Andreas Traube

Matrix manufacturing for cost-efficient cell and gene therapy production

Fraunhofer IPA

Fraunhofer-Institut für Produktionstechnik und Automatisierung IPA

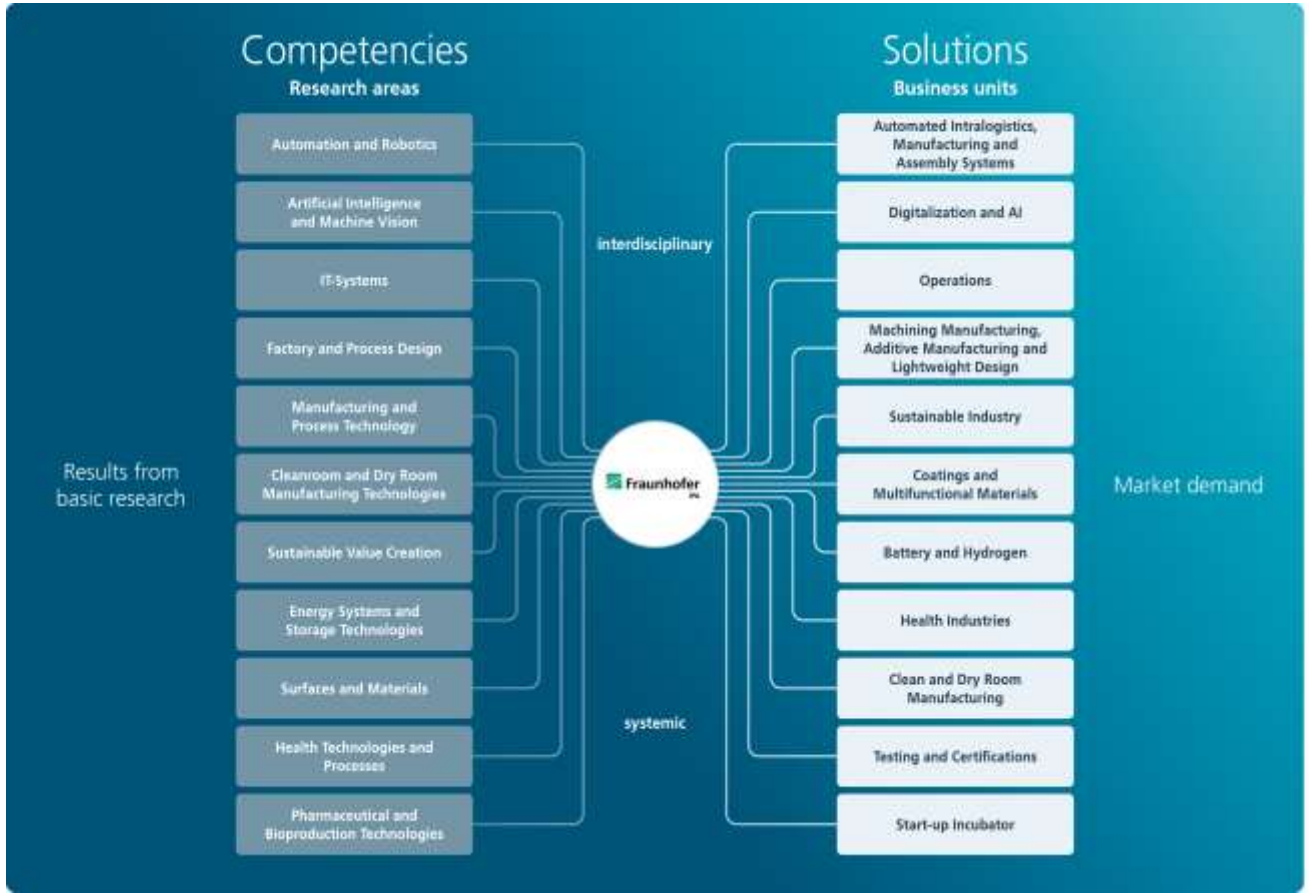
Fraunhofer IPA

A Strong Partner for Many Different Industries

- Over 1,000 industrial projects per year
- Almost 1,000 employees at nine locations (headquarters: Stuttgart)
- 22 patents granted in 2024 (four in Germany, 18 internationally)
- 820 publications in 2024
- Key figures for 2024 in million euros[1)]
  - **total budget**: 100
  - **operating budget:** 95[2)]
  - **investment budget**: 5
  - **industrial revenues**: 25

1) all figures include Fraunhofer Austria Research GmbH, Vienna, Production and Logistics Management Division
2) adjusted operating budget: increased by cost-reducing internal cost allocations with IPA value added of approx. € 1 million

Fraunhofer
Interdisciplinary Organization



Fraunhofer IPA
Location Stuttgart

Directors
Prof. Dr.-Ing. Thomas Bauernhansl
Prof. Dr.-Ing. Alexander Sauer

Additional locations

Fraunhofer Project Group Sustainable Manufacturing
Bayreuth

Clinical Health Technologies
Mannheim

Reutlinger Zentrum Industrie 4.0
Reutlingen

Working group KI-noW – Artificial intelligence in manufacturing
Schweinfurt

Fraunhofer HNFIZ/ FIZ: AI-based Robotics
Heilbronn/IPAI Spaces

Fraunhofer Project Center for Electroactive Polymers at AIST
Kansai

Fraunhofer Austria Research GmbH
Vienna

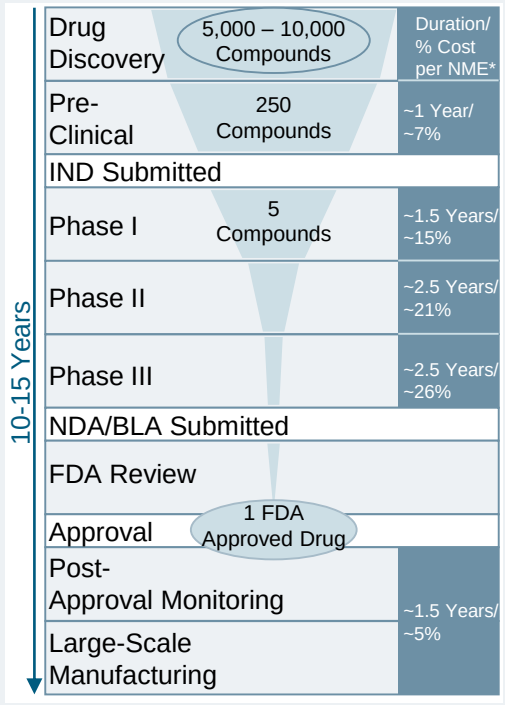
Paradigm shift in pharma manufacturing

The future of pharmaceutics by R&D+CT+P based on technology

Acceleration in today's fast-pacing world

Challenges in the pharmaceutical industry

- Increasing demands for shorter time-to-market challenge long development processes from discovery to market launch of a drug (10-15 years)
- High and increasing R&D spending ($1.6 billion on average to develop a new drug)
- Decreasing return on R&D investment (1.2% in 2022)
- Stagnant and declining R&D productivity Increasing competition and complexity from new players (high productivity and innovation potential of small pharma companies)
- Data breaches and cybersecurity
- Skills shortage



Sources:
Pharmaceutical research and manufacturers of America (PhRMA): Special 301 Submission 2021
https://catalyst.phrma.org/phrma-member-companies-rd-investments-reach-record-high-of-102.3-billion-in-2021
Deloitte: Seize the digital momentum – Measuring the return from pharmaceutical innovation 2022
Wouters, Oliver J. et. al.: Estimated research and development investment needed to bring a new medicine to market
Sun, D. et. al.: Why 90% of clinical drug development fails and how to improve it?
*NME: New Molecular Entity

Technology based future

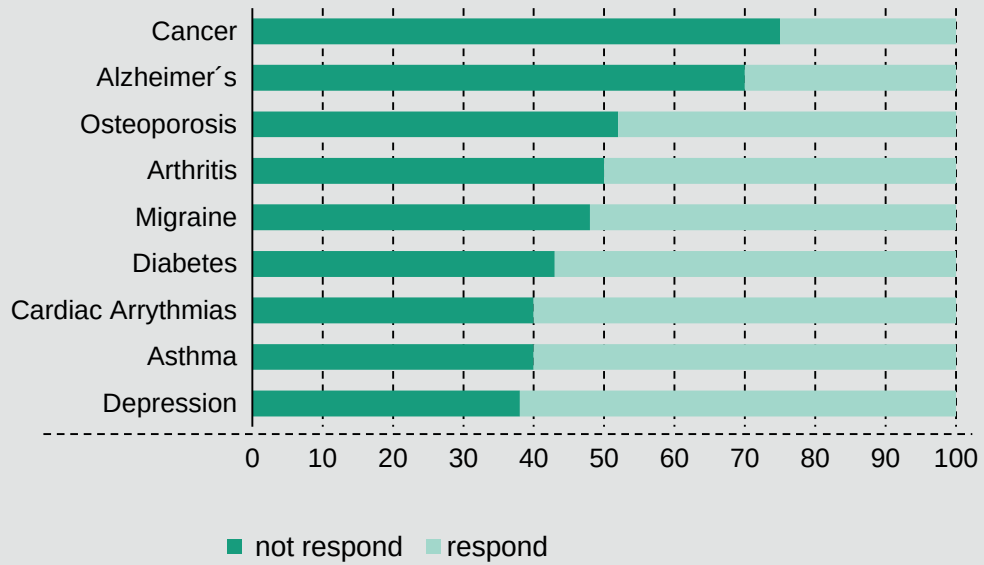
Goals

- Increasing the availability of new drugs
- Increasing efficiency in research, development and regulatory affairs through the use of digitization technology and automation
- Establishment of small-scale, scalable and variant-rich production based on the model of matrix production
- Strengthening research-based pharmaceutical companies

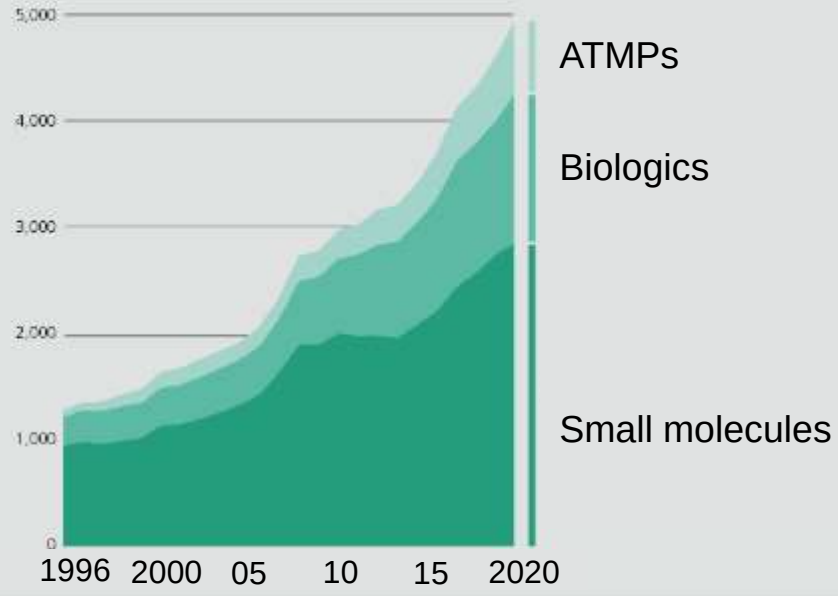
Motivation and Relevance

There is a high demand for increasingly personalized medicine

Percentage of patients who do not respond to medication (FDA)[1]



Number of innovative pharmaceutical products in phase I to III globally[2]



- Low response rates of individual drug groups reflect the heterogeneity of the patient population and the underlying individual disease pattern
- Cell and gene therapies as showcase examples of individualized therapies are becoming increasingly important

Pharma production on a Lab-Scale

Cell & Gene Therapies – What We're Trying to Make (and Why It's So Hard)

How a cell therapy is made (super simplified)

Step 1 – Take cells from patient
→ (Leukapheresis – blood filtering).
Step 2 – Modify them in the lab
→ Add or fix genes using viral or CRISPR tools.
Step 3 – Grow the new cells
→ Cultivate until enough "trained" cells are ready.
Step 4 – Test and freeze
→ Each batch must be checked for quality and identity.
Step 5 – Ship back to the same patient
→ Must match perfectly — every batch is unique.

⊘**Problem:**
Every patient = one batch = one mini-factory.

No economies of scale, lots of manual work, and delays are critical.

Pharma production on a Lab-Scale

The Technology Medley of CGT…

handle steps such as cell isolation, activation, transduction, expansion, and formulation under GMP conditions.

Fancy tech for cool stuff, sounds great - so, what‘s the problem?

ATMP Manufacturing

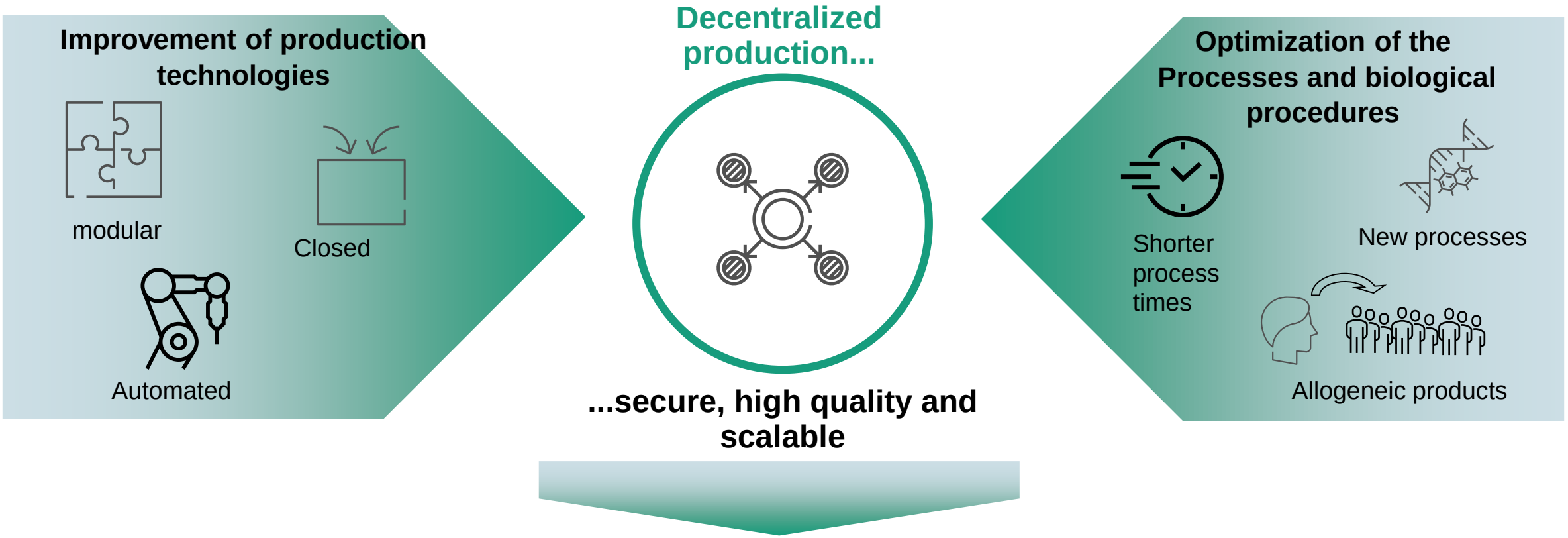
Transition of manufacturing setup is urgently required

- (Semi-) Manual, rigid and cost-intensive processes
- Stand-alone devices
- Non-digitalized process control
- At-line/offline control of biological parameters (e.g. identity)

- Fully automated and integrated
- Transferable and closed processes
- Modular and adaptable systems
- Complete inline/online analytics
- Self-optimizing and self-learning

Possible solutions for future cell and gene therapy needs

Adaptation of manufacturing processes for greater availability

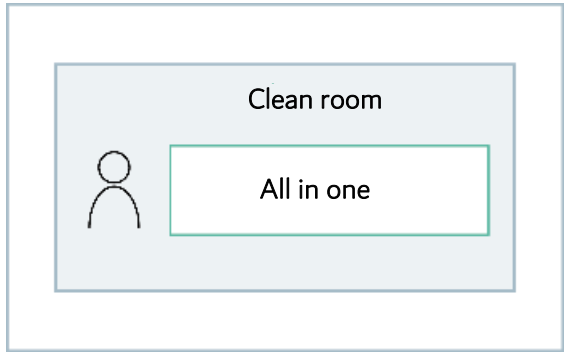


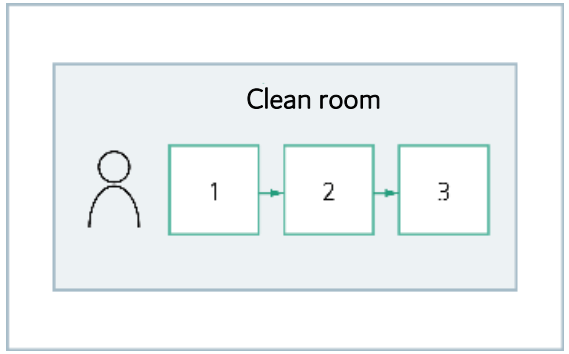
- **Production capacities can be flexibly and quickly adapted to demand and the latest findings**
- **Patients benefit faster from new therapies**

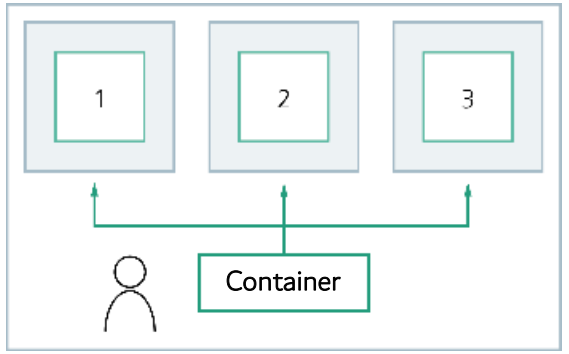
Automated ATMP production

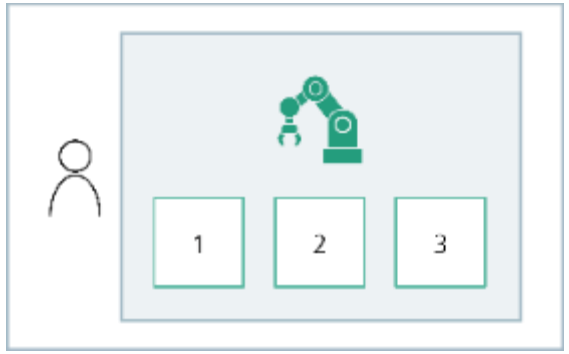
Different concepts address individual production strategies and products

All-in-one	Connection of individual stand-alone units	Modular system structure	Closed system concept



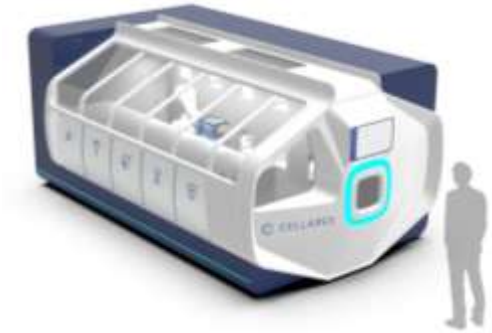






Lonza from pharma.lonza.com

Cytiva from cyivalifesciences.com



Cell Shuttle from cellares.com

ValueCell COMBI from https://www.comecer.com/atmp-cell-gene-therapy/

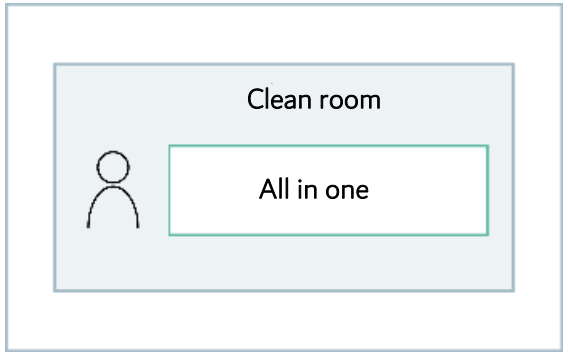
Transformation of ATMP production

From Industry 2.0 to 4.0

ATMP Production

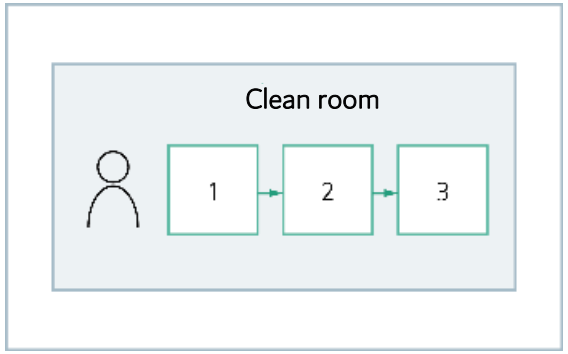
Different concepts address individual manufacturing strategies and products

All-in-one



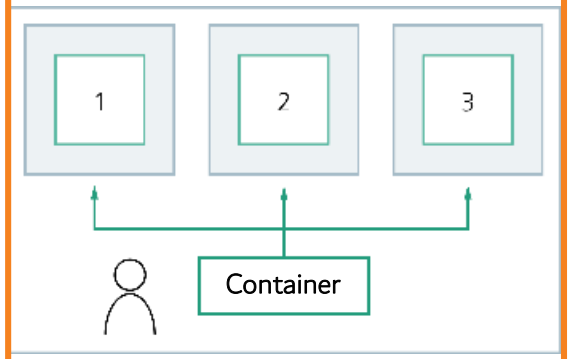
Lonza from pharma.lonza.com

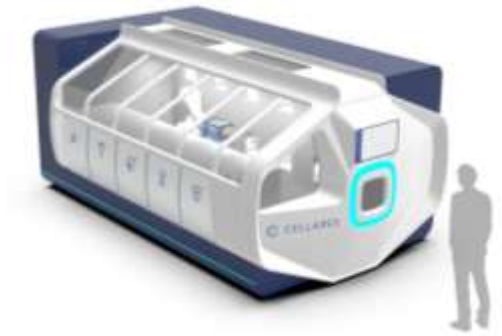
Connection of individual stand-alone units



Cytiva from cyivalifesciences.com

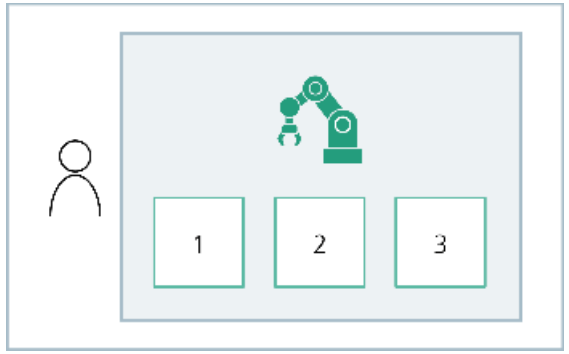
Modular system structure





Cell Shuttle from cellares.com

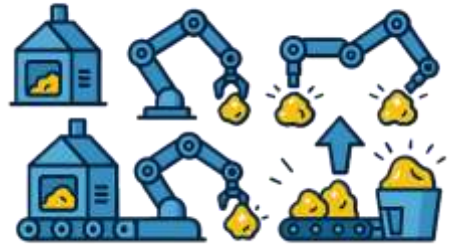
Closed system concept



Comecer https://www.comecer.com/atmp-cell-gene-therapy/

Scalable – from batch-of-one to real capacity

Make more therapies for more patients, without linearly multiplying cost or people.



- **Modular manufacturing** → small, standardized “Lego” units for parallel production (e.g., viral vector pods, cell processing modules).
- **Automation & robotics** → move from manual tasks to automated workflows (loading, feeding, sampling, QC).
- **Digital backbone** → MES + data integration for chain-of-identity, process control, and predictive maintenance.
- **Allogeneic platforms** → producing universal donor cell lines to replace patient-by-patient manufacture.

Key message*:* Scaling CGT means scaling *systems*, not people.

Flexible – technology that adapts, not locks you in

A future-proof setup that can handle new therapies without rebuilding everything.

- **Reconfigurable cleanrooms & modular facilities** (ballroom concepts).
- **Multi-product capability** → switching between CAR-T, TCR-T, AAV, LVV, LNP, etc.
- **Closed, automated platforms** → easy tech transfer, minimal revalidation.
- **Plug-and-play equipment integration** → data and control layers that allow system interoperability.

Key message*:* Tomorrow's facility must evolve as fast as the science it produces.

Our mission: We make ATMPs available for Everyone

- **Open**
  Flexible manufacturing for multiple therapeutic modalities and integration of best-in-class technologies

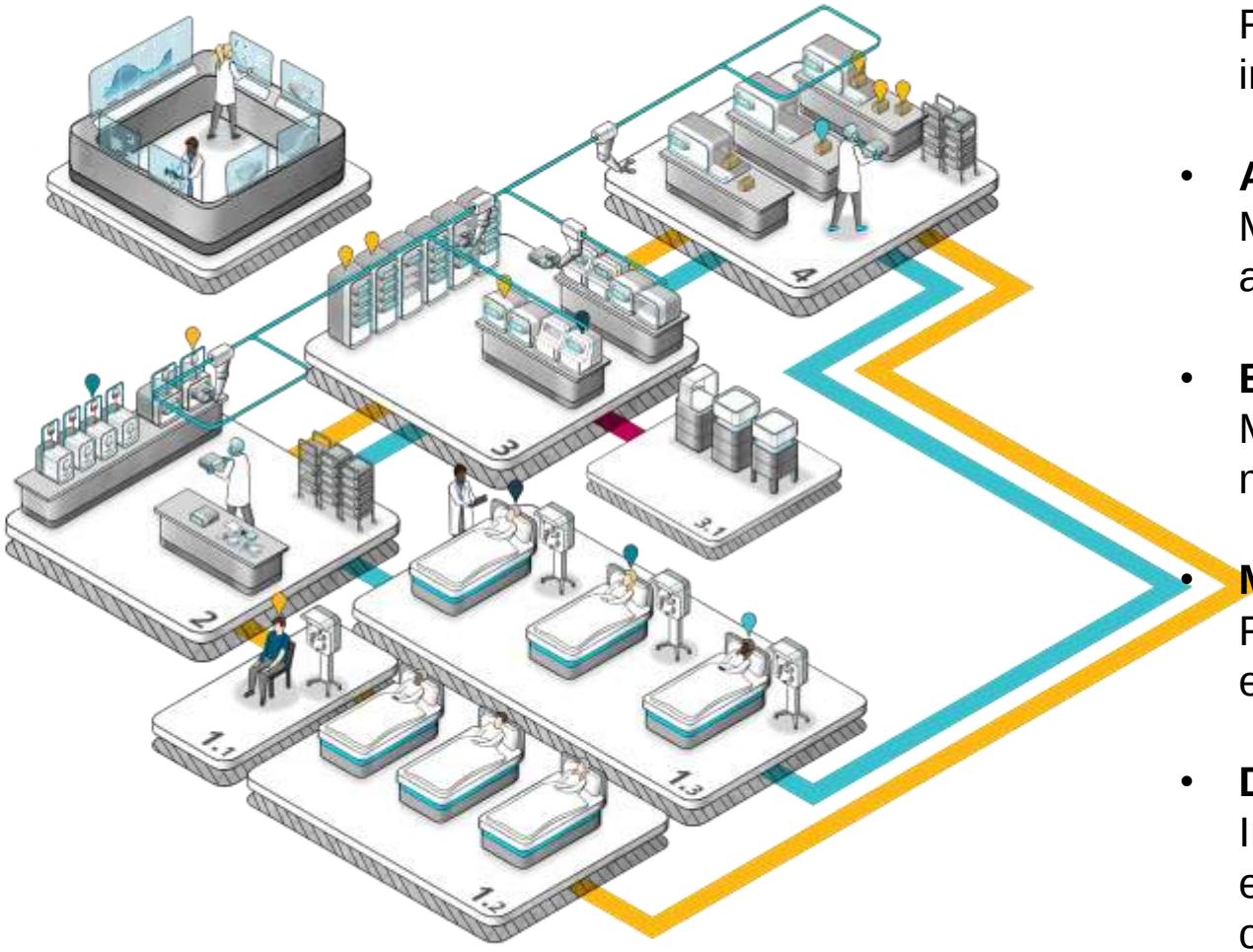
- **Adaptive**
  Matrix approach enables a scalable production environment adaptable to evolving needs

- **Efficient**
  Maximized utilization of resources and raw materials, while minimizing cleanroom footprint and personnel requirements

- **Modular & Closed**
  Fully modular GMP-in-a-box concept with closed processes to ensure sterility, compliance, and rapid reconfiguration

- **Digitalized**
  Integrated, centralized control and data management system enabling real-time monitoring, traceability, and predictive optimization

Our vision of production of cell and gene therapies



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Modular System Structure

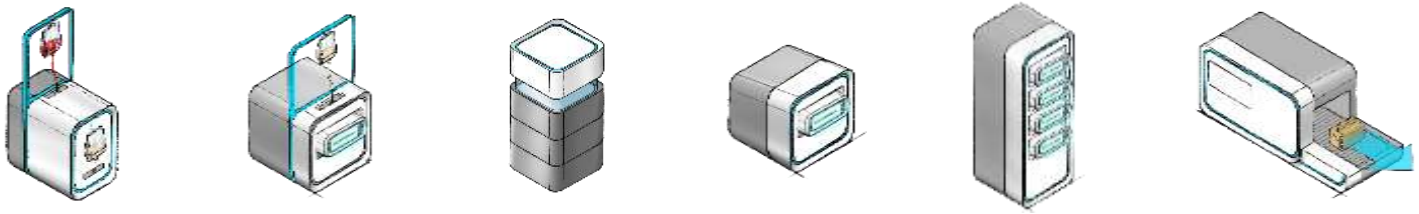
Automation to increase throughput while maintaining flexibility

Process

Step 1 — Step 2 — Step 3 — Step 4 — … — Step X — Step Y

Modules

A B C D E F …



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Products

Connection of individual modules

CAR-T-Cells: A B D …

CAR-NK-Cells: B C …

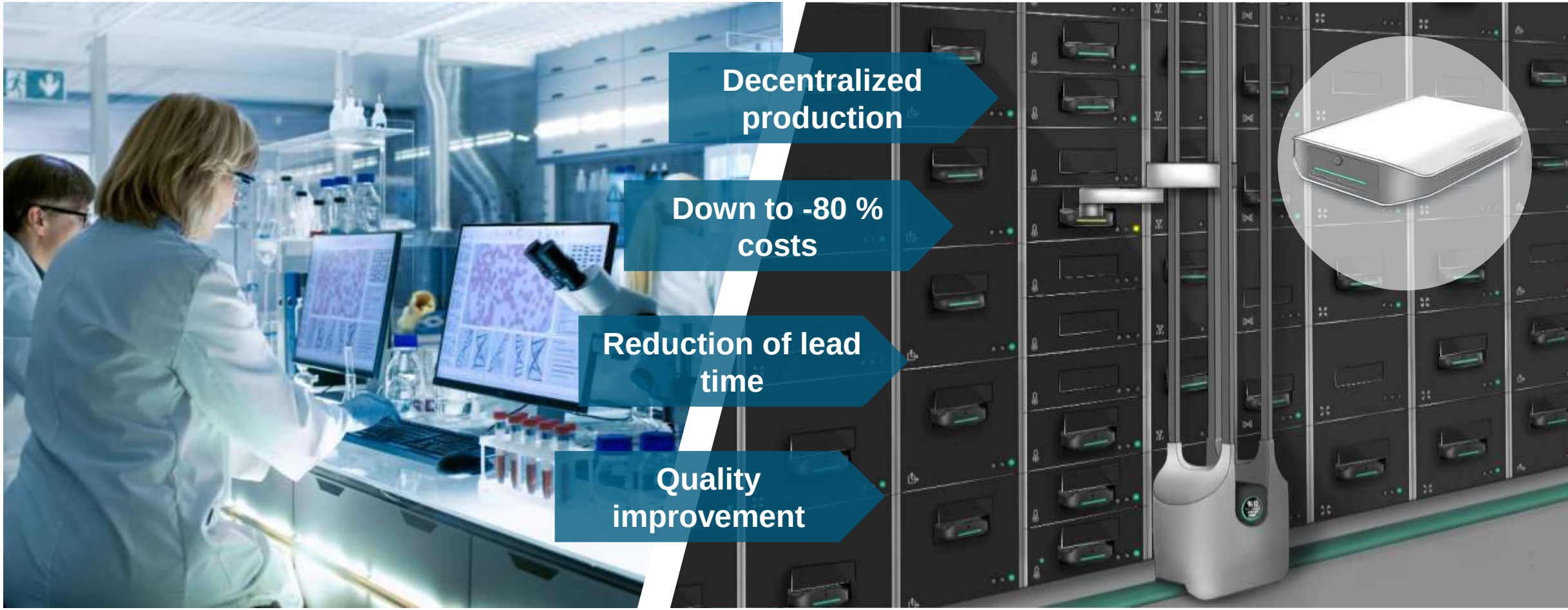
iPS-Cells: A B D … …

….

Goal: Flexible & scalable automation solutions

The future of medicine: Advanced Therapy Medicinal Products (ATMP)

Biointelligent production systems for manufacturing of cancer therapies



OUR Vision for the future: scalable, flexible, and cost-optimized

Standardized process formats for industrial automation

Cell culture chamber

- Contains cell material
- May come from different suppliers

Process Disc

- Mediates basic functionalities
- Modular design
- Adapter system
- Defined interfaces

Modul

- Takes over certain process steps
- Standardized interfaces (in particular software)
- Scalable

Factory

- Flexible scaling of individual subunits
- Fully automated handling of each module by robotic solutions

Enabling Technology

- Steril Re-Connectors
- Allowing “GMP in a Box”

Contact

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