CELL THERAPY TRANSLATION

Translational Challenges

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Summary

- Complex regulatory pathway
- Human Starting Materials
- Preclinical
- Clinical
- Licensing
- Supply
Cell and Gene Therapy Catapult
The Catapults

The **Catapults** are a force for innovation & growth

- Part of a **world-leading network** of technology and innovation centres
- **Bridge the gap** between businesses, academia, research and government
- Long-term investment to **transform** the UK’s ability to create new products and services
- **Regenerative medicine** is one of the UK government’s eight great technologies that support UK science strengths and business capabilities
- Open up global opportunities for the UK and **generate sustained economic growth** for the future
- Established by **Innovate UK** (formerly the Technology Strategy Board)
Why Cell Therapy?

- Identified significant and growing **unmet healthcare needs** that cell therapy could address.

- The UK is at the leading-edge of the cell therapy industry, with a disproportionate share of **world-leading scientists** and new developments in the field, creating an advantage upon which the country can capitalise.

- An opportunity to build a **large-scale industry** delivering health and wealth to the UK.
Strategic goals

Goal
- Build a £10bn industry

Pipeline
- Increased cell therapies in UK clinical trial and clinical use

Value
- Investible propositions created leading to cell therapy companies that succeed and stay in the UK

Attractiveness
- Demonstrating that the UK is the place to do this work, with increased inward investment
Catapults

Helping business to identify, adopt and develop innovative technologies

**Core Projects**
- Key challenges and barriers
- A unique technical capability
- Industry & research advisory groups
- Demonstration projects
- Disseminate to industry

**Industry R&D**
- Access to unique facilities & expertise
- Develop & demonstrate at scale
- Reduce risk of implementation
- Direct contracts for projects
- Easy access for SMEs

**CR&D**
- Innovation in collaborations
- Bring together customers, SME's & blue-chip companies
- Technical & management resource
- Partners in Projects (IUK & EU)
- Expertise at unlocking funding
## Assets

### facilities and teams

<table>
<thead>
<tr>
<th>Facilities</th>
<th>Teams</th>
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<tr>
<td><strong>£70m development laboratories</strong></td>
<td><strong>Business</strong></td>
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<tr>
<td>• London clinical research cluster</td>
<td>• Business development</td>
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<tr>
<td>• 1,200m² on 12th floor Guy’s Tower</td>
<td>• Business models</td>
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<tr>
<td>• 110 people</td>
<td>• Health economics</td>
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<td><strong>£55m large-scale advanced therapies manufacturing centre</strong></td>
<td><strong>Manufacturing and supply</strong></td>
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<tr>
<td>• Stevenage Biocatalyst</td>
<td>• Process development</td>
</tr>
<tr>
<td>• Opening 2017</td>
<td>• Analytical development</td>
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<tr>
<td>• 7,200m²</td>
<td>• GMP process proving</td>
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<tr>
<td>• 150 people</td>
<td>• Supply chain</td>
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<td>• Late clinical phase manufacturing</td>
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<td>• Initial in market supply</td>
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<td><strong>Clinical trial and regulatory</strong></td>
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<td>• Regulatory</td>
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<td>• Clinical trial sponsor</td>
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<td>• Clinical operations</td>
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<td>• Pre-clinical safety</td>
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Complex regulatory pathway
EU Tissues and Cells Directive or Blood Directive
30 years traceability requirement

STARTING MATERIAL Human Blood, Tissues or Cells

Substantial manipulation and/or non homologous use

Yes
ATMP

No
Transplants or Transfusions

Pre Clinical
Clinical Trials
Licensed Product
Post Marketing
30 Years Traceability Efficacy PhV follow-up

Clinical Trial Authorisation National (MHRA)
Marketing Authorisation European centralised licence (MAA) (CAT) EMA

Manufacturing Authorisation (MIA)

GMP Requirement (Eudralex Vol 4)

GLP

Manufacturing Authorisation Investigational Medicinal Products (MIA(IMP))

ATMP regulation EC 1394/2007
Guidance used for CT & G development

GUIDELINE ON VIRUS SAFETY EVALUATION OF BIOTECHNOLOGICAL INVESTIGATIONAL MEDICINAL PRODUCTS

NOTE FOR GUIDANCE ON QUALITY OF BIOTECHNOLOGICAL PRODUCTS: DERIVATION AND CHARACTERISATION OF CELL SUBSTRATES USED FOR PRODUCTION OF BIOTECHNOLOGICAL/BIOLOGICAL PRODUCTS (CPMP/ICH/294/95)

GUIDELINE ON HUMAN CELL-BASED MEDICINAL PRODUCTS

NOTE FOR GUIDANCE ON VIRUS VALIDATION

NOTE FOR GUIDANCE ON QUALITY OF BIOTECHNOLOGICAL PRODUCTS: STABILITY TESTING OF BIOTECHNOLOGICAL/BIOLOGICAL PRODUCTS (CPMP/ICH/968/96)

NOTE FOR GUIDANCE ON THE USE OF BOVINE SERUM IN THE MANUFACTURE OF MEDICINAL PRODUCTS

NOTE FOR GUIDANCE ON IMPURITIES TESTING: IMPURITIES IN NEW DRUG SUBSTANCES

VOLUME 2A
Procedures for marketing authorisation
CHAPTER 1
MARKETING AUTHORISATION

November 2005

Excipients in the label and package leaflet of medicinal products for human use

NOTE FOR GUIDANCE ON MINIMISING THE RISK OF LONGFORM ENCEPHALOPLASTY IN VETERINARY MEDICINAL PRODUCTS

GUIDELINE ON THE ENVIRONMENTAL RISK ASSESSMENT OF MEDICINAL PRODUCTS FOR HUMAN USE

European Medicines Agency pre-authorisation procedural advice for users of the centralised procedure
Human starting material
Translation challenges – Starting material

- Sourcing human derived starting material
  - Ethical
  - Consent
  - Regulatory
  - Donor to donor variability
Preclinical
Translation challenges - Preclinical

- Preclinical testing
  - Suitability of animal models
  - Impact of immunosuppression
  - GLP or not
Clinical
The challenges to translation - CT

- Licensing of procurement sites
- Logistics
- Clinical Trial design aspects – limited comparative data produced through non-standard pathways:
  - Small or extremely small number of patients
  - Most don’t follow the classical randomised, controlled PhI, PhII, PhIII, PhIV pathway
  - ‘Surrogate’ endpoints
  - May be administered to end-of life patients
  - Usually administer cautiously to patients in first instance (not healthy volunteers)
  - Sometimes already have some non-trial patient experience (eg specials route)
- Risk:benefit assessment for patient groups; informed consent
Licensing
Translation challenges - Licensing

• Europe wide licensing for ATMP
• Orphan or ultra-orphan products
• More likely to follow non-conventional licensing routes:
  • Conditional, Exceptional Use, Accelerated ie approved with small numbers of patients and with post approval commitments. Licence can be revoked if commitments not met
• Long-term supply of unlicensed products - Specials or Hospital exemption schemes
• Patient registries
Supply issues
Translation challenges - Supply

- Many autologous therapies
- Europe wide supply for ATMP
- High Cost of Goods
- Logistical supply significantly more challenging, with associated costs
- Post-marketing commitments
- More use of clinical champions
- Patients may travel within and between countries to receive treatment at centres of excellence
- Short-time frame for patients to receive treatment
- Uncommon for these products will be delivered on an ongoing basis
- Reimbursement