
**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): March 26, 2014

Mast Therapeutics, Inc.
(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction
of incorporation)

001-32157
(Commission
File Number)

84-1318182
(IRS Employer
Identification No.)

**12390 El Camino Real, Suite 150,
San Diego, California**
(Address of principal executive offices)

92130
(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))
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Item 8.01. Other Events.

Beginning on March 27, 2014, the information attached as Exhibit 99.1 to this report relating to Mast Therapeutics, Inc. (the “Company”) and its development programs will 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 filed with 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 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 MST-188 in sickle cell disease, arterial disease, heart failure, and AIR001, as well as the timing of activities related to those plans. 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 MST-188 in the EPIC study and the phase 2 clinical study in acute lower limb ischemia; the potential for delays in the commencement or completion of clinical studies, including as a result of difficulties in obtaining regulatory agency agreement on clinical development plans or clinical study design, opening trial sites, enrolling study subjects, manufacturing clinical trial material, completing manufacturing process development activities, and being subject to a “clinical hold”; the risk of suspension or termination of a clinical study, including due to lack of adequate funding or patient safety concerns; the potential for institutional review boards or the FDA or regulatory agencies outside of the U.S. to require additional nonclinical or clinical studies prior to initiation of phase 2 clinical studies of MST-188 in any particular indication in which the Company determines to develop MST-188, including heart failure, which likely would increase the total time and cost of development in the indication; the risk that clinical studies of the Company’s product candidates are not successfully executed and/or do not successfully demonstrate the drug’s safety or efficacy; the risk that, even if clinical studies are successful, the FDA or a regulatory agency outside of the U.S. determines they are not sufficient to support a new drug application; the risk 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, and regulatory activities for its product candidates and that such third parties may fail to perform as expected; the Company’s ability to obtain 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 the Company is not able to adequately protect its intellectual property rights relating to the MAST platform, MST-188 or AIR001 and prevent competitors from duplicating or developing equivalent versions of its product candidates; the risk that, even if the Company successfully develops and obtains marketing approval for its product candidates, it may not realize commercial success with its products and may never generate revenue sufficient to achieve profitability; 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.

March 26, 2014

By: /s/ Patrick L. Keran

Name: Patrick L. Keran

Title: President and Chief Operating Officer

Exhibit Index

Exhibit No.

Description

99.1 Mast Therapeutics, Inc. corporate overview presentation, March 26, 2014



Corporate Overview

Brian M. Culley, CEO

March 26, 2014

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

- **Publicly-traded biopharmaceutical company based in San Diego**
- **Developing MST-188 for diseases with high unmet need;**
 - **Near-term focus on rare (“orphan”) diseases**
 - Sickle Cell Disease (SCD)
 - Acute Limb Ischemia (ALI)
 - **Longer-term growth into larger markets**
 - Heart Failure
 - Stroke
- **Recently acquired Aires Pharmaceuticals (AIR001)**
 - Phase 2 asset in Pulmonary Hypertension (PH)
 - Complementary to MST-188



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NYSE MKT: **MSTX**

Lead Program MST-188



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MST-188 Overview



API Structure:	$\text{HO} - (\text{CH}_2\text{CH}_2\text{O})_{79} - (\text{CH}_2\text{CHO})_{30} - (\text{CH}_2\text{CH}_2\text{O})_{79} - \text{H}$ <p style="text-align: center;"> CH₃</p>
CMC:	Large polymer (8,500 Daltons) manufactured by chemical synthesis and proprietary purification process
Drug Product:	Formulated as a clear, buffered solution
Administration:	IV infusion



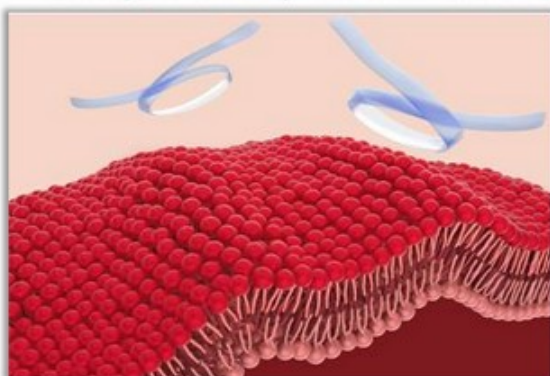
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NYSE MKT: MSTX

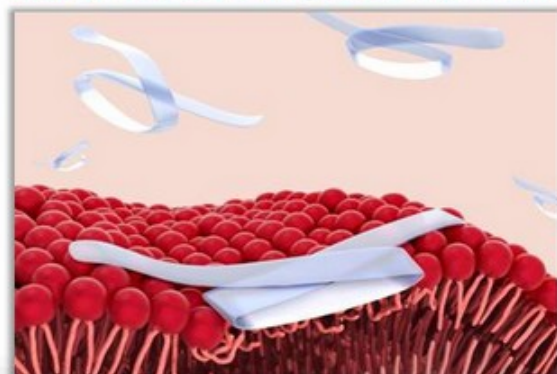
MST-188 Mechanism of Action

Hydrophobic core adheres to hydrophobic domains in circulation (e.g., damaged cell membranes)

No Affinity for Healthy Cell Membranes...



But Adheres to Damaged Cell Membranes

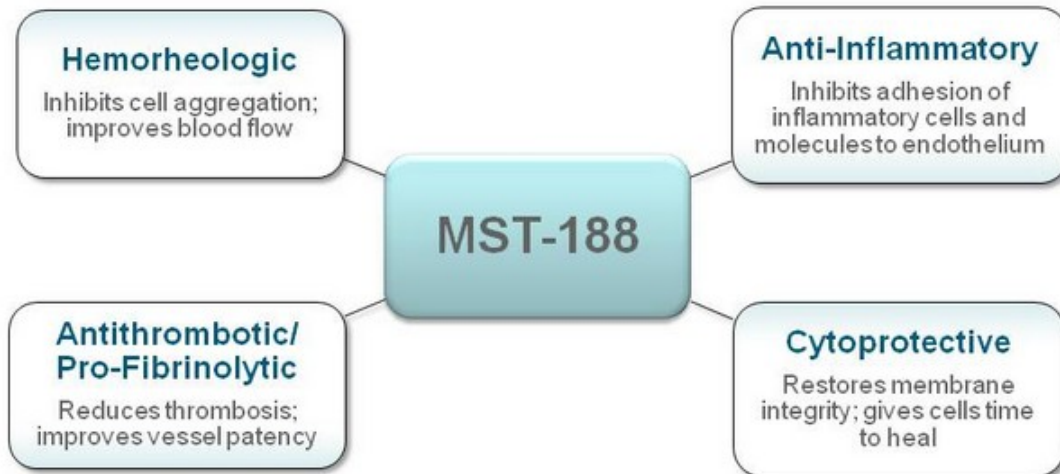


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MST-188 Pharmacodynamics

Biophysical mechanism confers multiple pharmacodynamic features



MST-188 Clinical Development

	Preclinical	Phase 1	Phase 2	Phase 3
2014				
Sickle Cell Disease (orphan)	▶			Enrolling
Acute Limb Ischemia* (orphan)	▶		Trial initiated Q1 2014	
Acute Heart Failure	▶	Positive nonclinical data: developing clinical strategy		
Stroke*	▶	Planned initiation: 2H 2014		

**In combination with thrombolytics*

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”**
 - 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)

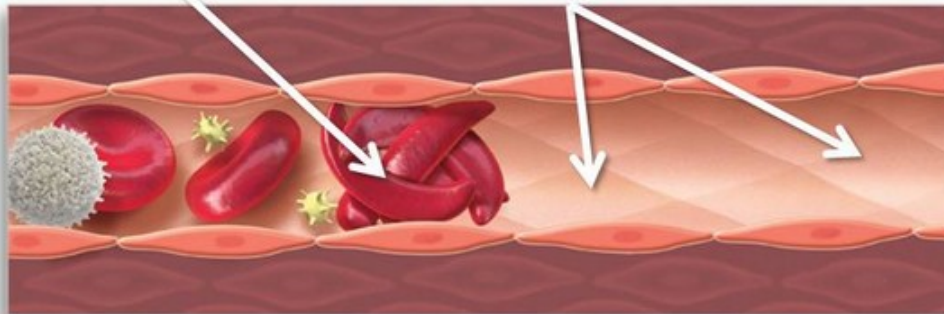
Role of MST-188 in Sickle Cell Disease

Vaso-Occlusion:

- Adhesion of poorly-deformable, "sticky" cells to endothelium
- Physical entrapment of rigid, sickled cells and vessel obstruction

Ischemia:

- RBCs cannot traverse occlusion to deliver oxygen to tissue, resulting in ischemia, hypoxia and infarction



MST-188:

- Reduces adhesion of cells to endothelium (anti-inflammatory)
- Reduces RBC aggregation, improves RBC deformability, lowers viscosity, and restores flow (rheologic)

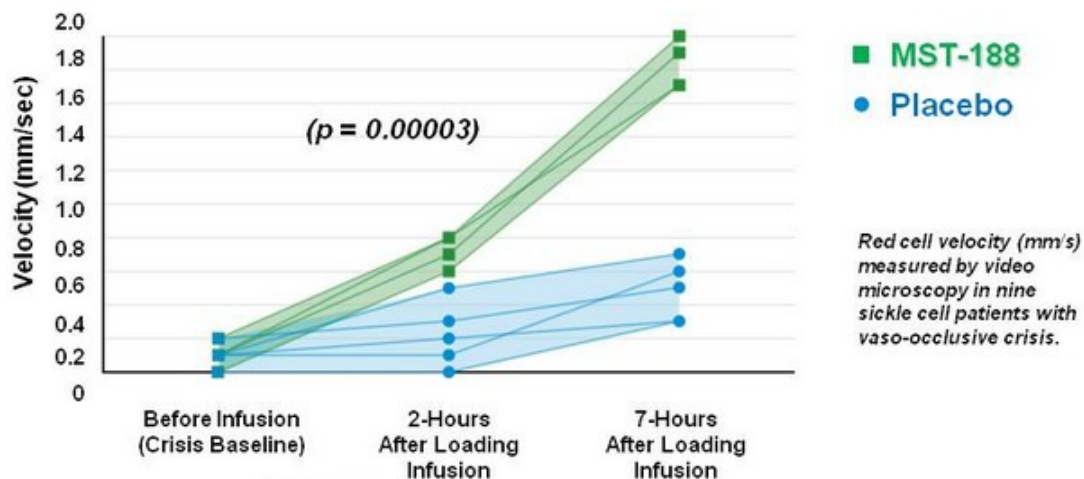


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MST-188 Improves Blood Flow

MST-188 improved microvascular blood flow in SCD patients in crisis



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

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Phase 2 Study

- Randomized, double-blind, placebo-controlled, multi-center study of MST-188* in SCD patients hospitalized for crisis
- MST-188 significantly improved important efficacy parameters

	Subjects Who Received Full Dose [‡]		
	MST-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 MST-188 and placebo.
^{±±} Proportional hazards model adjusted for baseline pain.

Source: Blood, September 1, 1997 – Vol 90, No. 5
 * 1st generation (non-purified) formulation

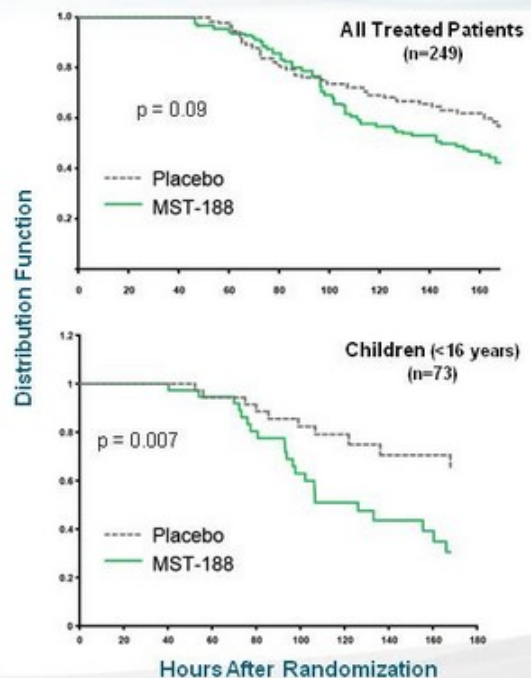


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Phase 3 Study

- Randomized, double-blind, placebo-controlled, multi-center study of MST-188 in 255 patients with SCD
- Time-to-event analysis demonstrates consistent trend in achievement of crisis resolution
- Original statistical plan, which required 350 patients, **was reduced by almost 30%** by prior sponsor (capital constraints), lowering statistical power.
- Observation period **was stopped at 168 hours** (“right censoring”), diminishing observable treatment differences



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



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Phase 3 Study

- Responders analysis (proportion of patients responding at a point in time) is not impacted by “right-censoring” (discontinuation of observation period)
- MST-188 significantly increased the proportion of patients achieving crisis resolution at 168 hours (end of the observation period)

Group	MST-188	Placebo	p Value
All treated patients (n=249)	51.6%	36.6%	0.02
Patients <16 years (n=73)	59.5%	27.8%	0.009

Evaluation of Purified 188 In Crisis (EPIC): Pivotal Phase 3 Study Design

- **Randomized, Double-Blind, Placebo-Controlled, Multicenter**
 - 388 patients
 - Standard of care +/- MST-188
- **Primary Efficacy Assessment**
 - Duration of crisis (from randomization to last dose of parenteral opioid)
- **Secondary Efficacy Assessments**
 - Re-hospitalization for crisis within 14 days
 - Occurrence of acute chest syndrome
- **Power**
 - 90% power to detect a 16-hour difference (p=0.05)
 - 85% power to detect a 24-hour difference (p=0.01)

EPIC Success Factors

- **Enrollment on-track at 6-months** (*announced Jan 2014*)
 - 40 U.S. sites opened in 2013
 - First ex-U.S. sites opened Q1 2014
- **Most Advanced New Drug in SCD**
 - Potential to be first approved drug to treat an on-going vaso-occlusive crisis
 - Substantial head start versus other SCD drugs in development
- **Positive Factors for Regulatory Decision-Making**
 - Significant unmet need – standard of care unchanged for years
 - Increased reliance on disease experts in rare disease
 - Support for MST-188 among medical / advocacy communities
 - Fast Track designation
 - Orphan Drug designation
 - Healthcare disparity

Arterial Disease

(MST-188 In Combination with Thrombolytics)

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

Overview of 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 markets

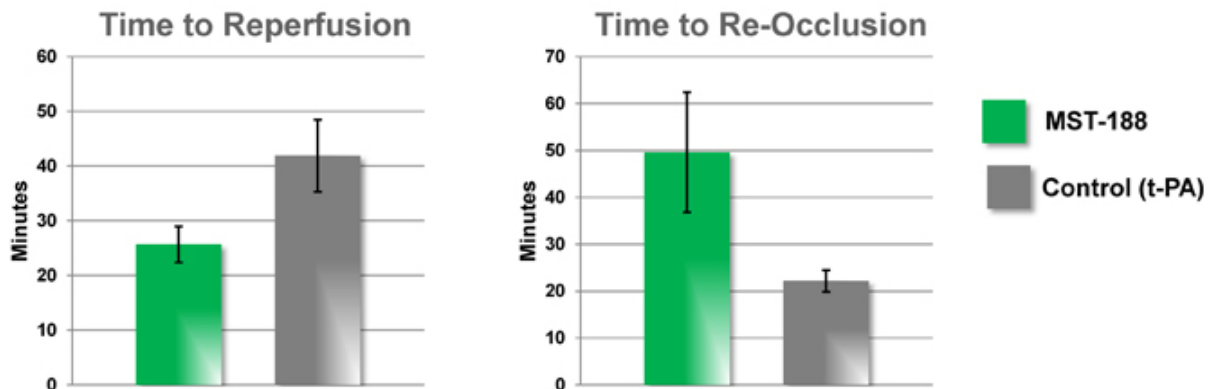


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MST-188 Improved t-PA Effectiveness

Animals randomized to t-PA (n = 10) or t-PA + MST-188 (n = 10)



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Source: Data on file
NYSE MKT: **MSTX**

MST-188 Showed Synergy with Thrombolytics in Heart Attack

Parameter	MST-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
*1st generation (non-purified) formulation



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Phase 2 Study in ALI

- **Clinical Proof-of-Concept Study**
 - Biomarkers
 - Clinical outcomes
- **Study Design**
 - Dose-finding, randomized, double-blind, and active-controlled
 - Rutherford Class 2A / 2B and catheter-directed thrombolysis
 - t-PA +/- low or high dose MST-188
 - 60 subjects (20 per arm)
- **Timing**
 - Study initiated Q1 2014
 - Enrollment: ~18 months
- **Data can be supportive of clinical development in stroke**



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Heart Failure (Acute Decompensation)

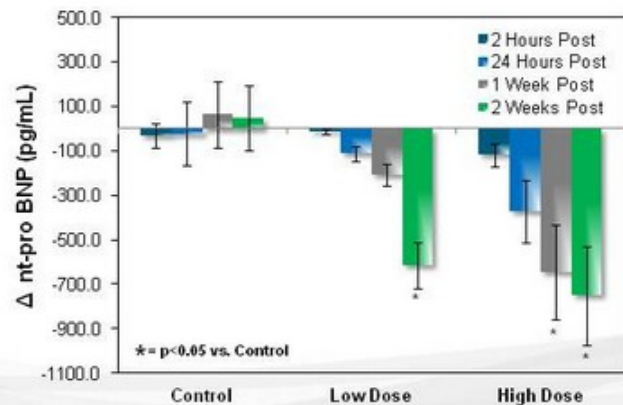
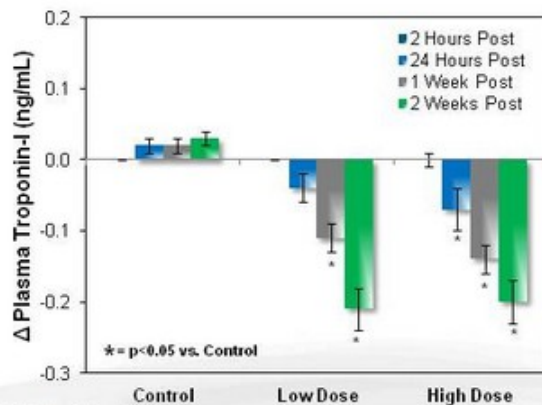
Overview of Heart Failure

- **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
- **Acute Decompensation**
 - Each decompensation event contributes to worsening heart failure and damage to vital organs, decreasing survival probability following the next event
- **MST-188**
 - Membrane-sealing activity may restore weakened cardiac cell membranes, minimizing calcium overload injury
 - Durable effect may indicate a direct improvement in cardiac function

Proof-of-Concept in Heart Failure

(nonclinical model of chronic heart failure)

- Single 2h infusion resulted in statistically significant improvements in hemodynamic parameters (LVEF, CO) and biomarkers (troponin, NT-proBNP)
 - Troponin associated with 180-day all-cause mortality
 - Elevated NT-proBNP associated with poor prognosis
- Potentially novel mechanism, compatible with existing treatments
- Clinical development plan in 2H 2014



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Source: data on-file

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AIR001

(sodium nitrite) inhalation solution



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AIR001

- **Nitrite for intermittent inhalation via nebulizer**
 - **Beneficial effects include dilation of blood vessels and reduction of inflammation and undesirable cell growth**
 - **Positive hemodynamic effects**
 - **Observed reductions in:**
 - pulmonary vascular resistance
 - pulmonary capillary wedge pressure
 - right atrial pressure
 - **Safety data in more than 120 subjects (well-tolerated)**
 - **Additional clinical data expected Q3 2014 in >20 pulmonary arterial hypertension (PAH) patients**

AIR001 for Pulmonary Hypertension

- **PH is high blood pressure affecting the blood vessels in the lungs**
 - **Leads to shortness of breath, dizziness, fainting, leg swelling, etc.**
 - **May result in heart failure**
- **Evaluating potential in World Health Organization (WHO) Group 2 Patients (PH associated with left heart disease)**
 - **Planned expansion of an ongoing Phase 2a study in PH**
 - **Evaluate whether AIR001 may be effective in reducing PVR, PCWP and RAP in WHO Group 2 patients**
 - **Data expected summer 2015**

MSTX Financial Overview

- **Cash/investments at 12/31/13: \$44.4 million**
- **Market capitalization: ~\$84 million***
- **Shares outstanding: ~114 million***
- **Average daily volume (3 mo): ~4.4 million***
- **No debt**
- **Evaluating strategic partnerships**



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* As of March 24, 2014

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Mast Investment Summary

- **A Leader in Areas of Significant Unmet Need**
 - **Sickle Cell Disease: Most advanced new drug in development (Phase 3)**
 - **Acute Limb Ischemia: Initiated Phase 2 study in Q1 2014**
 - **Heart Failure: potential new mechanism with durable effects**
- **Recently acquired Aires Pharmaceuticals (AIR001)**
 - **New opportunities in pulmonary hypertension and heart failure**
- **Cash and marketable securities**
 - **\$44.4 million at 12/31/13**
- **Non-Dilutive Financing Opportunities**
 - **Strategic partnerships**



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