CELL THERAPY TRANSLATION

Translational Challenges

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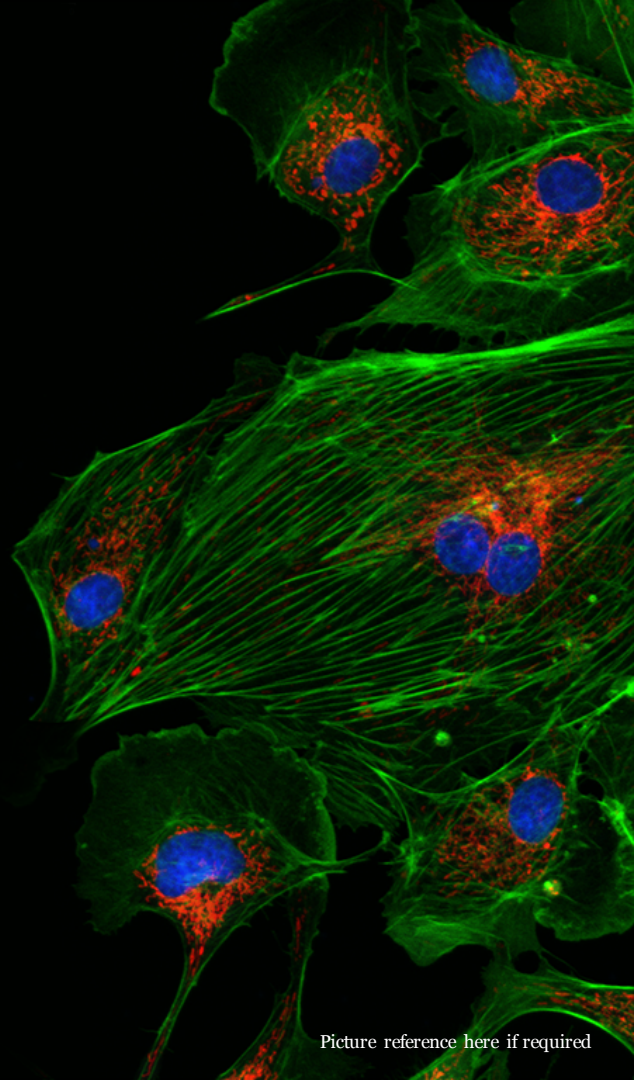

Picture reference here if required

Summary

- Complex regulatory pathway
- Human Starting Materials
- Preclinical
- Clinical
- Licensing
- Supply

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Cell and Gene Therapy Catapult

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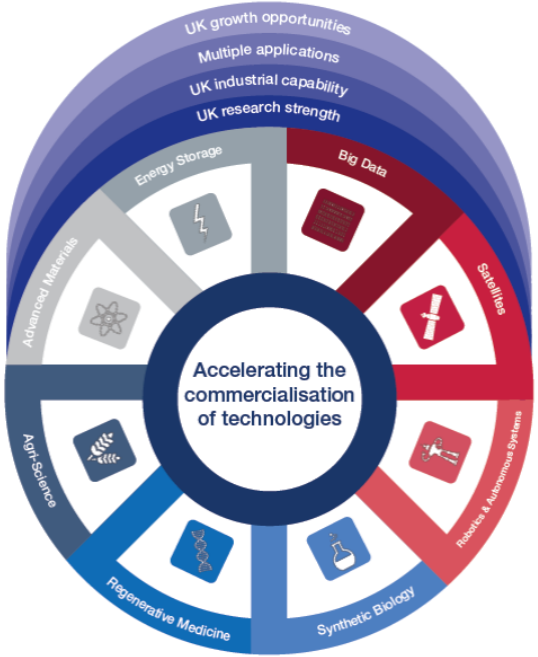
The Catapults

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)



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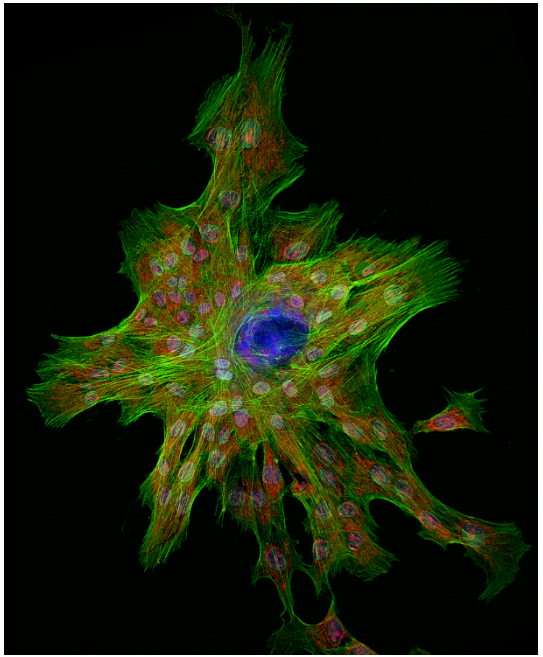
Why Cell Therapy?

- 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



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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

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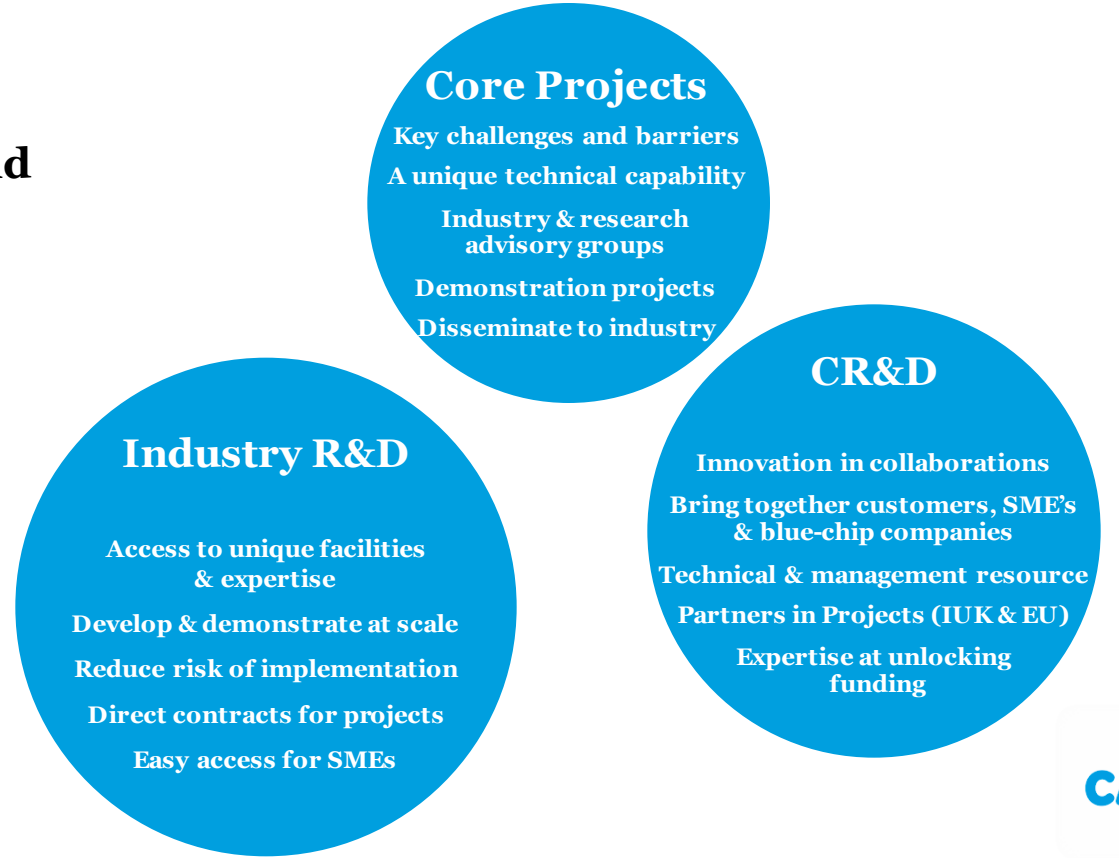
Catapults

Helping business to **identify, adopt and develop** innovative technologies



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Assets
- facilities and teams

Facilities

£70m development laboratories

- London clinical research cluster
- 1,200m² on 12th floor Guy's Tower
- 110 people

£55m large-scale advanced therapies manufacturing centre

- Stevenage Biocatalyst
- Opening 2017
- 7,200m²
- 150 people

Teams

Business

- Business development
- Business models
- Health economics

Manufacturing and supply

- Process development
- Analytical development
- GMP process proving
- Supply chain
- Late clinical phase manufacturing
- Initial in market supply

Clinical trial and regulatory

- Regulatory
- Clinical trial sponsor
- Clinical operations
- Pre-clinical safety

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Complex regulatory pathway

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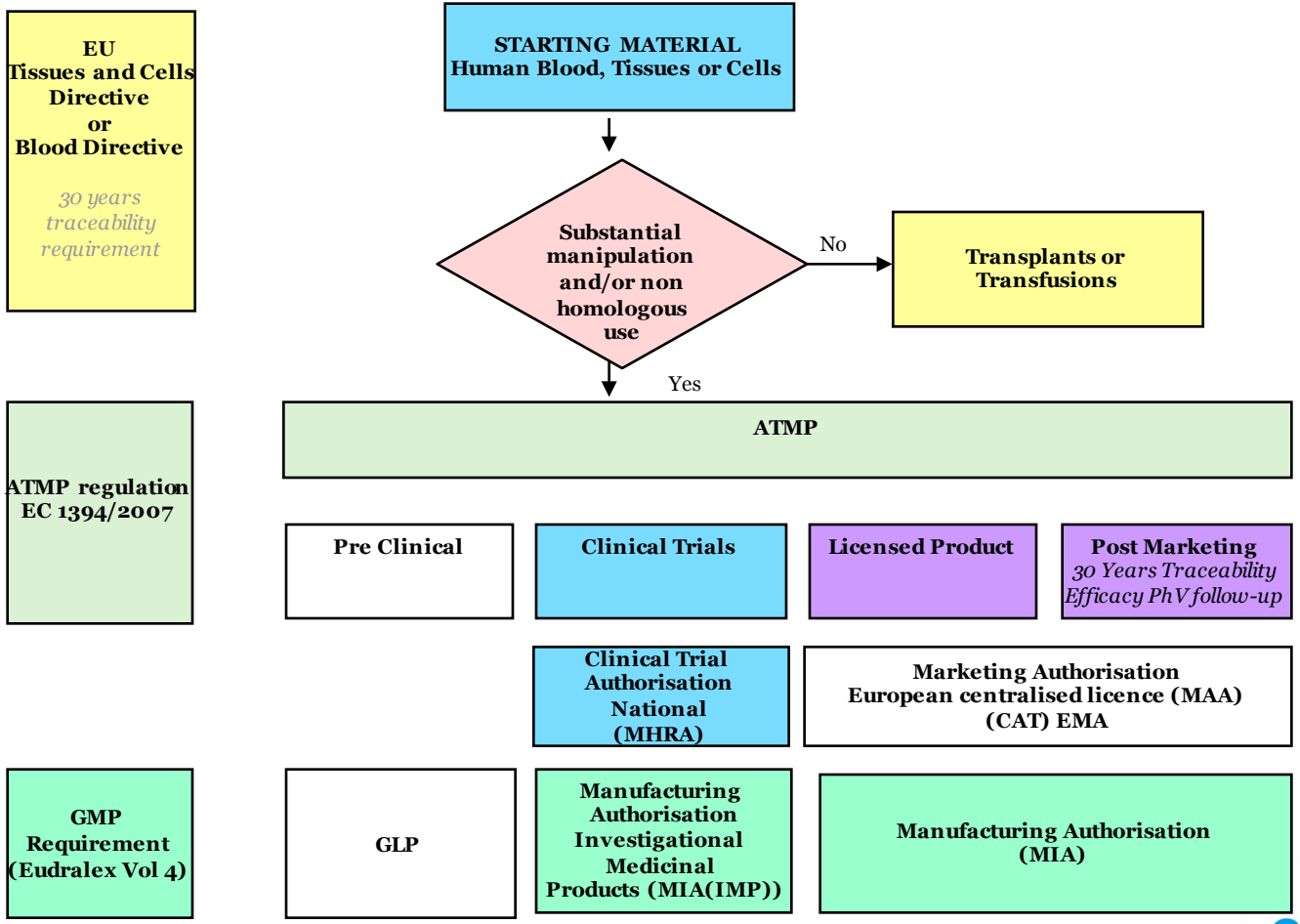

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Guidance used for CT & G development

GUIDELINE ON VIRUS SAFETY EVALUATION OF BIOTECHNOLOGICAL INVESTIGATIONAL MEDICINAL PRODUCTS

European Medicines Agency pre-authorisation procedural advice for users of the centralised procedure

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)

NOTE FOR GUIDANCE ON QUALIT
STABILITY TESTING OF BIOTECI
(CPM

NOTE FOR GUIDANCE ON
SPECIFICATIONS: TEST PROCEDURES AND ACCEPTANCE CRITERIA FOR BIOTECHNOLOGICAL/BIOLOGICAL PRODUCTS
(CPMP/ICH/365/96)

NOTE FOR GUIDANCE ON VIRUS VALIDATIO

NOTE FOR GUIDANCE ON THE USE OF BOVINE SERUM IN THE
UCTS

GUIDELINE ON HUMAN CELL-BASED MEDICINAL PRODUCTS

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

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

NOTE FOR GUIDANCE ON GUIDANCE ON MINIMISING THE R
ONGIFORM ENCEPHALOPAT
RINARY MEDICINAL PRODU

ECTIONS 6.2 AND 6.3

VOLUME 2A
Procedures for marketing authorisation
CHAPTER 1
MARKETING AUTHORISATION

November 2005

NOTE FOR GUIDANCE ON
QUALITY OF BIOTECHNOLOGICAL PRODUCTS: VIRAL SAFETY EVALUATION OF BIOTECHNOLOGY PRODUCTS DERIVED FROM CELL LINES OF HUMAN OR ANIMAL ORIGIN
(CPMP/ICH/295/95)

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

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Human starting material

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Translation challenges – Starting material

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

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Preclinical

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Translation challenges - Preclinical

- Preclinical testing
  - Suitability of animal models
  - Impact of immunosuppression
  - GLP or not

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Clinical

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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

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Licensing

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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

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Supply issues

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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

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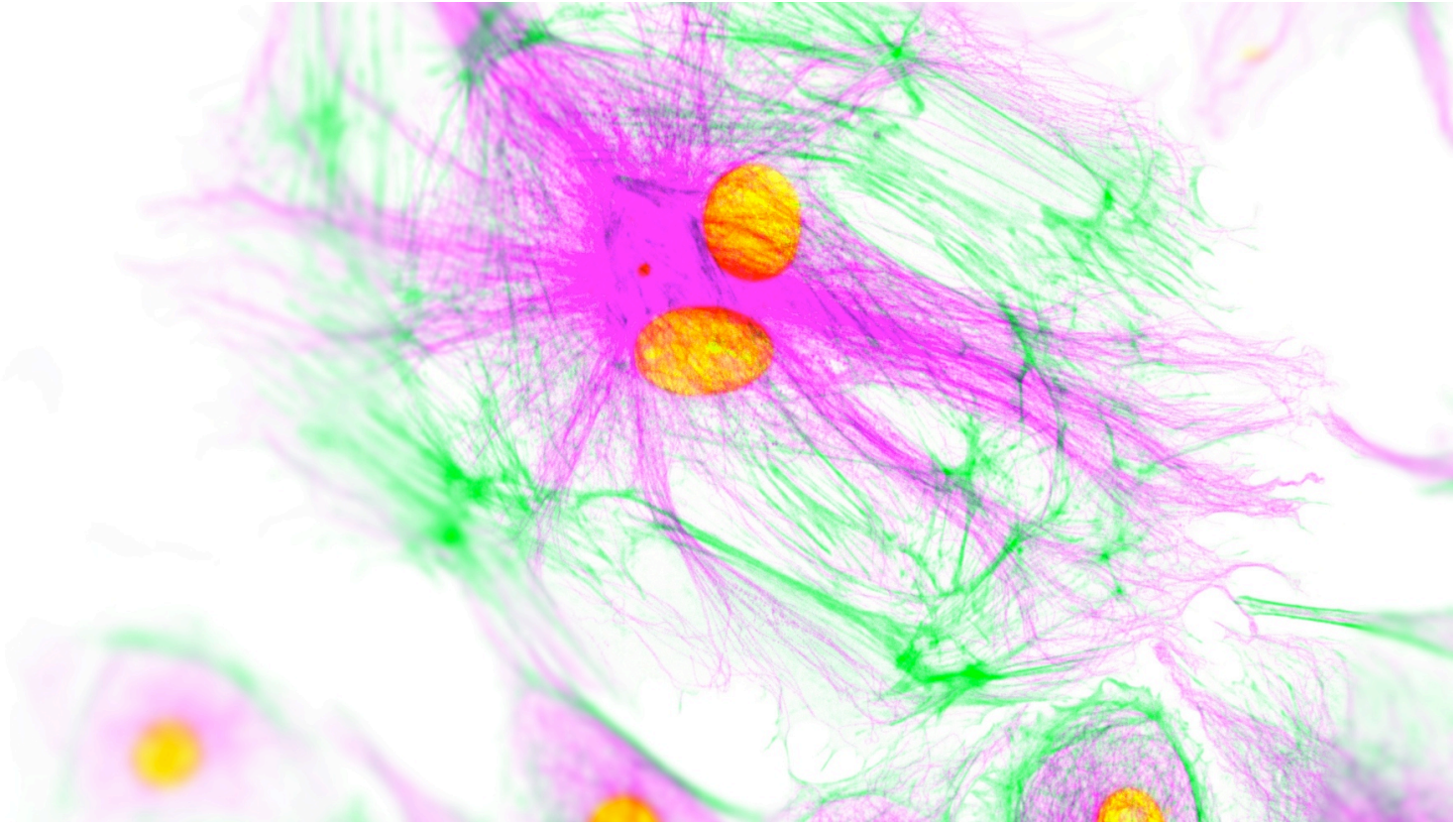

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