Living the digital transformation in a biotech company

DataHow Symposium 2025
26.06.2025

Dr. Dietmar Andreas Lang

Forward-Looking Statements

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Forward-looking statements are subject to many risks, uncertainties and other variable circumstances, including negative worldwide economic conditions and ongoing instability and volatility in the worldwide financial markets, ability to obtain funding, ability to conduct current and future preclinical studies and clinical trials, the timing, expense and uncertainty of regulatory approval, reliance on third parties and collaboration partners, ability to commercialize products, ability to manufacture any products, possible changes in current and proposed legislation, regulations and governmental policies, pressures from increasing competition and consolidation in the company's industry, ability to manage growth, reliance on key personnel, reliance on intellectual property protection, ability to provide for patient safety, and fluctuations of operating results due to the effect of exchange rates or other factors. Such risks and uncertainties may cause the statements to be inaccurate and readers are cautioned not to place undue reliance on such statements. Many of these risks are outside of the company's control and could cause its actual results to differ materially from those it thought would occur. The forward-looking statements included in this presentation are made only as of the date hereof. The company does not undertake, and specifically declines, any obligation to update any such statements or to publicly announce the results of any revisions to any such statements to reflect future events or developments, except as required by law.

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Presenter Introduction

Dr. Dietmar Andreas Lang, MPharmMed
Senior Director Platform Development PM

- Structural biologist / biotechnologist by training
- > 30 years of experience in biotechnological R&D
- ~ 24 years working at international organization & companies
- Leading multiple projects in research, development & manufacturing of **(i)** biopharmaceuticals (biologics), **(ii)** medical devices/companion diagnostics & **(III)** consumer goods
- Since 10/2023 at Curevac

AGENDA

- Introduction to the company CureVac
- The digital use case
- Summary & Outlook

CureVac at a Glance

Pioneers in Medical mRNA Applications

Founded in
2000

Headquartered in
Tübingen,
Germany

Manufacturing Expertise

Scalable Solutions

Inhouse GMP manufacturing complements end-to-end mRNA capabilities

Deep Clinical Pipeline

Oncology — Infectious Diseases — Molecular Therapy

The RNA Printer®

Rapid and highly automated

Financing Business Transformation

€438.3 m
cash position*

CVAC
Nasdaq Listed

Nasdaq
Biotech
Index

Strategic partnerships

MD Anderson

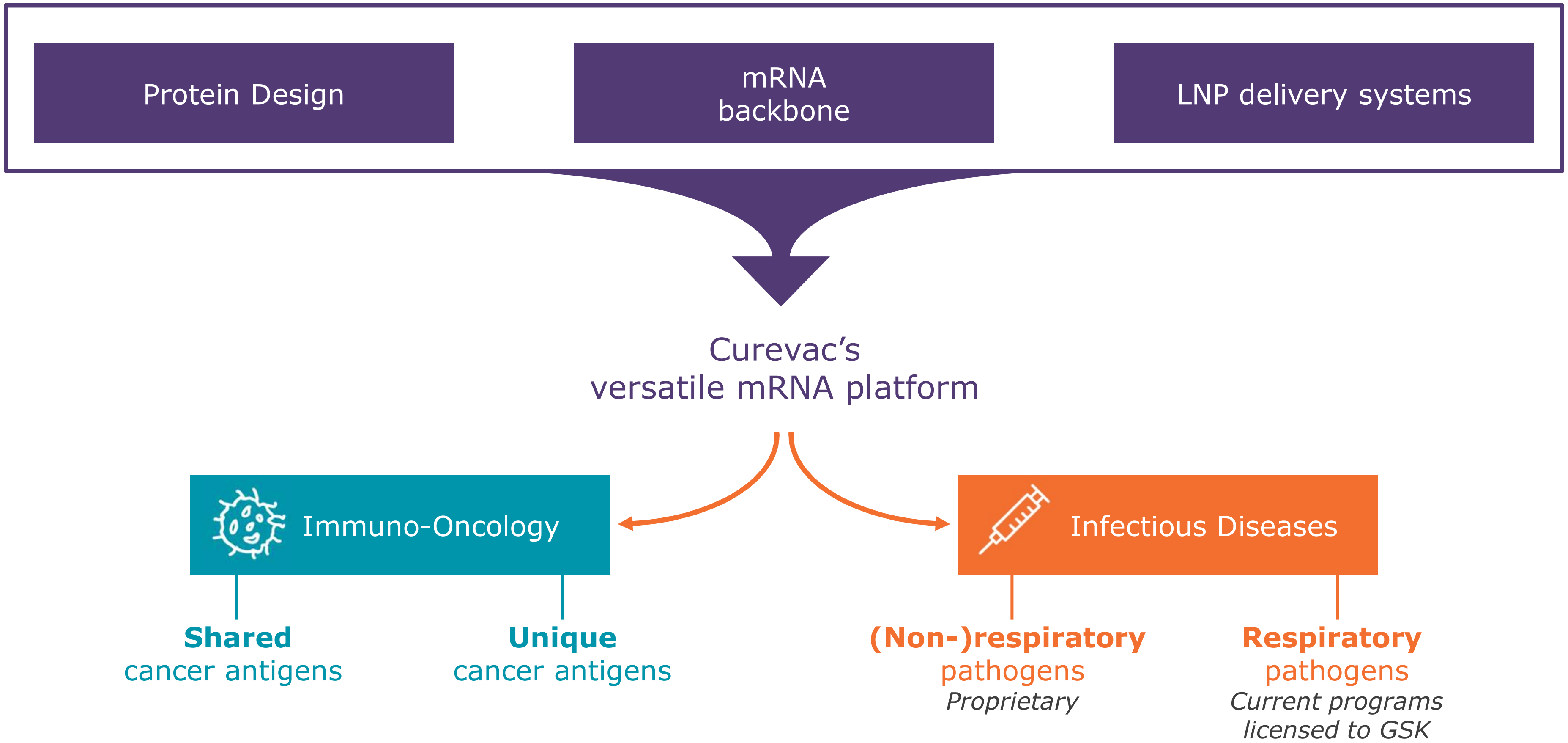
CRISPR Therapeutics

myNEO Therapeutics

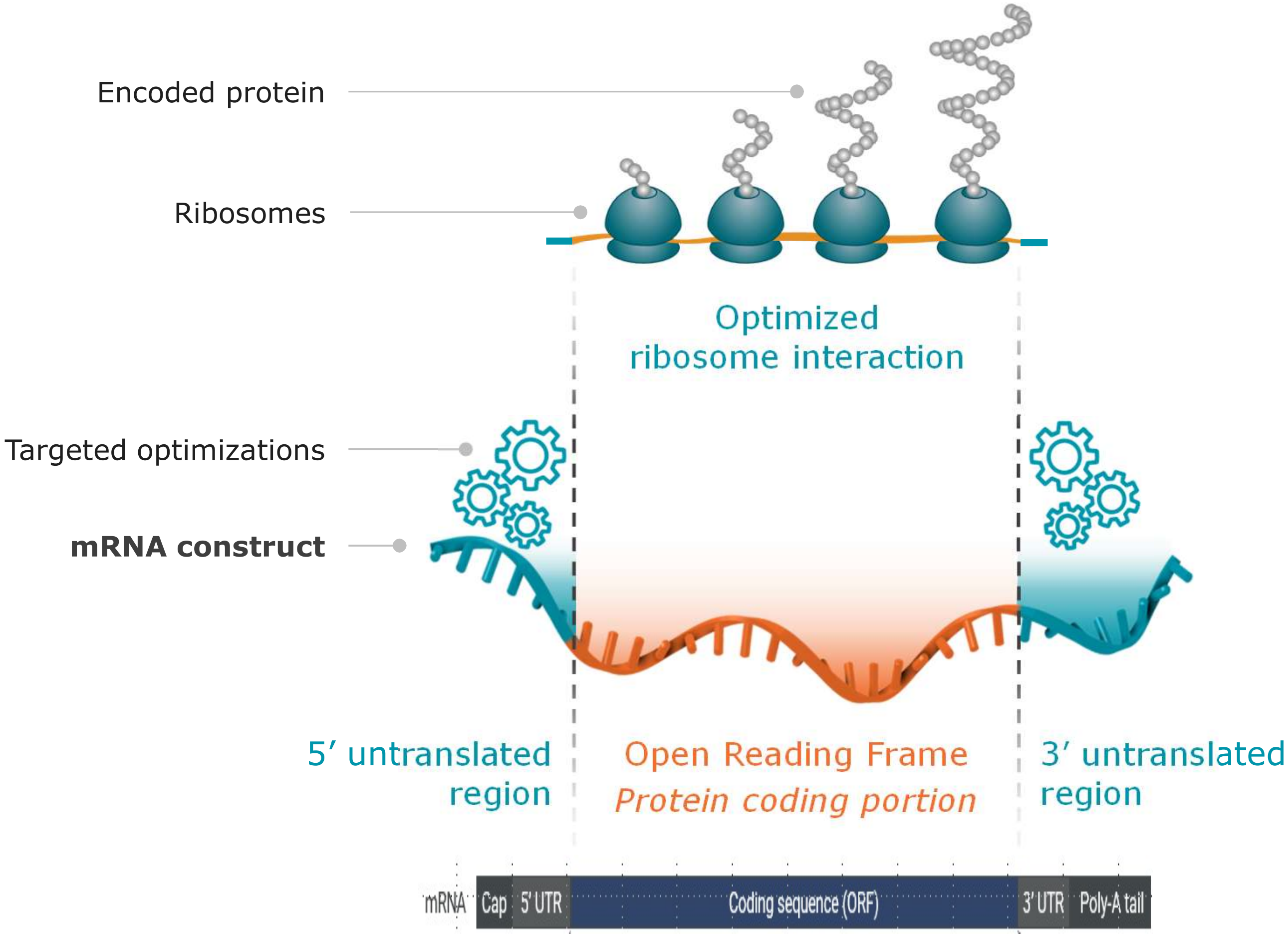
- Operational expertise
- Development support
- Commercial execution power

*As of March 31, 2025

mRNA technology Driving Our Pipeline Strategy



Optimizing mRNA for Broad Range of Vaccine Applications



- Optimizing untranslated regions based on **potent, tissue-specific** regulatory elements
- Optimizations allow for increased **translation efficiency** and **immunogenicity**
- Maximizing ribosome interaction for increased protein expression enables **low dose activity**

mRNA platform is composed of 3 components:

mRNA technology
- Sequence-based stability
- Coding sequence optimisation
- UTR optimisation
- RNA modality

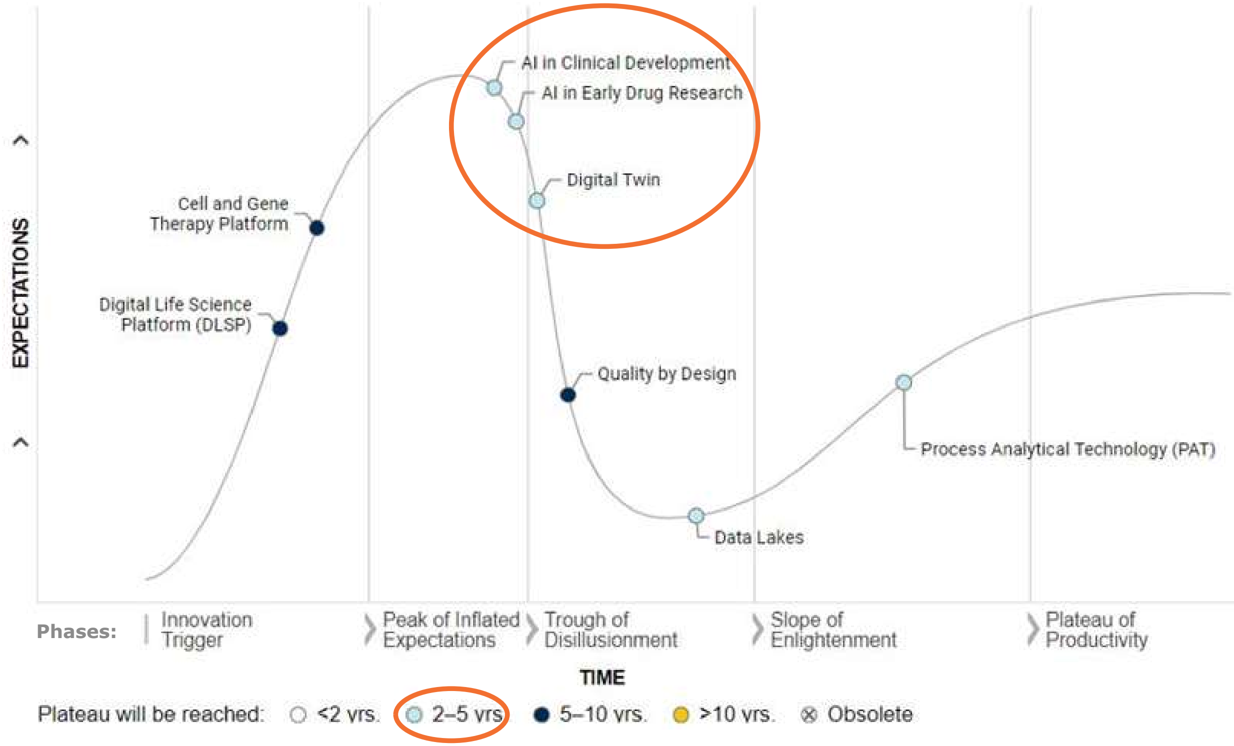
Optimizations allow for increased translation efficiency and immunogenicity

Manufacturing & Process technology
- DNA process
- mRNA process
- Formulation process (e.g. LNP)

Delivery technology
- Novel ionizable lipids — driving the efficacy (and tolerability)
- Novel helper lipids — enabling tissue and cell-specific delivery
- Novel non-PEG lipids — stabilizes the particle against aggregation
- Novel immune cell targeted lipids

Analytical methods

Life Science “Technology” Hype Cycle

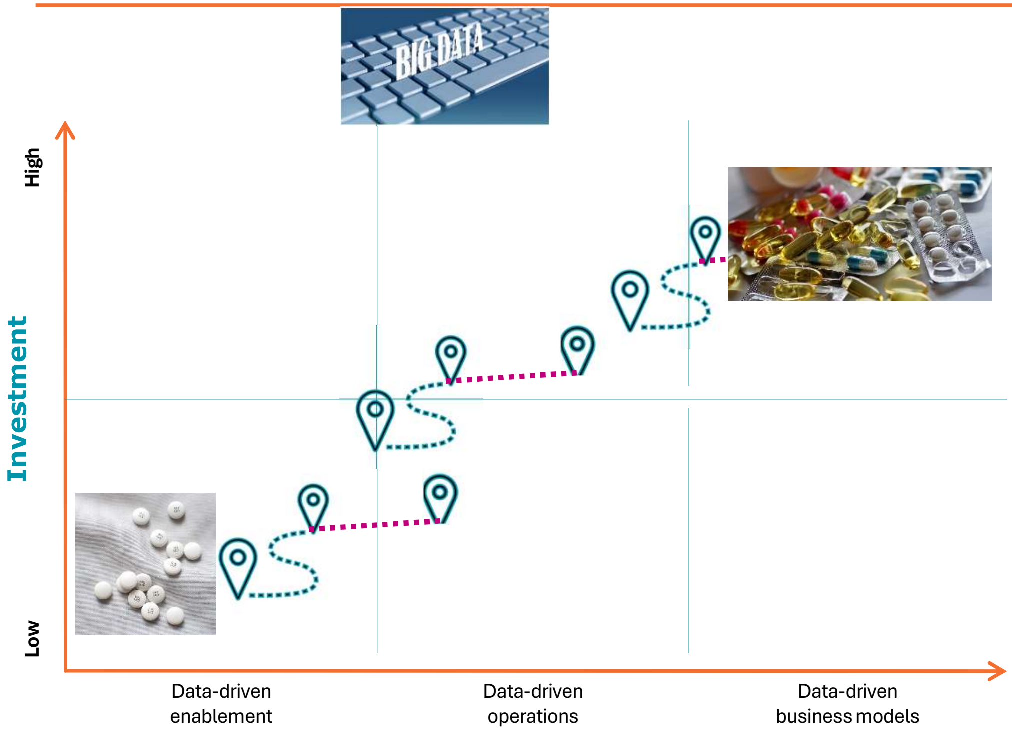


www.gartner.com,
Status 07/2021

The graphic shows the expectations for given technologies to mature (5 phases) over time from innovation idea to daily life productivity

Pharma companies are re-inventing their business based on data and AI, …

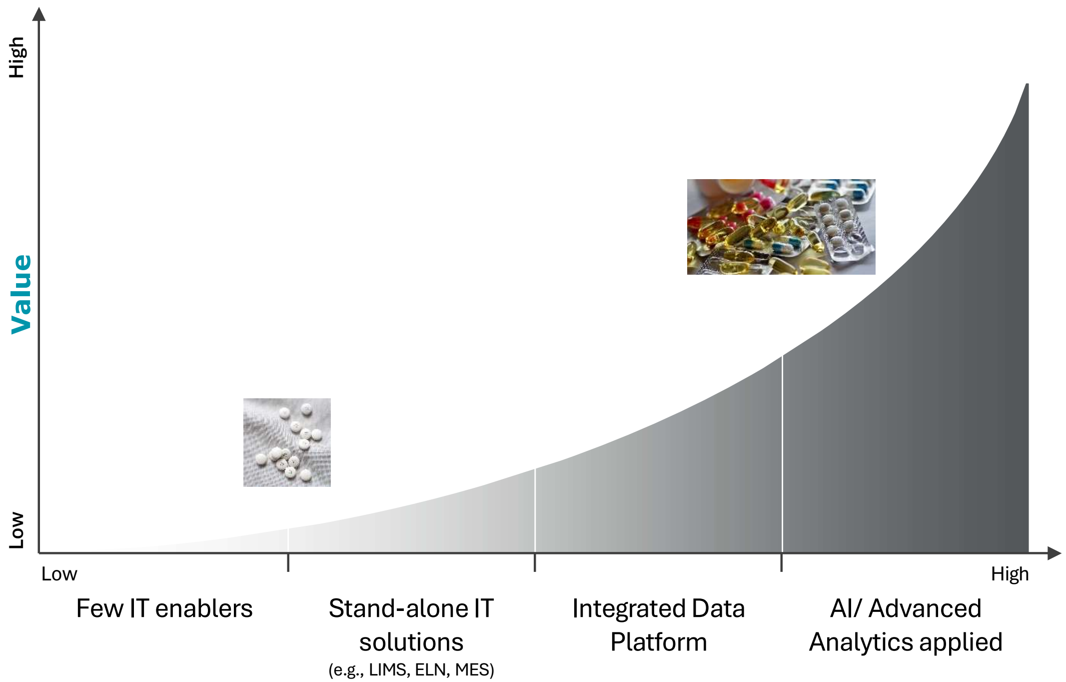
The data-driven journey



General considerations - Biotech

- Speed up development to get to market quickly and to **be prepared to scale up later**
- *Choose targeted areas of investments given no market revenue is generated*
- **Leverage the tech ecosystem to gain momentum in digital & data journey**

Digital & Data Maturity Curve



Considerations

- Technical process enablement is key to accelerate data value by applying AI/ML and other digital enablers
- **An integrated data platform** fueling use cases **in combination with data governance and standardized data models** is essential to driving efficiency and business growth

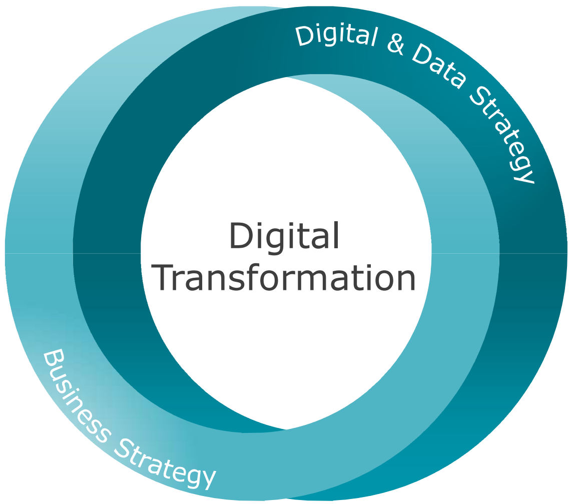
Digital & Data (D&D) Strategy Objectives

Our Digital & Data (D&D) Strategy is key to achieving our business goals by strengthening our IT foundation, sparking data-driven innovation, and **fostering a culture that sees data as a vital, cross-departmental asset**

OBJECTIVE

Business Imperatives

1. Strengthen our R&D Pipeline
2. Innovate our mRNA Platform
3. Ensure Financial Sustainability
4. Increase Manufacturing Flexibility and Efficiency
5. Enhance organizational efficiency and drive culture change

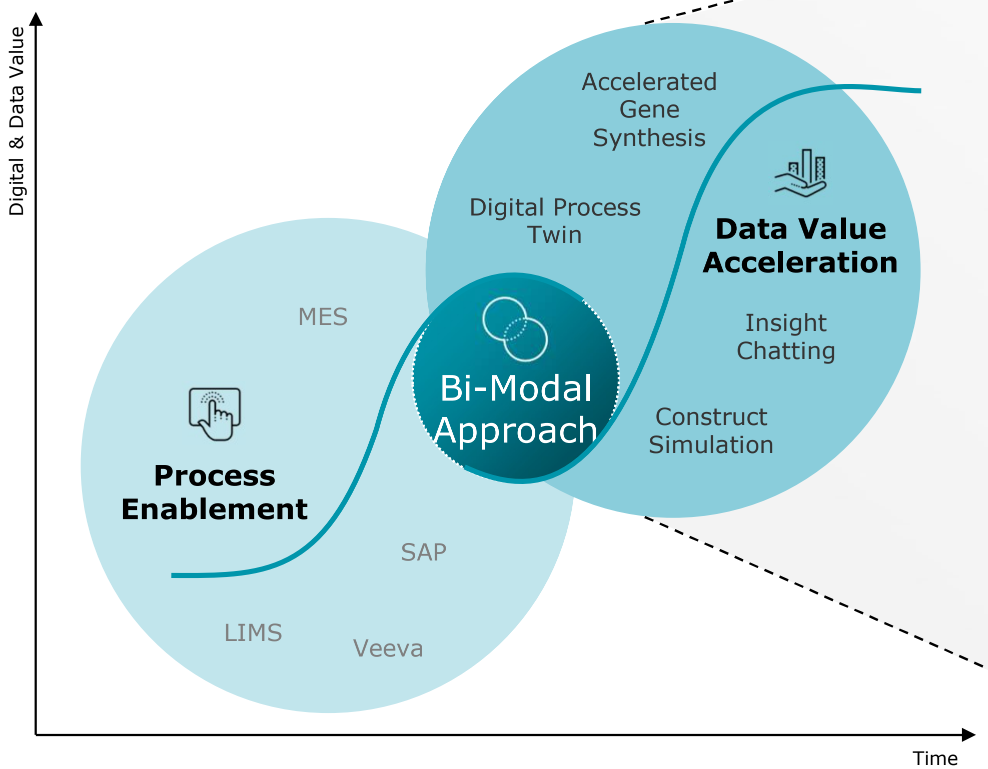


D&D Vision Imperatives

- Digitize processes and drive data value acceleration at the same time
- Focus available resources on internal game-changing data & AI readiness & value
- Follow CureVac's design principles while operationalizing D&D capabilities

Process Enablement and Data Value Acceleration are mutually dependent

Digital & Data Scope



Building blocks for our success in Data Value Acceleration

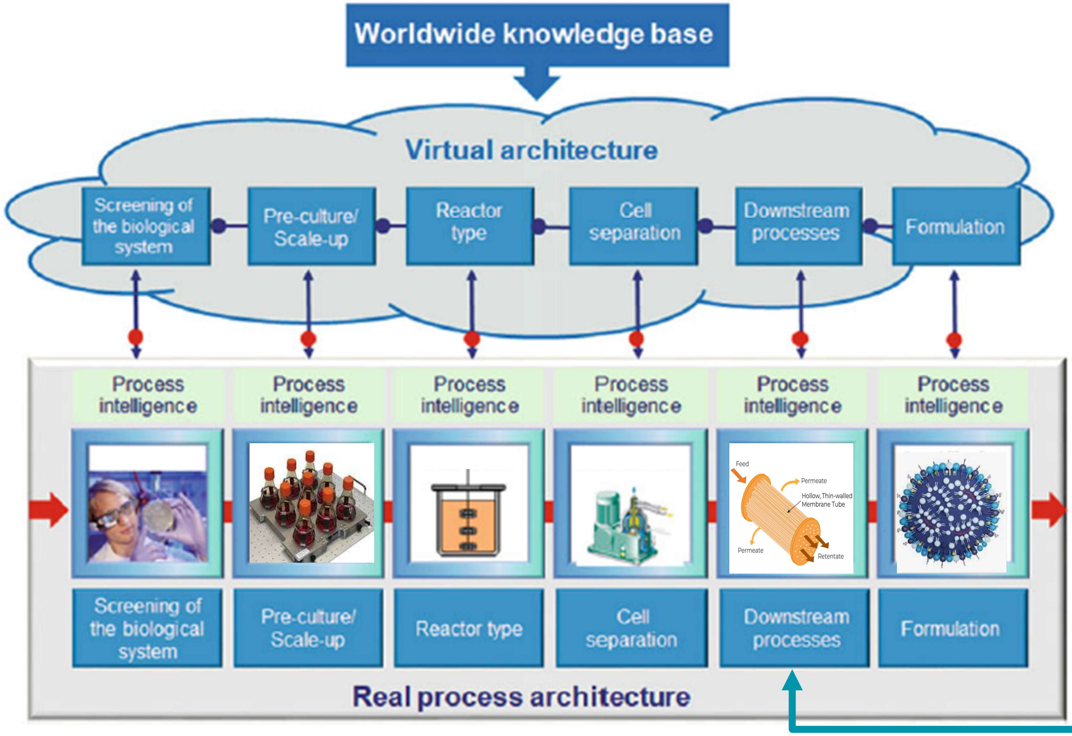
Priority Solutions and D&D Services
Create focus on value drivers and services

Foundations
Implement organizational and technical foundations to deliver D&D

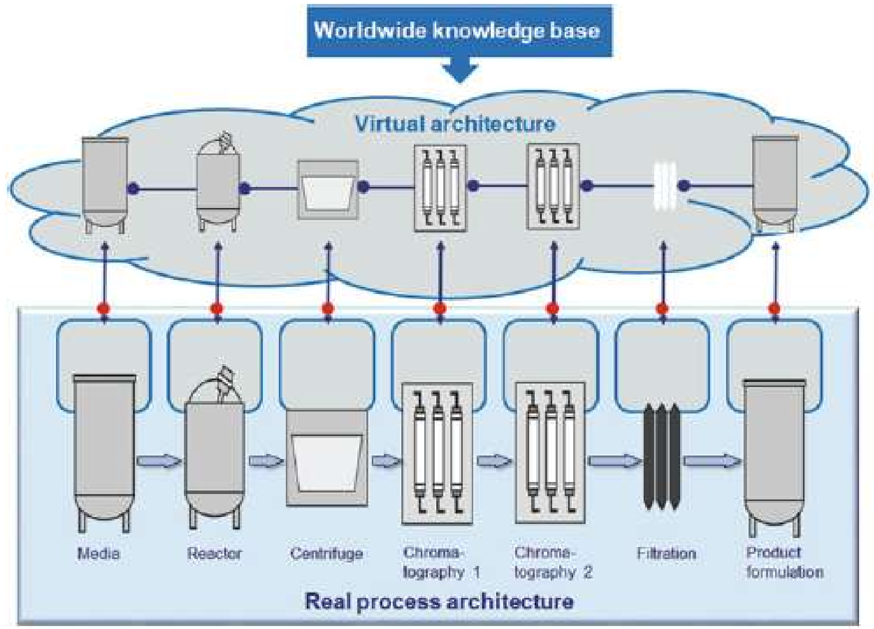
Governance & Discipline
"Draw the line in the sand" & ensure upskilling

Bioprocess Intelligence

Interaction real vs virtual process architecture;
Bioprocess is divided into 6 main modules



Control of biotechnological process
via digital twin virtual architecture



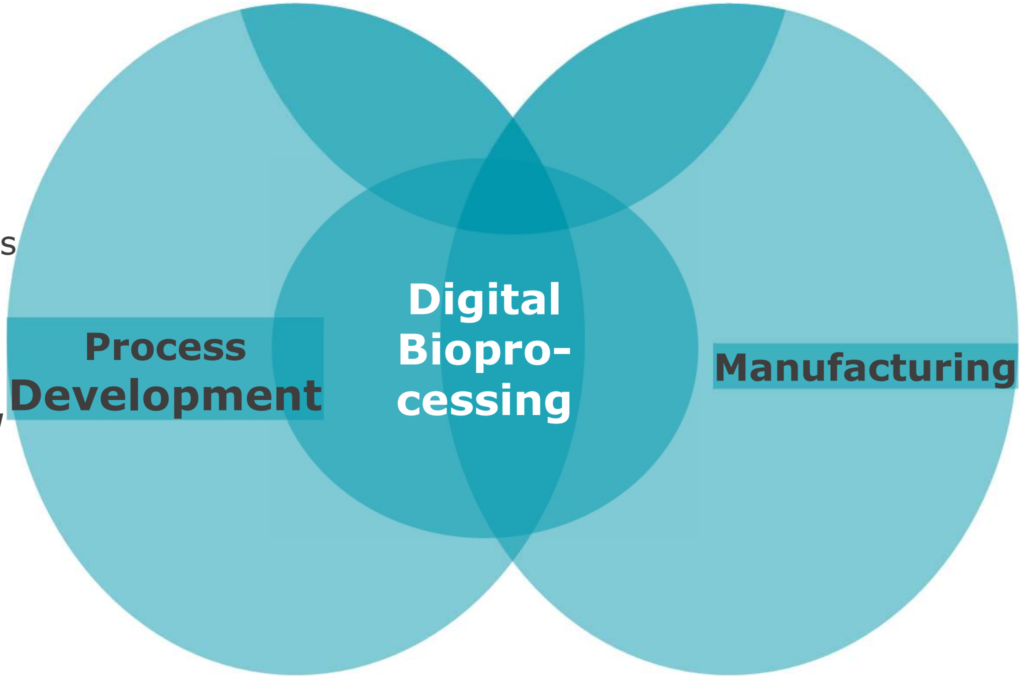
for mAbs / non-mAbs / mRNA products

Scheper et al., 2021

Digital Bioprocessing – holistic view

- Generation of data depth
- Prediction of bioprocessing steps
- Simulation of new whole bioprocesses

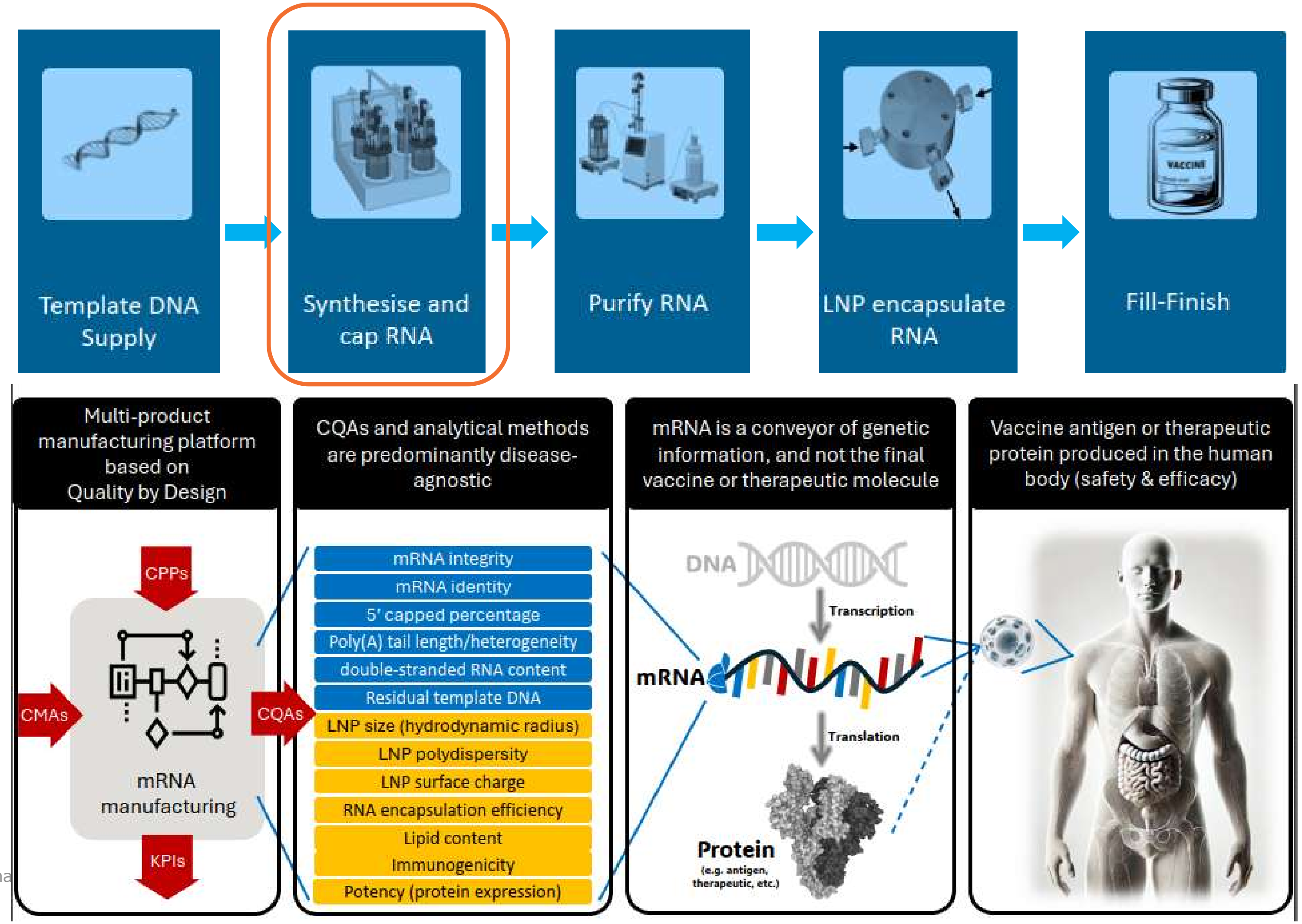
Computational Bioprocessing



- Process-optimized data
- Automation
- Control & Validation

Digital Manufacturing

Overview of mRNA manufacturing process (multi-product mRNA platform)

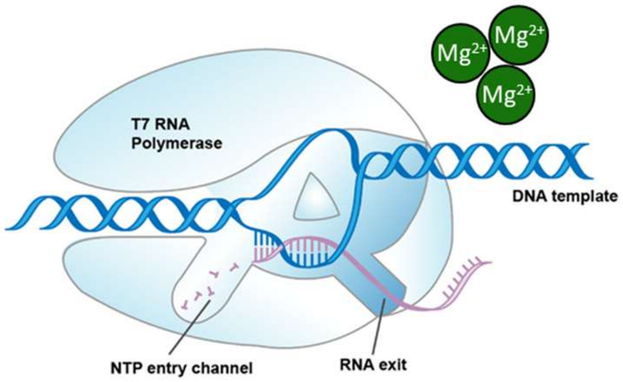


Nair et al., 2024, Zoltan Kis, 2025

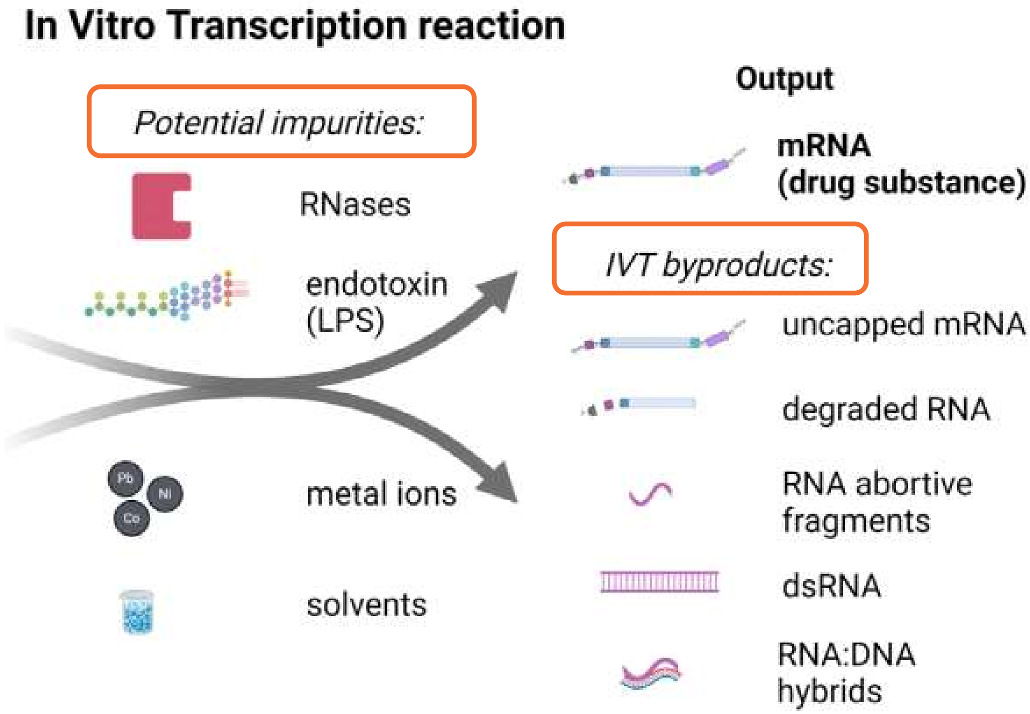
mRNA process: the IVT reaction step – a bio-catalytical step

IVT-Mix

NTPs (A,G,U,m1Ψ,..), CleanCap, DNA template, Mg^{2+}, T7 polymerase, buffer, DTT, RNAse inhibitor, Pyrophophatese, additives



Shaking, temperature, pH, incubation duration



Modified after Lenk et al., 2024

Impact on critical quality attributes like yield , integrity, capping, (im-)purity…

Digital use case: Setting the scene

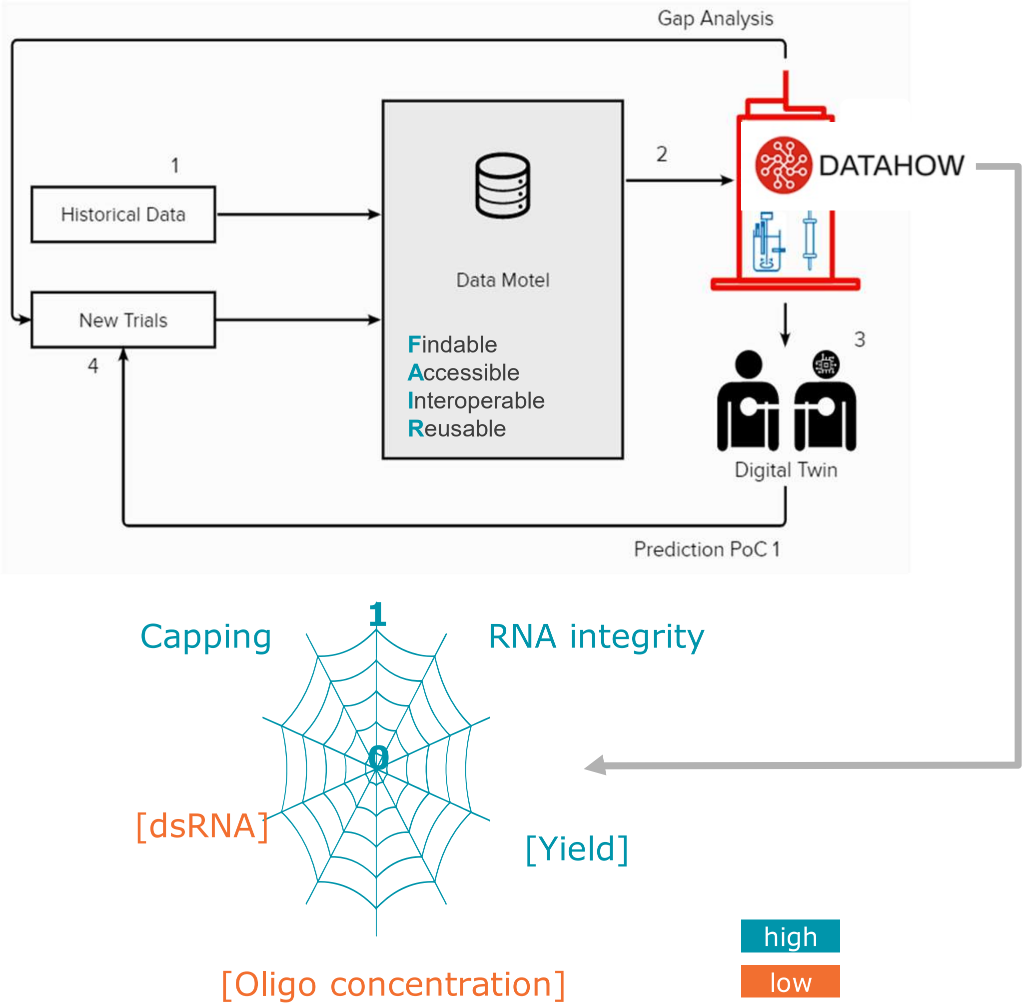
Build digital process model for IVT reaction step

Scope

- **Reaction optimization** by model-directed condition selection (e.g. higher yield, with less experimental effort)
- **Reduce experimental effort** for technology transfer (non-GMP to GMP)

1)

2)



Digital use case:
Digital process step model to predict and optimize CQAs developed

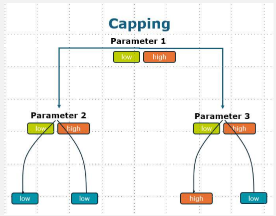
External support onboarding

- Partner selection process (RfP, Proposal review & evaluation),
- Onboarding partner

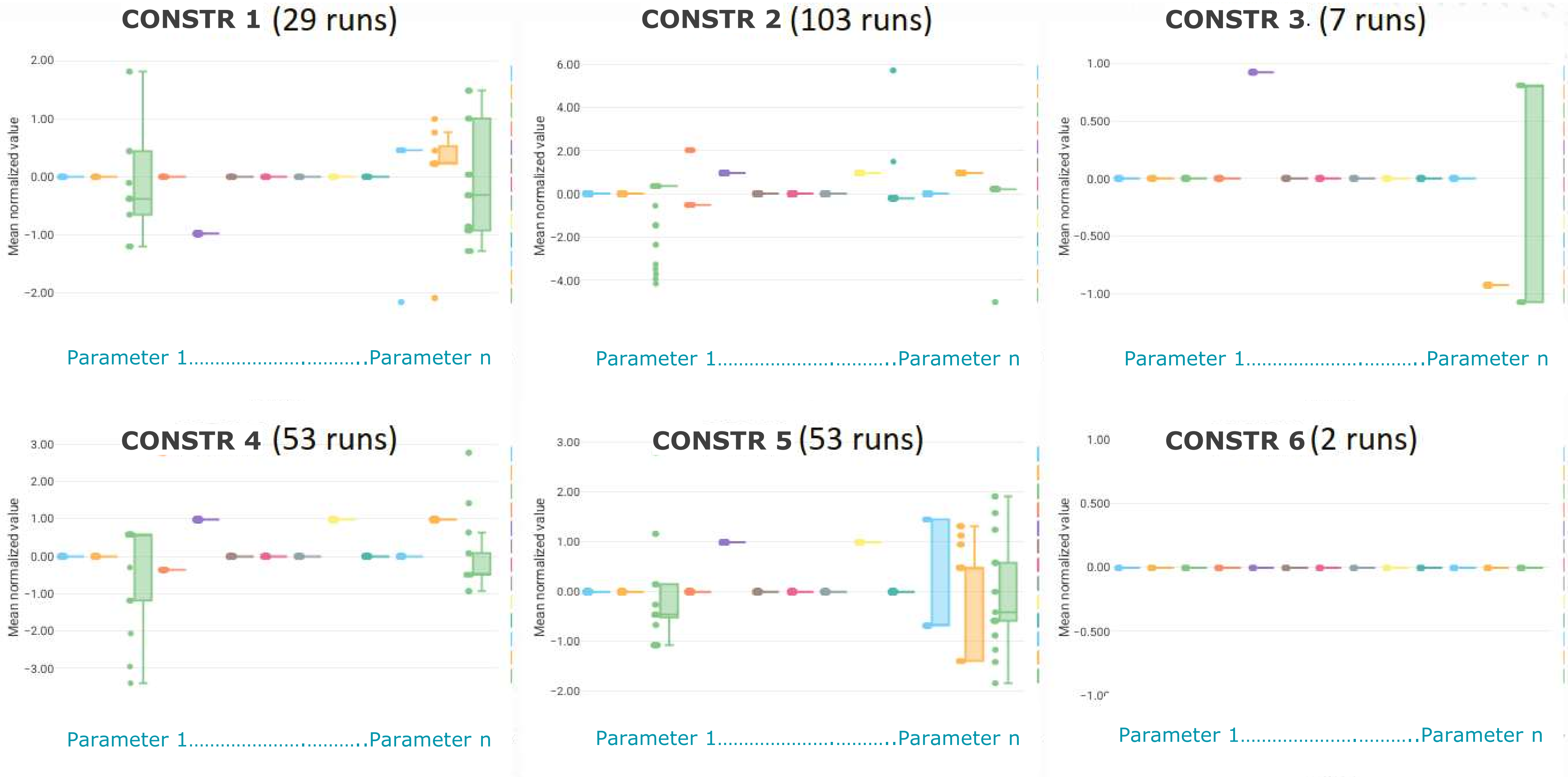
DATAHOW

Analysis of non-GMP & GMP data

- Assessed data needed for model building / training
- *Limited data variability, limited model quality expected*
- *thus, planing of additional experiments*



Digital use case:
In historical data, not all factors have been varied for all constructs (!)



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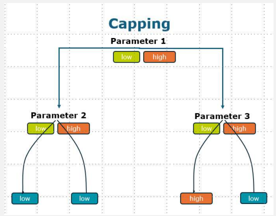
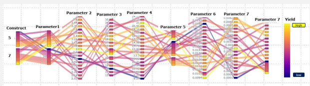


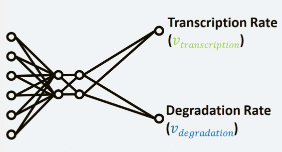
Additional experiments

- *Conducted 20 additional experiments for model enhancement*
- High sampling frequency for kinetic interpretation
- Reflecting on different parameter setting outside of usual boundaries



Build and trained AI process model

- hybrid process model developed by
   - Artificial neural network to model process dynamics
   - Partial Least Square (PLS) model to model product quality



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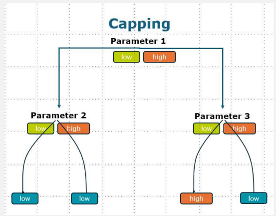

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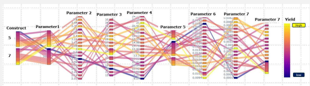

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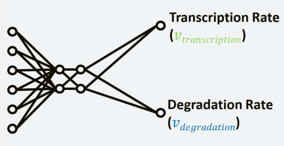
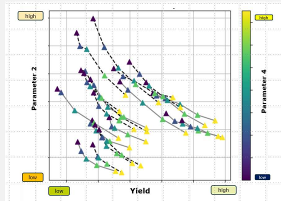


Used model to optimize IVT conditions

- Defined thresholds for targeted CQAs
- Assigned weight to CQAs within acceptable ranges to direct model optimization
- *Model suggested experimental conditions to validate optimized IVT*

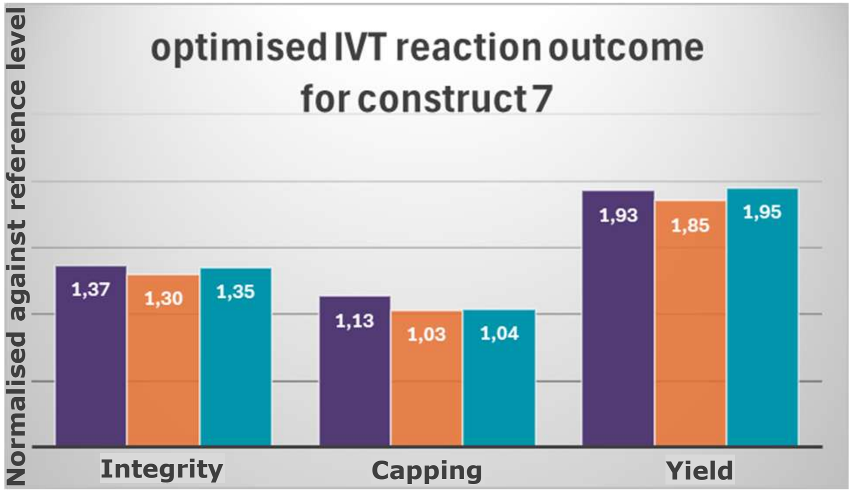


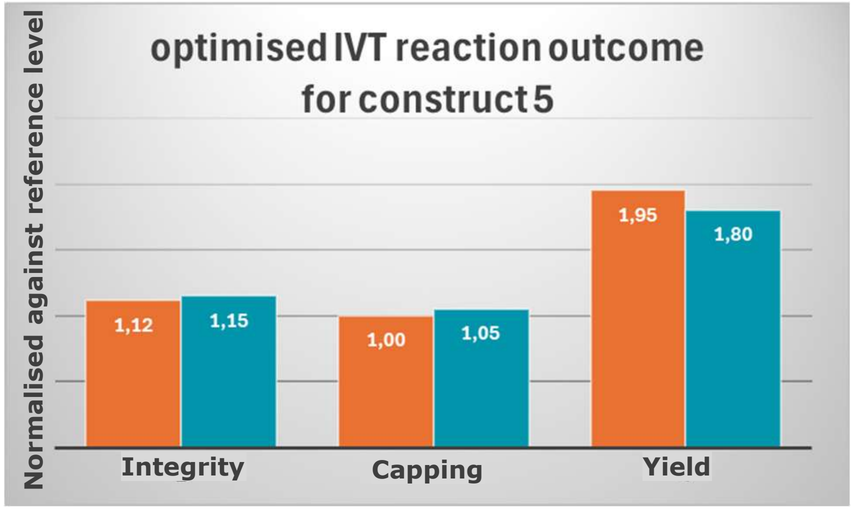
Experimental validation

- *Conducted experiments for validation of model selected conditions*
- Evaluated model prediction vs. measured results

Knowledge transfer / data ingestion in cloud

Digital use case:
Model-derived conditions for IVT showed similar quality



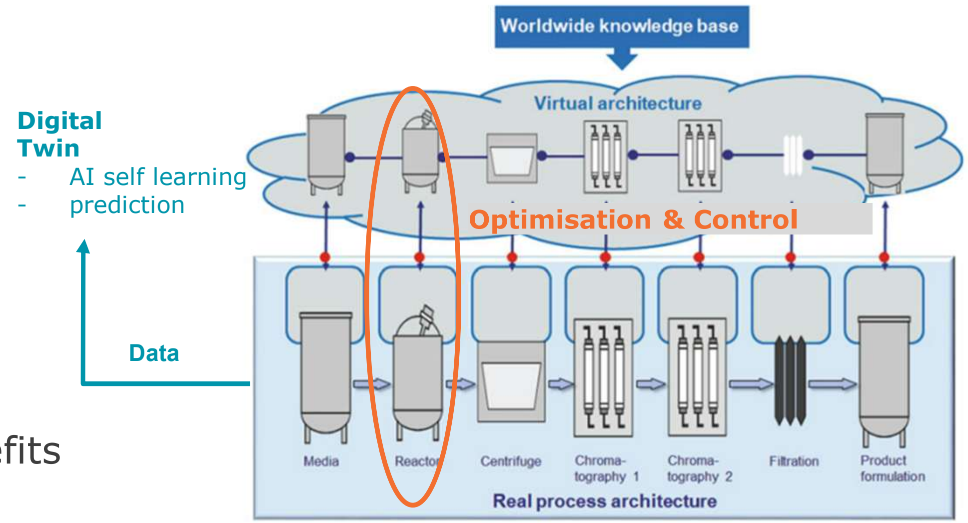


Reference experiment
Model prediction
Validation experiment

- ***Validation*** experimentation ***confirmed*** the model-based parameter **prediction** !
- A **business relevant parameter** sweet spot **for cost savings** identified

Summary

- Partnered with DATAHOW for IVT bioprocess modelling (PoC)
- Leveraged existing IVT data and generated more data with additional experiments (» F.A.I.R)
- Digital process twin for 2 constructs built
- Model-based DoE application for process optimization of construct 7 successfully applied (with business related benefits identified)
- Integrated data into cloud platform for future use cases & model refinement



Schepers et al., 2021, Helgers et al, 2021

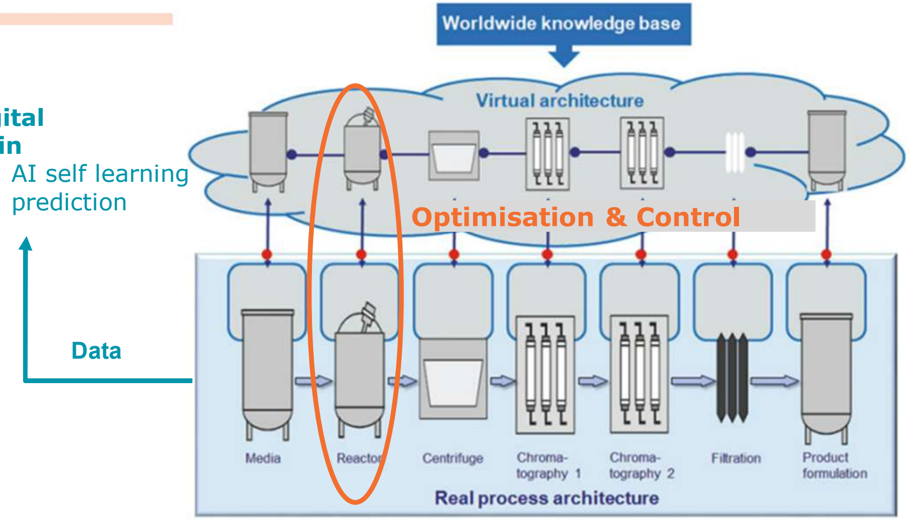
Outlook into the future

1) Hybrid modelling of reaction parameters (mechanistic modelling with data-driven modelling) including machine learning using modified reaction conditions, Co-factors, employing alternative stabilizers / protector molecules

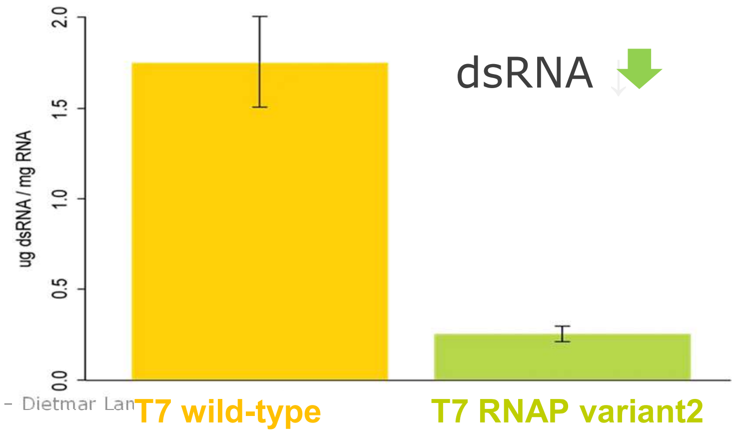
2) together with **machine-learning based structure prediction tools** (structural fold modifications or even de novo scaffolding) for the **catalytic protein(s) of the reaction** (engine – T7 RNA Polymerase & conductor – IPP)

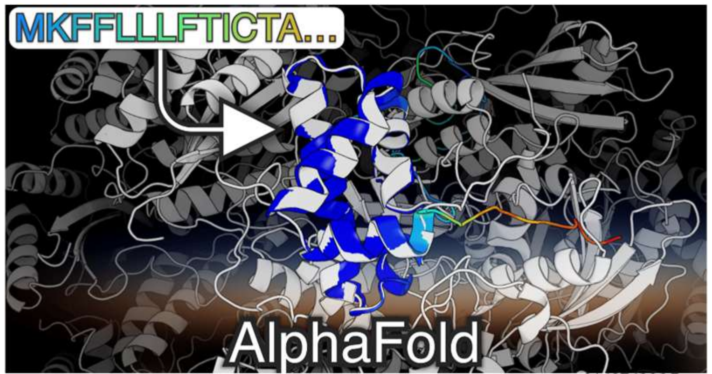
will further improve the mRNA product (therapeutic) quality in the future

Digital Twin
- AI self learning
- prediction



Schepers et al., 2021, Helgers et al, 2021





Yang et al., 2023, Jumper et al.,2021

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- Alessandro Butto

RNA Printer Unit

- Patrick Zägel

Technical Development

- Sven Trucks
- Janina Rehder
- Jochen Stehle
- Claudia Baar-Schut
- Akanksha Moga

MSAT Unit

- Regina Brockmann
- Jan Wolfgramm

Thank you for your attention

CureVac
www.curevac.com

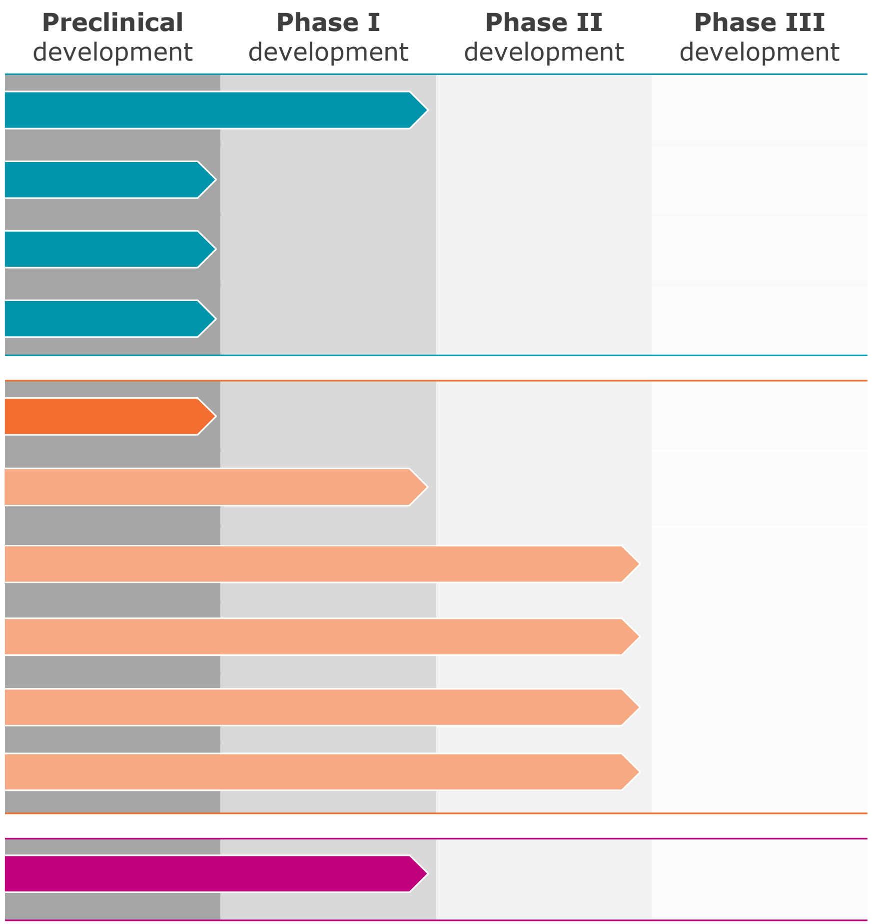

LEARNING
KNOWLEDGE
EXPERIENCE
SKILLS
ABILITY
COMPETENCE
TRAINING
GROWTH

BACK-UPs

Diversified Pipeline Targeting Urgent Medical Needs

CureVac the RNA people®

			Collaborator
Oncology	Resected glioblastoma	CVGBM	*Proprietary*
	Squamous NSCLC	Off-the-shelf cancer vaccines	myNEO Therapeutics
	Undisclosed indications	Off-the-shelf cancer vaccines	MD Anderson
	Undisclosed indications	Personalized cancer vaccines	*Proprietary*
Infectious Diseases	Urinary tract infections	UPEC vaccine candidates	*Proprietary*
	Seasonal influenza/ COVID-19 combination	Multivalent candidate	*Fully licensed to* GSK
	Seasonal influenza	Multivalent candidate *(B strain optimization)*	*Fully licensed to* GSK
		Multivalent candidate	*Fully licensed to* GSK
	Avian influenza	Monovalent candidate	*Fully licensed to* GSK
	COVID-19	CV0601 / CV0701	*Fully licensed to* GSK
Molecular Therapies*	Gene editing	Cas9 enzyme	CRISPR Therapeutics



T7 RNAP - structural changes at the active site (single nucleotide addition cycle)

Potential reagents required for IVT reaction

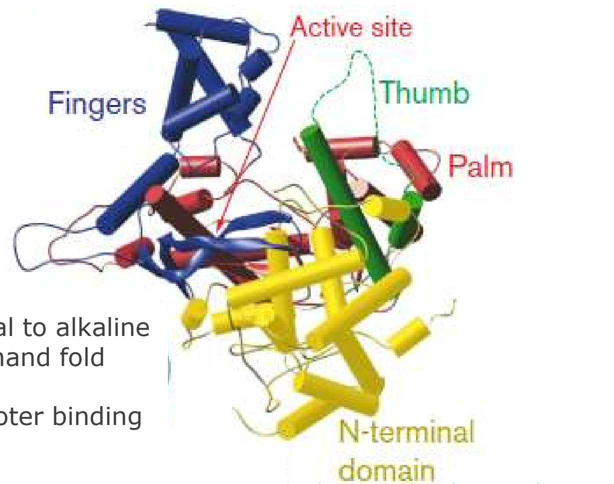
Compound	Type	Comments (impact)
DNA	template	
ATP, GTP, CTP	Nucleotides	
UTP *or* m¹ΨTP	Modified/ Unmodified Uridine	
CleanCap	Protector molecule	Stability
Tris-HCl, HEPES	Buffer	Chelating effect, enzyme functionality
Dithiothreitol	Reducing agents	Conformational stability
Spermidine	Polyamine	Chelating effect
Mg^{2+}	Cofactor	Activity (alternatives ?)
RNase Inhibitor	Protector	Stability
Pyrophosphatase	Enzyme (mesophilic)	Activity
Triton X100 / other additives	Nonionic detergents / salts etc.	Educt/product solubility

Steitz, 2008;McMinn et al., 2024; Sousa, 2000

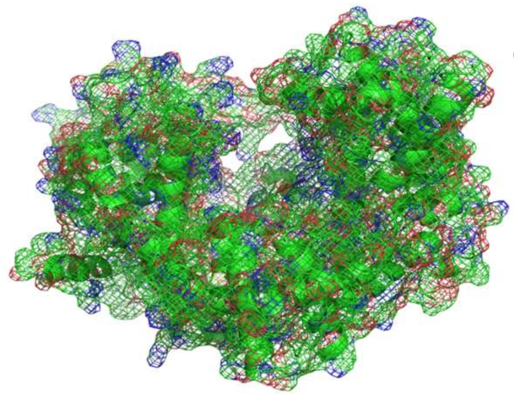
plus phage T7 DNA dependent polymerase (EC 2.7.7.6)

Characteristics

- Monomer
- 98 kD (883 amino acids)
- Mg^{2+} as co-factor
- mesophilic
- pH activity range > neutral to alkaline
- C-terminal region> right hand fold (thumb, palm, thumb)
- N-terminal region – promoter binding domain



Castro et al. 2007, Cheetham et al., 1999
PDB: 1ARO, 1MSW, 1QLN, 2pi4, 2pi5



Overall fold with surface (polar – red/blue, non-polar –green)

Benefits

Efficiency win by 20-50%

(higher throughput (more projects), higher product yield, less lab work)

Accelerated timelines

from sequence to clinic

-fast project execution-

Enabler for

Improved process robustness

(QbD and PAT)

Enabler for

Global data management

(i) ensures data integrity,

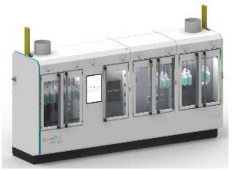
(ii) handles data complexity,

(iii) simplifies data transfer across scales & sites

The RNA Printer® & Personalized Therapies: Highly Automated Tool to Manufacture mRNA Therapeutics: Details

Fast manufacturing with the RNA Printer®

1 DNA production



2 RNA production

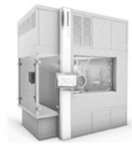
3 LNP formulation

GMP framework manufacturing license obtained & clinical trial material supplied (1, 2)

GMP manufacturing license in progress (3)

Potential extension

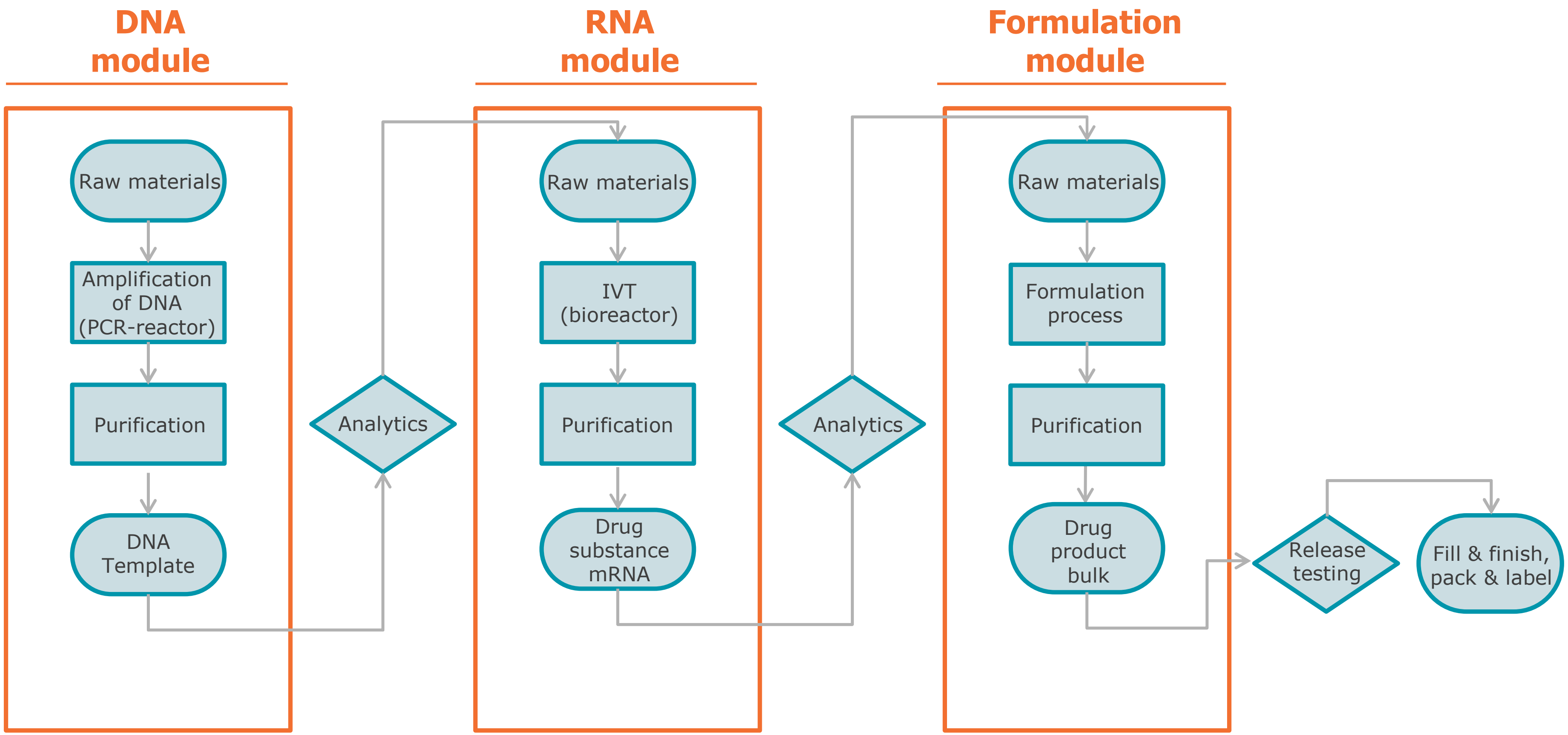
4 Fill & finish



Not considered differentiating for clinical trial phase 1

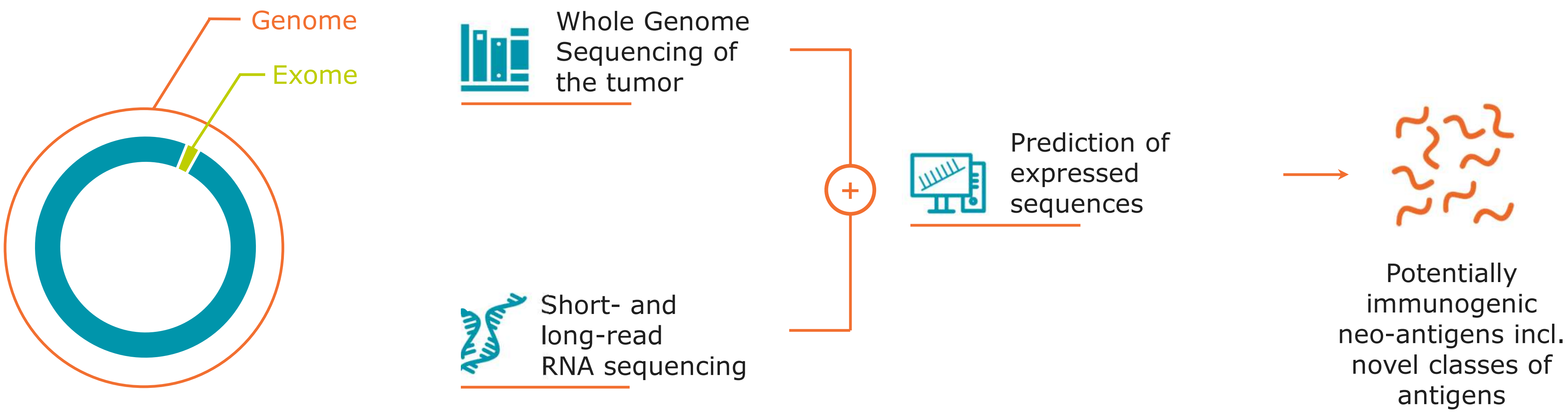
GMP, good manufacturing practices; LNP, lipid nanoparticle.

The RNA Printer® & Personalized Therapies: Process Flow Overview



IVT, in vitro transcription; PCR, polymerase chain reaction.

Antigen Discovery by Leveraging Full Inventory of Genomic Changes



Conventional antigen discovery is restricted to mutations in the **tumor exome** accounting for only **1-1.5%** of the human genome

CureVac leverages the **full tumor genome** and tumor-specific **expression analysis**

Powerful bioinformatics use the full genetic inventory to identify potentially immunogenic neo-antigens including novel **cancer vaccine candidates**

Summary

IVT reaction

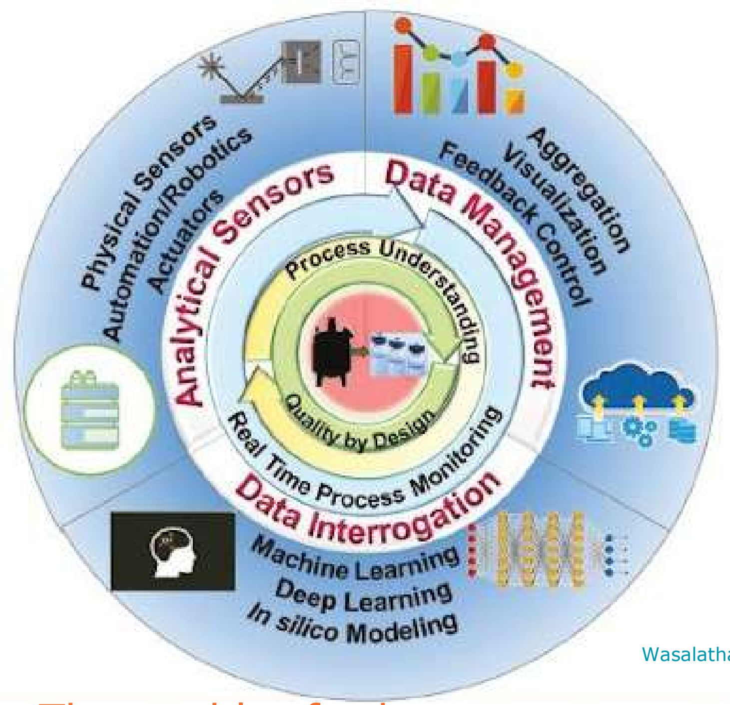
Complex reaction with impact of multiple parameters on reaction success

Protein molecules (T7 RNAP & IPP) are the catalyzers (engine – T7 RNAP & conductor – IPP) for the reaction

Applying machine-learning based **structure prediction tools** (structural fold modifications or even de novo scaffolding)

together with hybrid **modelling of reaction parameters** (mechanistic modelling with data-driven modelling) including machine learning will improve

- **development & manufacturing, in particular**
  - **Product quality**
  - **Product costs**
  - **overall timeline reduction for bringing a new drug idea to market**



Wasalathanthria et al, 2020

The enabler for better process understanding and quality by design of biopharmaceuticals.

This entails analytical sensors, data management and interrogation tools.