Issuer Free Writing Prospectus Dated June 7, 2013
(to the Preliminary Prospectus dated June 5, 2013)
Filed Pursuant to Rule 433
Relating to Registration Statement on Form S-1
Registration No. 333-188870

MAST THERAPEUTICS, INC.

Corporate Overview

NYSE MKT: MSTX

June 2013

Forward-Looking Statements

This presentation includes forward-looking statements about our business prospects, financial position, and development of MST-188 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 MST-188; and other risks and uncertainties more fully described in our press releases and our filings with the SEC, including the prospectus included in our registration statement on Form S-1 (File No. 333-188870).

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

Corporate Overview

- **Developing MST-188 for "microcirculatory insufficiency"**
  - Platform technology targeting multiple indications
- **Initially focused on rare/orphan diseases**
  - Sickle Cell Disease (SCD)
  - Acute Limb Ischemia (ALI)
- **Currently enrolling subjects in a pivotal phase 3 study in SCD**
  - Most clinically-advanced new molecular entity in development for SCD
- **Planned expansion into larger markets**
  - Resuscitation Following Major Hemorrhage
  - Acute Decompensated Heart Failure
  - Transfusion (Storage Lesion)
  - Acute Ischemic Cerebrovascular Infarction (Stroke)

MST-188 Overview

API Structure:	$HO-(CH_2CH_2O)_{80}-(CH_2\underset{\displaystyle CH_3}{\underset{\vert}{C}}HO)_{27}-(CH_2CH_2O)_{80}-H$
Drug Product:	Formulated as a clear, citrate-buffered solution
CMC:	Large polymer (8,500 Daltons) manufactured by chemical synthesis and proprietary purification process
Administration:	~12-48 hour IV infusion in acute-care settings (hospital, ICU, specialized out-patient)

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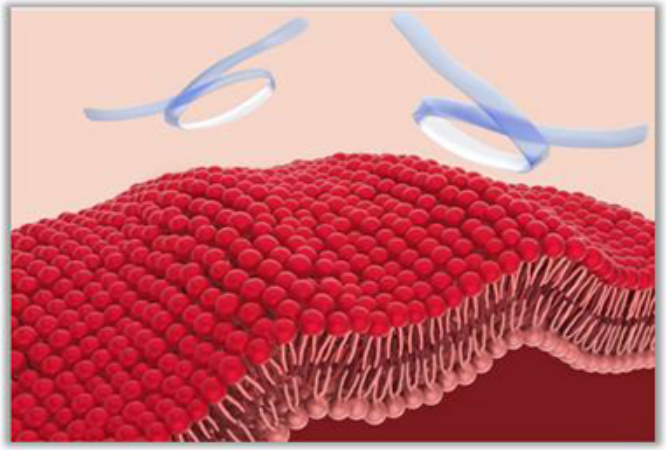
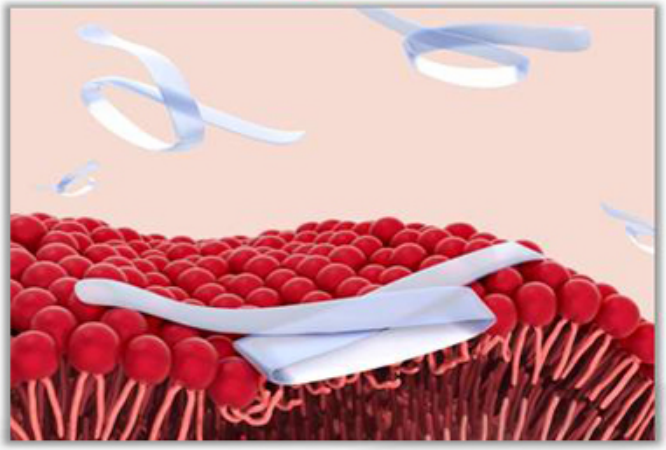
MST-188 Mechanism of Action

- Hydrophobic core binds to hydrophobic domains in circulation (e.g., damaged cell membranes, acute phase reactant proteins)

No Affinity for Healthy Cell Membranes



Adheres to Damaged Cell Membranes



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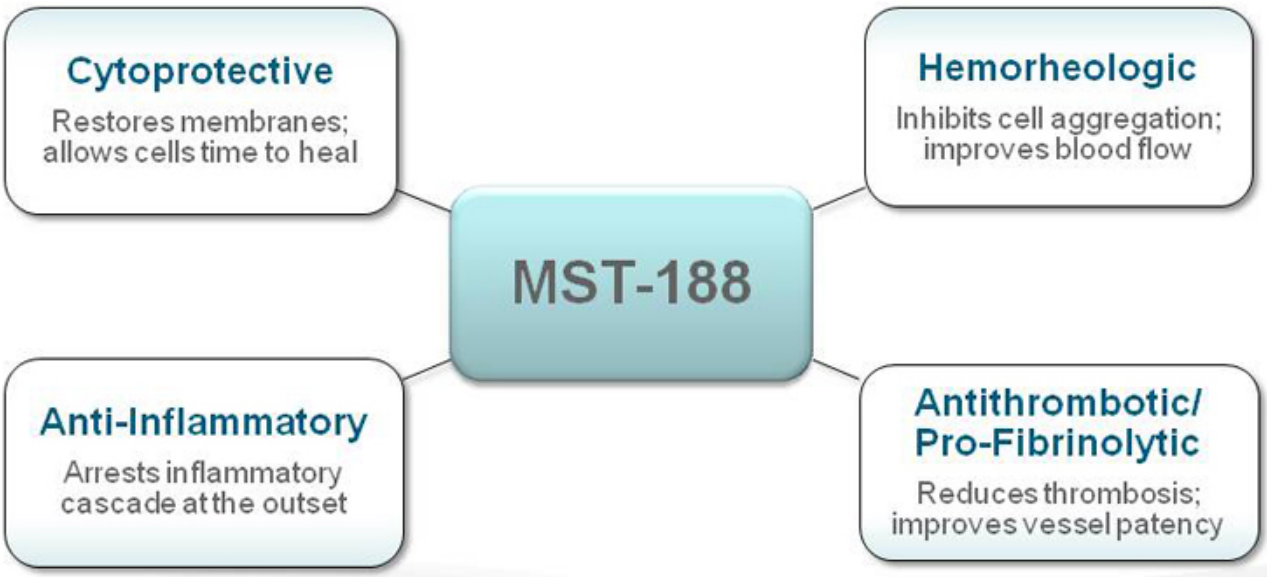
MST-188 Pharmacodynamics

- **Single mechanism with numerous effects addresses multiple pathophysiologic processes**



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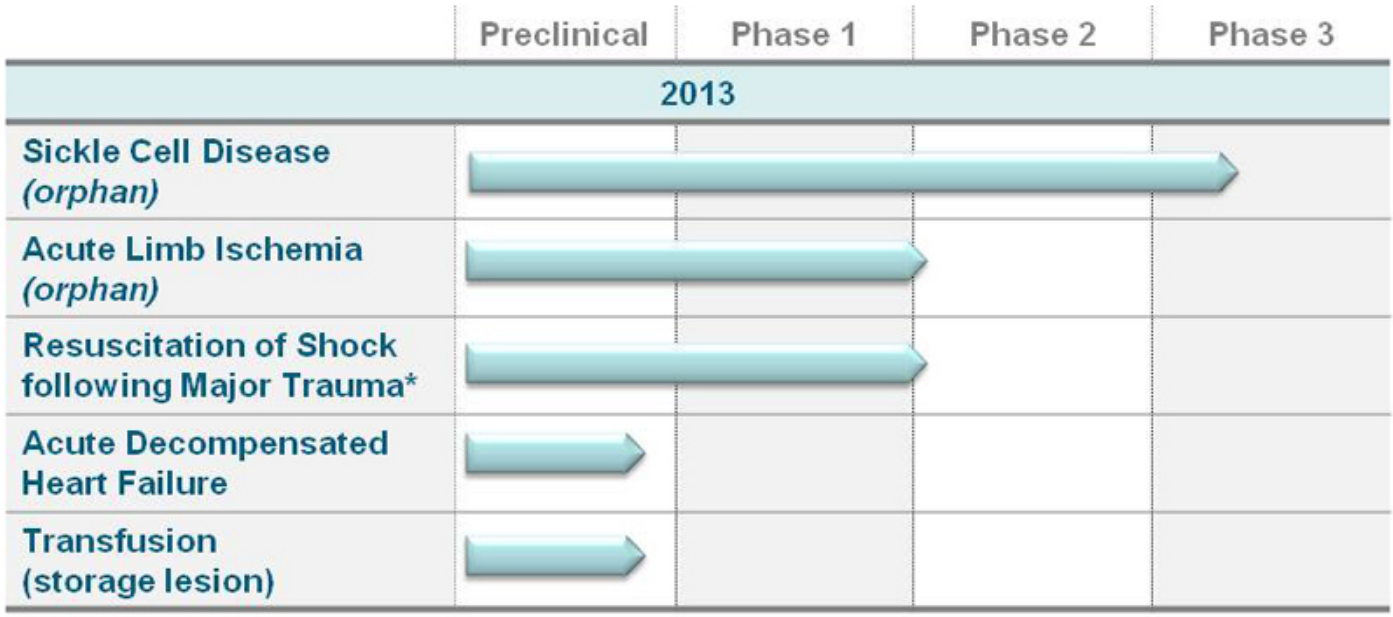
The MST-188 Pipeline



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* Contingent on U.S. government funding/other collaborator

Sickle Cell Disease

(vaso-occlusive crisis)

Sickle Cell Disease Overview

- **An inherited genetic disorder and orphan disease**
  - 90,000 to 100,000 people with SCD in the U.S.‡
  - Characterized by severe deformation (i.e., "sickling") of red blood cells
  - Sickled cells cannot navigate the microcirculation
- **Presents as recurring episodes of extreme pain ("crisis")**
  - Episodes typically last 4 to 5 days, but may last a week or longer
  - Patients "suffer at home" until pain requires IV analgesia (hospital visit)
- **Significant unmet need**
  - Average death: ~40 years old
  - Standard of care; hydration and pain meds
  - ~100,000 hospitalizations/year for crisis
  - No approved agents to shorten duration or severity of crisis
- **Substantial recent interest from Big Pharma**
  - Pfizer: $395 million* for phase 2 investigational drug (Oct 2011)
  - Novartis: $650 million* for phase 2 investigational drug (Sep 2012)

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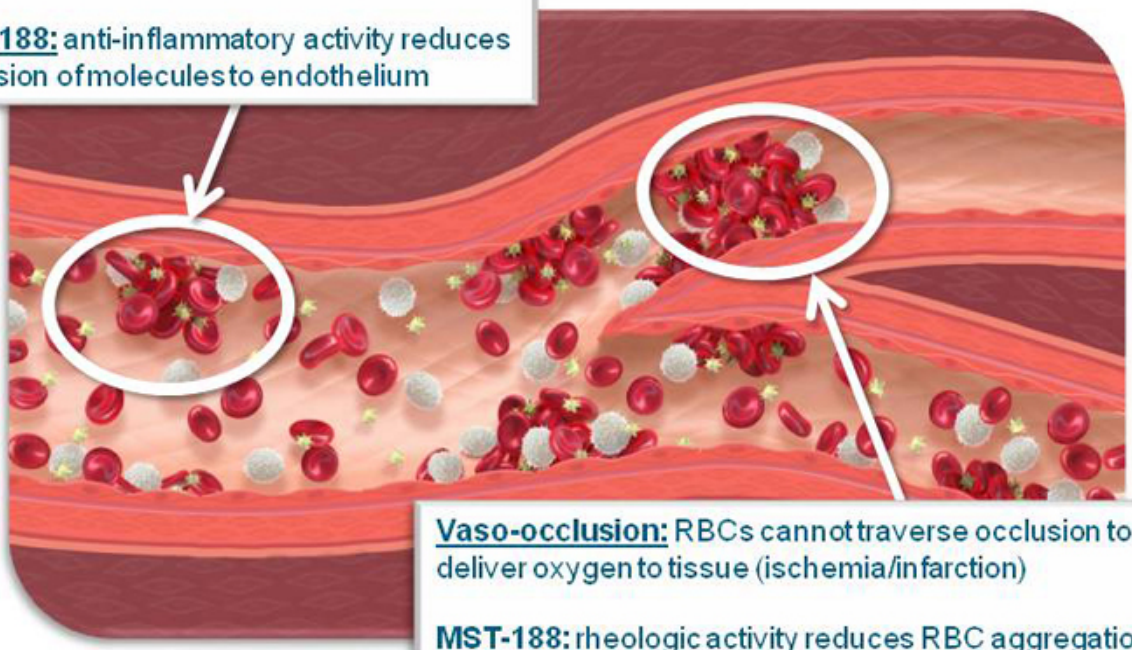
‡Source: Centers for Disease Control and Prevention
* Reported deal value

Pathophysiology of SCD: Impaired Blood Flow

Early stages: adhesion of circulating blood products to endothelial cells

MST-188: anti-inflammatory activity reduces adhesion of molecules to endothelium



Vaso-occlusion: RBCs cannot traverse occlusion to deliver oxygen to tissue (ischemia/infarction)

MST-188: rheologic activity reduces RBC aggregation, improves RBC deformability, lowers viscosity

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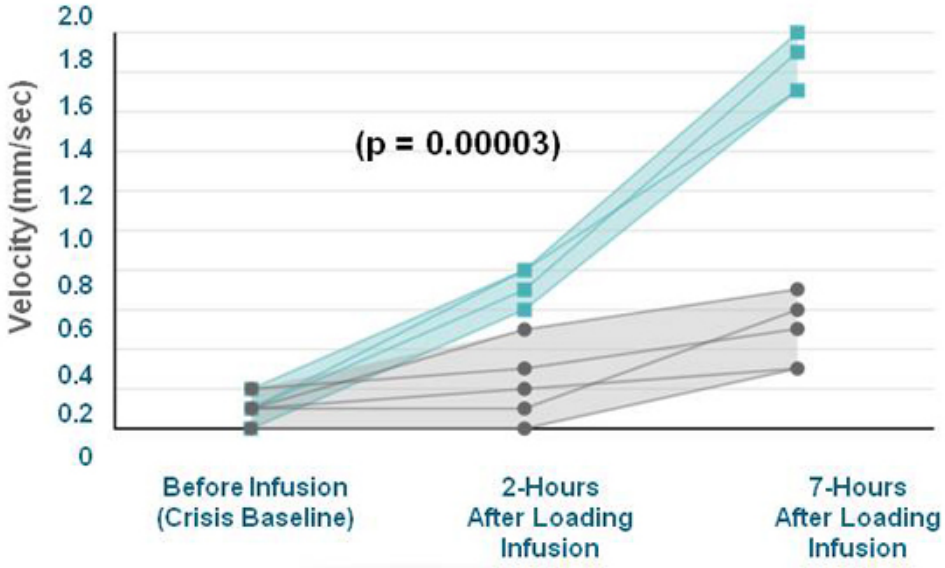
MST-188 Improves Blood Flow

- Improvement in microvascular blood flow in SCD patients in crisis following treatment with MST-188



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

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Completed Phase 2 Study in SCD

- Improvement in various endpoints in SCD patients in crisis following treatment with MST-188*

	Subjects who received ≥ 24h infusion (n=45)		
	MST-188*	Placebo	Improvement
Duration of Crisis	60 hours	88 hours	32% shorter
Duration of Hospitalization	5 days	7 days	2 days shorter
Total Analgesic Use	49mg	169mg	71% less
Parenteral Analgesic Use	40mg	150mg	73% less

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

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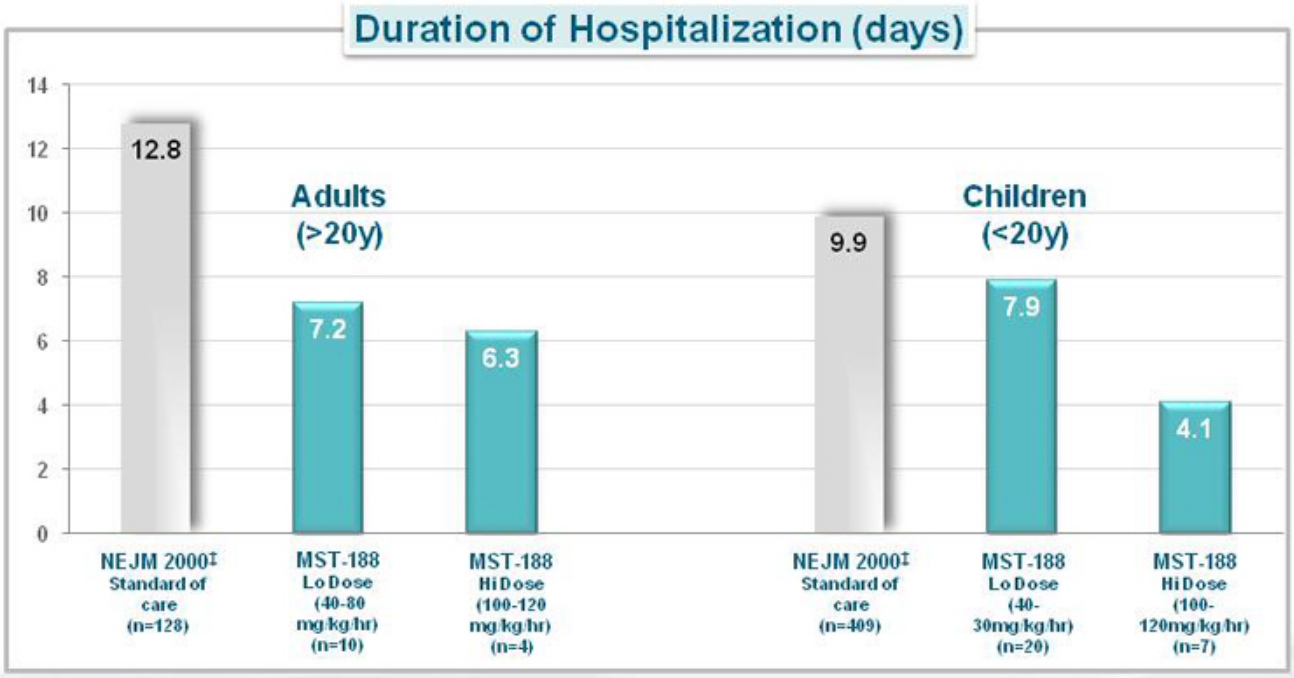
Additional Clinical Data in SCD – Acute Chest Syndrome

- Reduction in duration of hospitalization in SCD patients with acute chest syndrome (n=41) following treatment with MST-188*



*Source: Study C97-1243 (1997-99); data on file
‡Source: NEJM, June 22, 2000 – Vol 342, No. 25

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Completed Phase 3 Study in SCD

(Primary and post-hoc analyses)

- Improvement in duration of crisis in SCD patients following treatment with MST-188

Group	MST-188	Placebo	p Value
All treated patients (n=249)	132 hours	140 hours	0.07
Patients <16 years old (n=73)	127 hours	149 hours	0.01

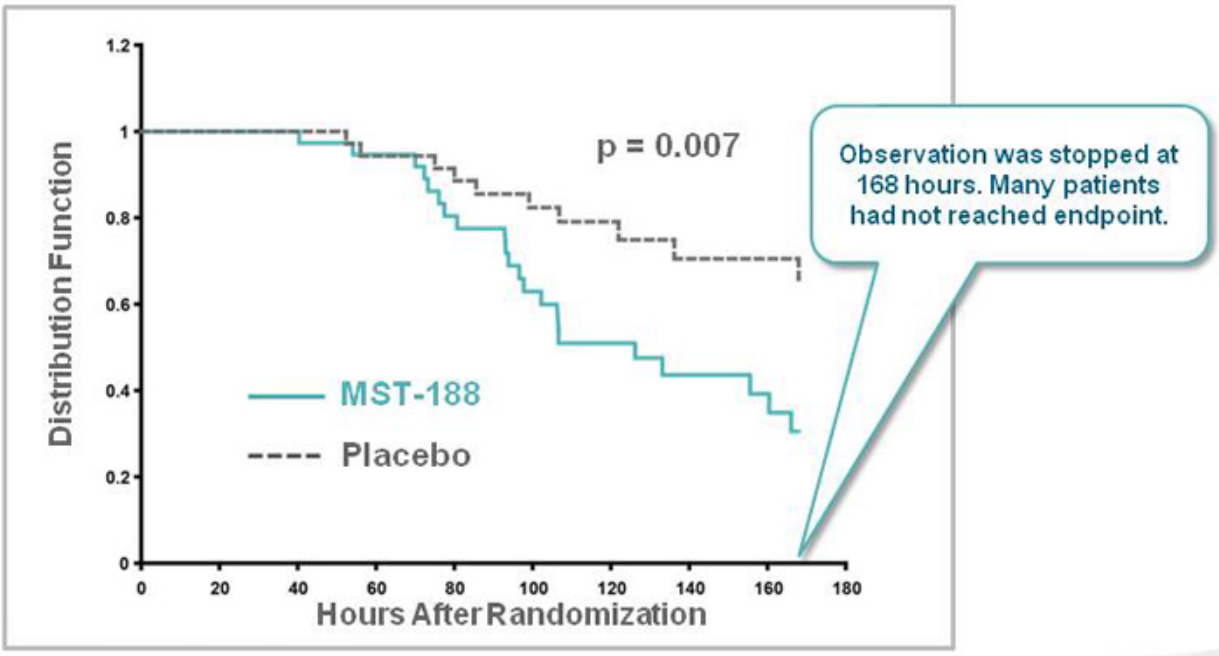
Original trial design required 350 patients.
Reduced by almost 30% by prior sponsor (capital constraints).

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

Completed Phase 3 Study in SCD

(Post-hoc analysis)

- Proportion of patients <16 years remaining in crisis over time (n=73)



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

Completed Phase 3 Study in SCD

(Post-hoc analysis)

- Proportion of patients achieving crisis resolution within 168 hours

Group	MST-188	Placebo	p Value
All treated patients (n=249)	51.6%	36.6%	0.02
Patients <16 years old (n=73)	62.2%	27.8%	0.01

Responder's analysis reached statistical significance for both adults and peds

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

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Lessons Learned

- Prior Phase 3 was the first large interventional study in SCD
- Simplify endpoint to minimize protocol violations and missing ("left-censored") data
- Follow subjects until hospital discharge to avoid truncated ("right-censored") data
- Avoid subjective endpoints, which increase variability
- Standardize pain management practices across study sites
- Increase homogeneity in terms of cumulative disease burden (chronic pain)
- Control duration of crisis ("suffering at home") prior to randomization
- Limit SCD genotypes

Pivotal Phase 3 Trial (EPIC)

Evaluation of Purified 188 In Children

- **Study design**
  - Randomized, two-arm, double-blind, placebo-controlled
  - 388 patients ages 8-17 from ~40 centers in the U.S. and ~30 centers outside the U.S.
  - 90% power to show 16h benefit versus standard of care
- **Primary endpoint**
  - Duration of crisis
  - Time from randomization to last dose of parenteral opioid
- **Secondary endpoints**
  - Re-hospitalization rate (for vaso-occlusive crisis) within 14 days
  - Acute chest syndrome within 120 hours of randomization
- **First Active Site: March 2013**
- **Expected enrollment completion and data read-out: 2015**

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MST-188 Phase 3 Trial Comparisons

	1248 (Prior Study)	EPIC (Ongoing)
Primary Endpoint	Duration of crisis	Duration of crisis
Assessment tool	Pain score plus	Last dose parenteral opioid
Secondary endpoint	Total analgesic use; Length of hospitalization	14-day rehospitalization rate; Acute chest syndromes
No. Patients	350 (255 actual)	388
Patient age	8-65	8-17
No. Centers	40 US	40 US + 30 ex-US
Power (alpha)	80% (0.05)	90% (0.05)

Potential Competition in SCD

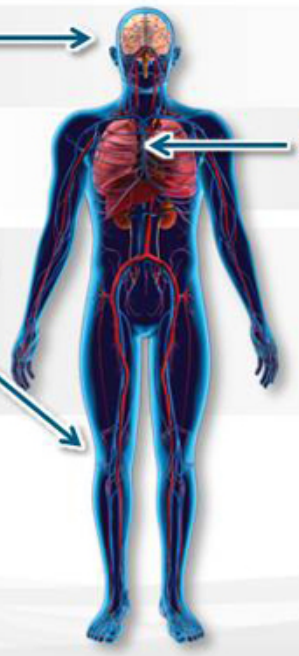
Drug	Sponsor	Challenges
GMI-1070 (Phase 2)	Glycomimetics (Pfizer)	• Only blocks selectins; other adhesion molecules not affected • Subjectivity of pain scores • Variability inherent in hospital discharge as endpoint
Sel-G1 (Phase 1)	Selexys (Novartis)	• MOA targets only 1 aspect of multi-factorial SCD pathophysiology; blocks P-selectin, one of many CAMs • Early stage, no efficacy data (phase 1 was in healthy subjects)
Prasugrel (Phase 3)	Lilly (Daiichi)	• MOA targets only 1 aspect of multi-factorial SCD pathophysiology • Modest benefit (trend) observed in phase 2, and only in secondary endpoints, not in primary endpoint • Risk of hemorrhage
LentiGlobin® (Phase 1/2)	bluebird bio	• Early stage (phase 1/2 in beta-thalassemia to start July 2013) • Regulation of expression control and insertion location • Historical challenges related to gene therapy

Acute Limb Ischemia

Arterial Disease

- A progressive circulatory problem in which obstructed arteries <u>reduce blood flow</u> to tissue
  - Thrombolytic agents (tPA) 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 larger markets

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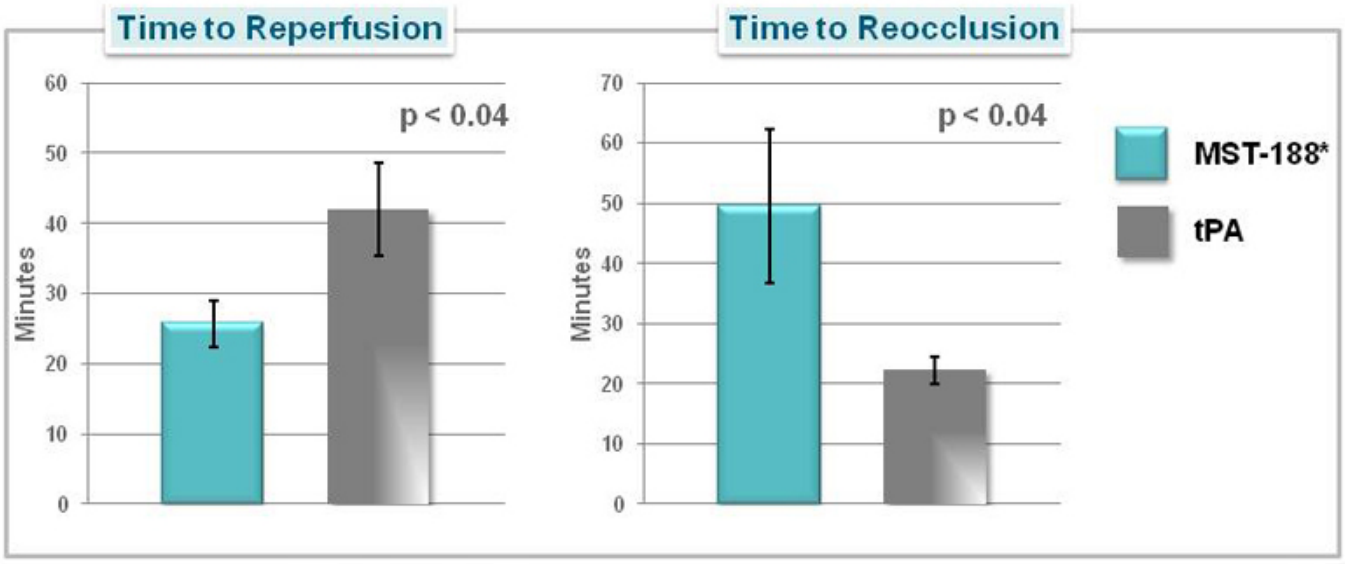
MST-188 Improved tPA Effectiveness

- Animals randomized to tPA (duteplase) (n = 10) or tPA + MST-188* (n = 10)



Source: Data on file
* 1st generation (non-purified) formulation

Planned Phase 2 Study

- **Generate Clinical Proof-of-Concept Data**
  - Biomarkers
  - Clinical outcomes
  - Protocol under development
- **Study Concept**
  - Design: dose-finding, randomized, double-blind, active-controlled
  - Population: Rutherford Class 2A / 2B and catheter-directed thrombolysis
  - Arms: tPA vs. tPA + MST-188
  - Sample Size: 60 subjects
- **Timing**
  - Initiation: late 2013/early 2014
  - Enrollment: ~15 months

MST-188 Exclusivity

Multiple Barriers to Entry	
Marketing Exclusivity	➢ SCD: orphan drug designation in U.S. and EU ➢ ALI: will seek orphan drug designation in U.S. and EU
Patents	➢ Filed applications cover: ▪ proprietary purification process ▪ methods of using poloxamers ▪ use of poloxamers in combination therapy ➢ Additional applications in-process
Trade Secrets	➢ Macromolecules difficult to characterize ("biosimilars") ➢ Non-patented / non-published manufacturing steps ➢ Proprietary specifications (in-take; in-process; release) ➢ Evaluating proprietary analytical standards / bioassays

Financial Overview

- **Cash/investments at 3/31/13: ~$32.0 million**
- **Market capitalization: ~$33 million***
- **46.3 million shares outstanding**
  - Warrants for 16.5 million shares (10.6m @ $1.10; 5.9m @ $3.04‡)
- **Average daily volume (3 mo): ~215,500***
- **No debt**
- **Opportunities for U.S. government funding**
- **Evaluating ex-U.S. partnerships to fund U.S. development**

‡ Weighted average exercise price
* As of May 31, 2013

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2013 Activities

Event	Timing
Initiate tQT/QTc Study	Completed
Secure Orphan Designation for MST-188 for SCD in EU	Completed
Activate First Site in Phase 3 Study	Completed
File New Patent Applications	Completed
Request "Rare Pediatric Disease" Designation for SCD	Completed
Dose First Subject in Phase 3 Study	Completed
Report data from tQT/QTc Study	Q3
Submit Applications for U.S. Government Funding for Phase 2 Study in Resuscitation of Shock following Major Trauma	Q3
Request Orphan Designation for MST-188 for ALI in U.S.	Q3
Initiate Nonclinical Proof-of-Concept Study in Heart Failure	Q3
Open First Ex-U.S. Clinical Site in Phase 3 Study	Q4
Initiate mBF Sub-Study	Q4
Initiate Phase 2 Study in ALI	Q4 '13/Q1 '14

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Management and Board

Management Team

- **Brian Culley, M.A., M.B.A. - *Chief Executive Officer***
- **Patrick L. Keran, J.D. – *President and Chief Operating Officer***
- **Santosh Vetticaden, M.D., Ph.D. - *Chief Medical Officer***
- **Brandi Roberts, CPA, M.B.A. - *Chief Financial Officer***
- **R. Martin Emanuele, Ph.D., M.B.A. - *Senior VP, Development***
- **Gregory D. Gorgas, M.B.A. – *Senior VP, Commercialization***

Board of Directors & Affiliations

- **Jack Lief – *Chairman*** - Arena, Cephalon, Abbott
- **Ted Love – *Director*** - Onyx, Nuvelo, Theravance, Genentech
- **David Ramsay – *Director*** - Halozyme, Lathian, Valeant
- **Lewis Shuster – *Director*** - Kemia, Life Technologies, Pharmacopeia
- **Brian Culley - *CEO & Director*** - iTherx, Neurocrine, UC San Diego

Investment Summary

- **Balanced Platform Pipeline**
  - Mitigates corporate-level development risk
  - Multiple partnering opportunities
- **Multi-Stage Development Strategy**
  - Initial focus on rare diseases; expand into larger markets
- **Late-Stage Program in Sickle Cell Disease**
  - Only company with new drug in phase 3 development
  - Increasing trend for Big Pharma deal-making
- **Non-Dilutive Financing Opportunities**
  - U.S. government funding
  - Ex-U.S. partnerships to fund U.S. development
- **Attractive Valuation**
  - Market capitalization: ~$33 million*

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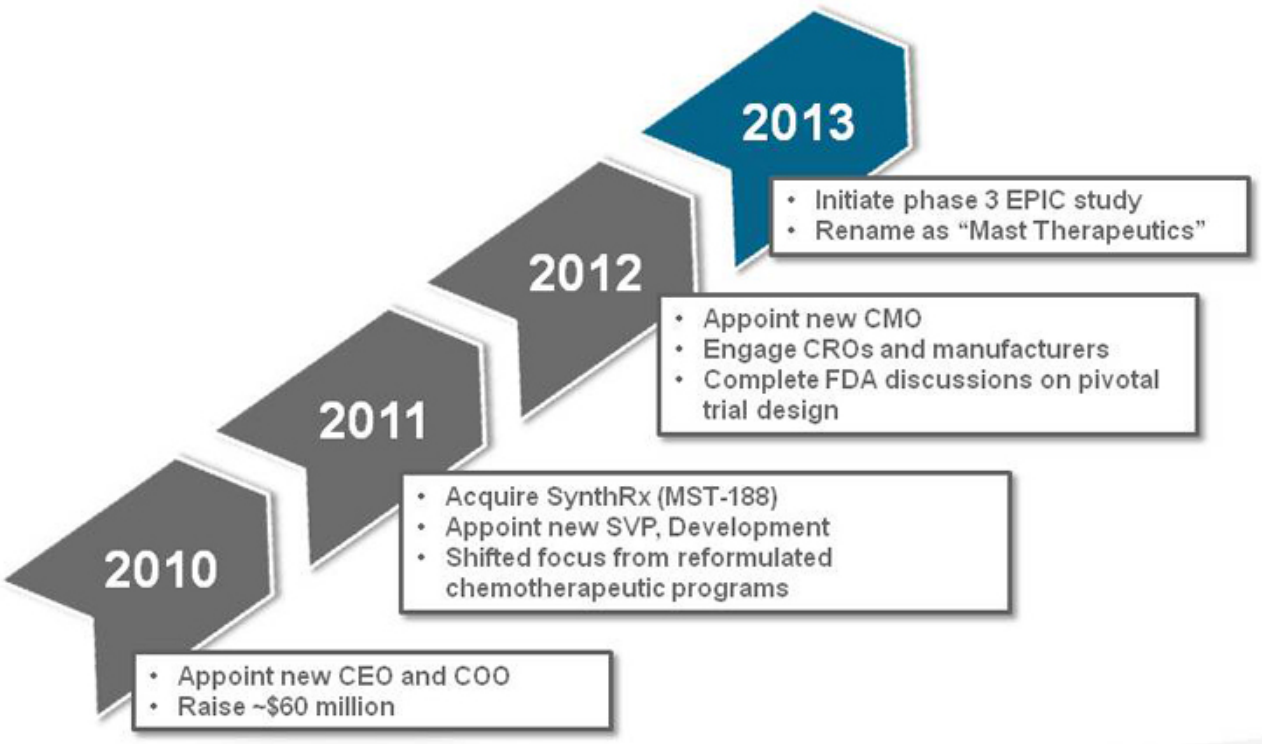
* Based on closing price of $0.71 on May 31, 2013

Additional Slides

Corporate Evolution



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Phase 3 CRO/CMOs

- **Theradex**
  - 30 year collaboration with National Cancer Institute
  - Experience with pediatric trials, minority populations, and sickle cell disease trials, including phase 3
- **Pierre-Fabre Medicament**
  - Manufacturing active ingredient in MST-188
  - Second largest independent pharmaceutical group in France
  - Supercritical Fluids Division has expertise and specialized facilities for purification of products via supercritical extraction
- **Patheon**
  - Formulation, fill and finish of MST-188
  - A leading global provider of manufacturing services

MST-188 Safety Data

- **MST-188: generally well-tolerated**
  - Transient elevations in liver function tests, return to baseline during follow-up
- **Evaluated in 6 clinical studies***
  - 255-subject phase 3 randomized, controlled study in sickle cell disease
  - ~250 subjects* exposed to active drug
- **Thorough QT/QTc Study**
  - Standard design to assess cardiac repolarization (QT interval)
  - Initiated: Jan 2013

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* Numbers include only subjects exposed to 2nd generation (purified) formulation. Over 2,250 additional subjects exposed to 1st generation (non-purified) formulation.

Thorough QT/QTc Clinical Study

- **Four-period, four-way cross-over, placebo- and positive-controlled, double-blind randomized trial in 60 healthy volunteers**
- **Subjects receive each of four treatments:**
  - Placebo (saline)
  - Positive control
  - MST-188 therapeutic dose
  - MST-188 supra-therapeutic dose
- **Primary objective: evaluate the effect of MST-188 on cardiac ventricular repolarization (specifically the QT interval)**

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VOC Market Summary

Preclinical	Phase I	Phase II	Phase III	Marketed
SHAPE platform	Aes-103	Vorinostat	MST-188	Hydroxyurea
Enhoxy	MP4CO	Decitabine	L-glutamine	
Sanguinate	Gene Therapy	HQK 1001	Prasugrel	
CLT 001	Pomalidomide	GMI-1070		
Gene Therapy	Panobinostat	Regadenoson		
Zinc Finger	SelG1	Eptifibatide		
ACP-501		LMWH		
Piper Genus Botanical Extract		Antioxidant Therapy		
		Immune Globulin		
		Magnesium Sulfate		

Intervention
- Physiological enhancer
- Anti-inflammatory
- Anticoagulant
- Oxygenator

Prevention
- Dietary supplement
- HbF stimulant
- Gene correction (curative)

- Other/TBA

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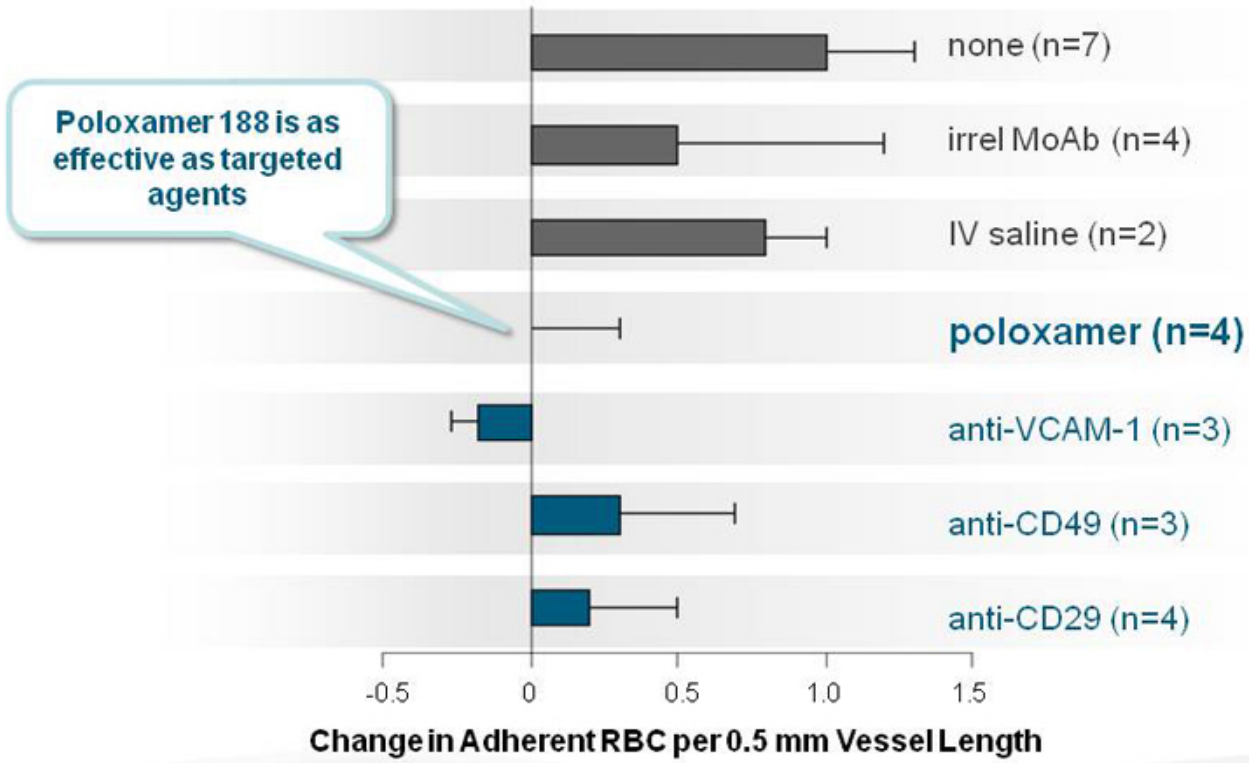
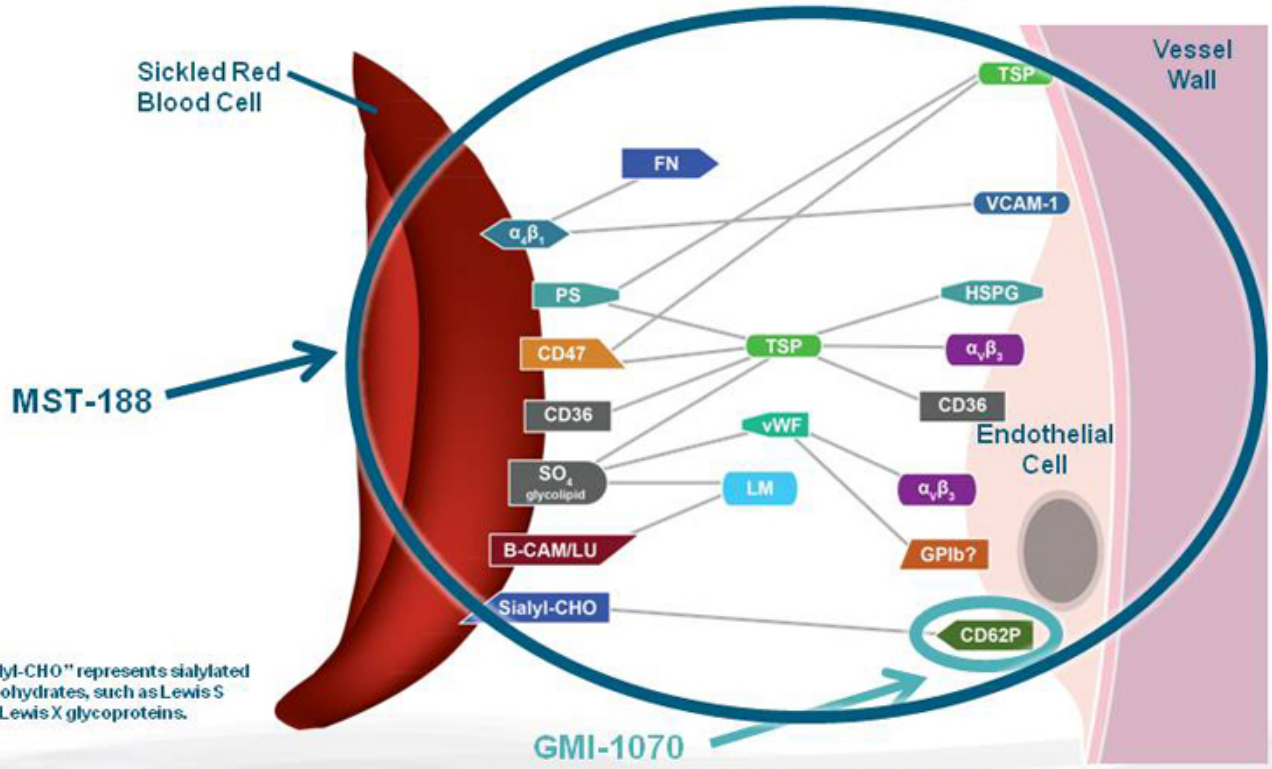
Effect of IV blocking agents on RBC adhesion following topical LPS



Source: Microcirculatory Effects Of Blocking Cell Adhesion Molecules In Transgenic Sickle Cell Mice, Dr. L.L. Hsu

MST-188 vs. GMI-1070 (Glycomimetics)

- Sickle cell adhesion to endothelium: MST-188 vs. GMI-1070



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MST-188 Improved Survival in Numerous Experimental Models

- MST-188* studied in 5 controlled models of hemorrhagic shock / resuscitation by 4 different investigator groups
- Consistently improved survival (reproducibility across studies)

Resuscitation (2011) (DARPA-funded)	MST-188 (n=7)	Control (n=16)	p Value
Median Survival Time (min) (95% CI)	161 (80 - 180)	55.8 (36.5 - 86)	0.0186

Shock (2009)	MST-188 + Hextend	Hextend	p Value
Survival time from onset of hemorrhage (min) (n=10/arm)	589±99	289±37	0.002

Source: Resuscitation 82 (2011) 1453-1459, SHOCK, Vol 32, No. 4, pp. 442-450, 2009
*Some studies evaluated 1st generation (non-purified) formulation

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Resuscitation of Shock following Major Trauma
Planned Phase 2 Study & Funding

- **Generate Clinical Proof-of-Concept Data**

- **Study Protocol (complete)**
  - Design: dose-ranging, randomized, double-blind, controlled
  - Population: admitted to ICU for resuscitation following major torso trauma
  - Arms: standard resuscitation protocol (SRP) vs SRP + MST-188
  - Sample Size: 60 subjects
  - Enrollment: 18 - 24 months

- **Collaboration with University of Florida**
  - A leader in clinical research and trauma care

- **U.S. Government Funding**
  - MST-188 prior recipient of funding (DARPA)
  - Preparing / submitting new applications
  - Timeline: 9 - 12 months

MAST THERAPEUTICS, INC.

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Mast Therapeutics, Inc. has filed a registration statement (Registration No. 333- 188870, including a prospectus) under the Securities Act of 1933, as amended, with the Securities and Exchange Commission for the offering to which this communication relates. Before you invest, you should read the prospectus in that registration statement for more complete information about the Company and the Offering. You may get these documents for free by visiting EDGAR on the SEC website at www.sec.gov. Alternatively, copies of the prospectus may be obtained from Piper Jaffray & Co., Attention: Prospectus Department, 800 Nicollet Mall, J12S03, Minneapolis, MN 55402, via telephone at 800-747-3924 or email at prospectus@pjc.com.