Regenerative Medicines Based on Autologous Stem Cells:
A New Era in Personalized Medicine

Somatic Cell Therapy
September 2008
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 and application of Tissue Repair Cell (TRC) technology, which involve certain risks and uncertainties. Actual results may differ significantly from the expectations contained in the forward-looking statements.

Among the factors that may result in differences are the results obtained from clinical trials and development activities, regulatory approval requirements, competitive conditions and availability of resources.

These and other significant factors are discussed in greater detail in Aastrom’s Annual Report on Form 10-K and other filings with the Securities and Exchange Commission.
Aastrom Leveraging Total Potential of Bone Marrow Using Mixed Population of Patient’s Cells to Treat Disease

- Cardiac Muscle
- Skeletal Muscle
- Bone Cells (Osteoblasts)
- Epithelial Cells
- Neurons & Glial Cells
- Fat Cells

- Bone Marrow Stromal Cells
- Hematopoietic and Endothelial Stem Cells
- Endothelial Precursor Cells
- Blood Vessels
- Macrophages, Lymphocytes & other Blood Cells
Novel Cell Products
Enabled by Advanced Manufacturing Technology

TRC technology creates cell products intended for target indications

Small amount of bone marrow collected from the patient

Over 290 patients treated to date

Cells produced in centralized GMP manufacturing facility

Patient-specific cell products with increased stem and progenitor cells

Bone
Liver
Pancreas
Kidney
Bone Marrow
Muscle
Joints
Neural
Cardiac
Vascular

Bone
Marrow
Muscle
Joints

Over 290 patients treated to date
Tissue Repair Cell (TRC) Based Products
Expanded Populations of Early Stage Cells Found in Bone Marrow

Frequency Distribution of Cell Types Shifts Towards Early Stem and Progenitor Cells
Regulatory Treatment Varies By Geography

<table>
<thead>
<tr>
<th>Marketing Authorization</th>
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<tr>
<td>• U.S. treats autologous cell therapy as biologics</td>
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<td>- Requires IND and BLA for market authorization</td>
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<td>• Rigorous multi-year process</td>
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<td>• Germany treats autologous cell therapy as tissue engineered products for tissue regeneration</td>
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<td>- Currently allows immediate marketing with licensed GMP production</td>
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<td>- New ATMP regulation requires centralized EMEA approval after 4 year transition period ending in 2013</td>
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<table>
<thead>
<tr>
<th>Manufacturing Authorization</th>
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<tr>
<td>• U.S. requires full GMP manufacturing as part of Phase III and BLA approval</td>
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<td>- Clinical trials do not require full GMP certification</td>
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<td>- Regulations cover product from arrival at manufacturing facility to administration by physician</td>
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<td>• EU requires licensed GMP manufacturing for all human use applications</td>
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<tr>
<td>- German regulations cover bone marrow aspirate collection through product administration by physician</td>
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German Manufacturing Regs Pose Challenges
Hospitals Drawing Aspirates Part of GMP Manufacturing Process

- Two regulatory options under German Drug Law AMG 14
  - Section 20c: hospital linked to central manufacturing license for bone marrow procurement
  - Section 20b: hospital as independent manufacturer of GMP bone marrow aspirate
- 20c, easier to implement for hospitals but greater burden on company
  - Best for single manufacturing site supporting small number of hospitals
- 20b, greater flexibility and places responsibility for bone marrow with hospitals
  - Best for multiple manufacturing sites and large number of hospitals
Aastrom Approach to German Manufacturing
Leverages Multiple Manufacturing Sites

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<tr>
<th>Typical Approach</th>
<th>Aastrom Model</th>
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<td>Mfg site 1  →  Hospital 1</td>
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<td>Mfg site 3  →  Hospital 4</td>
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- Manufacturing sites can be changed without impacting hospitals
- More reliable and efficient product supply due to redundant back-ups and sourcing options
- New hospitals can be licensed prior to finalizing product supply plans
Current EU Efforts Offer Two Value Propositions

• Support entry into U.S. clinical trials (via traditional regulatory pathways, eg. IND) by leveraging EU for…
  – Access to patients outside of clinical trial environment
  – Opportunity to modify treatment procedures without protocol amendments
  – Access to experienced centers with greater general acceptance of cell therapy

• Develop EU markets ahead of U.S. market entry
  – Build broad clinical experience
  – Refine patient-specific commercial model
Three-for-Three INDs Using Early EU Data

U.S. INDs supported by early EU data

- **IMPACT-DCM**
  - 40 patient Phase II trial for dilated cardiomyopathy
- **RESTORE-CLI**
  - 150 patient Phase II trial for critical limb ischemia
- **ON-CORE**
  - 120 patient Phase III trial for osteonecrosis of the femoral head

Example: IMPACT-DCM

- **Challenges**
  - Cells as sole therapy in first cardiac trial with TRC products
  - Direct injection into the heart
- **Value of EU patient experience**
  - Addressed potential for acute toxicity
  - Demonstrated feasibility of novel surgical approach
Cardiac Regeneration
Need for therapy to reverse disease progression

Normal Heart

Enlarged Heart due to Dilated Cardiomyopathy

Cardiac Repair Cell (CRC) Treatment Approach
EU Cardiac Compassionate Use Cases
Early clinical data supported IND filing

**Patient #1**

**Profile**
- 74 year old male patient diagnosed with ischemic dilated cardiomyopathy
- Suffered extensive three-vessel coronary heart disease, renal insufficiency and unstable angina pectoris (chest pain)
- Cardiac ejection fraction of 10%
- Met clinical criteria for class IV heart failure (New York Heart Association classification guidelines)

**Results from Surgical Center**
- Treated with CRCs in November 2007
- Discharged from the hospital in January 2008 with improved ejection fraction of 25-30%
- Clinical improvement of his heart failure stage had been noted

**Patient #2**

**Profile**
- 69 year old female diagnosed with severe dilated cardiomyopathy
- Suffered from extensive three-vessel coronary heart disease and had experienced multiple previous heart attacks
- Cardiac ejection fraction of 25-30%

**Results from Surgical Center**
- Treated with CRCs in December 2007
- Discharged from the hospital in February 2008 with improved ejection fraction of 45%

Source: Hans Michael Klein, MD, Professor of Cardiac Surgery at the Dusseldorf University Hospital in Dusseldorf, Germany
IMPACT-DCM Clinical Trial
U.S. Phase II Dilated Cardiomyopathy (DCM) Trial

**Trial Design**
- 40 patient, randomized, controlled, open-label study
  - 20 patients with ischemic DCM; 20 patients with non-ischemic DCM
  - Randomized 3:1 treatment vs. control
  - Up to 5 treatment centers
- CRCs delivered as monotherapy
  - Direct injection via lateral thoracotomy or minimally invasive thoracoscopy
- 12 month patient follow-up

**Target Patients**
- Diagnosed with ischemic or non-ischemic DCM
- New York Heart Association class III or IV heart failure
- Left ventricular ejection fraction ≤ 25% (60-75% is typical for a healthy person)
- 18-86 years old

**Data Collection**
- Safety data
- Incidence of MACE (Major Adverse Cardiac Events)
- New York Heart Association classification for heart failure
- Left ventricular ejection fraction
- Left ventricular dimensions/mass/volume
- Myocardial perfusion and viability
- Pulmonary function
- Exercise tolerance (six minute walk)
- Quality of life

Status: FDA approval within first 30 day review period; Finalizing IRB approvals at trial sites
Developing Personalized Stem Cell Therapies for Regenerative Medicine