Cell and Gene Therapy Supply Chain Challenge or Opportunity?

December 2016
Agenda

• Introduction to the Cell and Gene Therapy Catapult
• What are cell and gene therapies?
  • Clinical impact
  • Supply chain terminology
    • Auto, allo, vector
  • Industry growth/potential
• Challenges - current supply chain
• Opportunities – future supply chain
Why cell and gene therapy

01
Identified significant and growing unmet healthcare needs that cell and gene therapy could address

02
The UK is at the leading-edge of the cell and gene therapy industry.

03
An opportunity to build a large-scale industry delivering health and wealth to the UK.
Introduction to the Cell and Gene Therapy Catapult
• Part of a world-leading network of technology and innovation centres

• Bridge the gap between businesses, academia, research and government

• Access technical facilities and expertise to help adopt, develop and exploit innovations

• Established by Innovate UK

Growing the UK cell and gene therapy industry, delivering health and wealth.
Everything you need under one roof

Our capabilities complement each other across the cell and gene therapy lifecycle

**Safe and effective**

- Non-clinical safety
- Clinical operations
- Regulatory expertise
- Industrialisation

**Scalable**

- Investment in infrastructure - GMP facility and state-of-the-art laboratories
- Regulatory expertise
- Industrialisation

**Affordable**

- Health economics and market access
- Industrialisation
UK industry growth 2012 to 2015

£400m+

Investment 2015
Investment attracted by UK companies in 2015 vs. £35m in 2012¹

42
ATMP therapy developers
50% are rapidly growing

+1,000
Jobs created
are up from 540 in 2012 (expected to exceed 2,000 in 5yrs)

90%
Growth in the number of ATMP therapy companies since 2012

+50%
Growth in UK clinical trials since 2013

+50%
GMP footprint
22 facilities/11,800m². A 50% increase vs. 2013

¹Excludes Smith & Nephew acquisition of Healthpoint for $782M in 2012
Cell and gene therapies
Potential of cell therapies

Potential cell sources include:

- Pluripotent stem cells
- Adult stem cells e.g. MSCs
- Hematopoietic stem cells
- Immune cells

Stroke
Traumatic brain injury
Alzheimer’s disease
Parkinson’s disease
Missing teeth

Baldness
Lou Gehrig’s disease
Blindness
Deafness

Wound healing
Myocardial infarction

Bone marrow transplantation
(currently established)
Spinal cord injury
Osteoarthritis
Rheumatoid arthritis
Multiple sites: cancers

Muscular dystrophy
Diabetes
Crohn’s disease

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Diagram of the human body showing potential sites for cell therapy treatments.
Major milestones and key data events

Examples of major milestones and key data events: Q3 2016

- Fate Therapeutics receives FDA Orphan Drug Designation for ProTmune in allogeneic hematopoietic cell transplantation — September 26, 2016
- Kite Pharma announces positive topline KTE-C19 data from ZUMA-1 pivotal trial in patients with aggressive non-Hodgkin lymphoma — September 26, 2016
- Cellular Dynamics International, a FUJIFILM company, announces launch of iCell Hepatoblasts to enable research into therapies that stimulate liver regeneration — September 22, 2016
- bluebird bio’s LentiGlobin investigational gene therapy for transfusion-dependent beta-thalassemia is accepted into European Medicines Agency’s PRIME Program — September 21, 2016
- Alliqua BioMedical announces commercial introduction of Interfyl Connective Tissue Matrix — September 19, 2016
- Asterias Biotherapeutics announces positive efficacy data in patients with complete cervical spinal cord injuries treated with AST-OPC1 — September 14, 2016
- Sangamo BioSciences receives Orphan Drug Designation from U.S. FDA for SB-FIX, first application of therapeutic in vivo genome editing — September 6, 2016
- Spark Therapeutics announces new positive data from continuation of Phase 3 trial of voretigene neparvovec, its most advanced product candidate, for treatment of inherited retinal disease — August 10, 2016
- Mesoblast Phase 2 trial results of MPC-300-IV show dose-related improvements in biologic refractory rheumatoid arthritis — August 9, 2016
Example – T cell therapy

Collect patient’s white blood cells

Isolate and activate T cells

Engineer T cells with CAR or TCR gene

Grow and expand number of T cells

Infuse patient with engineered T cells

Modified from Kite Pharma
Terminology and logistics challenge

Allogeneic

Autologous

Courtesy of Lonza
Challenges in current supply chain
**Low volume - orphan indication (20 patients/yr)**

### Bone marrow donation

<p>| | |</p>
<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Volume</td>
<td>20/yr</td>
</tr>
<tr>
<td>Temp</td>
<td>Controlled ambient</td>
</tr>
<tr>
<td>Container</td>
<td>Blood bag</td>
</tr>
<tr>
<td>Shelf Life</td>
<td>&lt;24hrs</td>
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### Viral vector

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<tbody>
<tr>
<td>Volume</td>
<td>“Large” single shipment</td>
</tr>
<tr>
<td>Temp</td>
<td>-80°C</td>
</tr>
<tr>
<td>Container</td>
<td>Vials</td>
</tr>
<tr>
<td>Shelf Life</td>
<td>Months</td>
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### Final product

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<tbody>
<tr>
<td>Volume</td>
<td>20/yr</td>
</tr>
<tr>
<td>Temp</td>
<td>2-4°C</td>
</tr>
<tr>
<td>Container</td>
<td>50-80ml in 120ml syringe</td>
</tr>
<tr>
<td></td>
<td>Shipped in metal box</td>
</tr>
<tr>
<td>Shelf Life</td>
<td>&lt; 24 hrs</td>
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**NB**

- One EU manufacturing site supplying EU, one US site supplying North America.
- Contingency planning is vital.
- No consolidation with other shipments possible.
- Maximum visibility at all points during shipping.
High volume allo therapy (100,000 patients/yr (globally))

**Initial Donation**
- This will only required once as will form “bank” for later therapies

**Manufacture**
- Large central manufacturing
- Deliveries will be restocking as opposed to patient specific
- Consolidation of final product is essential
- Different product formulations and final packaging may decrease number of doses per shipper significantly.
- Significant space required for dry shippers, insulated boxes, dry ice and LN2 storage

**Final Product**
- **Volume**: 100s / hospital
- **Temp**: -180°C
- **Container**:
  - Dry shipper (13l LN²=27kg)
  - 500 vials/shipper
- **Shelf Life**: 10 dys

**Satellite**

**Patient**

**NB**

- Large central manufacturing
- Deliveries will be restocking as opposed to patient specific
- Consolidation of final product is essential
- Different product formulations and final packaging may decrease number of doses per shipper significantly.
- Significant space required for dry shippers, insulated boxes, dry ice and LN2 storage
Growth = challenge

**More** cell and gene therapy trials are now being sponsored by *commercial organisations*.

<table>
<thead>
<tr>
<th>Year</th>
<th>Research Institution Sponsor</th>
<th>Commercial Sponsor</th>
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<tbody>
<tr>
<td>2013</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2014</td>
<td></td>
<td></td>
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<tr>
<td>2015</td>
<td></td>
<td></td>
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<tr>
<td>2016</td>
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**Oncology** remains the dominant therapeutic area in clinical trials.

There is **continuous progression** of the cell therapy clinical trial portfolio.

<table>
<thead>
<tr>
<th>Year</th>
<th>On-going</th>
<th>Total</th>
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<tbody>
<tr>
<td>2015</td>
<td>34</td>
<td>51</td>
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<tr>
<td>2016</td>
<td>41</td>
<td>51</td>
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CATAPULT
Cell and Gene Therapy
Hidden challenges

Cell is the product

Complicated systems

Manual supply chain

Variable supply chain

Duration

European centre
Benchmarking

- Limited number of specialist providers
- White glove service
- “No” shipment integration
- Data from clinical trial is critical
- Cost “irrelevant”
- Limited development of shipping technologies
Opportunities in future supply chain
Updating the supply chain

- Digital real time tracking
- Distribution hub
- Improved container
- Thaw in clinic
This is not a new challenge

High volume, high value shipping

1.85m cell therapies per year

Validated, track and trace

Cold Supply Chain for “cells”
Opportunities – working together to…..

...meet patient/clinician needs.

...create a viable, supply chain.

...repurpose existing technology.

...enable a global industry.
Introduction