Preclinical Stage Cell Therapeutics Company
Focused on Rare Diseases

- Chimeric Cell therapy platform
- Lead program, DT-101 DEC, completed extensive in vivo studies in Duchenne’s muscular dystrophy and is ready for clinical trial (IRB, GMP manufacturing, clinical protocol completed)
- Being studied in additional indications with opportunity to broaden across a large variety of disorders (e.g. GVHD, pulmonary fibrosis, sarcopenia, others)
- Distinctive advantages over competitive approaches
  - Universal therapy for all Duchenne’s genetic mutations
  - Does not require immunosuppression
  - Excellent safety profile - no tumor formation
  - Novel chimeric cell approach - no other companies developing
- Technology licensed from the University of Illinois
- Robust IP real estate with patents that expire in 2036
Dystrogen Therapeutics
Pipeline

<table>
<thead>
<tr>
<th>Candidate</th>
<th>Therapeutic Area</th>
<th>Discovery</th>
<th>Pre-Clinical</th>
<th>Clinical (First-in-Human)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DT - 101 DEC</td>
<td>Duchenne’s Dystrophy</td>
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<tr>
<td>DT - 200</td>
<td>Sarcopenia</td>
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<tr>
<td>DT - 201</td>
<td>Pulmonary Fibrosis</td>
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<tr>
<td>DT - 202</td>
<td>GVHD</td>
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</table>
1st Product (Most Advanced)

DEC Therapy for Duchenne Muscular Dystrophy
Duchenne Muscular Dystrophy

- Rare disease
- Most common lethal X-chromosome linked progressive muscle-wasting disorder
- Over 20,000 boys are living with the disease in the US and over 300,000 worldwide
- Caused by a variety of dystrophin gene mutations
- No cure currently exists
DT-101 DEC Goal of Clinical Treatment – Slow or Halt Disease Progression
Chimeric Cell Therapy

Prof. Maria Siemionow
Inventor

- 10+ years of scientific studies
- Patented technology by prof. Maria Siemionow (global protection)

**CHIMERIC CELLS** are created by fusing the patient’s diseased cells with healthy cells from a donor. In case of DMD healthy **myoblasts** are fused with the patient’s **myoblasts**

- A novel approach to mitigate the side effects of immunosuppression and conditioning regimens as well as to **enhance cell engraftment**

**No cancer** demonstrated in small and large animal model
Chimeric Cell Therapy improves functional outcomes
Dystrophin Expressing Chimeric (DEC) Cells

Express Dystrophin

Normal Donor of Myoblast (MB^N)

Muscle biopsy

Myoblasts Isolation

Stained RED with PKH26 dye

Myoblast Labelling

Stained GREEN with PKH67 dye

Ex vivo fusion & Sorting

SORT + PKH26+/PKH67+

EXPRESS DYSTROPHIN

DMD Donor MHC

DMD Donor of Myoblast (MB^DMD)

Does Not Express Dystrophin

Stained ORANGE – DEC
(fusion of RED and GREEN cells)

SORT + PKH26+/PKH67+

EXPRESS DYSTROPHIN

DMD Donor MHC

SORT - PKH26-/PKH67+

NO DYSTROPHIN EXPRESSION

DMD Donor MHC

Stained RED with PKH26 dye

Stained GREEN with PKH67 dye

Normal Donor of Myoblast (MB^N)

Normal Donor MHC

Stained RED with PKH26 dye

Normal Donor MHC

NO DYSTROPHIN EXPRESS

DMD Donor MHC
DEC Cells - Mechanism of Action

**Intraosseous systemic delivery**

**DEC engraftment**

**MB\textsuperscript{DMD} + DEC fusion**

**Dystrophin production**

**Improved muscle strength**

---

**ENGRAFTMENT**

Chimeric DEC: MB\textsuperscript{N}/MB\textsuperscript{DMD}

**SPONTANEOUS FUSION - DIFFERENTIATION**

Chimeric DEC: MB\textsuperscript{N}/MB\textsuperscript{DMD}

**DYSTROPHIN DELIVERY**

Chimeric DEC: MB\textsuperscript{N}/MB\textsuperscript{DMD}

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**Chimeric DEC:**

- MHC
- Myotubes
- Express dystrophin
- Myofibers

**DMD Donor MHC**

- Myotubes
- Express dystrophin

**Normal Donor MHC**

- Myotubes
- Express dystrophin

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**Dystrophin production**

**Improved muscle strength**

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**Full-length dystrophin**

- Actin-binding domain
- Hinge
- Cysteine-rich domain
- Rod domain
- C-terminal domain

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Regenerative Medicine Life Sciences Company Focusing on Rare Diseases
Significant increase of Dystrophin expression at 30 days after DEC transplant to the gastrocnemius muscle (GM) of mdx mice

Biological marker: 37.3% increase in Dystrophin level at 30 days

After administration to gastrocnemius muscle in DEC injected mdx host compared to vehicle and not-fused MBwt and MBmdx controls; (n=6, mean±SD, 5 ROI/3 sections/6 animal/group, (One-way ANOVA)

Immunofluorescence images of dystrophin expression in GM of: wild type (wt) mice (left, positive control); Dystrophin-deficient mdx mice injected with vehicle; not fused MBwt with MBmdx; MBwt/MBmdx DEC

Improved Respiratory Function after Systemic DEC Therapy in *mdx/scid* mice on Plethysmography

Improved respiratory function after systemic-intraosseous transplant of DEC cells confirmed by whole-body plethysmography. One-Way Anova with post-hoc Tukey’s test, p<0.05.
Improved Muscle Force Function after Systemic DEC Therapy in \textit{mdx/scid} mice

Reduced skeletal muscle disease after systemic-intraosseous transplant of DEC cells confirmed by \textit{ex vivo} Aurora Muscle Force test
One-Way Anova with post-hoc Tukey's test, $p<0.05$
Improved Cardiac Outcomes After Systemic DEC Therapy in \textit{mdx/scid} mice

Systemic DEC administration demonstrated statistically significant increase in cardiac ejection fraction at day 90 as confirmed by echocardiography.

With a p-value of 0.031, EF was statistically significantly higher at day 90 for the mice injected with snjMB/mdxMB fused cells at an 0.05 compared to EF at day 0.
Reduced Cardiac Disease at 90 Days after Systemic DEC Therapy in \textit{mdx} mice

Confirmed by M and B-mode echocardiography
Representative images of Hematoxylin-eosin (H&E) stained cross-sections of heart, diaphragm and gastrocnemius muscle of mdx/scid mice confirming reduced fibrosis at 90 days after DEC transplant when compared to vehicle control. Magnification 10X, scale bar 200μm (Olympus, Japan)
Confirmation of Safety after Systemic DEC Therapy in mdx/scid mice

Assessment of organs of the highest tumor risk rate and the right hind limb revealed lack of tumor or tumor-like structure formation confirming safety of DEC cell lines after transplant.

MRI evaluation was made using a standard T2 – weighted protocol and T1 – weighted scanning for brain and liver. 31cm bore size 9.4 Tesla Agilent MRI System
# Competitive Advantages

<table>
<thead>
<tr>
<th>Features</th>
<th>DEC Therapy</th>
<th>Gene therapy</th>
<th>Stem Cell</th>
</tr>
</thead>
<tbody>
<tr>
<td>Targets 100% DMD patients</td>
<td>✓</td>
<td>✗</td>
<td>✓</td>
</tr>
<tr>
<td>Functional Outcomes</td>
<td>✓</td>
<td>✗</td>
<td>?</td>
</tr>
<tr>
<td>Dystrophin Expression</td>
<td>✓</td>
<td>✓</td>
<td>?</td>
</tr>
<tr>
<td>Not observed adverse effects</td>
<td>✓</td>
<td>✗</td>
<td>✓</td>
</tr>
<tr>
<td>No gene manipulation</td>
<td>✓</td>
<td>✗</td>
<td>✓</td>
</tr>
<tr>
<td>No need for immunosuppression</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
</tr>
</tbody>
</table>
Patenented Manufacturing Process
Regulatory

- ATMP classification – Tissue Engineering Product
- Orphan Designation FDA/EMA
- Rare Pediatric Disease Designation FDA
- Scientific Advice EMA
Intellectual Property – Cellular Therapy Platform

- Japanese Patent granted no. 2017-564642
- Canadian Patent granted no. 2988137
- Australian Patent granted no. 2016274797
- Filing date: 11 June 2015
- PCT Application
  Title: Muscular Dystrophy Chimeric Cells and Method for Treating Muscular Dystrophies
  Published on: December 15, 2016 as WO/2016/201182
- Proprietary Fusion Technology Know-How
- Basic Science Pre-clinical Data
- Exclusive Worldwide License From University of Illinois, Chicago, USA
Company Founders

Prof. Maria Siemionow MD, PhD
CHIEF MEDICAL OFFICER

- Professor of Orthopaedics, Director of Microsurgery Research, the University of Illinois in Chicago
- Lead surgeon of team that performed the world’s first near-total face transplantation, December 2008
- Over 300 scientific publications in the peer reviewed scientific journals

Dr. Kris Siemionow MD, PhD
CHIEF EXECUTIVE OFFICER

- Chief of Spine Surgery and Associate Professor of Orthopaedics and Neurosurgery at the University of Illinois in Chicago
- Entrepreneur & experienced manager (12 patents developed & commercialized). Developed and sold technology, patents, and licenses. Co-founder Holosurgical Inc, Inteneural Networks Inc, Kardiolytics Inc

Prof. Paul Lewicki PhD
CO-FOUNDER, DIRECTOR

- Founder and CEO of StatSoft (acquired by Dell in 2014)
- Big Data Pioneer
- Entrepreneur, large multinational company CEO (StatSoft had 30 overseas offices in all major markets and over 1 M B2B users across various industries)
Experienced Management Team & Scientific Board

Management Board

Prof. Maria Siemionow MD, PhD
Founder, CMO

Dr. Kris Siemionow MD, PhD
Co-Founder, CEO

Prof. Paul Lewicki PhD
Co-Founder, Board Member

Marta Osęka
VP Business Development

Research Directors and R&D Team

Prof. Wojtek Juzwa, PhD
Head Flow Cytometry

Prof. Ahlke Heydemann PhD
Scientific Advisory Board

Prof. Natalia Rozwadowska, PhD
Head Cell Therapy

Regenerative Medicine Life Sciences Company Focusing on Rare Diseases
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