Navigating the Future of Biologics and mRNA

Dr Clare Trippett & Dr Helen Young

Overview of CPI and our role supporting global pharmaceutical innovation

CPI is an independent, deep-tech innovation centre addressing the global challenges and opportunities of society, industry and the environment.

We help companies to develop, prove, scale-up, and commercialise their disruptive and transformative novel innovations.

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cpi

Bringing your bright idea to market

We help companies to deliver, re-risk, and accelerate their ideas into successful products and processes.

- Founded in 2004
- 600+ staff
  - 450+ Scientists and Engineers
- £250m of innovation facilities (~25000 m^2)
- Founding member of UK's High Value Manufacturing Catapult
- >1500 R&D&I projects delivered
- Unlocked over £3billion of private investment into R&D&I

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CPI capabilities and markets supported

ALIGNMENT WITH MISSIONS

- Life Sciences
- Defence
- Advanced Manufacturing
- Clean Energy
- Digital and Technologies

THEMES AND INDUSTRIES

Pharmaceuticals

Medicines manufacturing innovation for multi-modalities including, biologics, small molecules, nucleic acids (mRNA, siRNA, oligos), microbiome and phage therapies, under appropriate quality systems (e.g. GMP)

Development and scale-up of **nanotherapeutic delivery systems for intracellular delivery**.

Healthtech

Development and scale-up of **medical devices including in vitro and point-of-need diagnostics, wearables and digital health innovations under appropriate quality systems (e.g. ISO 13485)**

Defence & National Security

Development and scale-up of **Advanced Materials, Pharmaceuticals, Healthcare and Biotechnology** with applications across the sector

Sustainable materials and chemicals

Development and scale up of **materials for clean energy** including generation, storage, recovery and recycling

Development and scale-up of sustainable materials and fossil free chemicals for **circular supply chains including critical minerals, polymers, fibres and composites**

Biomanufacturing

Development and scale up of **bio-derived ingredients and products such as agrichemicals, alternative proteins, functional ingredients** for food, feed, nutraceuticals, agritech and consumer goods

TECHNICAL CAPABILITIES

- Engineering biology
- Process chemistry and process engineering
- Materials chemistry and formulation science
- Fermentation and cell free synthesis
- Software, Hardware and Mechanical design and Engineering
- Nanotechnologies and 2D materials
- AI and data science
- Flexible hybrid electronics
- Coatings and thin films
- Robotics and high-throughput screening
- In silico modelling
- Additive manufacturing
- Pilot and process line planning and modelling
- Technoeconomic analysis
- Life cycle assessment

UNDERPINNING ACTIVITIES

- Place and Academia
- Skills
- SMEs
- Access to Finance
- Global partnerships

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Examples of global partnerships in pharmaceuticals

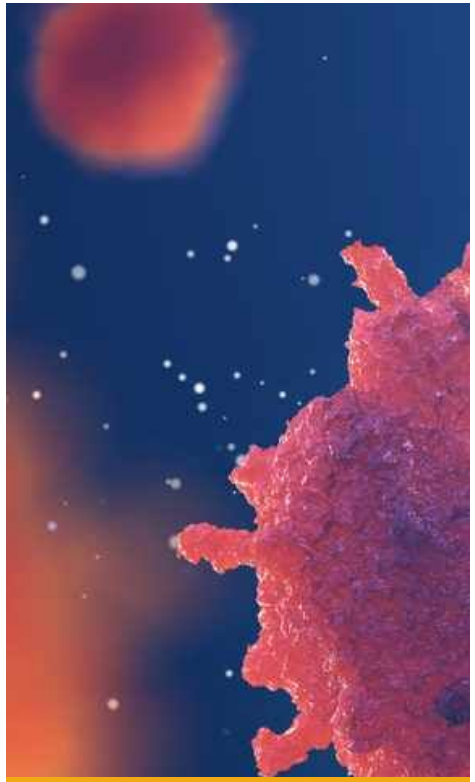
CPI has worked with international partners to develop and scale innovative pharma manufacturing processes

CSIR-NCL
India

Sustainable pharmaceutical processing

Alnylam Labs
United States

Oligonucleotide manufacture



NRC
Canada

Viral vector production and AI-powered bioreactors

CPI Pharma: Biologics

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The future of biologics manufacturing

Process intensification

Digitalisation & AI

Process Analytical Technology (PAT)

Personalised & Decentralised Manufacturing

mRNA & Next-Generation Therapies

Sustainability & Green Biomanufacturing

Overview of facility

1. Established in **2015**, we support the design, development, optimisation and demonstration of bespoke manufacturing processes specific for biologic product.

2. £38m state-of-the art, 5,000m^2 facility in Darlington, UK.

3. **10 flexible laboratories** designed to handle BSL1 and BSL2 organisms

4. **ISO 9001 Certified** scale-up and manufacturing approach, **GMP Certified** for RNA-LNP clinical supply

5. **Independent facility** with no alignment to proprietary technologies or contract manufacturing lock in.

6. **Expertise** in evolving manufacturing technologies, help increase performance, productivity and flexibility

Biologics focus

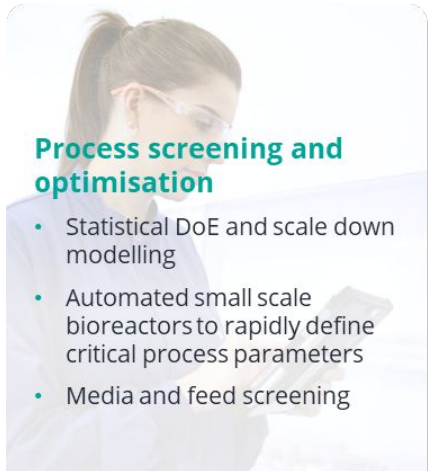
Comprehensive expertise in **synthetic**, **microbial** and **mammalian** expression systems for the production of a wide range of products including monoclonal antibodies, gene therapies, mRNA-LNPs, microbiome therapeutics and recombinant proteins.

How we can help you:

1. High-throughput development and scale up
2. Technology evaluation in our established processes
3. Material supply for preclinical studies
4. Supply of clinical material for mRNA-LNPs

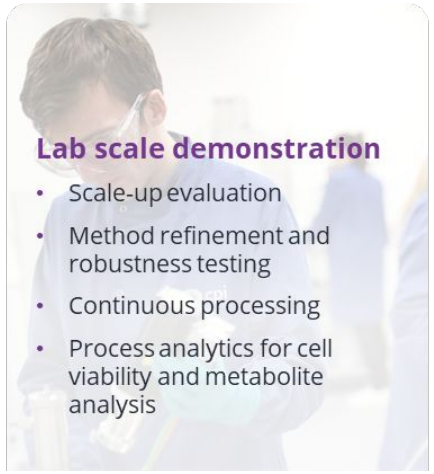
Upstream and downstream process development

Upstream



Process screening and optimisation

- Statistical DoE and scale down modelling
- Automated small scale bioreactors to rapidly define critical process parameters
- Media and feed screening



Lab scale demonstration

- Scale-up evaluation
- Method refinement and robustness testing
- Continuous processing
- Process analytics for cell viability and metabolite analysis

Process scale-up

- Process demonstration
- Scale-up studies
- Material supply

Upstream Capability

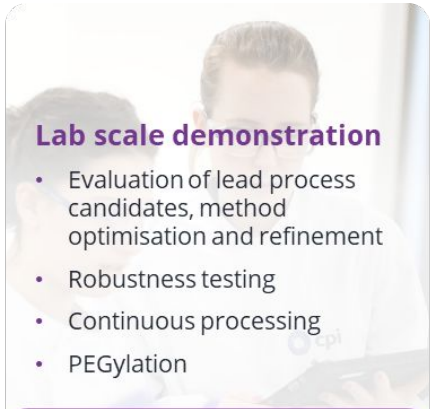
- **Optimisation & scale up from plate to 100L (micro); 200L mammalian**
- **Experience using all relevant Biologics expression systems & cell free/ enzymatic**
  - CHO, HEK293, E. Coli, Yeasts, Bacillus, Sf9 etc

- **Key equipment:**
  - Ambr15
  - Ambr250 HT & Perfusion (w/ data bridge to MS)
  - ATF perfusion
  - 50 & 200L SUB, 100L SIP

Downstream

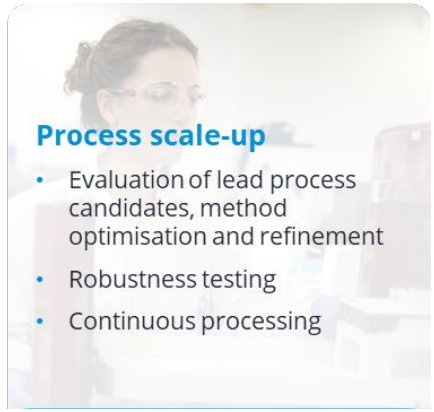
High throughput process screening and optimisation

Robotic liquid handling platforms and high throughput analytics for rapid screening of filtration and chromatography conditions



Lab scale demonstration

- Evaluation of lead process candidates, method optimisation and refinement
- Robustness testing
- Continuous processing
- PEGylation



Process scale-up

- Evaluation of lead process candidates, method optimisation and refinement
- Robustness testing
- Continuous processing

Downstream Capability

- **Optimisation & scale up, from resin plates to process scale, chromatography & filtration**
- **Experience encompassing all biologic types, and different conjugation chemistries**

- **Key equipment:**
  - Ambr crossflow
  - Liquid handler for resin plates & robocolumns
  - Continuous purification – Akta PCC

Analytical development & Formulation

Process support: Product quality, residuals and impurities

CAPABILITIES

- UPLC / HPLC
- Capillary electrophoresis
- Biolayer interferometry (Octet)
- Ella (automated immunoassay)
- Jess (automated western blot)
- qPCR, ddPCR
- Endotoxin analysers
- SDS-PAGE / Agarose gels
- NGS

Product characterisation

CAPABILITIES

- cIEF, CE-SDS, cIEF fractionation
- UPLC / HPLC
- LC-MS(/MS) (intact/subunit/peptide mapping, *N*-glycan profiling)
- Mass Photometry
- Circular Dichroism
- DSC
- Particle/aggregate analysis across the nanometer, submicron, micron and visible size ranges

Stability studies and Lyophilisation

CAPABILITIES

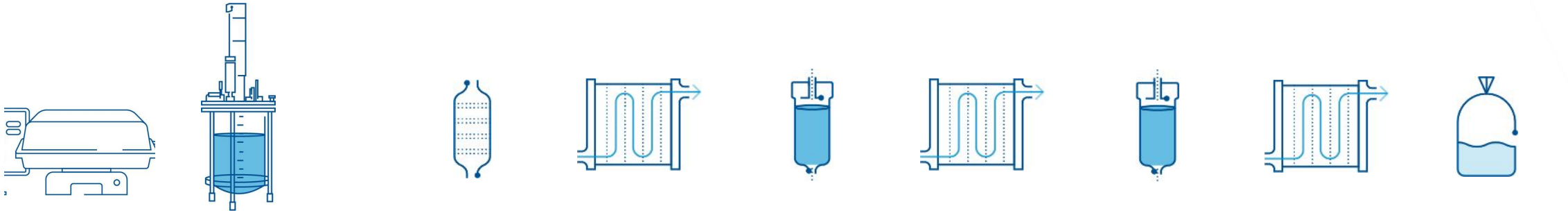
- Accelerated/forced degradation
- Understand degradation pathways
- Identify critical quality attributes
- Support formulation development
- Develop stability indicating assays
- Lyophilisation screening and optimisation
- Excipient screening

Analytical method development

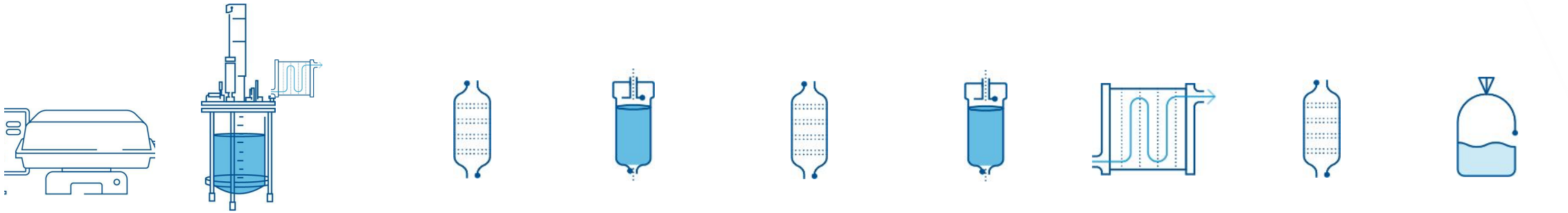
CAPABILITIES

- Design, optimise and validation of analytical methods
- Analytical method transfer

Conventional bioprocessing



Intensified processing



N-1 perfusion
Perfusion culture

Continuous & semi-continuous purification
In-line diafiltration and concentration

Process Analytical Technology

Project UK Continuous 2

PROJECT AIM

Develop a continuous biologics manufacturing testbed with integrated advanced process analytics and control to allow predictive real-time analysis of critical process parameters and critical quality attributes

PROJECT OUTPUTS

1. An industrial-grade operational control and data collection system
2. A digitally integrated advanced process control system, with real-time cloud storage of ALL process data from each integrated unit
3. A home-made automated upstream bioreactor platform with perfusion
4. A modular continuous downstream testbed
5. An integrated USP-DSP continuous development platform
6. 1x Repligen XCell Lab Controller, 2x Akta PCC75 chromatography systems + 2x BiologIC Technologies Smart Surge Tanks
7. Extensive technical experience with continuous process challenges
8. White papers, journal articles and conference presentations
9. 55-day automated perfusion process, lights-out operation and 7-day steady-state continuous DSP

Progress

100%

From Apr 2021

To Jan 2024

Funding

£3.1m Innovate UK

£2.1m
Grant

£1.0 m
Industrial Match

Antibody intensification

E2E intensified test best developed at CPI

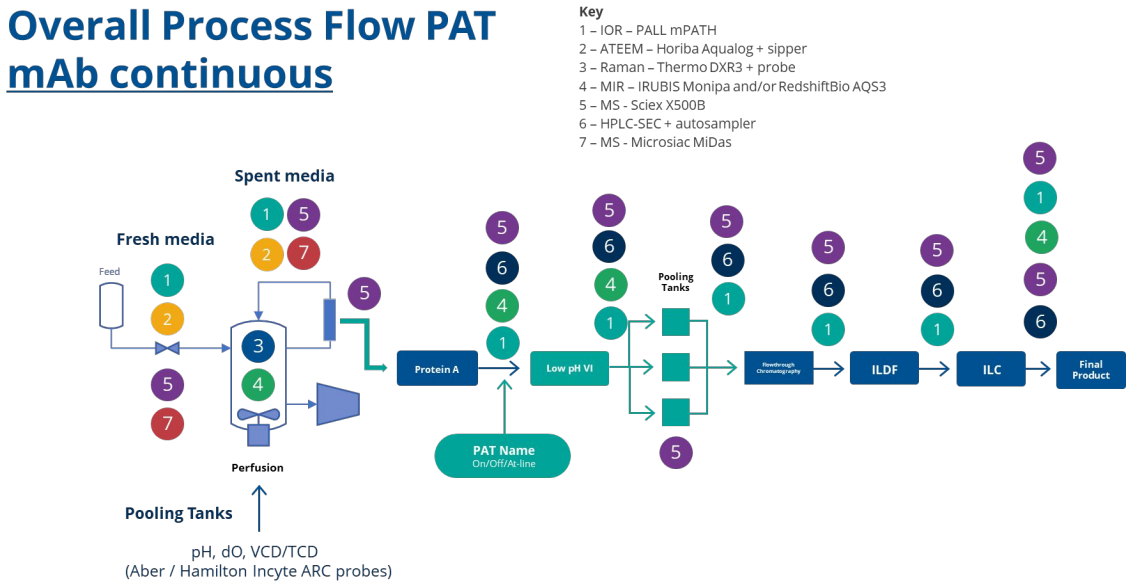
Perfusion upstream culture, SMB semi-continuous downstream with integrated PAT

Key learnings now applied to projects:

- Defining the “right” PAT
- The right decision layers & models
- Integration of equipment
- Unified data layer

- Programmes in progress to show scale up, and evaluate additional PAT

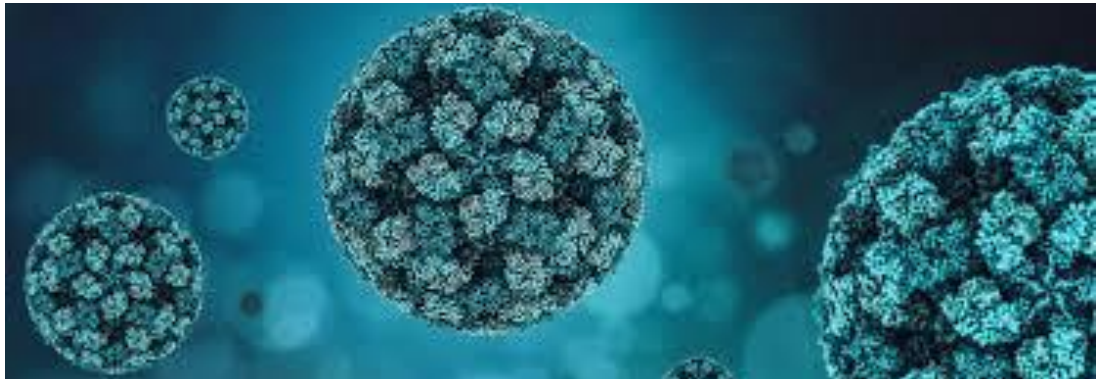
Overall Process Flow PAT mAb continuous



Antibody intensification

Case study: Platform for decentralised vaccine production through cell free expression

Scalable and rapid vaccine manufacturing without cells



*Developing an **automated cell-free platform** for decentralised manufacture of viral-like particles (VLPs) using **Pichia-based lysate**, integrating global expertise in expression, purification, automation, and product design.*

Outcomes

- **Integrated System**: Combines cell-free expression, purification, automation and VLP technology into one platform
- **Accelerated candidate selection**: Enables rapid clinical material supply
- **Decentralised manufacturing**: Reduces dependency on large-scale infrastructure

Impact

- **Fast pandemic response**: Scalable, distributed production at point of need
- **Cost-effective supply**: Lower capital requirements and simplified logistics

University of Waterloo · CEPI · University of Leeds · FIOCRUZ · University of Toronto · Liberum · cpi · Imperial College London

Collaborative R&D project

2 years

RNA Centre of Excellence

RNA Centre of Excellence

Research and Development

Future optimisation of our RNA-LNP capabilities and improvement of platform process

Early-phase Manufacturing

Platform process for clinical manufacturing up to early phase clinical

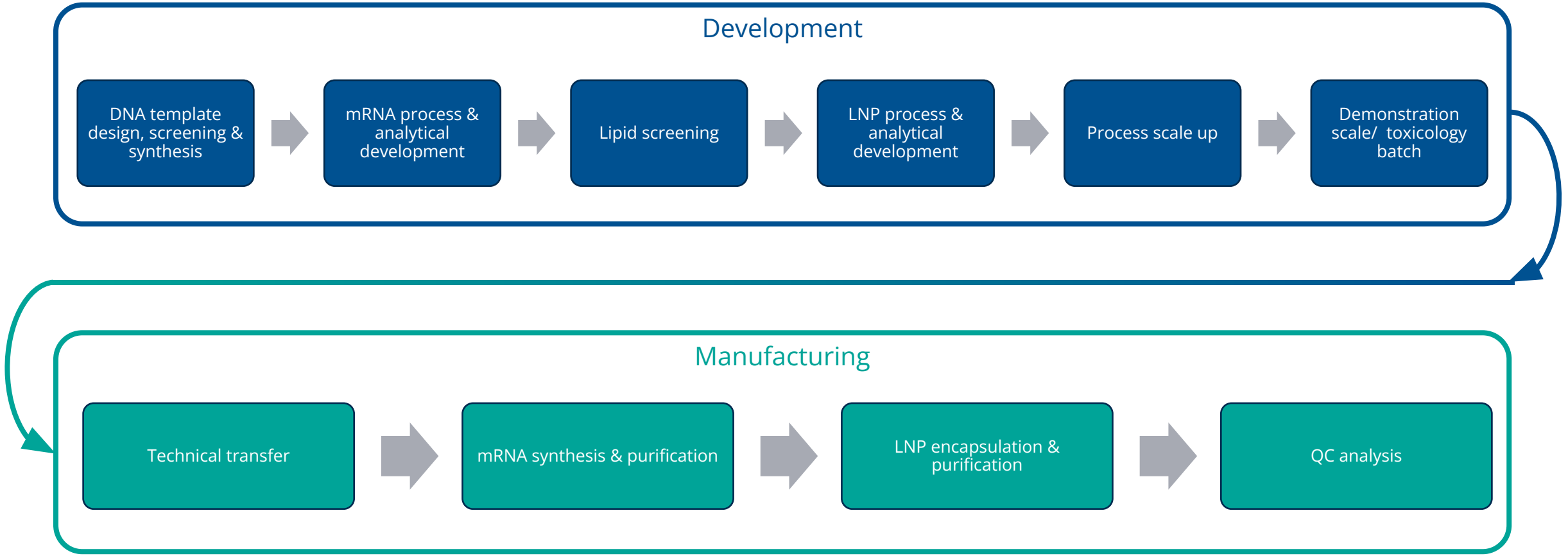
Training Academy

Industry CPD accredited training courses from basics to process development

UK RNA service now fully operational

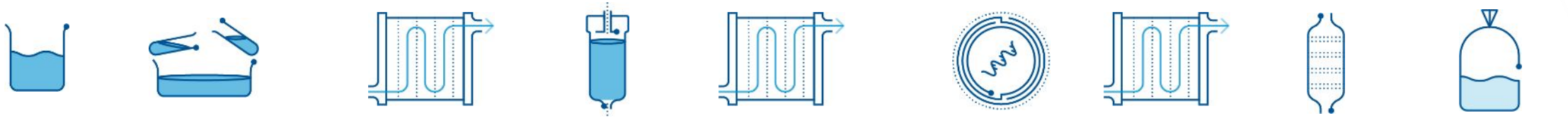
- Only UK-based open access RNA Facility offering
  - Process Development and scale-up
  - Manufacture and encapsulation ready for use in Clinical trials (Phase I and Phase II)
- Backed by UK Government
- End to end process all in one location
- Platform process
  - Plug and play
  - Accelerate vaccine development and scale-up
- Independent facility – no ties to process
  - Tech transfer in
  - Co-develop
  - Transfer out to CDMO

End to end, from development through manufacture



mRNA-LNP intensification

mRNA–LNP Platform Overview



Template linearisation | In Vitro Transcription | Tangential Flow Filtration | Chromatography | Tangential Flow Filtration | Encapsulation | Tangential Flow Filtration | Filtration | Bulk product

Making RNA

Purifying RNA

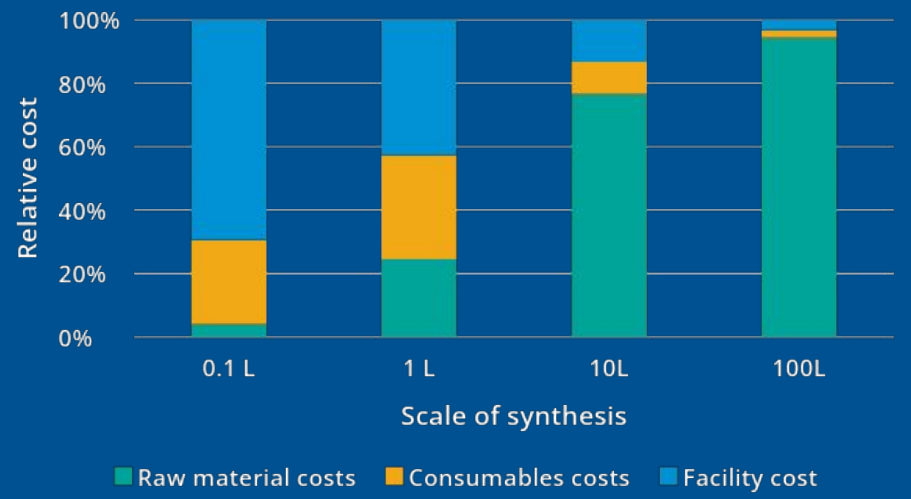
Encapsulation + Formulation RNA

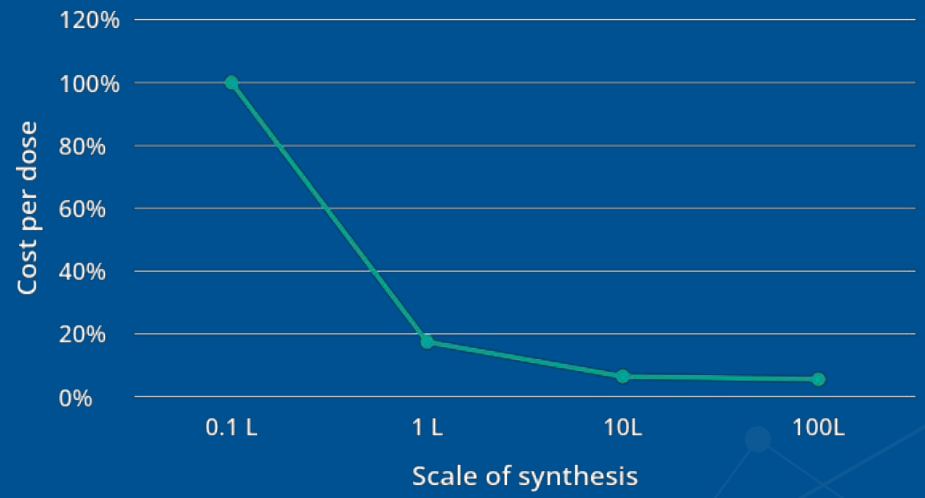
Analytics

Intensification driver – dose size

- Infectious disease vaccines <100ug
- Therapeutic vaccines <10mg
- Enzyme replacement & *in-vivo* expressed therapeutics >10mg (potentially over 100mg in some cases)

- All driving increased demand for mRNA-LNPs





All for one, and one for all – UK RNA Biofoundry

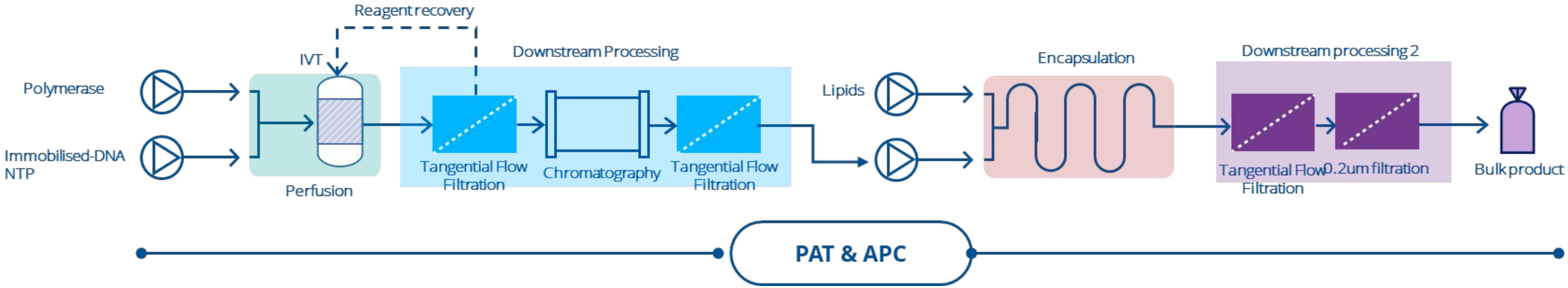
Different modality, same approach

RNA-LNP production is similar but different to conventional biologics

Evaluating scalable, intensified by design, integrated manufacturing systems

- Simplicity vs opportunity in complexity

Applying best practice from previous experiences



The BioFoundry Concept

Vision: To build a global network of scalable, state-of-the-art biological treatment manufacturing facilities – also known as **BioFoundries.** Each BioFoundry will be flexible enough to cost-effectively and safely produce a single individualised treatment or millions of treatments.

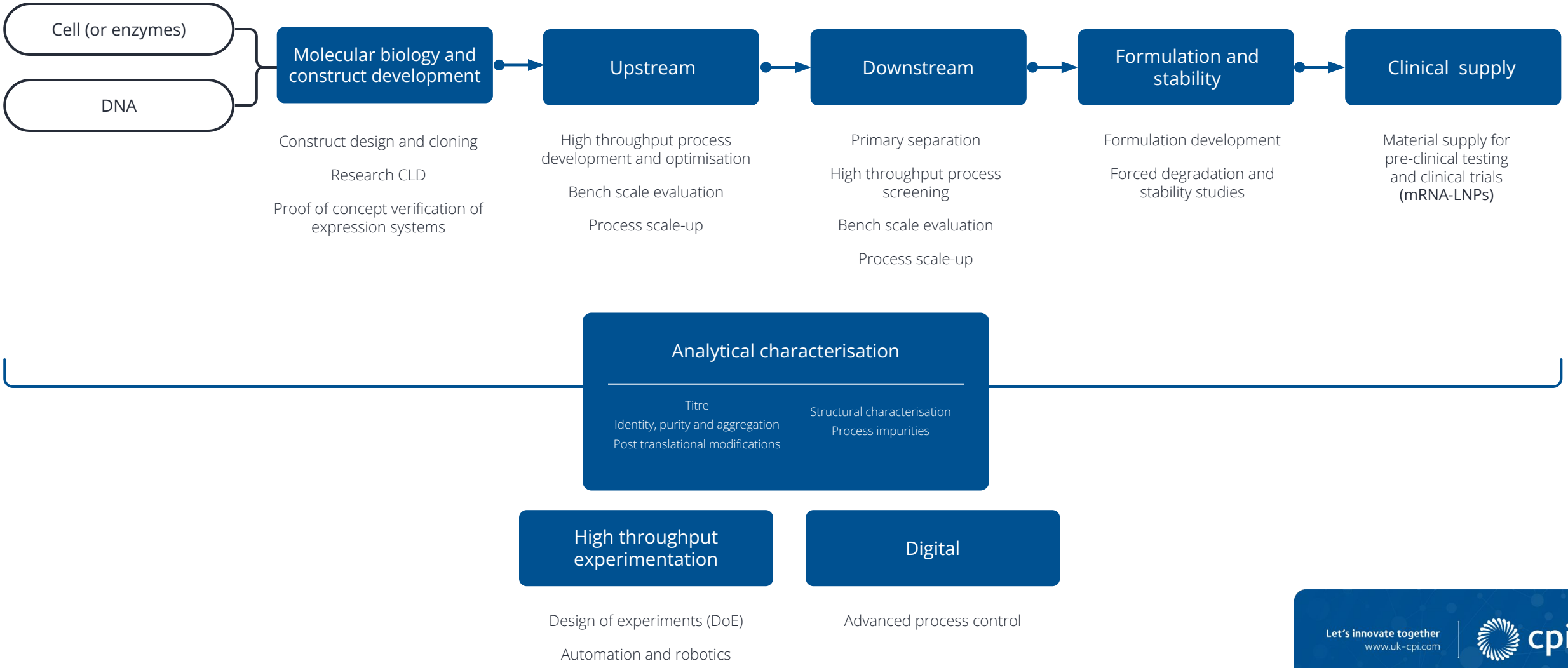
Goals:

- **Agile:** To produce research, pre-clinical and clinical grade encapsulated RNA continuously
- **Scalable:** From milligram to pandemic scales
- **Rapid:** Reduced production timelines and risks to enable rapid response
- **Cheap:** Lower cost of drug development and production to provide affordable, equitable and accessible cures

wellcomeleap.org/r3-global/

UKRI Innovate UK

Summarised capabilities



Working together with CPI

Here to help your company

Demonstration of **disruptive** and **market-creating** technologies

Industry level input on policy-making for local and national innovation strategies

Driving capital efficiencies with access to over £250m of innovation assets

Driving **industry-level standards** with pre-competitive collaboration

Cross-industry knowledge that drives horizontal innovation and accelerates commercialisation

Reduce risk and decrease your time to profitability

Support in navigating the complex **grant funding landscape**

Access **innovative start-ups** developing the technologies of tomorrow

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Fee for service

- **One-to-one** project with CPI
- **Flexible scope** and project size
- **Rapid initiation** of projects
- Can encompass a range of services including business and innovation support, consultancy, and lab-based projects

Offers flexibility and speed

Collaborative projects

- **One-to-one** with CPI or together with a larger consortium
- Projects initiate after completion of a **detailed funding protocol**
- We offer a bespoke service for **bid development** and **grant landscape navigation**

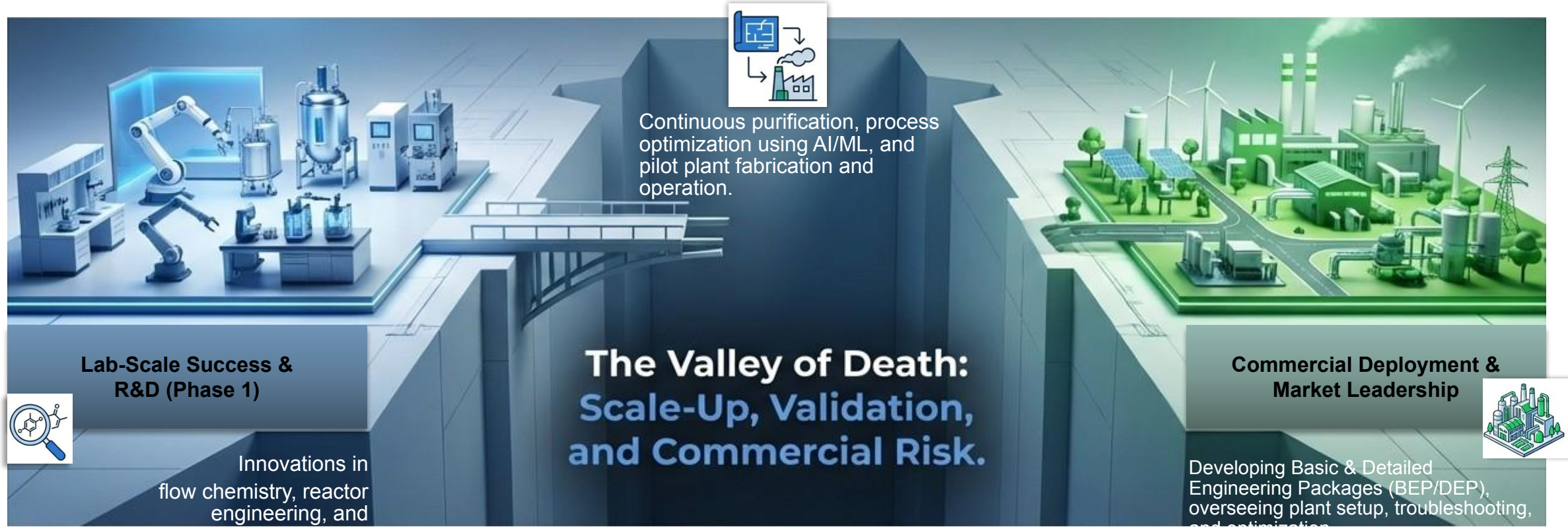
Best option for highly innovative projects you can't fund fully yourself

Decarbonisation of the Indian Pharmaceutical industry –

Living Lab Phase I & II enabled by the CPI–NCL Partnership as a model

Dr Arun Harish

From Proven Innovation to Widespread Impact: Bridging the "Valley of Death"



The Indian ecosystem currently lacks established models to reliably scale-up, pilot, and commercialize innovative platform technologies through shared risks and rewards.

This is the gap we are aiming to bridge through the CPI – NCL partnership, initially for flow chemistry, solvent-free chemistry and digitally-enabled medicines manufacturing

Foundation Built: Living Lab Phase 1 Enables the Shift to Competitive Deployment

Phase-1: Living Lab (The Foundation)

@CSIR-NCL, Pune

Fully Operational & Validated: Located at CSIR-NCL in Pune.

Government Backed: Jointly supported by UK and Indian governments via the **UK-India Net Zero Innovation Partnership.**

Industry Integrated: Active participation from core members, technology partners, and the Indian Pharmaceutical Alliance (IPA).

Proven Triple Helix Model of Powerful Public - Private Partnership

- **Approach: CSIR-NCL, CPI-UK, Tier-1,2,3 industry partners**
- **Focus:** Pre-Competitive, collaborative innovation in platform chemistries
- **Activities:** Early-stage innovation, integrating components, demonstrating platform chemistries.
- **Scale:** Lab-scale and Mini-pilot (0.1 – 1 kg/day)
- **Output:** Proven concepts and processes.

Phase-2: **Public-Private Translational Centre**

Phase 2 is designed to take validated, early-stage technologies and carry them across the commercialization gap. It will operate in the competitive landscape to:

→ Validate, scale-up, and optimize technologies for specific, high-value molecules for specific industries.

→ Pilot and de-risk these technologies to meet techno-commercial demands and assess the viability

→ Develop concrete plans for commercial-scale production.

Phase 2 is the Strategic Bridge from the Lab to the Market

- **Approach: NCL + ICT + CPI + Process Engineering Firm + SPV**
- **Focus:** Competitive Landscape
- **Activities:** Validating, scaling-up, piloting, and optimizing for specific industrial molecules.
- **Scale:** Pilot and Demo (50 – 100 kg/day)
- **Output:** Market-ready, commercially deployable technology packages.

Phase 2 will also serve as a landing pad for other India and UK innovators to bring novel technologies to the Indian and global chemical industries.

A Platform to De-Risk and Accelerate a Sustainable Transformation

Mission To accelerate the development and commercial adoption of sustainable manufacturing technologies for the pharmaceutical and fine & specialty chemicals sectors.

Model A first-of-its-kind India-UK collaboration between CSIR-NCL, ICT-Mumbai and CPI-UK, operating through a neutral, non-profit company and a process engineering partner in India for serving industry clients

Function Provide shared pilot-scale infrastructure, expertise, & collaborative environment that individual companies cannot build or access alone, including digital platforms.

Objective & Leadership Model

- To simplify the industry interface and maintain a highly outcome-focused approach to decarbonization and accelerated translation towards continuous manufacturing.
- Governed by a Board of executive leadership team, supported by an industry-led Strategic Advisory Committee (SAC) and a Technical Advisory Committee (TAC).

End-to-End Process Commercialization

- Near Future: Small molecules (Pharma, Specialty Chemicals)
- Next in Line: Biomolecules (Biosimilars, Enzymes, Proteins)

The Value Proposition: A One-Stop Solution for Commercializing Innovation – Value for Industry Clients

Access: Ready access to cutting edge innovations from premier Indian and UK research institutions.

Simplicity: A single point of contact for end-to-end, ready-to-commercialize technology solutions.

Network: Unparalleled opportunities for partnership with Indian, UK, and European industries and stakeholders.

Expertise: Engagement with experts for troubleshooting and future challenges.

IP Security: Fully confidential development and deployment with business-enabling IP terms.

Influence: A powerful, collective voice to engage with regulators and government agencies.

A World Class Collaboration: High-Level UK–India Engagement

Living Lab is a key strand within the UK-India NetZero Innovation Partnership (NZIP) with significant support from both governments.

The initiative was endorsed in the UK-India Science and Innovation Policy dialogue in London, co-chaired by the DST Secretary Prof. Abhay Karandikar and UK's National Technology Adviser, Dr. Dave Smith. This also forms a key part of UK-India Vision 2035. This backing provides unparalleled credibility that will help fast-track the adoption of new technologies.

CSIR-National Chemical Laboratory (NCL) Pune

- 75 years of excellence in process development
- 20+ years of excellence in R&D on continuous flow chemistry & process intensification
- Nationally and globally recognized as a CoE in translational research & consulting
- Translation of knowledge into TRL 3 technologies & successful licensing

Centre for Process Innovation - UK

- 20 years of deep tech innovation and commercialization with a focus on process development and scale up (TRL 3/4 to 8).
- Globally leading capabilities in medicines manufacturing innovation (multiple modalities including small molecule and biopharma), chemicals, materials and biomanufacturing.
- Founding member of UK's Catapult Network.

Institute of Chemical technology (ICT) Mumbai

- 90 years of excellence in chemical engineering and allied sciences
- Nationally and globally recognized institute for academic research & consulting
- Deep connects with Indian chemical industry
- Excellent infrastructure for research, education and skilling

Thank you

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