Scaling for ATMP commercialisation

Cell and Gene Therapy Catapult

Daria Marsh, Head of Bioprocessing

We are an independent innovation and technology organisation committed to the advancement of the cell and gene therapy industry

Our vision

A thriving industry delivering life-changing advanced therapies to the world.

Our role

Create powerful collaborations which overcome the challenges to the advancement of the ATMP sector.

How we work

We are a team of experts covering all aspects of advanced therapies.

Applying our own unique capabilities and assets, we collaborate with academia, industry and healthcare providers to develop new technology and innovation.

ATMP Demand and the Patient Access Challenge

- Patient demand for commercially approved ATMP products outweighs current supply
- CAR-T pricing >$180k; ~$1M with cost of administration. Drive to improve margins to ~80% by 2030.*[2]
- In the Allogeneic space at least 1,200 patients presenting with 34 different indications have been implanted with an accumulated dose of at least 190 billion hPSC derived cells + 200 billion platelets.*[4]

CAR-T Products

~10,000

CAR-T products manufactured/year[*1]

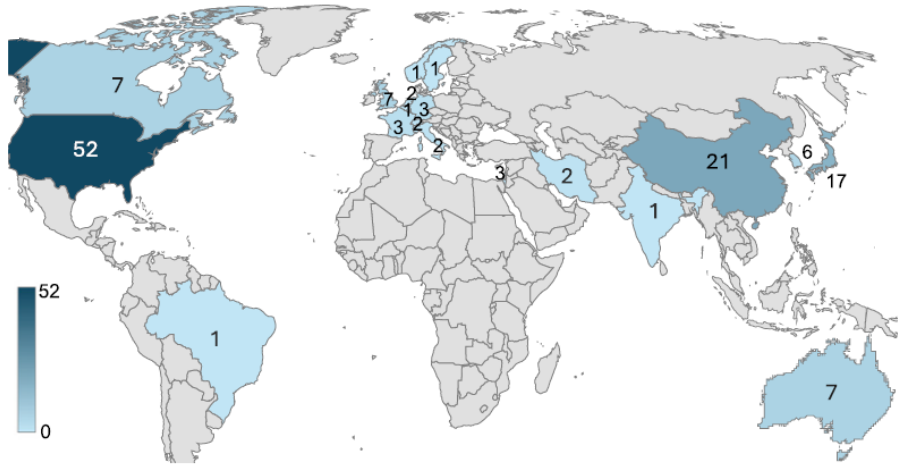
~1,894

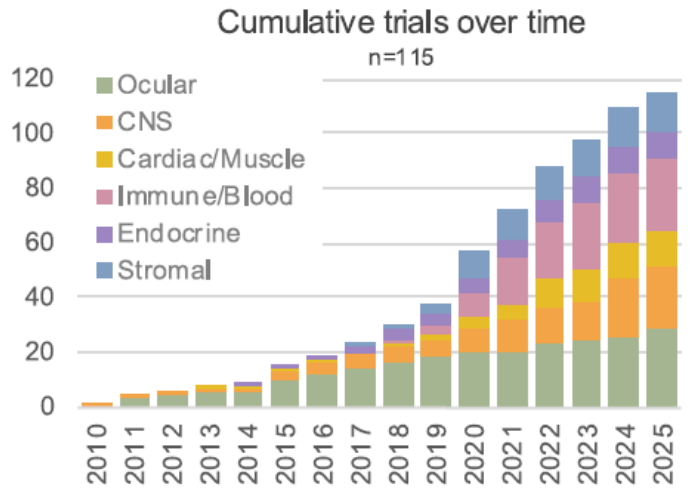
Clinical trials[*3] *underway*

2M

Hematological cancer patients eligible for CAR-T by 2029[*3]

hPSC Derived Products*[4]





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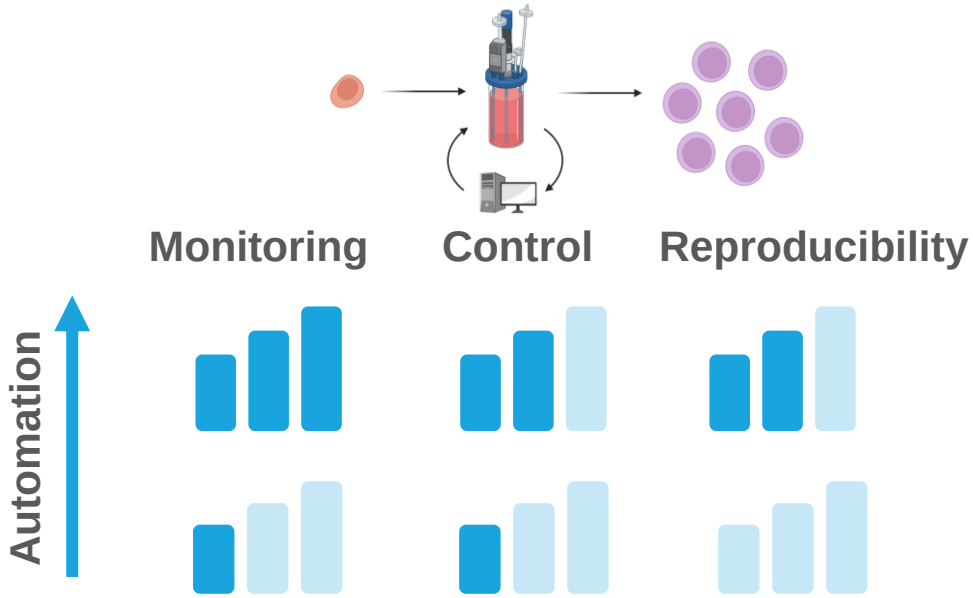
*[1] Patient Access Analytics | Ori Biotech, Oribiotech (2024)
*[2] *Alliance for Regenerative Medicine Meeting at the Med 2025*
*[3] *Driving the next wave of innovation in CAR-T cell therapies.* McKinsey (2019)
*[4] Kirkeby et al., 2025, Pluripotent stem-cell-derived therapies in clinical trial: A 2025 update, Cell Stem Cell 32, January 2
*[5] Adapted from ARM Cell & Gene State of the Industry Briefing, EvaluatePharma, Deliotte Analysis, Jan 2025

Challenges for Scaling

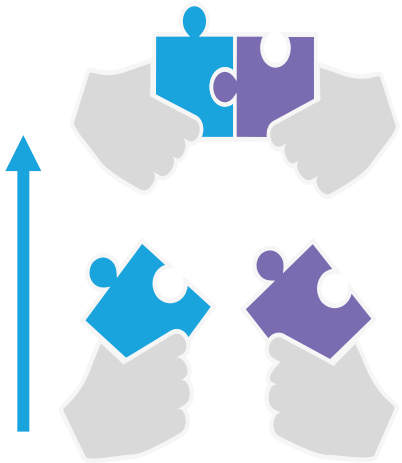
Scale up: iPSC derived case example

1. Close the process
2. Maximise yield and quality
3. Use PAT to automate control



Scale out approach

1. Min intervention, max reproducibility
2. Automate for controlled parallelization
3. QC Automation
4. Digital Integration & Advanced Control

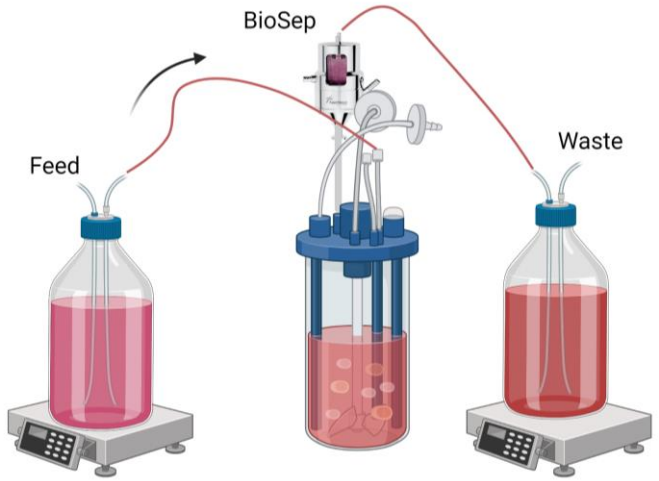


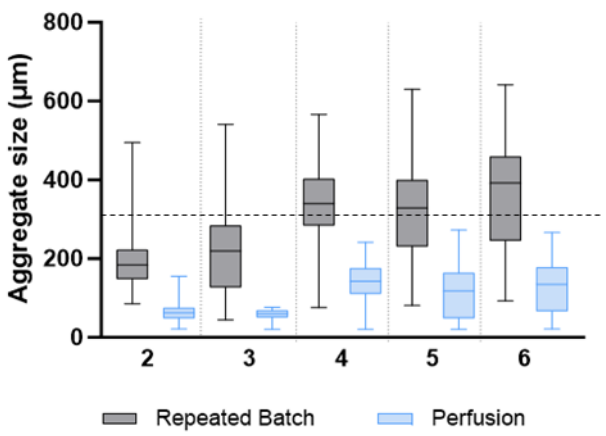
Deployment

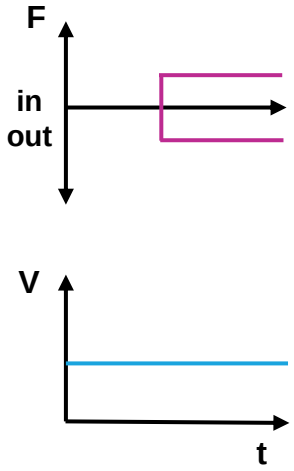
Innovation

Scale Up: iPSC Expansion

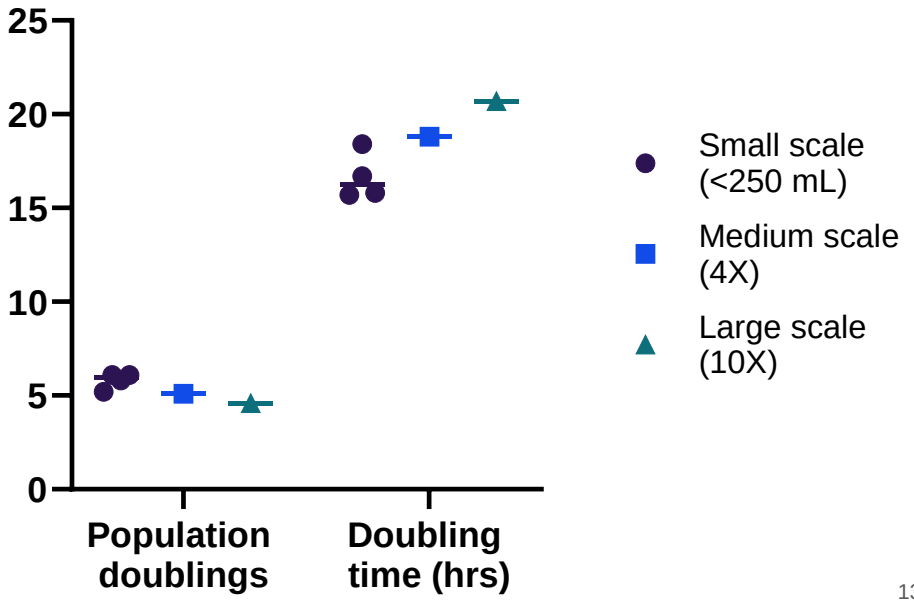
Close process, Maximise Yield and Quality





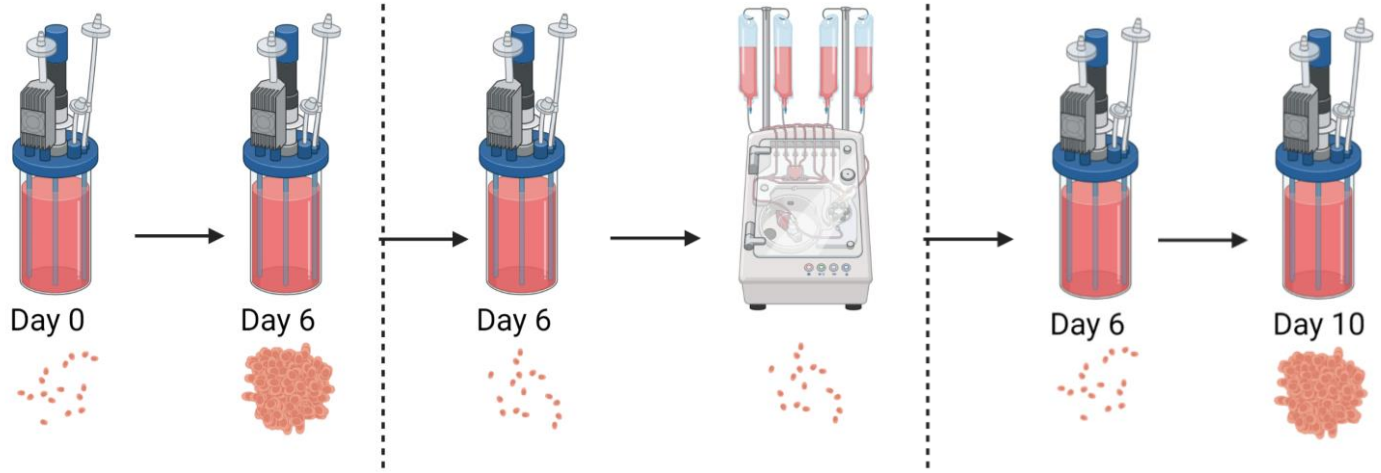


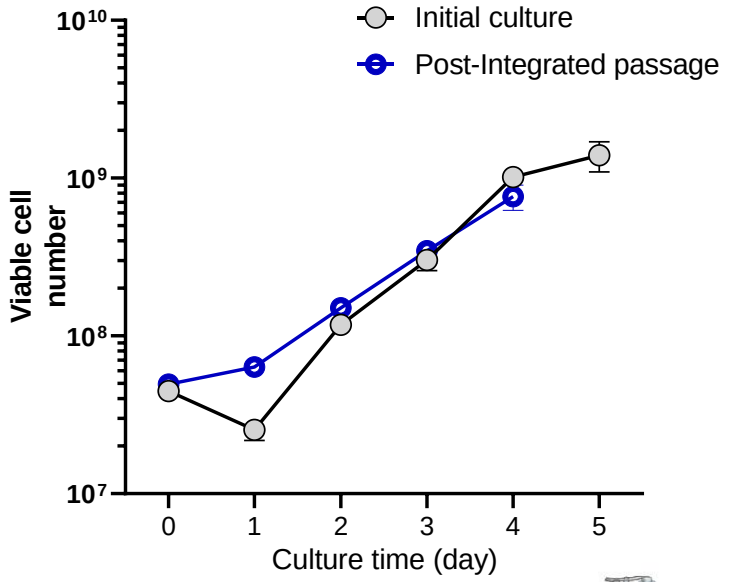
- Intensification: perfusion controlled cell expansion process in STR
- 30-fold expansion of iPSC in 5 days (**10^7 cells/mL**)
- More homogenous aggregate size
- Potential for further intensification and seamless downstream differentiation



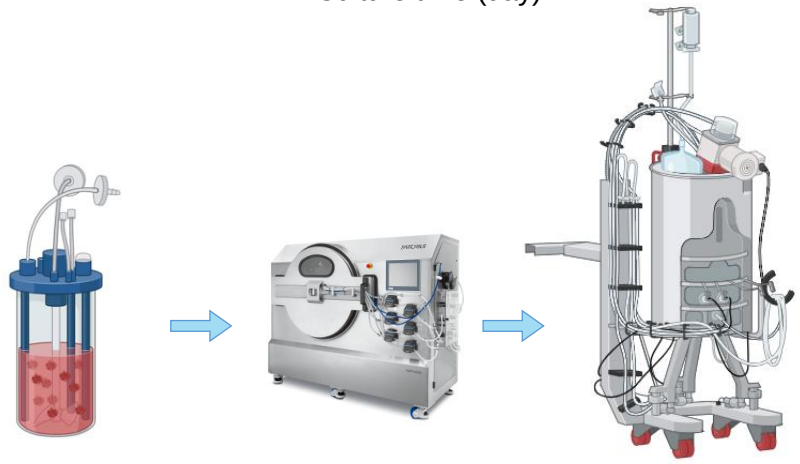
Scale Up: iPSC Integrated Passage

Close process, Maximise Yield and Quality





- **Semi-Automated** integrated passage to facilitate scale up
- Retains **closed processing** for all intermediate steps
- Proven at <250 mL scale
- **>80% cell recovery** achieved for in situ dissociation and inoculation into subsequent culture



PAT for Aggregate Size

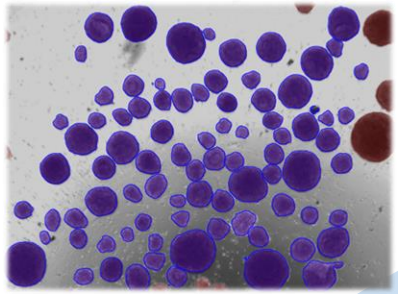
Aggregate size is a key in-process measurement

- Linked to PSC quality and differentiation efficiency

Existing manual workflows are inefficient with poor data integrity

- Manual
- Several points of manual data transfer and analysis
- Out-dated image analysis pipeline

Multi-day to 15 min workflow

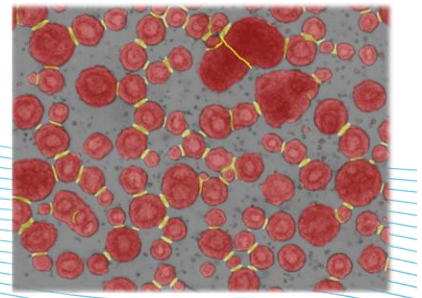


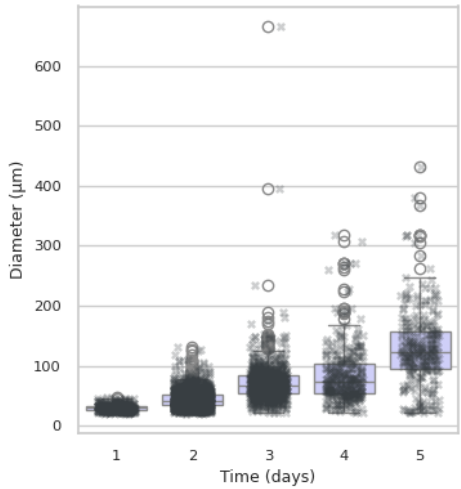
Train

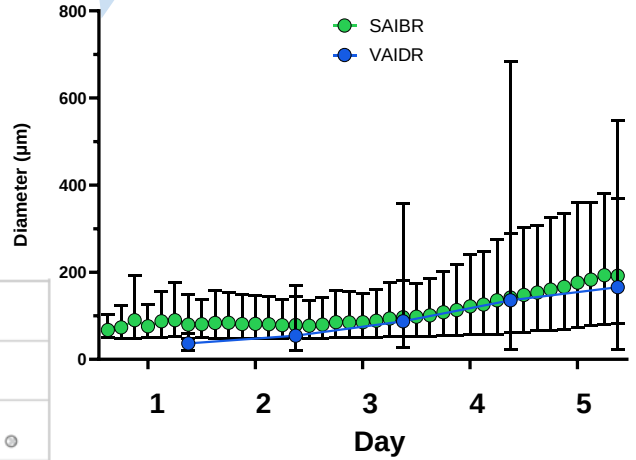
Analyse

Report

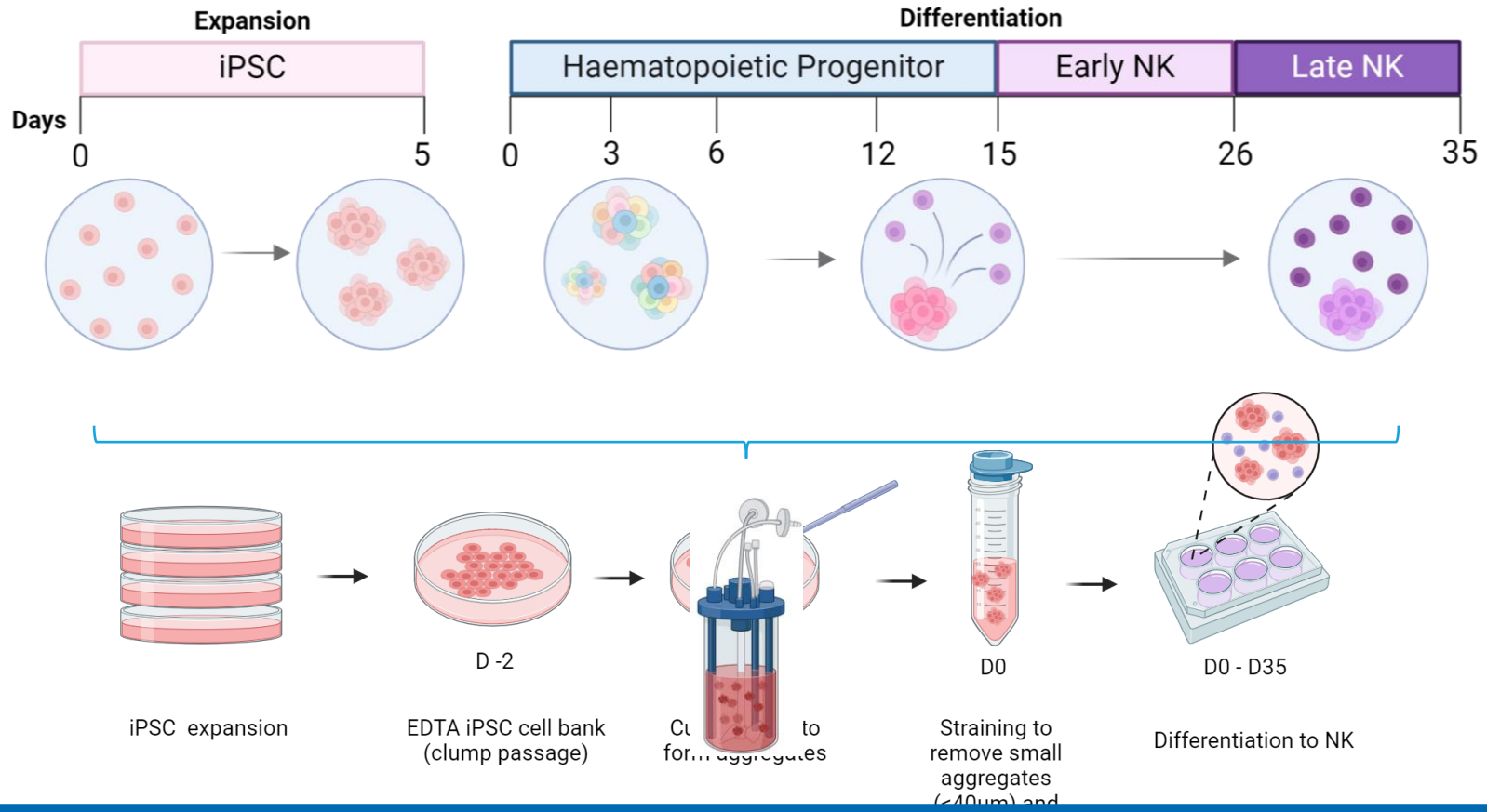
Integrate







Scale Up: NK Differentiation Case Study



Integrated iPSC expansion and NK differentiation in an STR system

Closed and Maximised Yield and Quality of iNK

YIELD

Integrated iPSC to NK differentiation in an STR, resulting in functional NK cells

- 10X improvement in yield
- High purity of NK cells

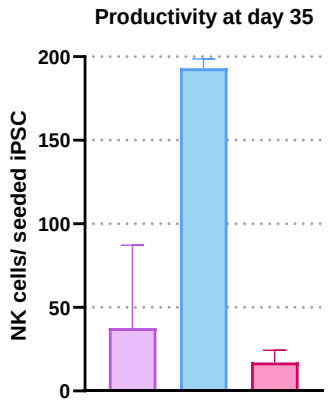
QUALITY

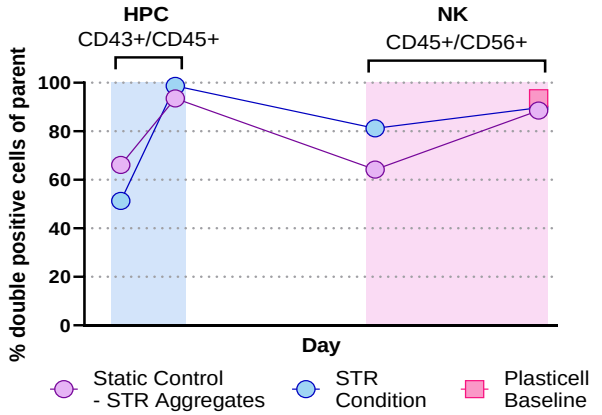
STR-generated iNKs showed cytotoxic function against 3 cancer cell lines.

Correlating these outcomes with FCM data, revealed different phenotypes associated with:

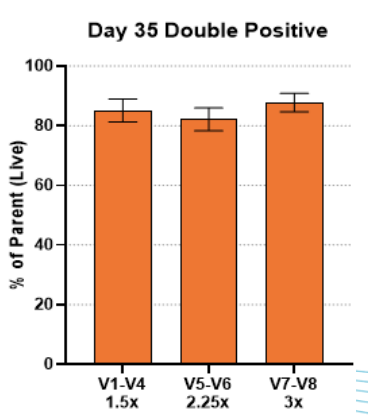
- iNKs from processes that were highly productive.
- iNKs that were highly functional.

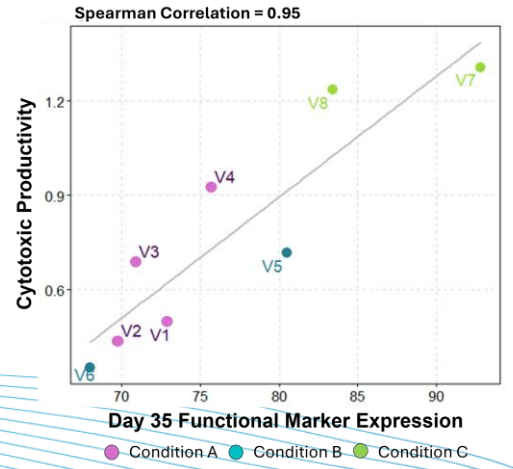
Feasibility Assessment

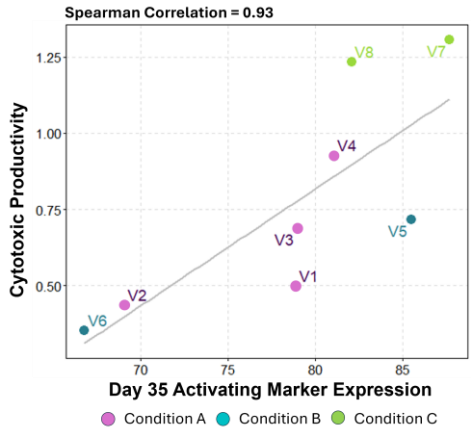




STR Condition Screening







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Product Characterisation

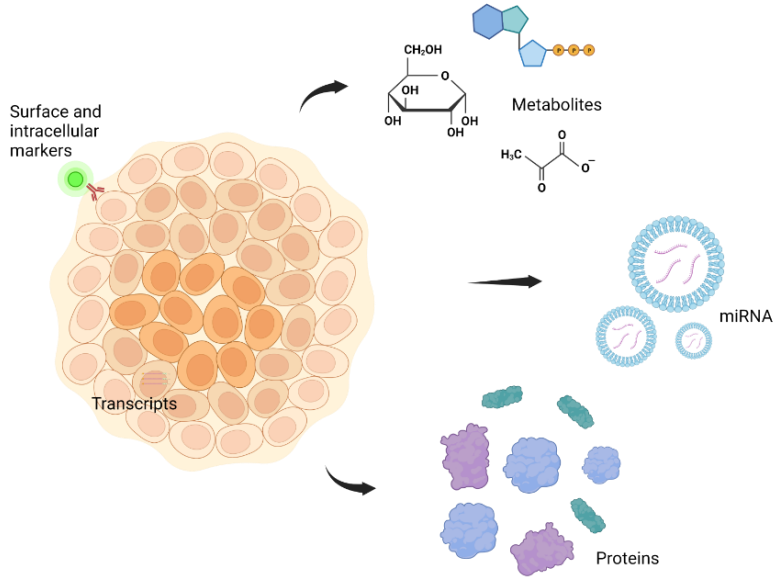
scRNAseq Screening

- Louvain clustering at day 35 - presence of different cell populations per condition, unique clusters in condition C.
- Modulation of cell density at a key transitional timepoint influenced the proportion of differentiated cell populations
- Cluster annotation (Human Cell Atlas) showed the largest population in all STR conditions consisted of target iNK cells, with small proportions of off-target cells

Targeted Protein Screening

- Olink screening platform
  - Uses proximity extension assay for high specificity
  - High throughput screening of 5400 proteins
- PCA of 1010 proteins

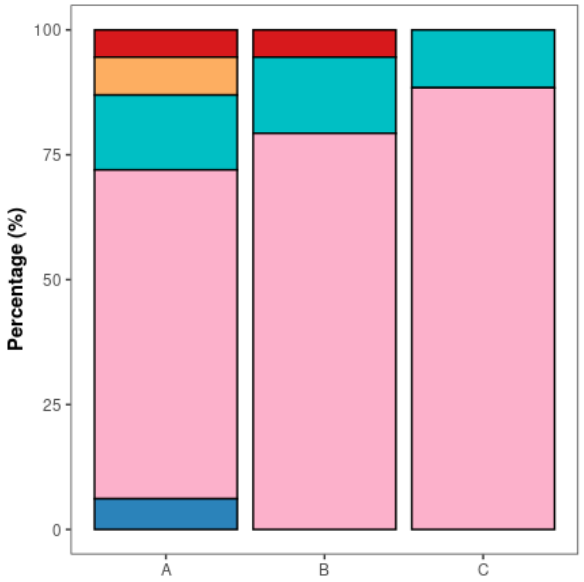
→ Selected proteins capture shift in proteome during NK differentiation



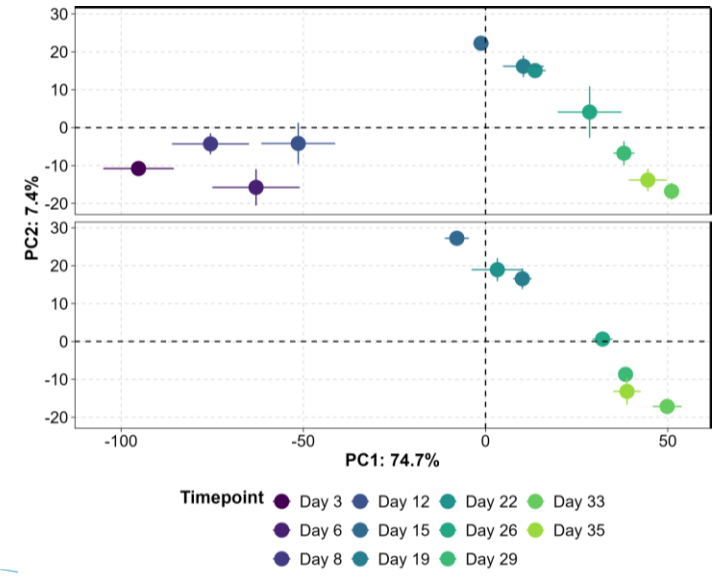
CATAPULT Cell and Gene Therapy

Olink

scRNAseq



Targeted Protein Screening



PAT and Biomarker Discovery Lab

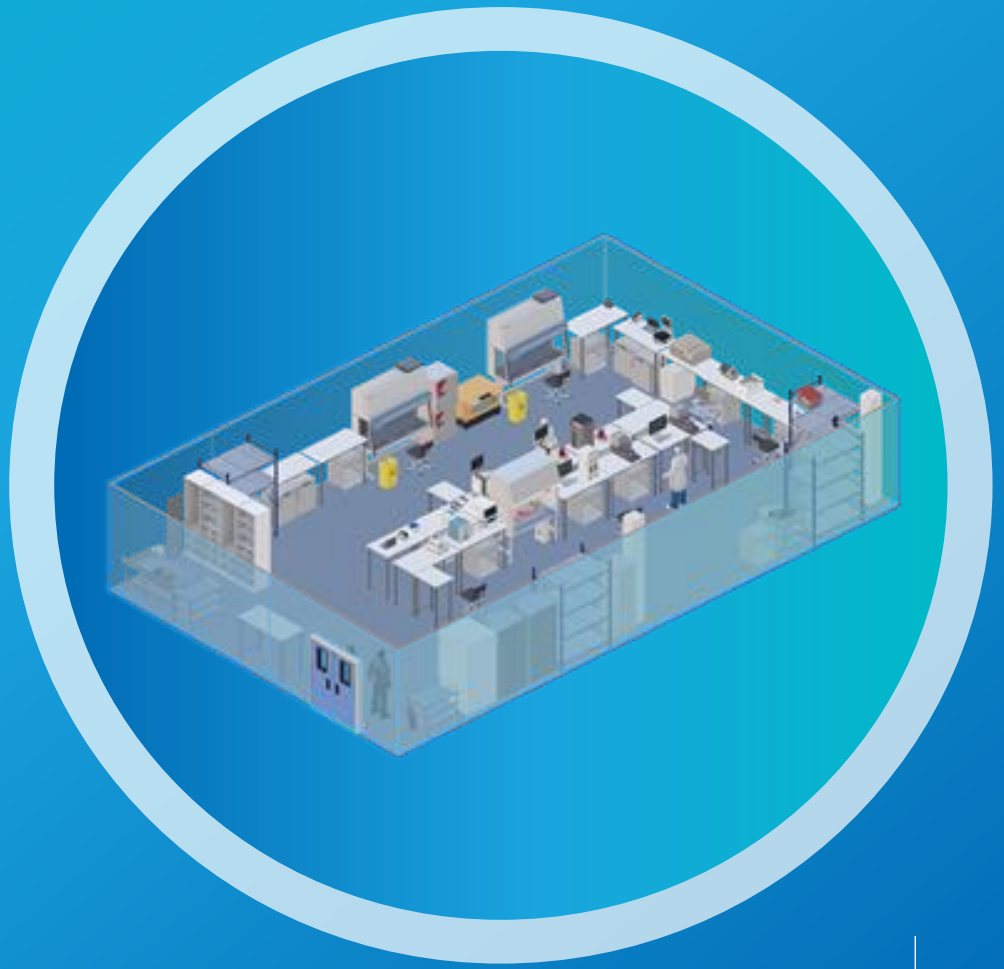
CATAPULT Cell and Gene Therapy

Gain greater understanding and **control** of your product and process through use of **in-line analytics and real-time data interpretation** to adjust and improve process performance

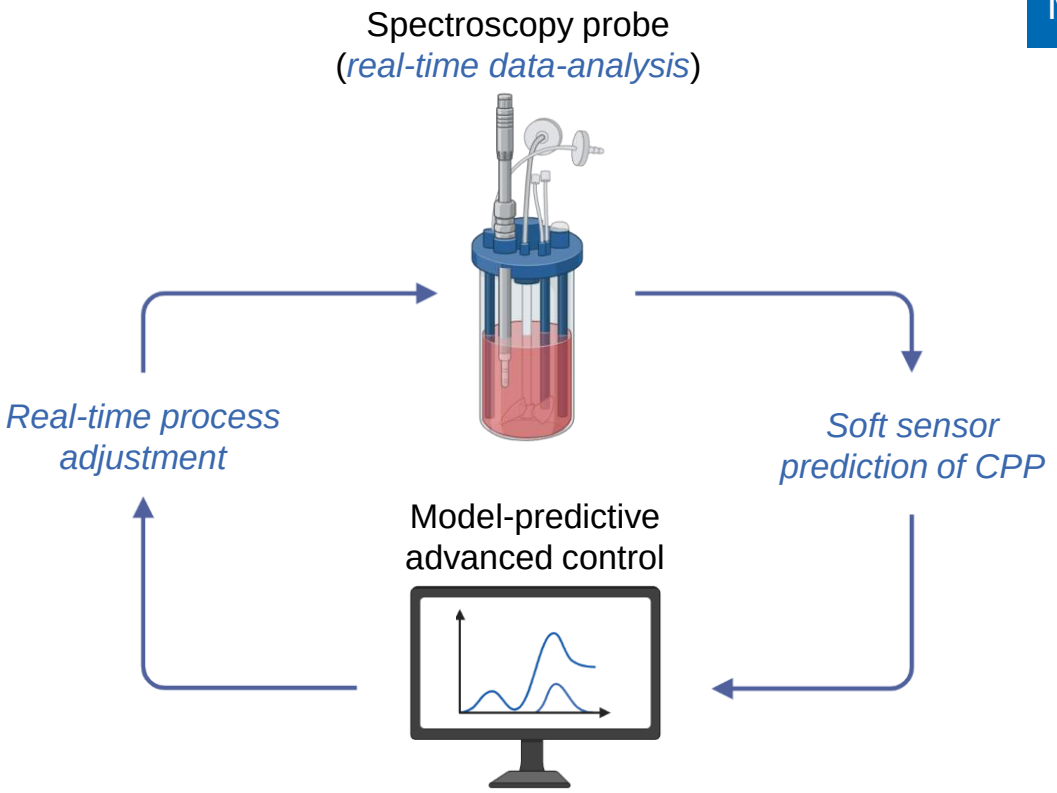
State-of-the-art **lab automation and digitalisation** allow rapid, high-throughput sample collection and analysis

Assess and integrate **process analytical technologies** and advanced analytical tools to build in-depth characterisation

Develop **digital twins and advanced process control strategies** to maintain critical process parameters and critical quality attributes



Digital Twin Build



Digitalisation and Automation of Medicines R&D and Manufacture

Advanced Control Development for AAV Manufacture

RE•FEYN

Rentschler Biopharma

UKRI Innovate UK

CATAPULT Cell and Gene Therapy

SMARTER Consortium

Advanced Control Development for TIL- like cells and DCs

ACHILLES THERAPEUTICS

Leibniz Universität Hannover

UKRI Innovate UK

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Challenges for Scaling

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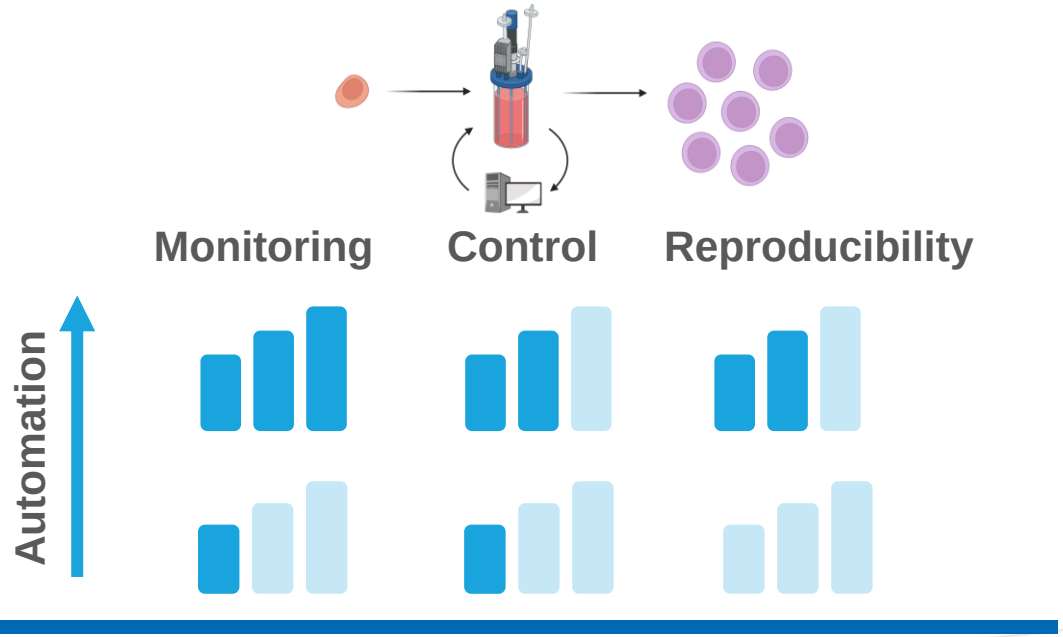
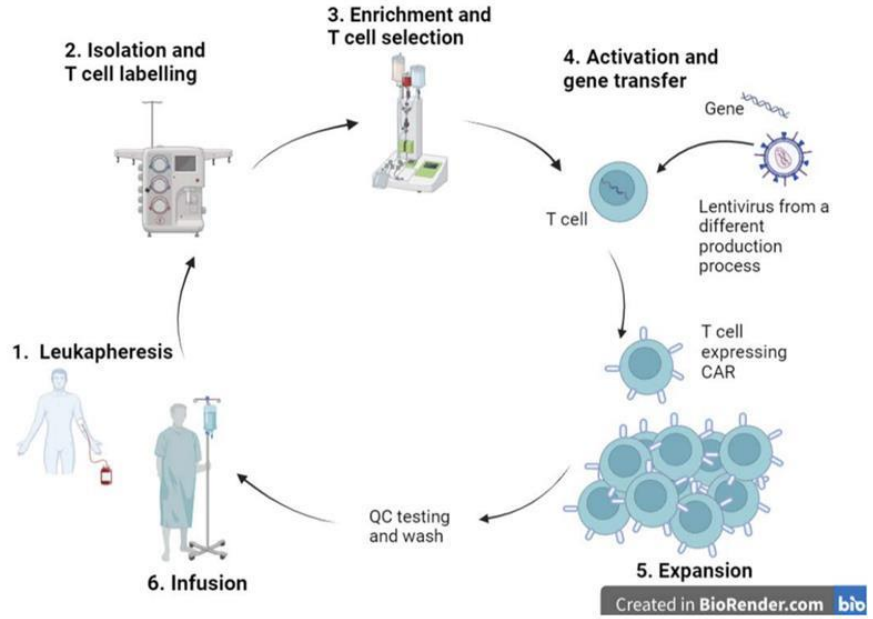
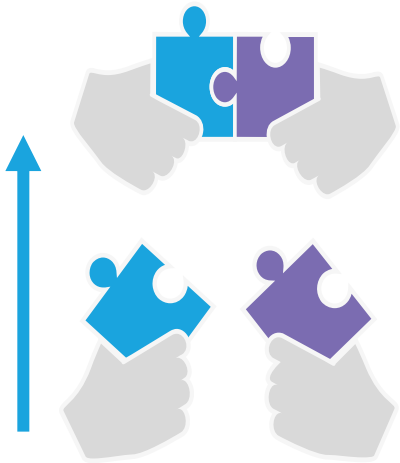


Challenges for Scaling



Scale Out: CAR-T case example

1. Min intervention, max reproducibility
2. Automate for controlled parallelization
3. QC Automation
4. Digital Integration & Advanced Control



Deployment

Innovation

Automate for controlled parallelization

Expert guidance and tailored activities in a controlled environment for de-risked testing, validation and adoption of next-generation technologies.

Phased Journey to Power Scalable Innovations

STAGE 1

Strategic Assessment & Feasibility Analysis

Address scalability and compliance challenges early in development

STAGE 2

PoC Testing and Real-World Data Generation

Showcase scalable processes/technologies ready for real-world application

STAGE 3

Qualification and Deployment

Facilitate clinical/commercial therapeutic manufacturing and technology market adoption

De-risk and accelerate time-to-market and strengthen value proposition

QC Automation: challenges of process scale up in manufacturing

25%* cost per batch attributed to QC/QA

QC bottle necks

Reliance on multiple offline instruments

Inherent variability of living samples – SMEs required

Labour intensive manual release testing

Lack of standardisation of methods/instruments

Need for automation/digitalisation

Increase throughput – fast release e.g. autologous cell therapy

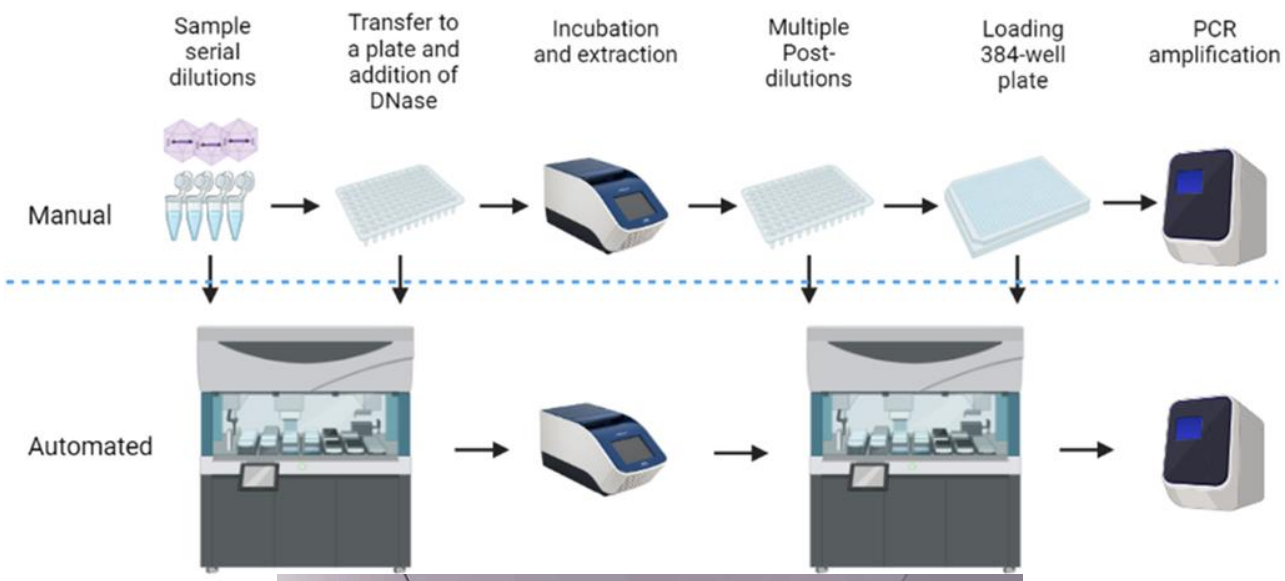
Improve quality – reduce variability, improve data integrity and reduce error

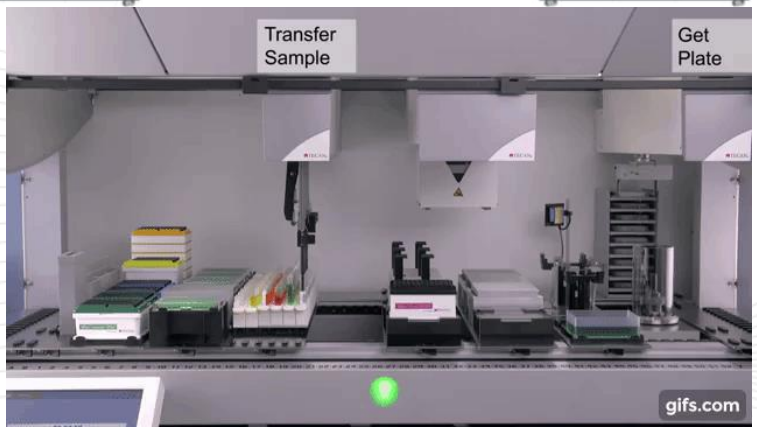
Reduce labour intensive analytics

Reduce overall complexity

Case Study – Introducing assay automation

Improvements in throughput, quality, reliability and data integrity



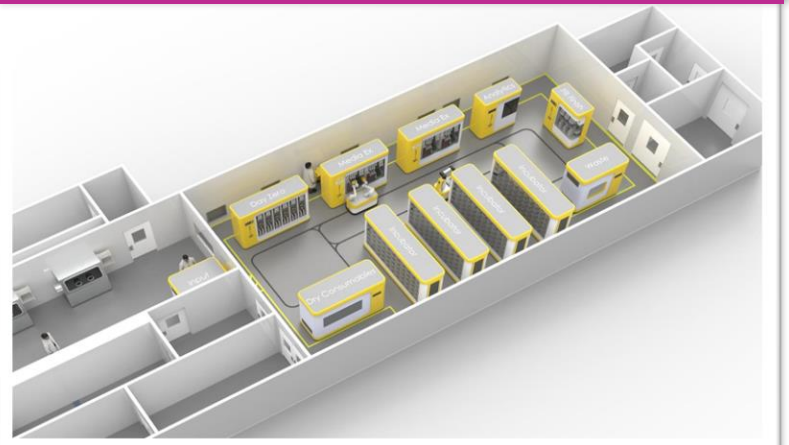


Workflow	Manual	Automated
Lab Hands-on time	6h/plate	2.5h/plate
Samples per run	Up to 15 samples	Up to 32 samples
Sample pass rate (%)	36%	96%
Costs per sample (%)	100%	56%

Digital and Automation Testbeds

"First-in-the-world" ATMP-specific GMP-mirroring testbeds for de-risked, accelerated testing and adoption of next-generation automation and digital technologies.

High profile GMP facilities for rapid real-world testing and deployment of automation and digital innovations.



MHRA licensed facilities

Adaptable non-GMP modules

Cost/risk sharing model

Co-located GMP modules

Co-located PAT and biomarker discovery lab

Operational, qualified manufacturing enterprise systems

Training and upskilling support

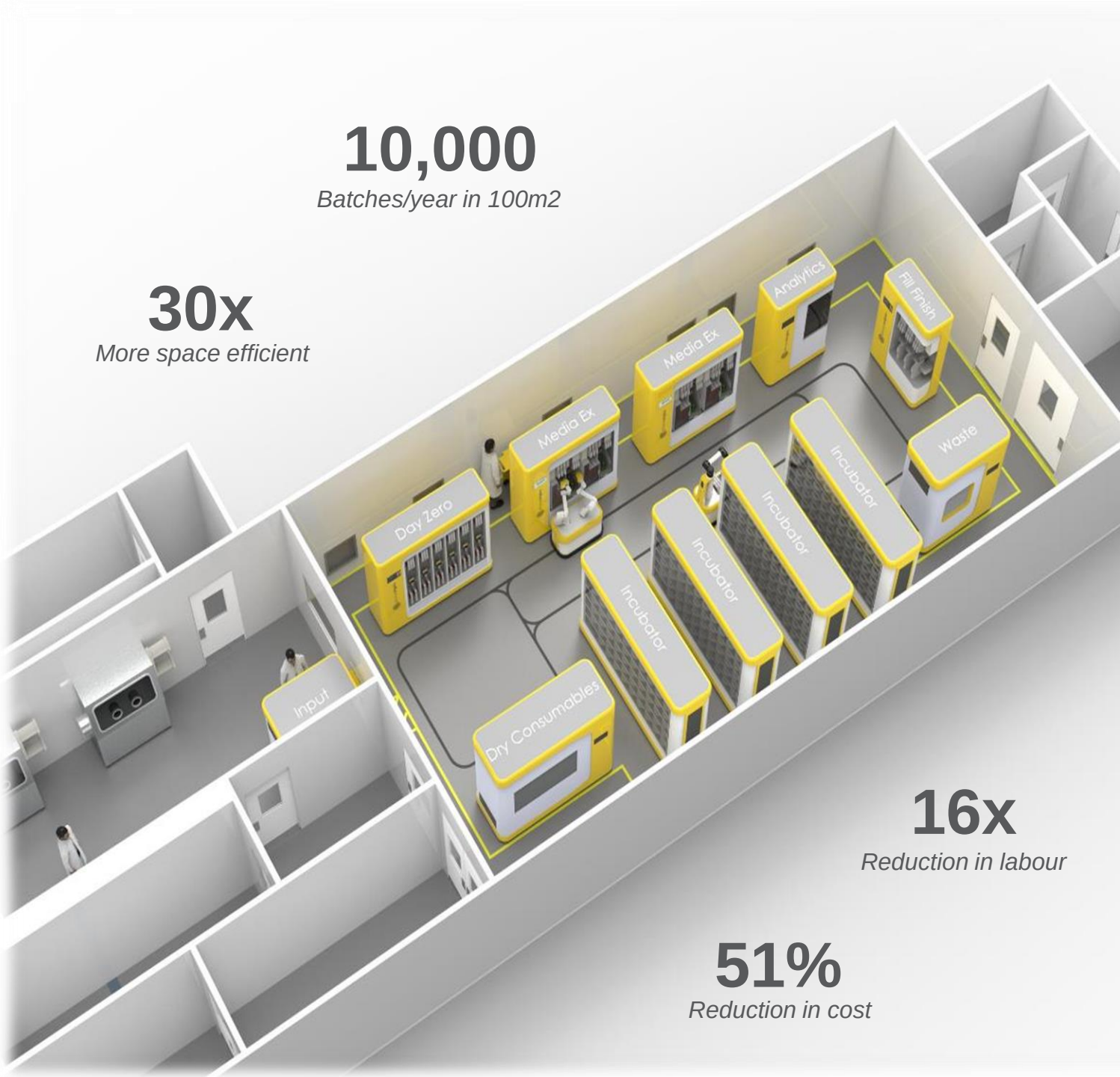
Process development, manufacturing, supply chain, quality, validation, regulatory expertise

Future Factory Concept

Integration of fully automated robotics and PATs for scalable, reproducible, high-quality and more environmentally sustainable manufacturing of CGTs.

Ensures regulatory compliance, product consistency and a scalable route-to-market.

Increased attractiveness of innovations for investors, enhancing the exit potential and overall commercial value.

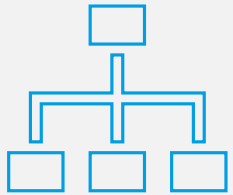


Scalable Therapy Development

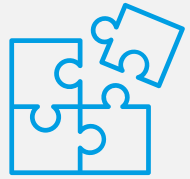
CATAPULT Cell and Gene Therapy

- **Skilled cell biologists, analytical scientists, bioprocess engineers, bioinformaticians**
- **Developing robust, scalable manufacturing processes for pluripotent stem cell production**
- **Knowledge of high-content metabolomics, and transcriptomics analysis to enable PSC analytics development**

20+ collaborators supported



Broad experience across cell therapy modalities



Disruptive innovation through key collaborative projects

Scottish National Blood Transfusion Service · Plasticell · Procella Therapeutics · Roslin CT your advanced therapy solution · Cell2Cure · Asterias Biotherapeutics · University of Cambridge · The University of Nottingham · Terumo · atelerix · HESI · Earlham Institute · The University of Edinburgh · University of Liverpool · Manchester 1824 The University of Manchester · Center for iPS Cell Research and Application, Kyoto University CiRA · Rinri Therapeutics · bit bio · novo nordisk · Alder Therapeutics · Imperial · University of Bristol · UCL

Thank you to everyone involved

CGT Catapult

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Dr Virginia del Solar Fernandez

Juline Guenat

Dr Marcia Mata

Dr Chris O'Grady

Dr Dragos Marginean

Dr Joseph Oddy

Coralie Nerincx

Dr John Churchwell

Dr Molly Tregidgo

Kevin Vela

Lee Elkington

Rhys Macown

Mohsen Shaeri

Andrew Riley

Majahar Sayed

Su Jayakody

Julie Kerby

Dr Stephen Ward

Plasticell

Dr Marina Tarunina

Dr Tanya Ponomaryov

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