Challenges of ATMP Development and Supply

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Dr. Michael Bennett
Director of Business Development
861+ regenerative medicine companies worldwide, including cell and gene therapies

464
North America

233
Europe and Israel

64
companies in the UK

126
Asia

15
South America

1
Africa

22
Oceania

Data from Alliance for Regenerative Medicine Q1 2018 data report
# Cell and Gene Therapy Trials Worldwide

Gene and Cellular Therapies and Other Regenerative Medicine Products – Q1 2018 Clinical Trials

**959**

Clinical trials underway worldwide by end of Q1 2018

<table>
<thead>
<tr>
<th>Ph. I</th>
<th>Ph. II</th>
<th>Ph. III</th>
</tr>
</thead>
<tbody>
<tr>
<td>320</td>
<td>549</td>
<td>90</td>
</tr>
</tbody>
</table>

**Number of Clinical Trials Utilizing Specific RM/AT Technology: Q1 2018**

<table>
<thead>
<tr>
<th>Gene Therapy</th>
<th>Gene-Modified Cell Therapy</th>
<th>Cell Therapy</th>
<th>Tissue Engineering</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total:</strong> 319</td>
<td><strong>Total:</strong> 284</td>
<td><strong>Total:</strong> 332</td>
<td><strong>Total:</strong> 24</td>
</tr>
<tr>
<td>Ph. I: 110</td>
<td>Ph. I: 121</td>
<td>Ph. I: 84</td>
<td>Ph. I: 5</td>
</tr>
<tr>
<td>Ph. II: 174</td>
<td>Ph. II: 152</td>
<td>Ph. II: 211</td>
<td>Ph. II: 12</td>
</tr>
<tr>
<td>Ph. III: 35</td>
<td>Ph. III: 11</td>
<td>Ph. III: 37</td>
<td>Ph. III: 7</td>
</tr>
</tbody>
</table>

*Total number of clinical trials represents an estimate; please note that products employing cell-based immunotherapy are accounted for in both the gene therapy & gene-modified cell therapy and cell therapy subsets. As a result, the total number of clinical trials does not equal the sum of the trials within the individual technology groups.*
In the UK the majority of therapies are in early phase trials
Growing numbers of UK clinical trials are sponsored by a commercial organisation

- Research institution sponsor
- Commercial sponsor
## Approved cell and gene products in Europe

<table>
<thead>
<tr>
<th>Product</th>
<th>Target</th>
<th>Year</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>ChondroClect</td>
<td>Cartilage repair</td>
<td>2009</td>
<td>withdrawn from use</td>
</tr>
<tr>
<td>MACI</td>
<td>Cartilage repair</td>
<td>2012</td>
<td>suspended for use</td>
</tr>
<tr>
<td>Glybera</td>
<td>Treatment of LPL deficiency</td>
<td>2013</td>
<td>Exceptional circumstances [License expires 25 October 2017, will not renew]</td>
</tr>
<tr>
<td>Provenge</td>
<td>Treatment of advanced prostate cancer</td>
<td>2013</td>
<td>withdrawn from use</td>
</tr>
<tr>
<td>Holoclar</td>
<td>Treatment of limbal stem cell deficiency</td>
<td>2015</td>
<td>conditional</td>
</tr>
<tr>
<td>Imlygic</td>
<td>Treatment of advanced melanoma</td>
<td>2015</td>
<td>Standard, Reimbursed in the UK</td>
</tr>
<tr>
<td>Strimvelis</td>
<td>Treatment of immunodeficiency due to adenosine deaminase deficiency (ADA-SCID)</td>
<td>2016</td>
<td>conditional</td>
</tr>
<tr>
<td>Zalmoxis</td>
<td>Adjunctive treatment in (HSCT) of adult patients with high-risk haematological malignancies</td>
<td>2016</td>
<td></td>
</tr>
<tr>
<td>Spherox</td>
<td>Cartilage repair</td>
<td>2017</td>
<td></td>
</tr>
</tbody>
</table>
Look at the price tags!

**Strimvelis**

Ex-vivo stem cell gene therapy to treat a very rare disease called ADA-SCID (Severe Combined Immunodeficiency due to Adenosine Deaminase deficiency)

Estimated to occur in ~15 patients per year in Europe

**KYMRIAH™**

An ex-vivo CD19 immunotherapy approved in the United States for the treatment of patients up to 25 years of age with B-cell precursor ALL that is refractory or in second or later relapse.

Expected to treat a few hundred children per year

**Yescarta™**

A CD19-directed genetically modified autologous T cell immunotherapy indicated for the treatment of adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy

**Luxturna™**

AAV gene therapy to treat biallelic RPE65 mutation-associated retinal dystrophy that leads to vision loss and may cause complete blindness in certain patients.
ATMP manufacturing and supply challenge

**Cells taken from patient**
- Challenges
  - Approved facility
  - Trained staff
  - Tracking

**Manufacture**
- Challenges
  - Cost of goods
  - Analytics
  - Product release
  - Scale

**Supply chain**
- Challenges
  - Temperature
  - Time restrictions
  - Patient specific

**Arrival at hospital**
- Challenges
  - Thawing
  - Registry

**Delivery to patient**
- Challenges
  - Pharmacy
  - Tracking
  - Training

**Payment**
• **Accelerate** the commercialisation of innovations from research
• **Complement** industry and academia with **unique technical facilities and expertise**
• **Innovate** in collaboration with academic and industry network
• **Facilitate** operating in UK as a global centre; working with Government, the NHS and international regulators

### Development laboratories
- 1200m² purpose built centre
- Analytical characterisation
- Process development
- Viral vector

### GMP manufacturing development centre
- 7200m² manufacturing centre designed specifically for cell and gene therapies
- 12 segregated large modules
- Secure supported collaboration model
- Centre of a CGT industry cluster

### Cell and gene therapy specialists (>170)

#### Industrialisation
- Process development
- Analytical development
- Manufacturing systems
- Supply chain

#### Regulatory and clinical development
- Regulatory
- Non clinical safety
- Clinical programmes
- Programme management

#### Engagement
- Collaboration formation
- Intellectual property and patent
- Health economics
- Reimbursement
What is CGT doing?

- **2012-2017**: Expertise, Facilities, Capabilities, Technologies
  - Commercialisation of research
  - Next generation gene delivery
  - Gene delivery technologies
  - Intelligent manufacture and productivity
  - Supply chain and manufacturing
  - Proof of adoption and reimbursement
  - Regulatory advantage
  - Research, Industry and Policy Engagement

- **2018**:
  - World leading research and translation ecosystem
  - Globally attractive research, development and manufacturing industry
  - World leading NHS clinical and reimbursement practice
  - UK Exports

- **2023**:
  - Global Industry
    - $16bn
    - $80bn
  - UK
    - 4000 jobs
    - £2bn industry
  - Productivity:
    - Average GVA £104,000 per employee

- **2025**
  - UK
    - 18,000 jobs
    - £10bn industry

- **2035**
  - UK Exports

**UK Exports**
- Jobs: 4000
- Industry: £2bn
- Jobs: 18,000
- Industry: £10bn

**Global Industry**
- 2018:
  - $16bn
  - $80bn

**UK Exports**
- Average GVA £104,000 per employee
ISCF funded Advanced Therapy Treatment Centres

- Northern Alliance Advanced Therapies Treatment Centre
- iMATCH - Manchester Advanced Therapy Centre Hub
- MW-ATTC - Midlands & Wales Advanced Therapy Treatment Centre
- CGT Manufacturing centre