
AVEVAWORLD

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APRIL 9, 2025

Cytiva & SyVento:
Enhancing Biomanufacturing Efficiency with FlexFactory™ Historian

SESS-146

Tim Wortley – Cytiva

AVEVA

Enhancing Biomanufacturing Efficiency with FlexFactory™ Historian

A Case Study from SyVento Biotech

Tim Wortley, Cytiva

Who are we

cytiva

syvento | BIO TECH

Vision

Our vision is a world in which access to life-changing therapies transforms human health.

Mission

Our mission is to advance and accelerate therapeutics.

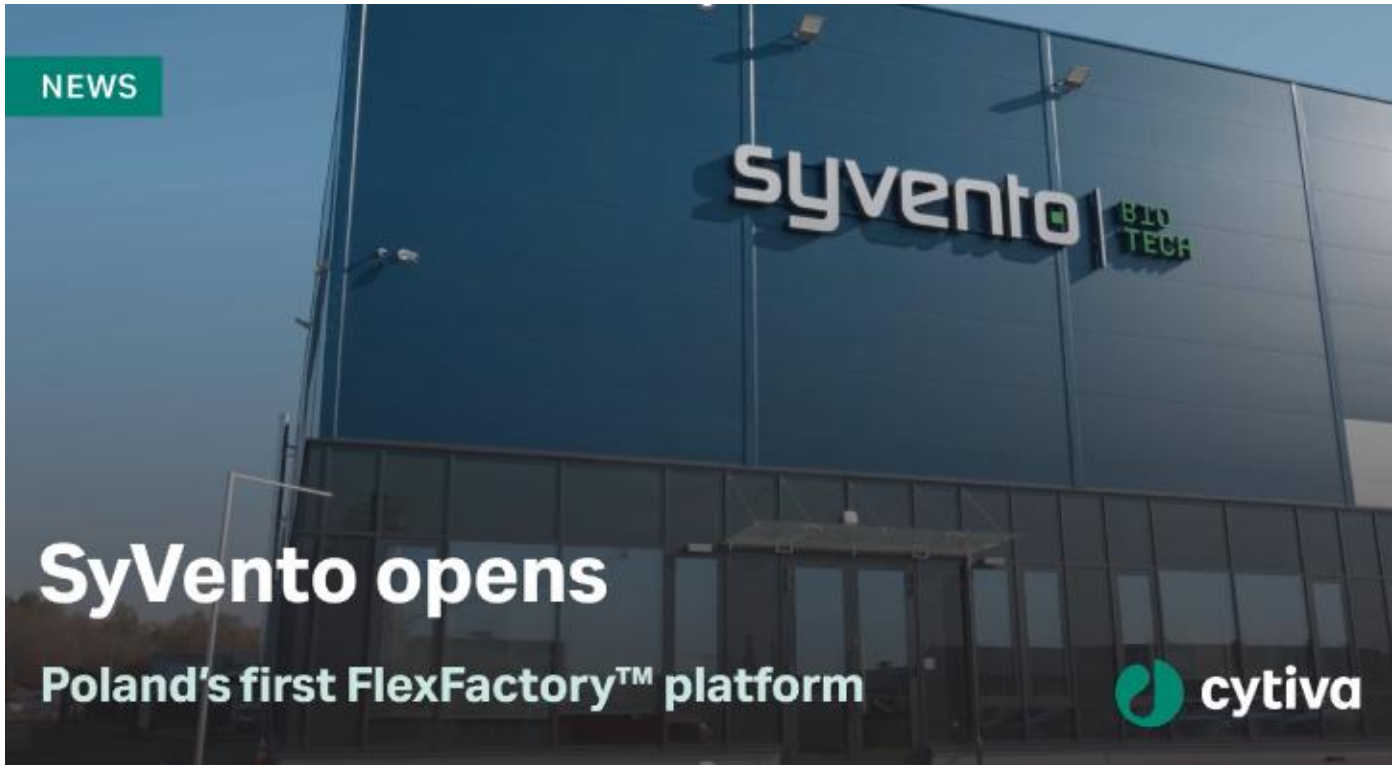
Why it matters
… Let’s meet Emily


FOCUS FORWARD
SHORT FILMS BIG IDEAS

Introduction

Cytiva's FlexFactory™ historian biomanufacturing solution built on top of AVEVA™ PI System transforms mRNA manufacturing at Syvento™ Biotech in Poland.

A discussion on the challenges in mRNA manufacturing and the transformative improvement on efficiency, costs and regulatory compliance from data management



The regulatory landscape and market trends

Why comply?

- Reputation, costs (fines), stay in business, access to global markets, directors & employees stay out of jail…
- Well recognized guidance documents on how to deliver safe and effective drugs. Similar standards apply globally.

How to comply (data)

- "If it didn't get documented (reviewed, approved, signed), it didn't happen"
- The (process, instrument, analytical, manufacturing) **data** is sacrosanct, must be original and proven tamperproof.

Complex Trends

- "Zoo" of biotherapeutics (mAbs, mRNA, AAV, pDNA, siRNA, EBT)
- Faster, cheaper, simpler (Viz SARS-COV2 vaccine in ~11months[2], typically many years[1,3])

1. The development of COVID-19 vaccines in the United States: Why and how so fast? – PMC
2. Emergency authorization Dec 2020, Approval Dec 2021 COMIRNATY | FDA
3. Merck's Gardasil was in development at U-Queensland in 1991 to approval in 2014 (23 years), Gardasil -Wikipedia

Bioprocessing is challenged with inefficiency

Over 300 error-prone manual interventions in average 2000L mAb SU process

More than 80% of company time is spent collecting and cleaning data sets[1]

10–20% of the time biopharma data can't be accessed[2]

Success of initial production run can be as low as 47%[3]

Biopharma scores lower than other industries in adoption of automation[4]

High batch failure rates and manufacturing deviations due to human error[5]

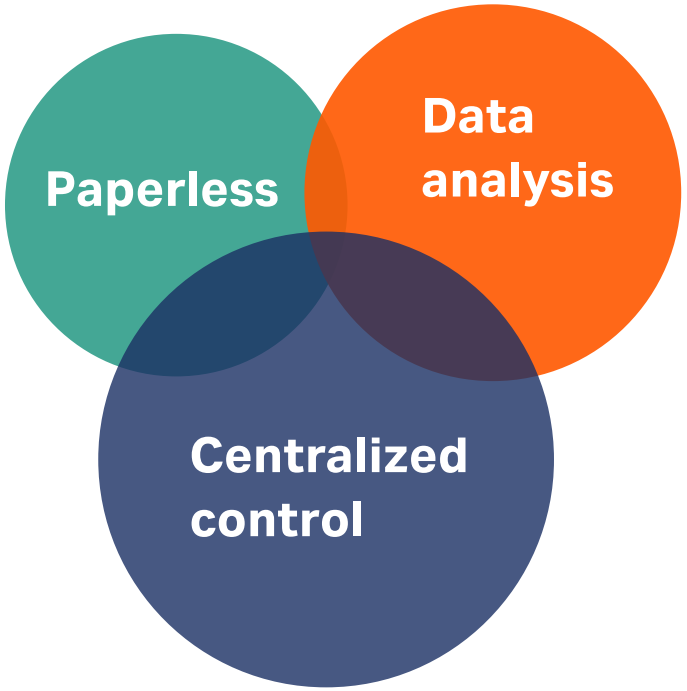
1 https://www.outsourcing-pharma.com/Article/2019/01/09/AI-and-improvements-to-pharma-manufacturing#
2 https://www.idbs.com/wp-content/uploads/2020/12/IDBS_Agility_Article_Sept_2020_V4.pdf
3 https://www.biopharminternational.com/view/review-exception-connecting-dots-faster-batch-release
4 https://www.mckinsey.com/industries/pharmaceuticals-and-medical-products/our-insights/automation-and-the-future-of-work-in-the-us-biopharma-industry
5 Bioplan Associates, "17th Annual Report and Survey of Biopharmaceutical Manufacturing Capacity and Production," April 2020: https://bioplanassociates.com/wp-content/uploads/2020/06/17th-Annual-Biomfg-Report_TABLE-OF-CONTENTS-2020.pdf

Automation and control can lead to large efficiency gains

Up to 75%
reduction in paper handling and storage[1]

Up to 20%
increase in employee efficiency[3]

Up to 38%
reduction in labor[5]



Up to 85%
reduction in batch review time[2]

Up to 79%
reduction in failed batches[4]

Up to 67%
reduction in deviations[5]

Enable electronic data capture, storage, access, and analysis

1, 2. http://www.sysiss.com/_fileupload/sysiss_documents/Systematic-Takeda%20EBRS%20case%20studyV1-600dpi.pdf
3. https://www.mckinsey.com/industries/pharmaceuticals-and-medical-products/our-insights/automation-and-the-future-of-work-in-the-us-biopharma-industry#
4. Bioplan Associates, "17th Annual Report and Survey of Biopharmaceutical Manufacturing Capacity and Production," April 2020: https://bioplanassociates.com/wp-content/uploads/2020/06/17th-Annual-Biomfg-Report_TABLE-OF-CONTENTS-2020.pdf
5. Cytiva – Biopharm Services study using BioSolve™, unpublished, March 2022

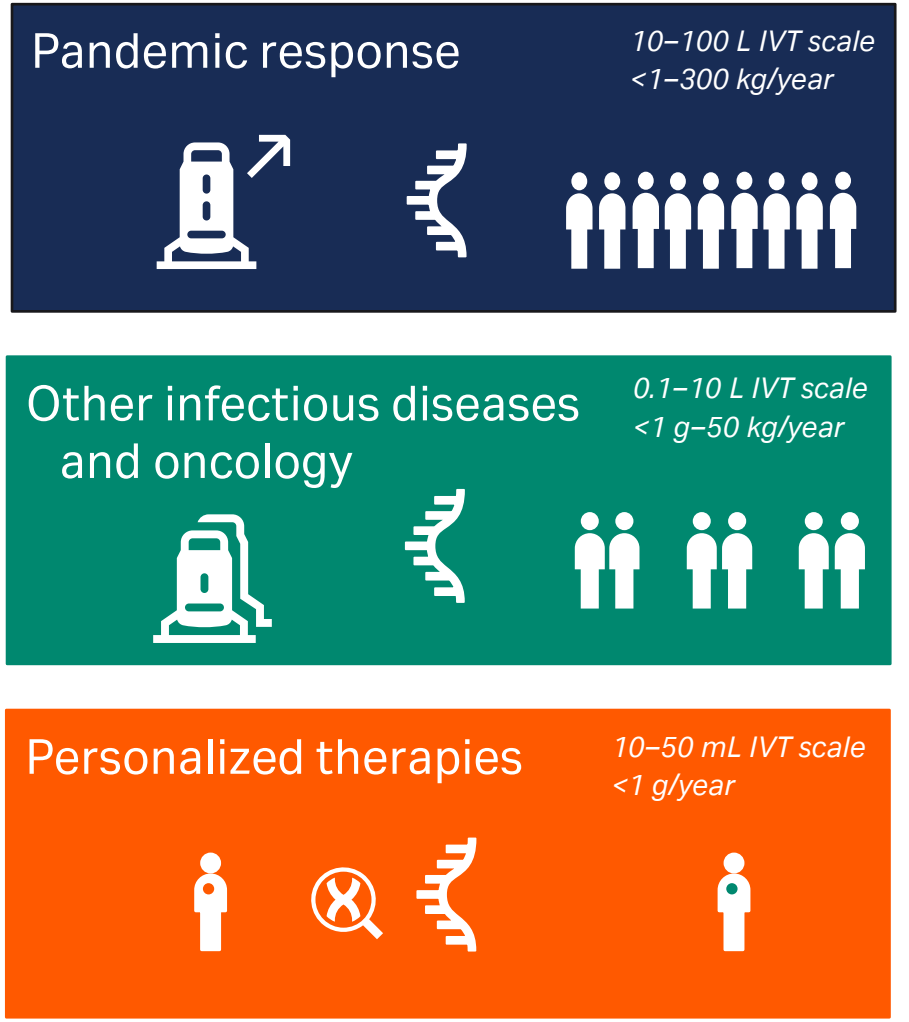
mRNA therapeutics

Synthetic messager RNA molecules are introduced and temporarily (hours-days) hijack our cells function to build the programmed target[1] to extend our immune system e.g.

- Infectious diseases (e.g. MERS-CoV, SARS-CoV2)
- Anti-cancer molecules / Oncology vaccines
- Cell & Gene therapties (CRISPR, CAR-T)
- Other vaccines (Rabies, HIV, Nipah etc)

Advantages

- **Rapid Development**: mRNA-based treatments can be designed and produced quickly, enabling swift responses to emerging health threats, such as pandemics[2]
- **Efficient Production**: mRNA therapeutics are produced in cell-free systems, which simplifies manufacturing and reduces resource intensity compared to traditional protein-based biologics[3]
- **Versatility**: mRNA can encode a wide range of proteins, making it adaptable for various applications, including vaccines, cancer immunotherapy, and protein replacement therapies[4]



1. ClinicalTrials.gov : mRNA search results
2. The rise of mRNA therapeutic vaccines - RSC Pharmaceutics (RSC Publishing) DOI:10.1039/D4PM00309H
3. https://jbiomedsci.biomedcentral.com/articles/10.1186/s12929-023-00977-5
4. Current landscape of mRNA technologies and delivery systems for new modality therapeutics | Journal of Biomedical Science | Full Text

Future proofing global manufacturing
flexible solutions required in-region-for-region

- mRNA technologies are relatively new (BioNTech founded 2008)
- Obscure (lost in Zoo?) until Covid
- Pandemic demonstrated need for in-region-for-region vaccine manufacturing
- mRNA vaccines can be mass-produced in a trailer.

Considerations

- Different process needs with different mRNA types
- No (new) platform process
- Rapidly evolving technology
- Unique problems need novel solutions (e.g. lipid nanoparticles)
- Few approved therapies
- Capital and operating costs critical.
- Substantial differences between pandemic response versus personalized therapeutics

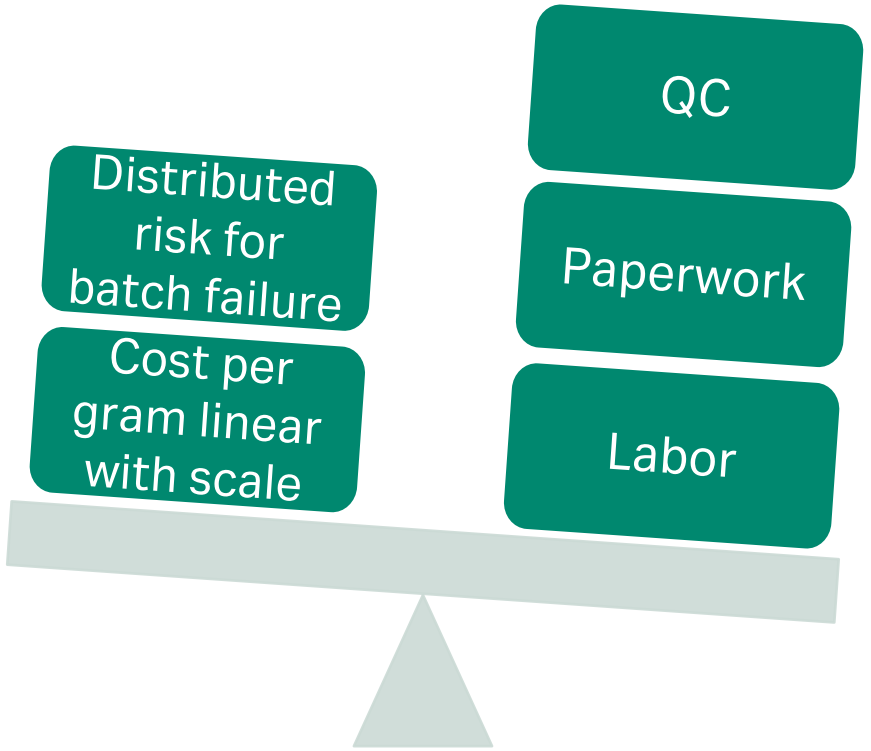
mRNA process – unique challenges

Process intensification

- 1-2 day process, many small batches (typical mAB is 15-30day cycle)
- Documentation, batch release (300 batches/year versus 30)
- High yield processes – 1L reactor → 4g mRNA[2] → 100,000 x 30µg dose[1]

Process needs

- Process, consumables, reagents, data usage 10-100x faster than conventional
- Paper processes (and staff) can no longer keep up, especially in a high stress (pandemic?) environment
- 2 day manufacturing process waiting for 2 month batch release not acceptable when patients are dying.
- Release by Exception



1. 2024-2025 Formula Pfizer-BioNTech COVID-19 Vaccine At A Glance
2. mrna production using the readytoprocess wave 25 rocker | Cytiva

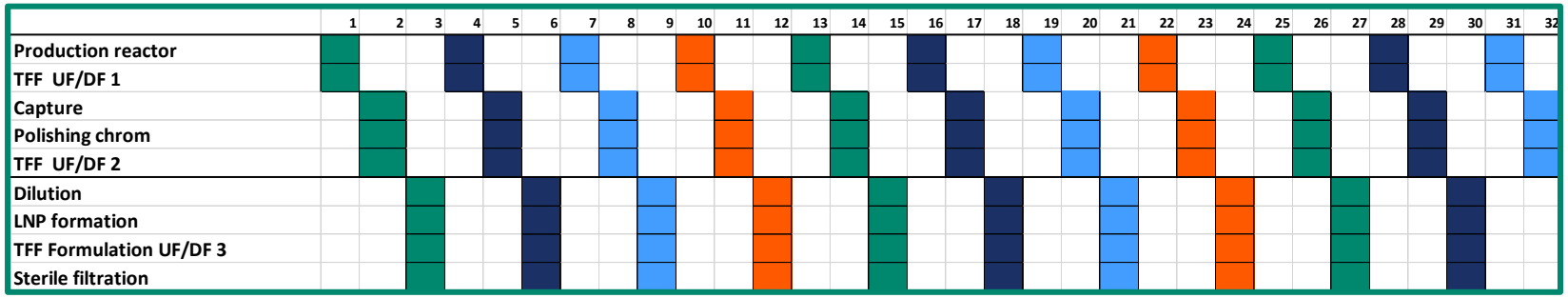
Intensified and complex manufacturing

The mRNA future manufacturing will have to handle multiple products and multivalent products.

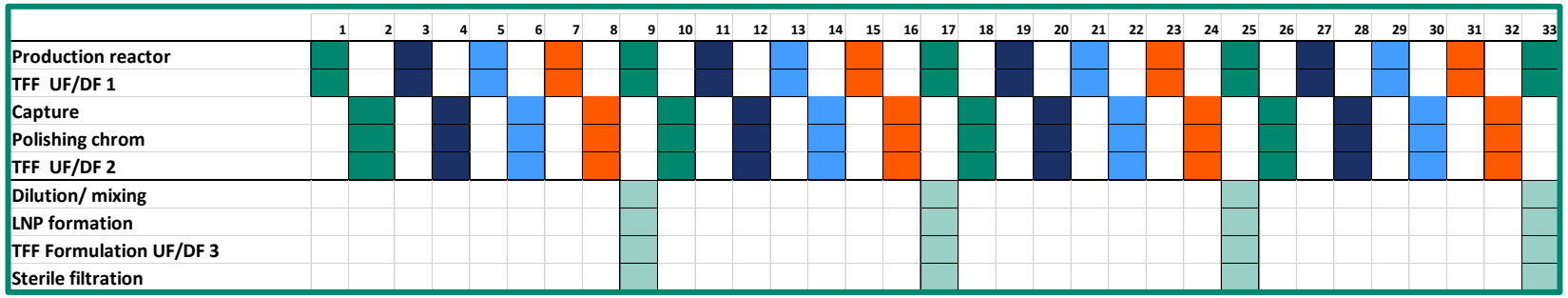
Challenge:

- short process and intensified manufacturing
- line clearance and batch-to-batch separation
- maximize facility utilization

mRNA multiproduct scheduling example



mRNA multivalent product scheduling example



LNP= Lipid nanoparticle

How historian technologies and pre-configured, pre-verified solutions improve manufacturing outcomes

Standard Cytiva and third party equipment

- Custom designed equipment is typical in industry, and not necessary
- Modern equipment have standard interfaces that are accommodated by PI Connectors and Interfaces2

Pre-design, pre-verified and documented solution

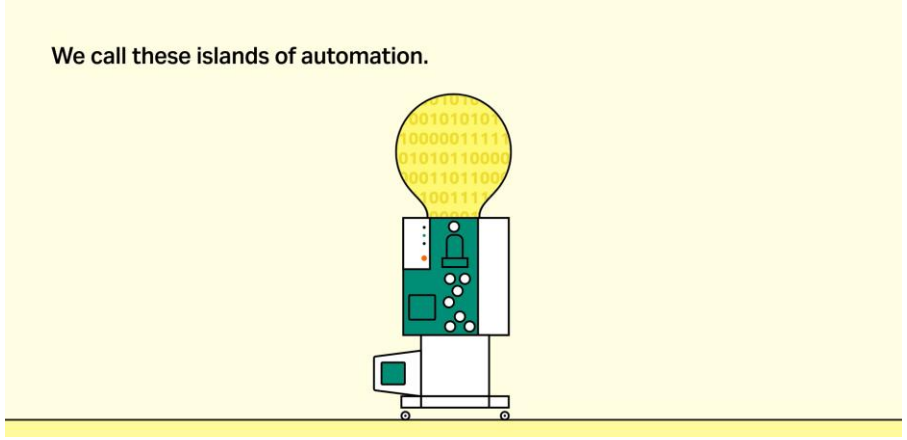
- Client receives an integrated solution from a single vendor that can rapidly configure, deploy and verify an industry standard expandable and flexible solution

Standard, templatized and automated AVEVA PI System build.

- PI System support can be deployed for standard equipment in hours, obviating need fo typical design-specification-build-test-document life cycle
- Standard PI System allows customers and their integrators to modify, extend and expand the deployed system.

Comprehensive CQV[1] documentation, protocols and support

- Working with standard equipment and software configuration optimizes the CQV process.
- Typically double+ the automation cost -- reduces significantly

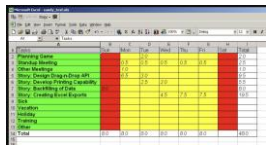


Cytiva

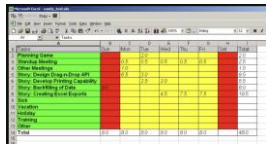
1. Explaining CQV, C&Q, and Commissioning and Qualification | Kneat

Typical FlexFactory historian deliverables

Specifications
- *General (Hardware)*
- *Functional*



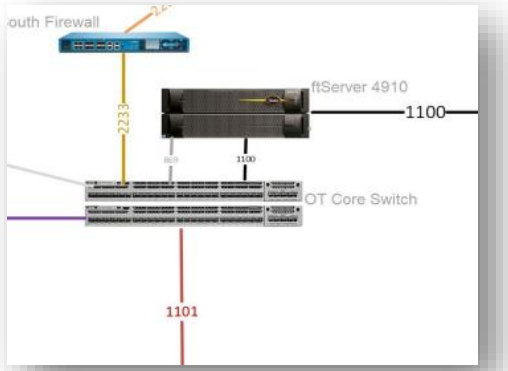
Configuration Specification (Template)



Configuration Specification
TOP documentation
Semi-Auto generated
- Tag & AF lists
- Test results docs
- Configuration docs

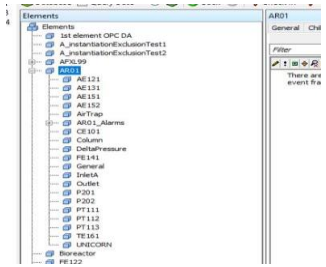
Automatically generated

Infrastructure Build

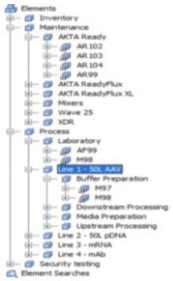


PI Vision Displays

Standard Build/ Work instructions
Process Euipment Config
PI System configuration
- Tags
- Audit trail interface
- Asset Framework



Tags, connectors and Interfaces



PIAF

Turn-over-Package (Commissioning & Qualification documentation)

Conclusion

FlexFactory historian powered by AVEVA PI System has delivered world class mRNA manufacturing capacity to Poland

- Syvento can deliver life saving therapeutics of a wide range of types, ensuring advanced treatments reach patients who need them.
- Improve access to personalized medicines and mRNA therapies across Europe to meet future CAR-T, oncology and pandemic vaccine needs.
- Enable creation of a new mRNA center of excellence, supporting global therapeutic drug research, development and manufacturing.

The FlexFactory provides a future-proofed and digitally enabled manufacturing platform

- Meet future regulators expectations for data integrity and analysis.
- Provide frictionless movement of data between manufactures, client biopharmaceuticals and regulators
- Provide for more rapid and smarter drug batch release, improve therapeutic drug development time to market.

For local office contact information, visit cytiva.com/contact

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