



# Aastrom Biosciences

## *The Future of Cell Therapy*

August 2013

## Safe Harbor



This presentation contains forward-looking statements, including, without limitation, statements concerning product-development objectives, clinical trial strategies, clinical trial timing and expected results, market data, potential market opportunities, market development plans, anticipated milestones and potential advantages of ixmyelocel-T, all of which involve certain risks and uncertainties which could cause actual results to differ materially from the expectations contained in the forward-looking statements. Any forward-looking statement speaks only as of the date of this presentation, and we undertake no obligation to update any forward-looking statement or statements to reflect events or circumstances after such date or to reflect the occurrence of unanticipated events.

Among the risks and uncertainties that may result in differences are: the results obtained from, and our ability to complete, clinical trials and development activities; our ability to obtain and maintain required regulatory approvals, including required FDA approvals; changes in regulatory requirements; competitive conditions; technological and market changes and the possibility that our products may become obsolete; commercial acceptance of our products such as our cell products for tissue repair treatments; our relationships with third parties and our reliance on third parties to conduct some of our clinical trials; the availability of resources, including those resources used in our cell manufacturing process; and our ability to develop or license intellectual property rights to protect our proprietary products and technologies.

These and other significant factors are discussed in greater detail in Aastrom's Registration Statement on Form S-1/A and other filings with the Securities and Exchange Commission.

# Free Writing Prospectus Statement



This presentation highlights basic information about us and the offering. Because it is a summary, it does not contain all of the information that you should consider before investing.

We have filed a registration statement (including a prospectus) with the SEC for the offering to which this presentation relates. The registration statement has not yet become effective. Before you invest, you should read the prospectus in the registration statement (including the risk factors described therein) and other documents we have filed with the SEC for more complete information about us and the offering. You may get these documents for free by visiting EDGAR on the SEC Web site at [www.sec.gov](http://www.sec.gov). The preliminary prospectus, as amended, dated July 25, 2013, is available on the SEC Web site at [http://www.sec.gov/Archives/edgar/data/887359/000110465913056497/a13-11022\\_1s1a.htm](http://www.sec.gov/Archives/edgar/data/887359/000110465913056497/a13-11022_1s1a.htm). Alternatively, we or any underwriter participating in the offering will arrange to send you the prospectus if you contact Aegis Capital Corp., Prospectus Department, 810 Seventh Avenue, 18th Floor, New York, NY 10019, telephone: 212-813-1010, e-mail: [prospectus@aegiscap.com](mailto:prospectus@aegiscap.com).

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## Offering Summary



### Issuer

Aastrom Biosciences, Inc.

### Exchange / Ticker

NASDAQ / ASTM

### Offering Size

\$15,000,000 of Common Stock (100 % Primary)

### Over-allotment

15% (100% Primary)

### Use of Proceeds

Clinical development of ixmyelocel-T; preclinical studies; technology platform development; working capital; general corporate purposes

### Sole Book-Runner

Aegis Capital Corp.

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## Leading Autologous Cell Therapy Platform

- Developing patient-specific multicellular therapies
- Highly automated and scalable GMP manufacturing system

## Highly Differentiated Product

- Ixmyelocel-T is a unique multicellular therapy
- Key effector cells have multiple activities that promote tissue repair & regeneration

## Consistent Positive Efficacy Data

- Focus on the treatment of severe ischemic cardiovascular diseases
- Appears well-tolerated with consistent positive preclinical and clinical efficacy results

## Phase 2b Study Enrolling



- Lead indication is for the treatment of advanced heart failure due to ischemic DCM
  - U.S. orphan drug designation with \$1+ billion peak revenue opportunity
- Study results expected in Q2 2015

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# Highly experienced management team in developing & commercializing cardiovascular and cell therapies

## Management Team

### Nick Colangelo – *President & CEO*

- More than 20 years of executive management and corporate development experience, most recently serving as the President and CEO of Promedior.
- Nearly a decade with Eli Lilly, including serving as Director of Strategy and Business Development for Lilly's Diabetes Product Group and founding Managing Director of Lilly Ventures.
- Extensive experience in the acquisition, development and commercialization of therapies to treat fibrovascular, metabolic and cardiovascular diseases.

### Ronnda Bartel, Ph.D. – *Chief Scientific Officer*

- More than 20 years of cell therapy research, development technical operations experience, most recently serving as executive director, biological research at Microslet.
- Previously served as vice president, scientific development at StemCells Inc.
- Senior principal scientist and director of research at Advanced Tissue Sciences, involved in the development and approval of some of the first cell-based products approved by the FDA.

### Daniel Orlando – *Chief Business Officer*

- More than 20 years of sales, marketing, and business development experience, most recently serving as Vice President of business development for North and South America at Takeda.
- Extensive commercial experience in cardiovascular, diabetes and metabolic disease areas.
- Original brand director for Actos, which became the #1 branded anti-diabetic agent in the U.S.

### David Recker, M.D. – *Chief Medical Officer*

- More than 20 years of drug development experience, most recently as Senior Vice President for Clinical Science at Takeda Global Research and Development.
- Responsibility for multiple development programs in a variety of therapeutic areas, including cardiovascular, diabetes, and metabolic disease areas.
- Numerous successful regulatory filings throughout the world.

### Brian Gibson – *Vice President, Finance*

- More than 13 years of finance and accounting experience, most recently as senior manager at PricewaterhouseCoopers.
- Served clients across multiple industries, including life science and healthcare companies.

## Board of Directors

**Robert Zerbe, M.D.**  
*Chairman of the Board*  
 CEO, QUATR<sub>x</sub>  
 Pharmaceuticals  
 Executive, Eli Lilly & Pfizer

**Nelson Simms**  
*Director*  
 CEO, Novavax; Executive, Lilly

**Ronald Cresswell, Ph.D.**  
*Director*  
 CSO, Warner-Lambert; COO,  
 Laporte Industries; COO  
 Burroughs Wellcome

**Alan Rubino**  
*Director*  
 CEO, Emisphere  
 CEO, New American  
 Therapeutics; CEO Akrimax;  
 Executive, Roche

**Nick Colangelo**  
*President and CEO, Astrom*

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## Scientific Advisory Board

### **Daniel R. Salomon, M.D., Chairman**

*Professor, Dept. of Molecular and Experimental Medicine and Medical Program Director, Scripps Center for Organ and Cell Transplantation, The Scripps Research Institute*

### **Mahendra S. Rao, M.D., Ph.D.**

*Director, NIH Center for Regenerative Medicine and Chief, Laboratory of Stem Cell Biology*

### **Karen K. Hirschi, Ph.D.**

*Professor, Dept. of Internal Medicine, Yale Cardiovascular Research Center, Yale University School of Medicine*

### **Joyce L. Frey-Vasconcells, Ph.D.**

*Founder, Frey-Vasconcells Consulting, LLC; Former FDA Deputy Director, Office of Cellular, Tissue, and Gene Therapies, CBER*

## ixCELL-DCM Steering Committee

### **Amit Patel, M.D., Chairman**

*Director, Clinical Regenerative Medicine and Tissue Engineering, University of Utah*

### **Anthony DeMaria, M.D.**

*Chair in Cardiology and Founding Director, Sulpizio Cardiovascular Center, UC San Diego*

### **Timothy Henry, M.D.**

*Director, Research at the Minneapolis Heart Institute Foundation*

### **Gary Schaer, M.D.,**

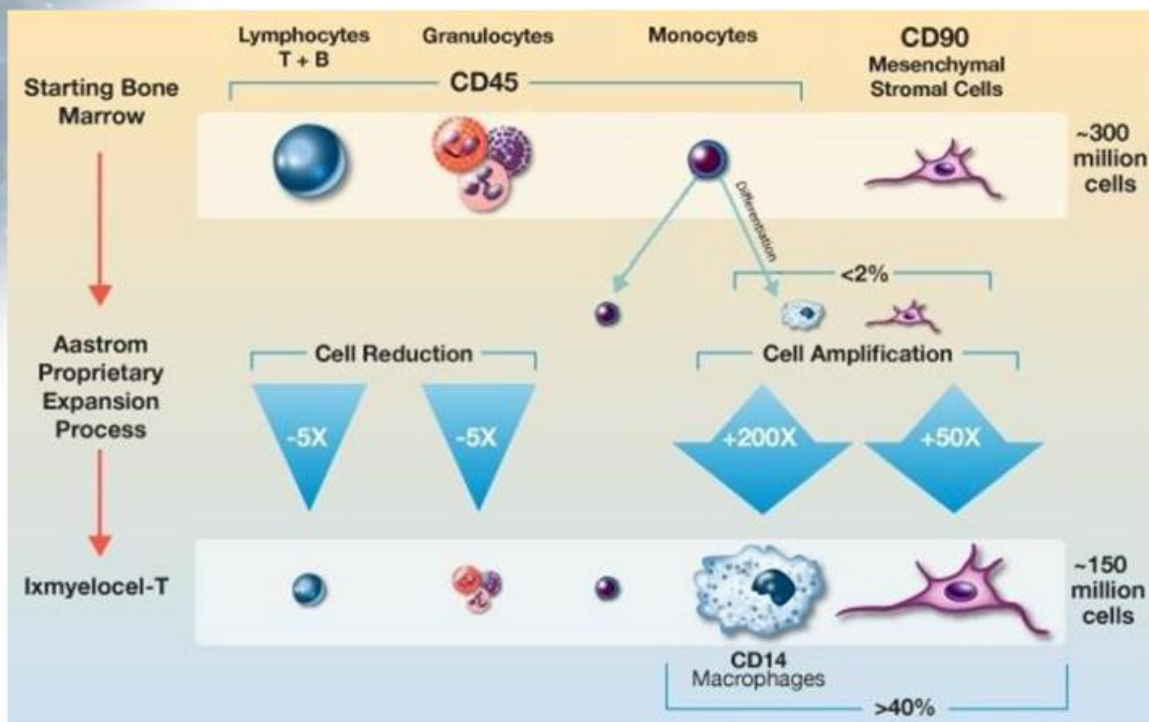
*Director, Cardiology Research at Rush University Medical Center*

### **David Recker, M.D.**

*Chief Medical Officer, Aastrom*

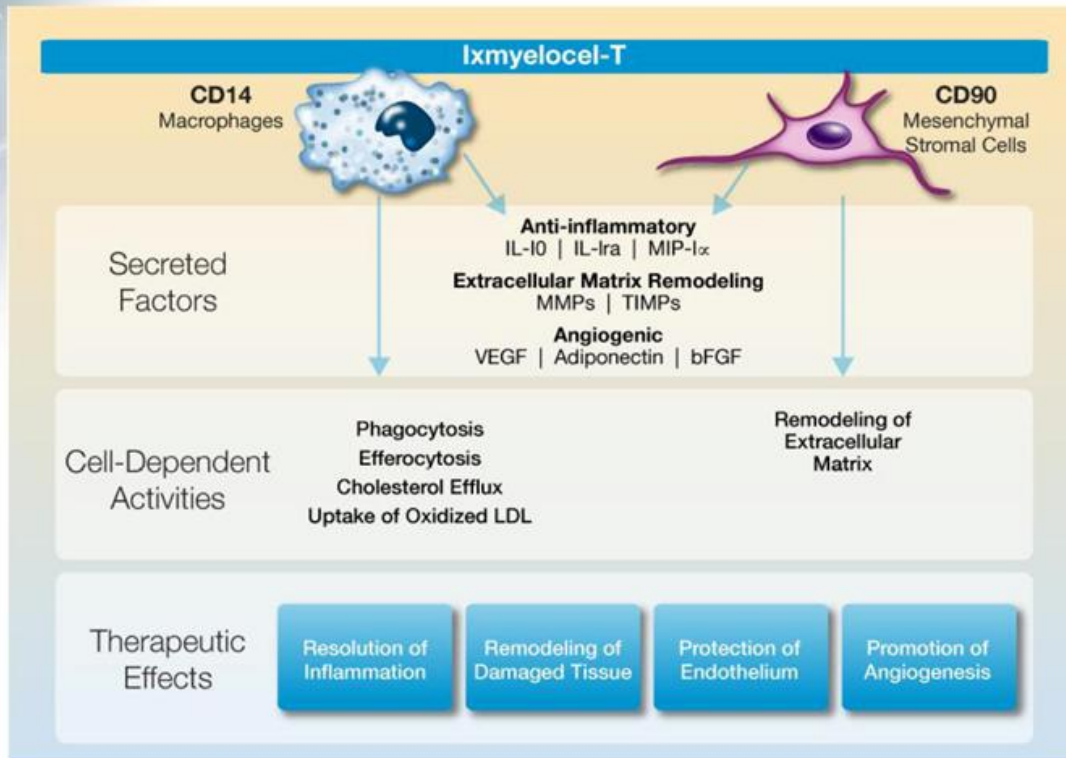
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# Ixmyelocel-T is a unique multicellular therapy; key effector cells are M2-like macrophages and MSCs



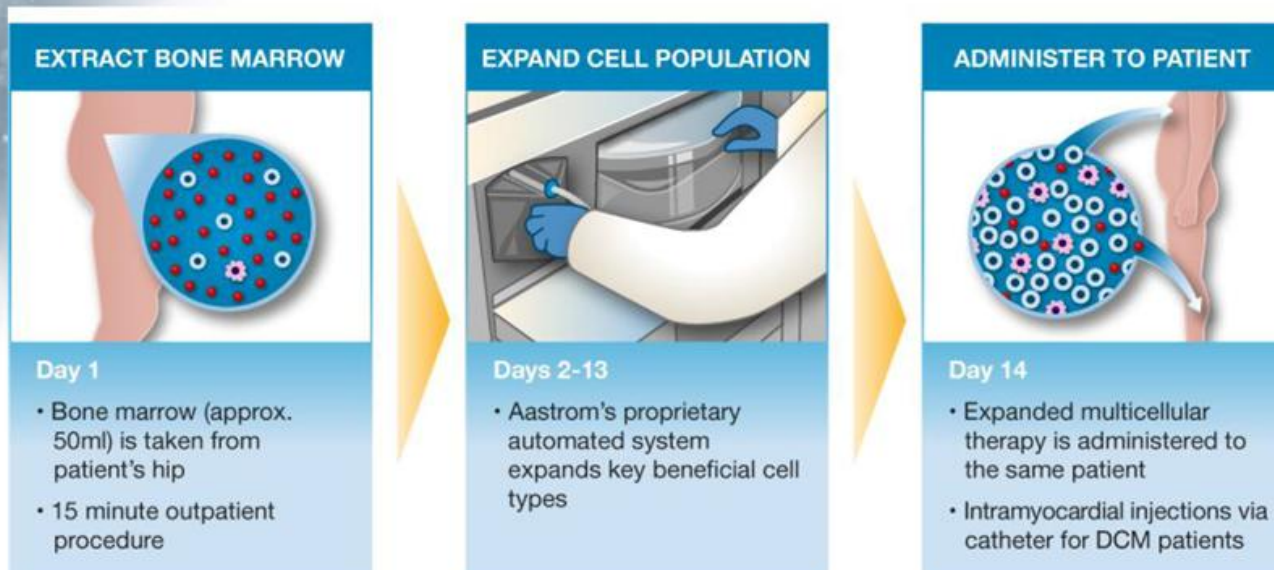
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# Ixmyelocel-T has multiple biological activities that promote repair & regeneration of ischemic tissue



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# Aastrom's therapeutic platform provides for efficient cell collection, production and delivery



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# Ixmyelocel-T GMP manufacturing platform is highly automated and expandable, with low COGS



## Automated, Fully-Closed GMP Manufacturing System

- Single-use disposable bioreactor cassette
- Application key
- Incubator
- Processor
- System manager



## Highly Scalable Modular Expansion

- Enables COGS < 10% at commercial scale



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# Ixmyelocel-T final product



- Manufactured to finished product specifications
- Streamlined logistics
  - Shipped via FedEx overnight in a qualified container
- Ready to use when received
  - No freezing or thawing
  - No refrigeration
  - No reconstitution
- 72-hour shelf life
- Easy to administer



Source: Perin EC et al. Circulation 2003;107:2294-2302  
Copyright © American Heart Association

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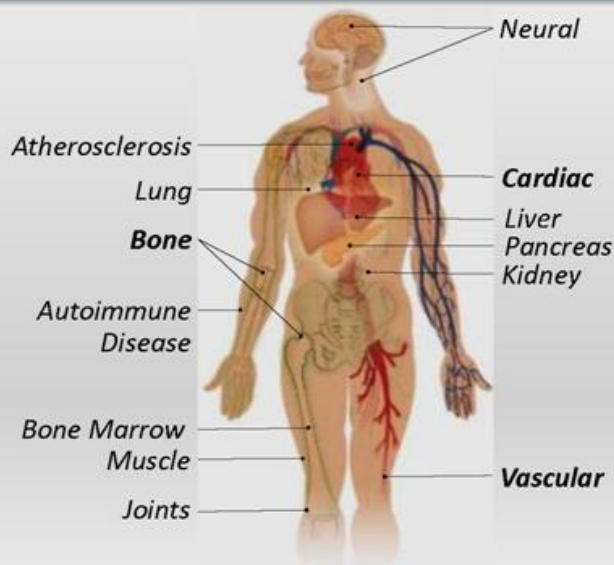
## Intellectual Property

- Comprehensive patent portfolio covering:
  - Composition of Matter
    - Provides protection through 2029
  - Manufacturing
  - Methods

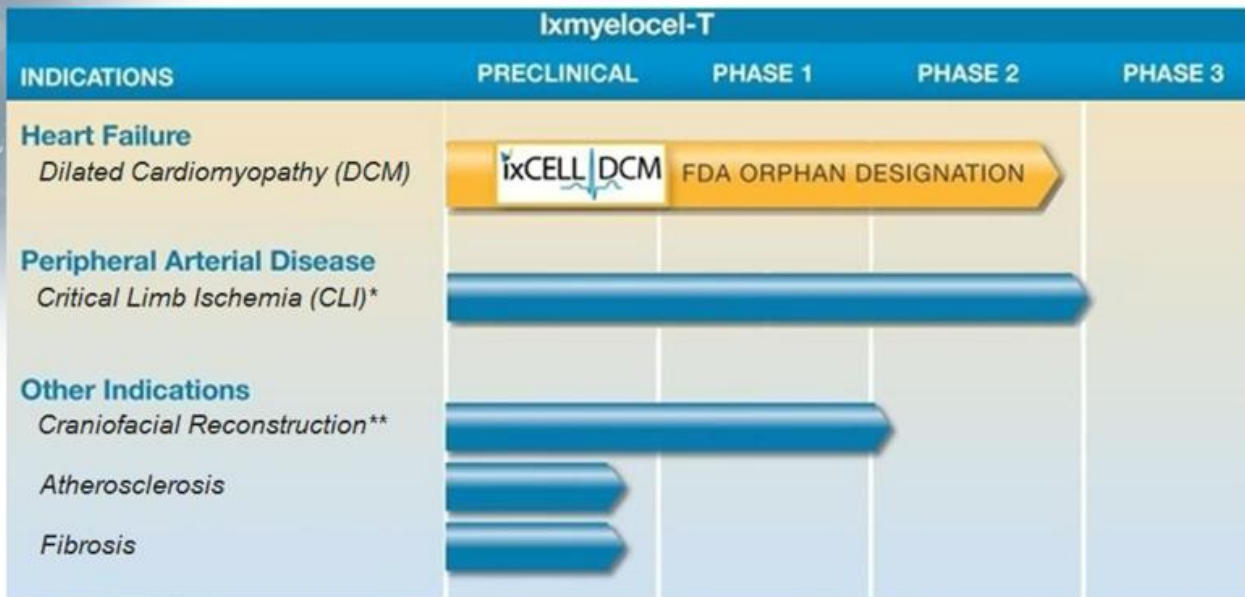


- Composition of Matter patents issued in US and EU in 2011 with broad claims covering:
  - Mixture of cell types derived from mononuclear cells, including MSCs and M2-like macrophages
  - Derived from bone marrow, blood or fetal liver
  - Hematopoietic, mesenchymal and/or endothelial lineages
  - Profile of anti-inflammatory cytokines and angiogenic factors
  - Low residual process reagents

## Ixmyelocel-T Potential Therapeutic Applications

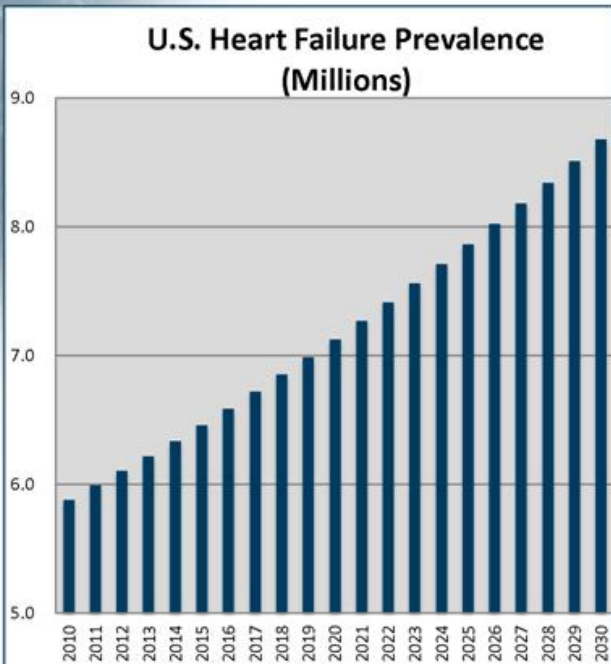


# Current focus is on developing ixmylocel-T to treat advanced heart failure due to ischemic DCM

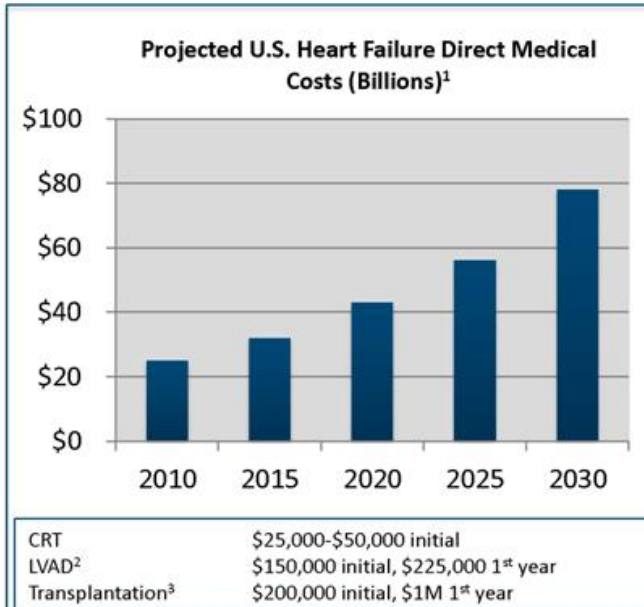


\* Not actively enrolling  
 \*\* Investigator-sponsored trial (University of Michigan)

# Heart failure represents a significant unmet medical need and growing public health problem



Sources: Health Research International; Heidenreich et al. Circulation 2011;123:933-944



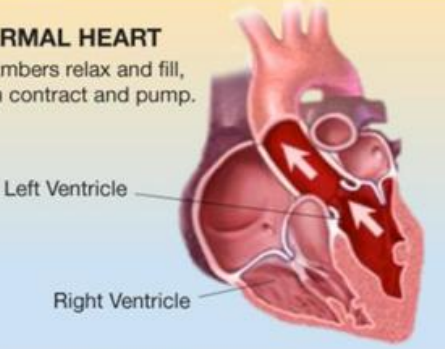
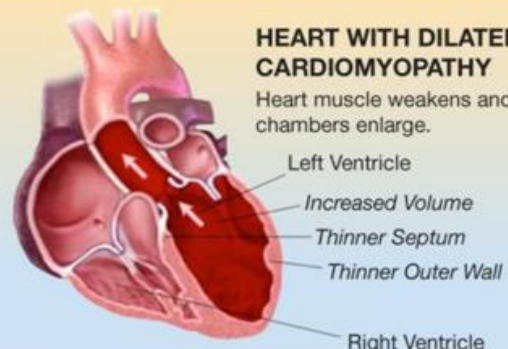
CRT	\$25,000-\$50,000 initial
LVAD <sup>2</sup>	\$150,000 initial, \$225,000 1 <sup>st</sup> year
Transplantation <sup>3</sup>	\$200,000 initial, \$1M 1 <sup>st</sup> year

Sources: 1. Heidenreich et al. Circulation 2011;123:933-944; 2. Moskowitz, Ann Thorac Surg 2001;71:S195-S198; 3. Transplant Living.org



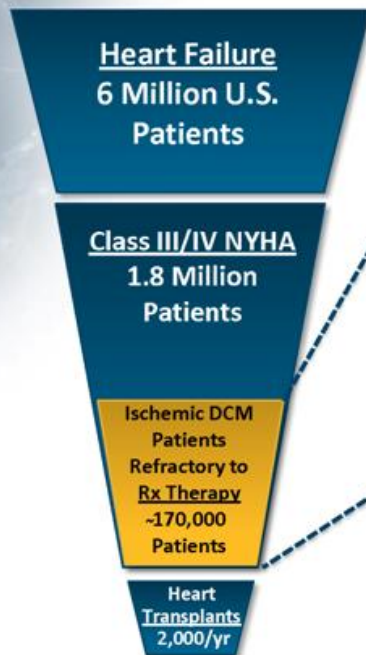
# Ischemic DCM is a leading cause of heart failure and heart transplantation



<p><b>NORMAL HEART</b> Chambers relax and fill, then contract and pump.</p>  <p>Left Ventricle Right Ventricle</p>	<p><b>HEART WITH DILATED CARDIOMYOPATHY</b> Heart muscle weakens and chambers enlarge.</p>  <p>Left Ventricle Increased Volume Thinner Septum Thinner Outer Wall Right Ventricle</p>
<p><b>Description</b></p>	<ul style="list-style-type: none"> <li>• Disease of the heart muscle characterized by weakened and enlarged chambers, reduced wall thickness, and inability to sufficiently pump blood</li> <li>• 3<sup>rd</sup> most common cause of heart failure</li> <li>• Leading cause of heart transplantation</li> </ul>
<p><b>Symptoms</b></p>	<ul style="list-style-type: none"> <li>• Chest pain</li> <li>• Shortness of breath</li> <li>• Fatigue</li> </ul>
<p><b>Causes</b></p>	<ul style="list-style-type: none"> <li>• <b>Ischemia/Atherosclerosis – 60% of DCM patients</b></li> <li>• Genetic; disease and toxin-induced</li> <li>• Idiopathic</li> </ul>
<p><b>Current Treatment Options</b></p>	<ul style="list-style-type: none"> <li>• Very limited therapeutic options available             <ul style="list-style-type: none"> <li>– Heart transplants limited</li> <li>– Left ventricular assist devices (LVADs) have high cost and poor QOL</li> </ul> </li> </ul>

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# A majority of advanced heart failure patients that are refractory to medical therapy have DCM



**Patient Profile**

- Majority of patients that are refractory to medical therapy have ischemic DCM (~170,000 patients)
- Generally have maximized Rx and device therapy
- Typically no longer candidates for revascularization procedures
- LVADs are commonly utilized as a bridge to heart transplantation
- ~2,000 heart transplants performed in the U.S. each year

**Product Positioning**

Refractory to:

- Rx therapy
- Revascularization
- CRT/ICD devices

> **lxmyelocel-T** <

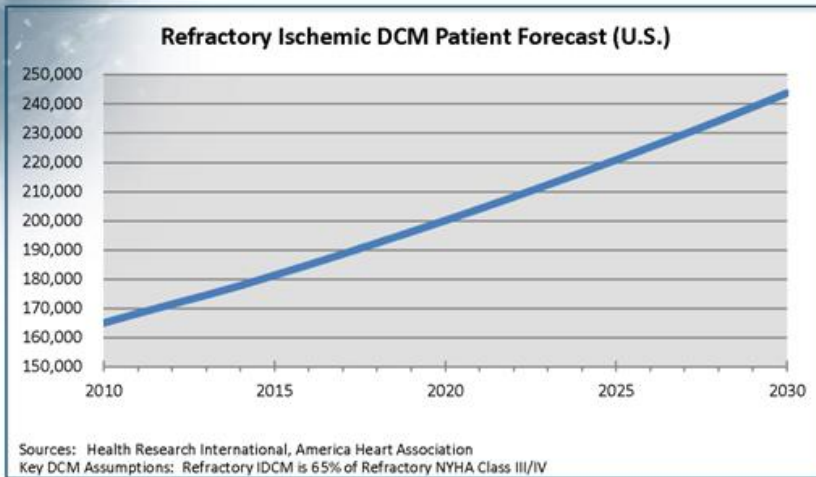
Prior to:

- LVAD
- Transplantation

Sources: Heidenreich et al. Circulation 2011;123:933-944; Health Research International; America Heart Association

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# The refractory ischemic DCM market represents a significant commercial opportunity for ixmyelocel-T



**Ixmyelocel-T Commercial Opportunity**

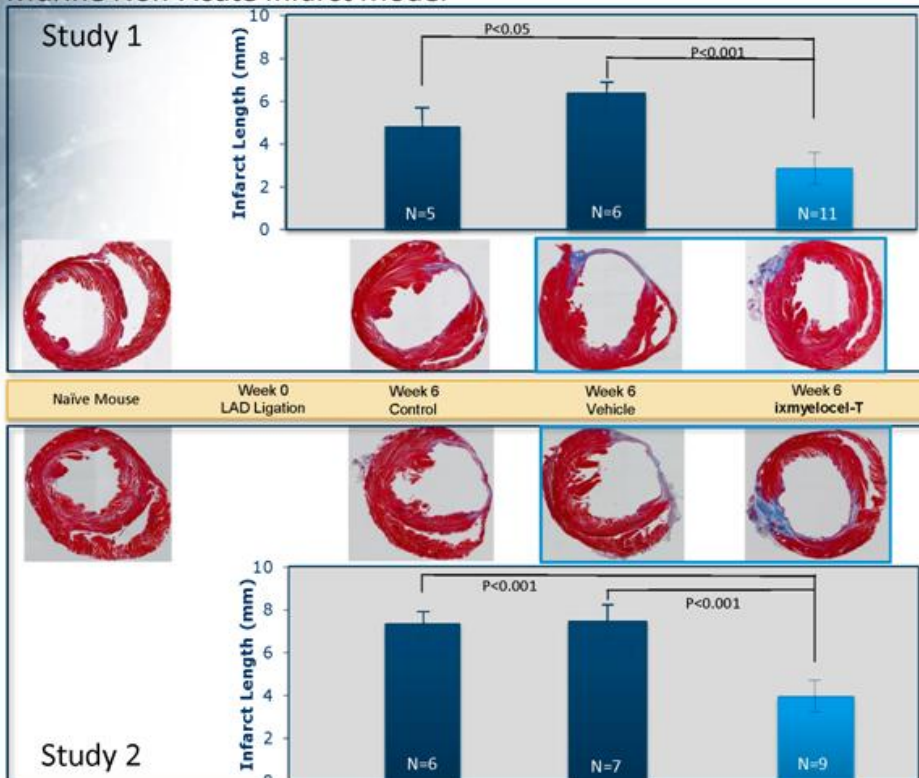
- First to market to treat advanced heart failure due to ischemic DCM
- Orphan indication
- Premium pricing
- > \$1B peak sales opportunity
  - \$40,000 price
  - 27% peak market share

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# Ixmyelocel-T significantly and reproducibly reduced tissue damage in a murine model of heart failure



## Murine Non-Acute Infarct Model



Statistically significant results reproduced across studies

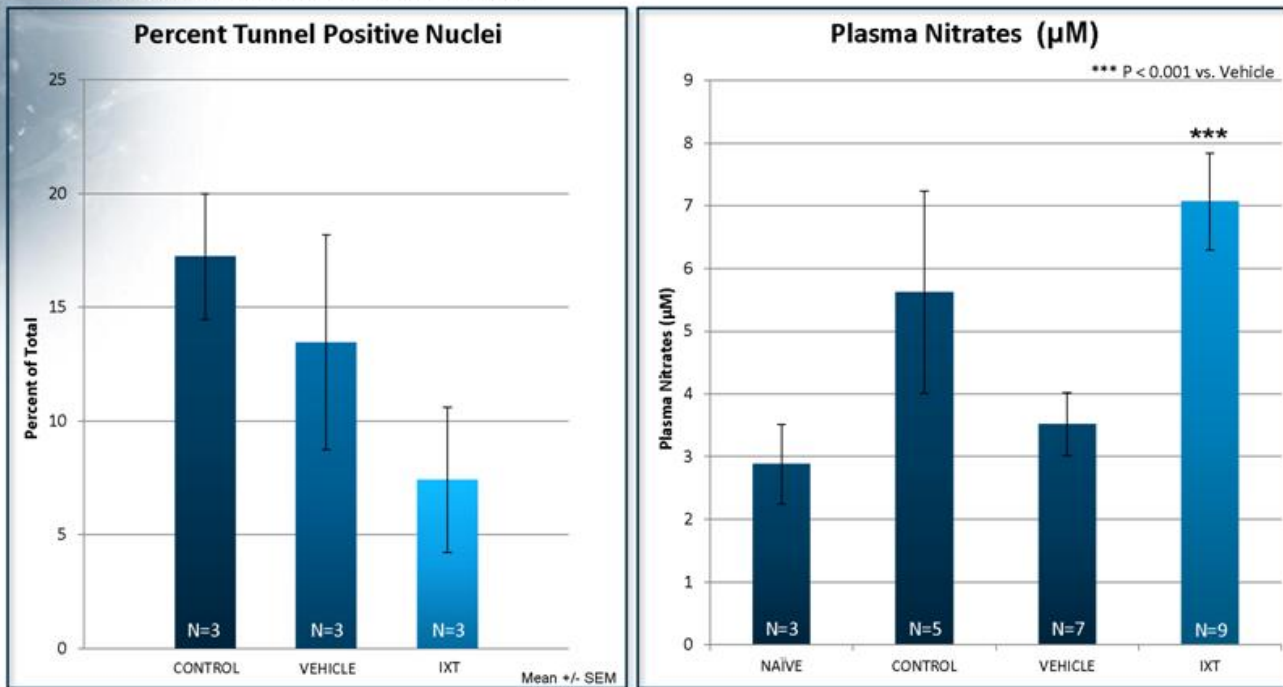
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Study conducted at Medigenix, LLC; data presented at the 18th Annual International Society for Cellular Therapy Meeting, June 2012.

# Ixmyelocel-T treatment reduced apoptosis in the infarct border zone and increased plasma nitrates



## Murine Non-Acute Infarct Model



21 Study conducted at Medigenix, LLC; data presented at the 18th Annual International Society for Cellular Therapy Meeting, June 2012.

# Phase 2a DCM clinical objectives focused on safety, optimizing delivery and patient selection



## Phase 2a Clinical Objectives

1. Demonstrate ixmyelocel-T safety in DCM patients
2. Evaluate delivery approaches
3. Gain clinical insight into patient selection

## Phase 2a Study Parameters: Two 12-month randomized open-label DCM studies

- Delivery: Surgical (IMPACT-DCM study) vs. Catheter (CATHETER-DCM Study)
- Patient Population: Ischemic vs. non-ischemic DCM

	IMPACT-DCM (n=39)		CATHETER-DCM (n=21)	
<b>Delivery</b>	Intramyocardial delivery to the myocardium via thoracotomy		Endocardial injections delivered via NOGASTAR® endomyocardial catheter	
	<b>Ixmyelocel-T</b>	<b>Control</b>	<b>Ixmyelocel-T</b>	<b>Control</b>
<b>Total n=60</b>	24	15	15	6
<b>IDCM</b>	12	7	9	3
<b>NIDCM</b>	12	8	6	3

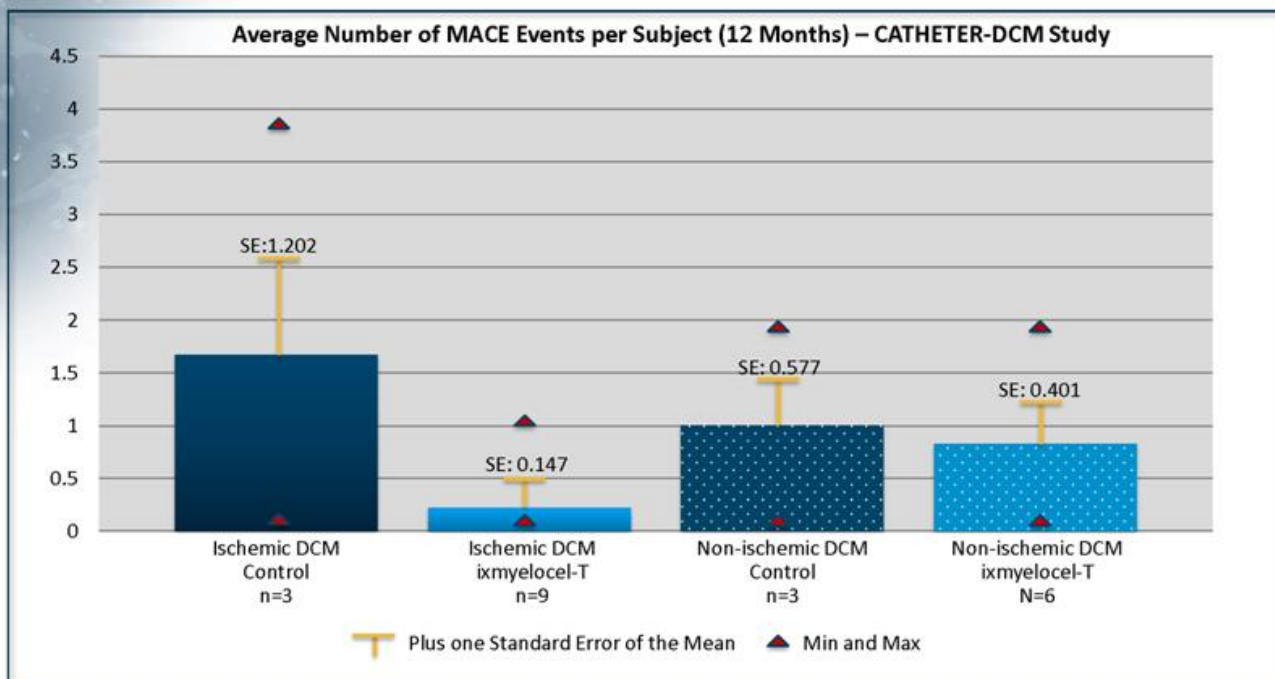
# Phase 2a safety results demonstrated that ixmyelocel-T was well-tolerated in DCM patients

## Summary Safety and Tolerability Conclusions

- Overall, ixmyelocel-T was well-tolerated in patients with DCM
  - IMPACT-DCM: Post-surgery, adverse event incidence was comparable between the ixmyelocel-T and control groups
  - CATHETER-DCM: Adverse event incidence was comparable between the ixmyelocel-T group and the control standard of care group
- Improved patient tolerance demonstrated with catheter administration

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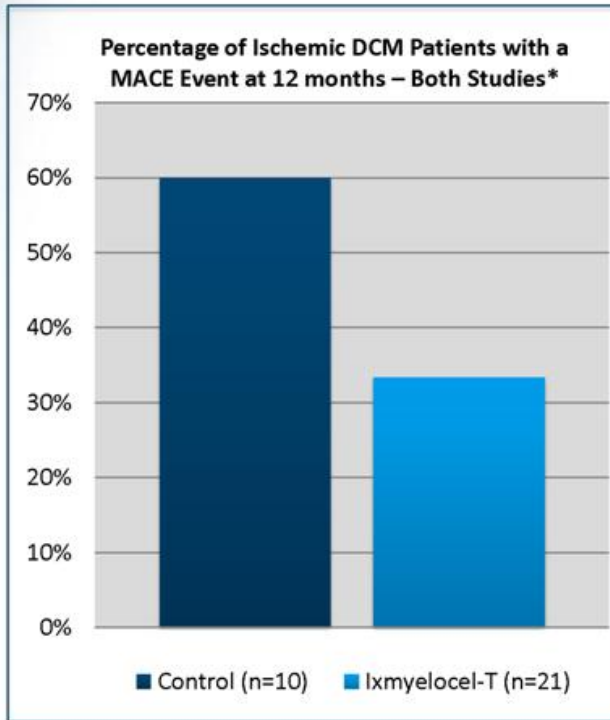
## Subjects treated with ixmyelocel-T in the ischemic DCM group had a lower number of MACE events



Note: MACE = cardiac death, cardiac arrest, myocardial infarction, sustained ventricular arrhythmia, pulmonary edema, CHF exacerbation (hospitalization), unstable angina, major bleed within one week of injection procedure

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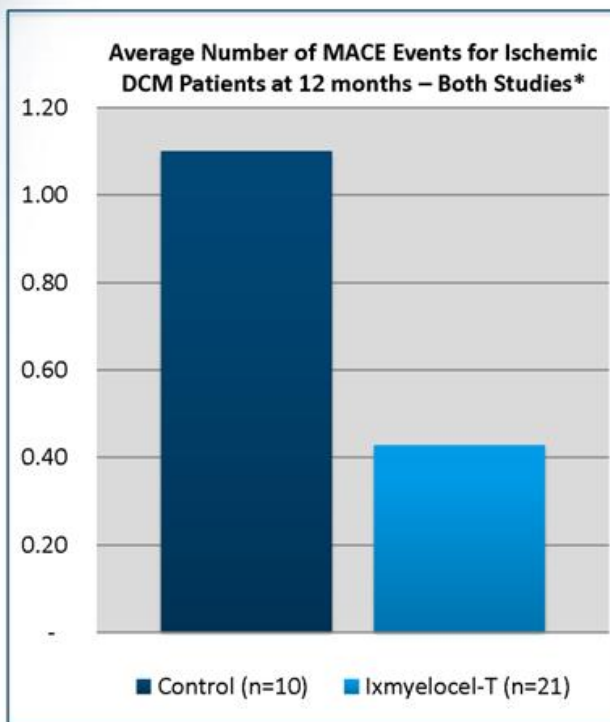
# Subjects treated with ixmyelocel-T in the ischemic DCM groups were less likely to have MACE events



45% reduction in the number of patients having a MACE event at 12 months

25 \*Combined IMPACT-DCM and CATHETER-DCM data in the ischemic DCM groups.

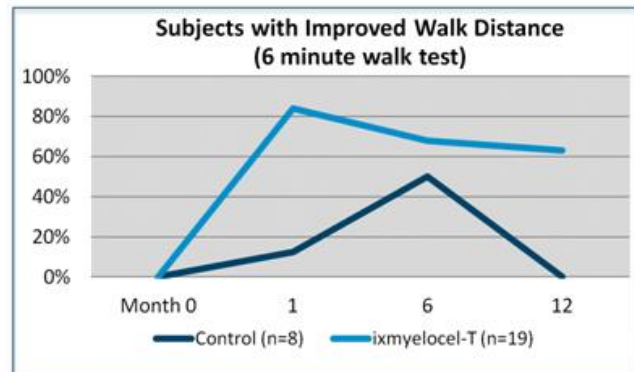
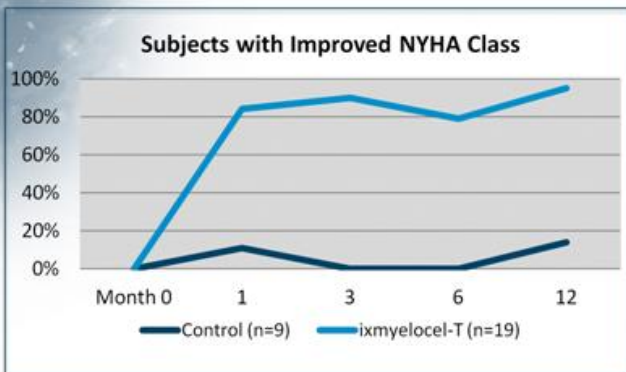
# Subjects treated with ixmyelocel-T in the ischemic DCM groups had a lower number of MACE events



61% reduction in the average number of MACE events per patient at 12 months

26 \*Combined IMPACT-DCM and CATHETER-DCM data in the ischemic DCM groups.

# Consistent positive trends observed in secondary efficacy measures in the ischemic DCM groups\*

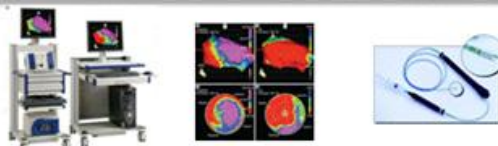


27 \*Combined IMPACT-DCM and CATHETER-DCM data in the ischemic DCM groups.

# The phase 2b ixCELL-DCM study is a robust clinical study of ixmyelocel-T in ischemic DCM patients

## Phase 2b ixCELL-DCM Study Design Highlights

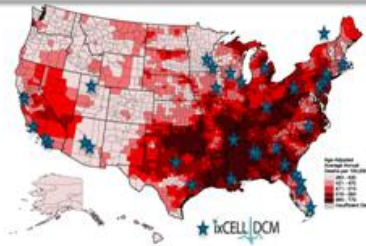
<b>Objectives</b>	<ul style="list-style-type: none"> <li>To evaluate the efficacy, safety and tolerability of ixmyelocel-T compared to placebo in patients with heart failure due to ischemic DCM</li> </ul>
<b>Patients</b>	<ul style="list-style-type: none"> <li>Males and females, age 30-85</li> <li>Diagnosis of ischemic DCM according to WHO criteria</li> <li>Not a candidate for reasonable revascularization procedures</li> <li>LVEF <math>\leq</math> 30%</li> <li>NYHA class III or IV heart failure</li> </ul>
<b>Design</b>	<ul style="list-style-type: none"> <li>Multicenter, randomized (1:1), double-blind, placebo-controlled phase 2b study</li> <li>108 patients at approximately 30 sites in the US and Canada</li> <li>Administration via catheter injection into the left ventricular endocardium using the NOGA® Myostar™ injection catheter</li> </ul>
<b>Key endpoints</b>	<ul style="list-style-type: none"> <li>Primary: Number of all-cause deaths, all-cause hospitalizations, and emergency department visits for IV treatment of acute worsening heart failure over 12 months</li> <li>Secondary: Additional clinical, functional, structural, symptomatic/QOL, and biomarker measures at 3, 6 and 12 months</li> </ul>
<b>Status</b>	<ul style="list-style-type: none"> <li>First patients enrolled and treated in April 2013</li> </ul>



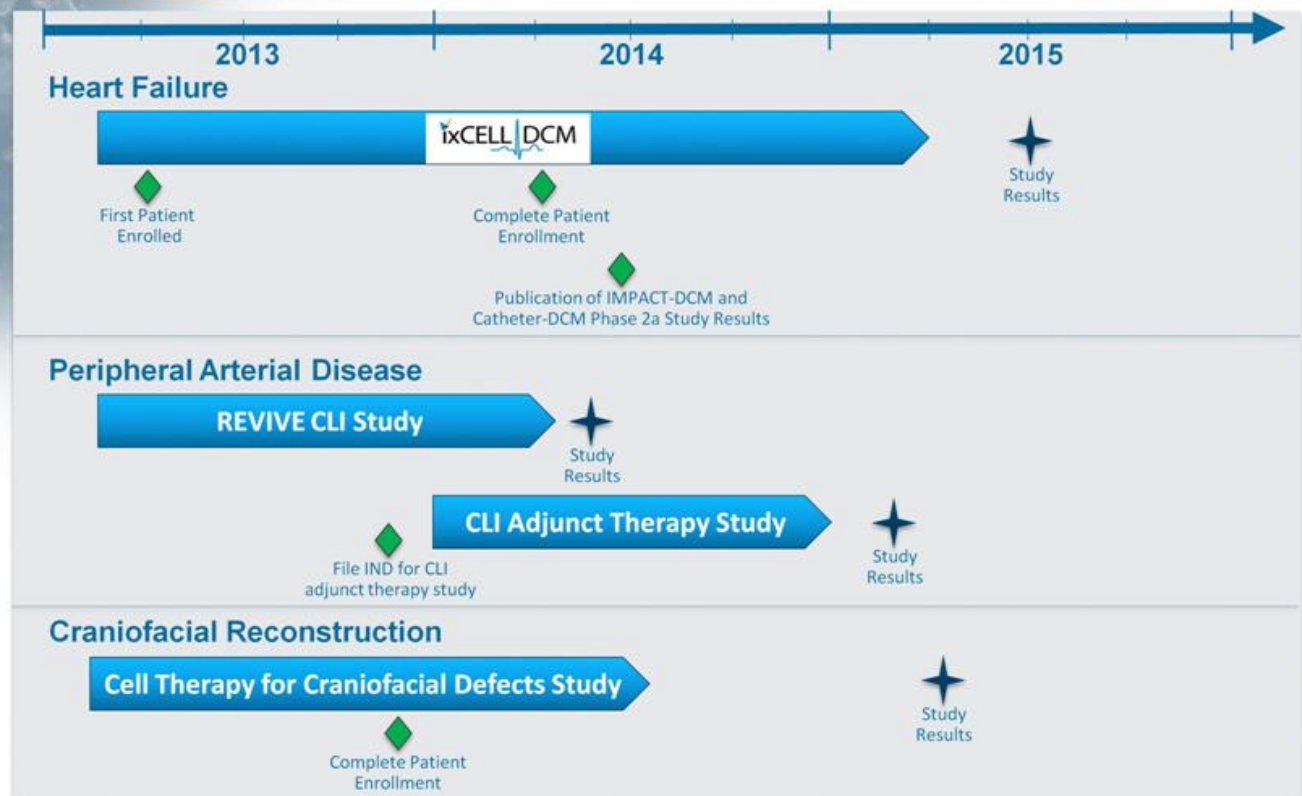
# ixCELL-DCM Phase 2b study execution is highly achievable

## ixCELL-DCM Study Execution Attributes

- Well-defined patient population at a well-defined point in disease progression
  - Advanced heart failure patients refractory to medical therapy
- Target physicians are motivated to perform catheter-based procedures
  - Standard practice for interventional cardiologists
- Strong coordination between heart failure specialists and interventional cardiologists
  - Existing relationships in management of patient care
- Study sites are experienced in using NOGA Myostar catheter for cell therapy studies
  - Myostar catheter is specifically designed for cell delivery (currently at 65 U.S. clinical sites)
- Manageable number of patients at a significant number of sites
  - 108 patients at 30 sites in U.S. and Canada
- Study sites are concentrated in areas of high disease prevalence
  - Target physicians located in these areas



# Aastrom has several value-creating Phase 2 clinical milestones over the financing period



## Cash Balance

- \$9.2 million at March 31, 2013

## Cash Burn

- ~\$4.5 expected in Q2
- ~\$3.5-\$4.5 million per quarter Q3 2013 through Q1 2014 (ixCELL-DCM enrollment)
- ~\$3 million per quarter thereafter

## Market Cap

- ~\$32 million public float
- ~\$40 million including preferred stock

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# Capital Structure

## Shares Outstanding (in millions) – June 2013

Common	45.7
Series B Preferred	<u>14.3</u>
Total	<u>60.0</u>

Employee Options	7.3 (WAV exercise price = \$2.05)
Warrants	4.8 (4.5M at \$2.44 ; 0.3M at \$1.25)

## Series B Preferred Stock

- Accruing PIK dividends at 11.1% through March 2017
  - Preferred shares convert to 21.9 million common shares in March 2017
  - 2 million dividend shares accrued to date
- No warrants or anti-dilution provisions

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## Leading Autologous Cell Therapy Platform

- Developing patient-specific multicellular therapies
- Highly automated and scalable GMP manufacturing system

## Highly Differentiated Product

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## Consistent Positive Efficacy Data

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ixCELL DCM

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