WP 3 Objectives

- Business Models
- Value Chains
- Innovation Ecosystems
- 10 Case studies in the UK
  - Private Firms (7)
  - Public Organisations (1)
  - University Spin Offs (1)
  - Research and Development Consortia (1)
- Case studies at various development and commercialisation stages
- None have marketing authorisation
- 1 used specials/unlicensed medicines during clinical trials for reimbursement
<table>
<thead>
<tr>
<th>Type of Organisation and Therapy Area</th>
<th>Funding Sources</th>
<th>Therapy Stage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Firm A</strong>: autologous - Immunotherapy</td>
<td>Grants + PE &gt; £70m</td>
<td>Clinical Trials</td>
</tr>
<tr>
<td><strong>Firm B</strong>: autologous - Immunotherapy</td>
<td>Public + PE + Financial Institutions ~ &gt;£5m</td>
<td>Clinical Trials</td>
</tr>
<tr>
<td><strong>Firm C</strong>: autologous - Cell therapy + Surgery</td>
<td>Grants and PE</td>
<td>Clinical Trials?</td>
</tr>
<tr>
<td><strong>Firm D</strong>: autologous – Tissue engineering + Surgery</td>
<td>Grants and PE &gt; £8m anticipating Euro 7m</td>
<td>Clinical Trials/Compassionate Use</td>
</tr>
<tr>
<td><strong>University Spinoff</strong> - Cell therapy</td>
<td>Grants</td>
<td>Animal Studies</td>
</tr>
<tr>
<td><strong>Firm E</strong>: drug discovery</td>
<td>Grant + Others</td>
<td>CMO</td>
</tr>
<tr>
<td><strong>Firm F</strong>: allogeneic - Cell therapy</td>
<td>PE + Grants &gt;£40 m</td>
<td>Clinical Trials</td>
</tr>
<tr>
<td><strong>Public Organisation</strong>: allogeneic – Cell and organs</td>
<td>Public</td>
<td>CMO</td>
</tr>
<tr>
<td><strong>Firm G</strong>: allogeneic - Cell therapy</td>
<td>PE + Public funds (£52 m). Burn rate £1 m p.m.</td>
<td>Clinical Trials – Specials / Unlicensed</td>
</tr>
<tr>
<td><strong>Research Consortium</strong>: allogeneic - Cell therapy</td>
<td>Grants: ~ £15m over 8 yrs</td>
<td>Pre-Clinical</td>
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</tbody>
</table>
Therapies and products covered in the case studies

- Ophthalmology
- iPSC (induced Pluripotent Stem Cells)
- Chimeric Antigen Receptor Technology
- Autologous Immunotherapies
- Solid Tumours
- Blood Cancer (myeloma)
- Epidermolysis Bullosa
- Meniscal tear repair
- Beta Thalassemia
- Osteoarthritis
- Parkinson’s and brain treatment
- Stem cells for drug discovery
- Organ generation
- Severe Influenza and Ebola
- HIV
- Pancreatic islets transplant
- Alzheimer’s
Innovation Pathway - Immunotherapy

Early Exit: Phase I/II business model
Translational Services business model
Material and service provision business model
Manufacturing and scale up business model

Program T Cells
Translation
Clinical Operations and Project Planning
Cancer Research UK Clinical Trial
CROs

Single Dose Therapy Development
Manufacturing and Process Development
Leukapheresis
Single Dose Therapy
Hospital Setting

Modify T Cell (CAR T cell)
Leukapheresis
Scheduling, Logistics etc
Machine designers and fabricators

Cancer Research UK Clinical Trial
Scheduling, Logistics etc
Machine designers and fabricators

CROs
Scheduling, Logistics etc
Machine designers and fabricators

Stevenage Plant: CGTC
CROs
Innovation Pathway - Tissue Regeneration

Early Exit: Phase I/II Business Model

Translational services Business Model

Material and service providers Business Model

Manufacturing and scale up Business Model

Donated Human Trachea
NHS BT (Speke)

Porcine Small Bowel

Porcine Liver

Contract Manufacture and Processing: UCL, Royal Free, CGTC, NHS BT (Liverpool)

Cell Manufacture

Off-shelf product
Proprietary technology

4-6 weeks

Cell Harvesting

Surgical Procedure

Seed vascularised organ

6 weeks later

Transplant Organ

Hospital Setting

Biological Scaffold Cell Seeding

Clinical Trials / Regulatory approval

Out-license technology or partner?
Why the Virtual Business Model?

- **Survival Strategy**
- **Keep cash burn rate low**

You need small amounts of money coming in regularly

<table>
<thead>
<tr>
<th>What burns cash?</th>
<th>Actors Supporting the Virtual Business Model</th>
</tr>
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<tbody>
<tr>
<td>Process Development</td>
<td>CMOs and Universities</td>
</tr>
<tr>
<td>Clinical Trial Design and Management</td>
<td>CROs</td>
</tr>
<tr>
<td>Clinical Trial Data Management</td>
<td></td>
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<tr>
<td>Regulatory Advice</td>
<td>Translational Services Providers</td>
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<tr>
<td>Manufacturing for Phases 1 &amp; 2</td>
<td>Academic CMOs</td>
</tr>
<tr>
<td>Manufacturing for Phase 3</td>
<td>CGTC Stevenage Plant</td>
</tr>
</tbody>
</table>
National Innovation System Support

It [CGTC] really is a perfect model because ... it de-risks the manufacturing for us. We don’t have to invest in building our own building, so we don’t have that cost. ...it also means we don’t have to give away, or trust someone else to do it [manufacturing] for us. We own the manufacturing and control it and also learn it, ...when the time is right and we've proven that the medicine works and it looks like we’re ready to commercialise it then we build our own facility... So you push the risk, the point at which you have to invest your own money in a building, further down the development pathway.

• The catapult was good for UK Plc [innovation infrastructure] as it was created to be internationally competitive and attract companies to the UK
• The NHS [clinical] and NHS Blood Transfusion has provided infrastructure for innovation
• Universities featured prominently in all 10 case studies and critical for training and retaining skills in niche areas
National Innovation System Support

- NHS
- Funders:
  - Research Councils
  - Regional Regeneration Funds
  - Charity Organisations and others*
- CGTC
  - Regulatory and translational service advice
  - CMO – Stevenage Plant
- Muscling out of the smaller service for a fee SMEs
- What happens when the state withdraws its support later on?
- How fast can SMEs step in to fill the innovation infrastructure/support system gap?

I think we were going to ... make more money selling shovels [instead of prospecting for gold]. And it was working... it was beginning to work. We were already cash neutral and we were beginning to work on interesting products. ... And then the Cell Therapy Catapult came along... So it pulled the rug completely from underneath us... they put 100 million in to it... We couldn’t compete with that...
Quick Takeaways

- Small indications attractive to small firms but not attractive to big pharma (not block-buster) especially for early exit [unmet need]
- Small indications come with clinical trial recruitment challenges
- Materials and service provision; CMOs and Translational Service: Only players with cash inflows from business activities
- Players in development activities are all in “cash-burn” activities
- University based players prefer the virtual business model to limit cash burn rate
Conclusion

- Field dominated by Small to Medium Enterprises (SMEs)
- Only 2 business models generating revenues
  - Material and service provision
  - Manufacturing and scale up
- CGTC – key innovation infrastructure supporting resource limited firms
- NHS - clinical and transfusion services key innovation infrastructure
- Skills development and retention critical for the sector
- There is a mix of Grant, Private Equity funding: ranging from £5 million to £70 million - most funding is for development work and clinical trials
- At some point re-imbursement needs to be addressed to act as an innovation puller [Innovative Procurement]
REGenableMed Project