Presenter:

James R. Stubbs, M.D.
Chair, Division of Transfusion Medicine

Department of Laboratory Medicine and Pathology
at Mayo Clinic, Rochester, Minnesota
Disclosures

• None

Regenerative Medicine

• Regenerative Medicine integral
• “Next evolution” of medical treatments
• Enables caregivers to provide specific, targeted medical care for difficult to treat or previously untreatable diseases
Regenerative Medicine

- Interdisciplinary expertise
  - Applied engineering, biochemistry, biology, chemistry, tissue engineering, and tissue science
  - Development of novel and innovative cures and therapies for diseases

- “Some Day” is not that far away (some of it is already here!)
  - Regenerate damaged tissues and organs while still inside patients’ bodies
    - Techniques – Stimulate damaged tissues and organs to heal themselves
  - Growth of organs and tissues in vitro – Implantation
    - Patients with conditions who cannot be stimulated to heal internally
  - Allow successful treatment of patients with previously untreatable diseases
Human Cellular Therapy Laboratory

• Initially created to support Mayo Clinic’s Bone Marrow Transplant Service
• Began processing hematopoietic progenitor cells (HPC) from marrow and blood in 1987
• Mayo Clinic HPC Transplant Service
  • One of the largest programs in the United States
  • Grown steadily
    • 74 transplants in 1996
    • 538 transplants in 2014
  • HCTL processed progenitors cells in support of over 6,000 HPC transplants

Human Cellular Therapy Laboratory

• 1998 Special development and manufacturing laboratory was built at Mayo Clinic
  • Complied with FDA requirements for drug manufacturing – cGMP facility
  • One of the first academic medical center-based cGMP-compliant cell manufacturing facilities in the United States
  • Since inception it is one of the most productive of such facilities
Human Cellular Therapy Laboratory

- Demand for HCTL services in development and clinical application of novel cellular therapies
  - Absence of current therapies for difficult to treat or rare diseases
  - Realization that evaluating new individualized cellular therapies drives novel investigative programs
  - End-to-end solution that provides regulatory support, clinical trial design, drug manufacturing, and patient monitoring services

Human Cellular Therapy Laboratory

- Total Solution for “First in Man” Trials
  - Design, write, submit and secure Investigational New Drug (IND) status for novel cellular therapies
  - Develop the technology platform
    - Identify the platform
    - Provide all the data in support of the platform that informs the parameters and use of the drug
  - Dedicated cGMP facility to meet the needs of investigators interested in using cells as drugs/drug manufacturing
    - Both proprietary and contract manufacturing
  - Clinical trial support
    - Methods for collecting patient samples
    - Proprietary methods for analyzing changes in peripheral blood of patients
**MSC Platform – First In Man Trials**

<table>
<thead>
<tr>
<th>Technology</th>
<th>Indication</th>
<th>Discovery</th>
<th>Preclinical</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autologous MSC-NTF Cells (NurOwn)</td>
<td>ALS</td>
<td></td>
<td></td>
<td>First in Man</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Autologous MSC</td>
<td>ALS</td>
<td></td>
<td></td>
<td>First in Man</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Autologous MSC</td>
<td>Bronchiolitis obliterans</td>
<td></td>
<td></td>
<td>First in Man</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Autologous MSC Coated Fistula plug</td>
<td>Perianal Crohn’s Disease</td>
<td></td>
<td></td>
<td>First in Man</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MSC Infected With a NIS-Expressing Derivative</td>
<td>Ovarian Cancer</td>
<td></td>
<td></td>
<td>First in Man</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Autologous MSC</td>
<td>Multiple System Atrophy</td>
<td></td>
<td></td>
<td>First in Man</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Autologous MSC</td>
<td>Atherosclerotic Renal Artery Stenosis</td>
<td></td>
<td></td>
<td>First in Man</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Autologous MSC</td>
<td>OA-joint</td>
<td></td>
<td></td>
<td>First in Man</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Autologous MSC</td>
<td>Type 1 Diabetes</td>
<td></td>
<td></td>
<td>First in Man</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**HOT TOPIC / Transfusion Medicine Part 2: Regenerative/Cellular Medicine**

**“Transformational” Medical Care**

<table>
<thead>
<tr>
<th></th>
<th>Fistula</th>
<th>Brain Cancer</th>
<th>Neurology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effectiveness</td>
<td>VERY PROMISING</td>
<td>VERY PROMISING</td>
<td>YES for MSA</td>
</tr>
<tr>
<td>Safety</td>
<td>Excellent</td>
<td>Excellent so far</td>
<td>Excellent</td>
</tr>
<tr>
<td>Potential use</td>
<td>40-100+ million/yr</td>
<td>50-100+ million/yr</td>
<td>40-100+ million/yr</td>
</tr>
<tr>
<td>Stage of discovery</td>
<td>Phase II in process</td>
<td>Phase I complete</td>
<td>Phase I complete</td>
</tr>
</tbody>
</table>