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# BIONTECH

Innovative Manufacturing Services



## EXPERTS IN CELL AND GENE THERAPY









## ABOUT BioNTech IMFS (FORMERLY EUFETS)

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BioNTech IMFS is a Contract Development and Manufacturing Organization specialized in the industrialization of cell and gene therapy products:

- **20 years** in the field of Cell and Gene Therapy
- **GMP certified** since 1999
- Products: **retroviral vectors, cells** and **ivt mRNA**
- State-of-the-art facility with: cleanrooms, development and QC labs
- Employees: **150 experienced staff members**
- Clinical supply of:
  - > 50 retroviral vector batches
  - > 100 mRNA batches
  - > 100 cellular products

# BioNTech IMFS – A COMPANY OF THE BioNTech GROUP

| <br><b>HOLDING</b> (with shared support functions)   |  |   |   |   |  |
|--|--|---|---|---|--|
| mRNA Technology  | Cell & Gene Therapy  | Protein Therapeutics  | Small Molecules   | Diagnostics   | GMP Production   |
| <p><b>Pharmacologically optimized protein coding RNA for targeted in vivo delivery</b></p> <ul style="list-style-type: none"> <li>• Cancer Immunotherapies</li> <li>• Prophylactic Vaccines</li> <li>• Protein Replacement</li> </ul>  | <p><b>Immunotherapy with genetically engineered T cells, adoptive T cell transfer</b></p> <ul style="list-style-type: none"> <li>• T cell receptor therapies</li> <li>• CAR therapies</li> </ul>  | <p><b>Engineered nano-particles for cancer immunotherapy</b></p> <ul style="list-style-type: none"> <li>• Bispecific antibodies</li> <li>• Microbodies</li> <li>• Virus-like-particles</li> </ul>  | <p><b>Small molecule drug discovery</b></p> <ul style="list-style-type: none"> <li>• Hit identification via <i>in silico</i> screening</li> <li>• Hit-to-lead</li> <li>• Lead optimization</li> <li>• Preclinical development</li> </ul>  | <p><b>Biomarker Discovery for individualized therapy</b></p> <ul style="list-style-type: none"> <li>• Molecular and Companion Diagnostics</li> </ul>  <ul style="list-style-type: none"> <li>• Peptides for Biomarker Discovery</li> </ul>  | <p><b>GMP Manufacturing Services</b></p> <ul style="list-style-type: none"> <li>• Retroviral Vectors</li> <li>• Cellular Products</li> <li>• mRNA</li> </ul>  |

# BioNTech IMFS FACILITIES

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BioNTech IMFS operates within a state-of-the-art facility providing a unique combination of GMP and BSL2 laboratories.



- Located in Idar-Oberstein, Germany (1.5 hrs from Frankfurt int. Airport)
- Facility complex: >4,500 m<sup>2</sup> (>48,000 sq ft)
  - Segregated manufacturing building with various clean room suites classified up to grade A/B (class 100)
  - Well equipped QC laboratories
  - Flexible development laboratories
  - Significant cryogenic storage capacity
- Biological Safety Level S2

# CLEAN ROOM FACILITIES

- BSL2 classified
- Cleanroom suites ISO 7 (B) -> A conditions under LAF
- Cleanroom suites ISO 8 (C)
- Separate flow of personnel, materials, and product
- 24/7 security system and HVAC monitoring system



**Dedicated to CGT**



**Dedicated to mRNA**

# BioNTech IMFS IN NUMBERS – INVESTMENT INTO THE FUTURE

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- Investment of ca. €25 Mio to more than double manufacturing capacities
- Two buildings added to existing facility
  - 3 floors of clean rooms
  - Development and QC lab
- Expected completion by mid 2020





# DEVELOPMENT AND MANUFACTURING SERVICES



## VIRAL VECTORS

### Technology Transfer

Explore how we ensure that your technology is transferred in an efficient and timely manner and with a particular attention to quality.

[EXPLORE](#)



## CELLULAR PRODUCTS

### Process Development

Process development for innovative new drugs is a complex task, requiring customized solutions for each product.

[EXPLORE](#)



## mRNA

### Assay Development

Our experienced analytical team offers customized assay development based on cell biology, virology, molecular biology, and microbiology technologies.

[EXPLORE](#)

### GMP Manufacturing

We have established robust GMP manufacturing processes for a variety of different retroviral vectors, cells and mRNA products. Learn more about our clinical and commercial supply capabilities.

[EXPLORE](#)

### GMP Quality Control

Our QC team ensures quality, safety and batch-to-batch consistency of all manufactured products. We have established more than 50 assays for the characterization of our customers' products.

[EXPLORE](#)

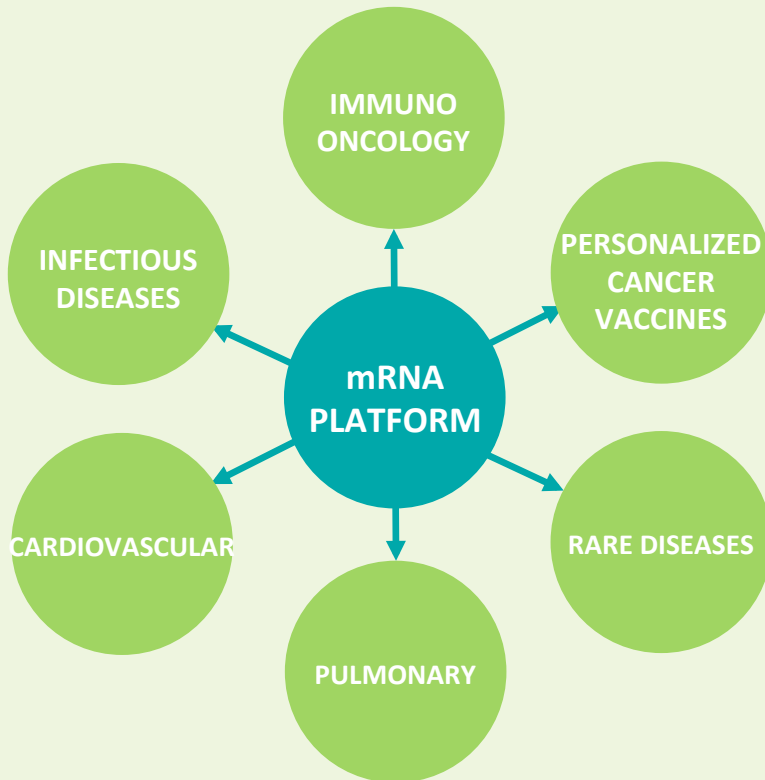
### Quality Assurance & QP Release

Learn how our QA team provides directions throughout each customer project to ensure quality and regulatory compliance of all products.

[EXPLORE](#)

# ADVANTAGES OF mRNA THERAPEUTICS

## Broad field of application



## Advantages of mRNA over:

### Gene therapy:

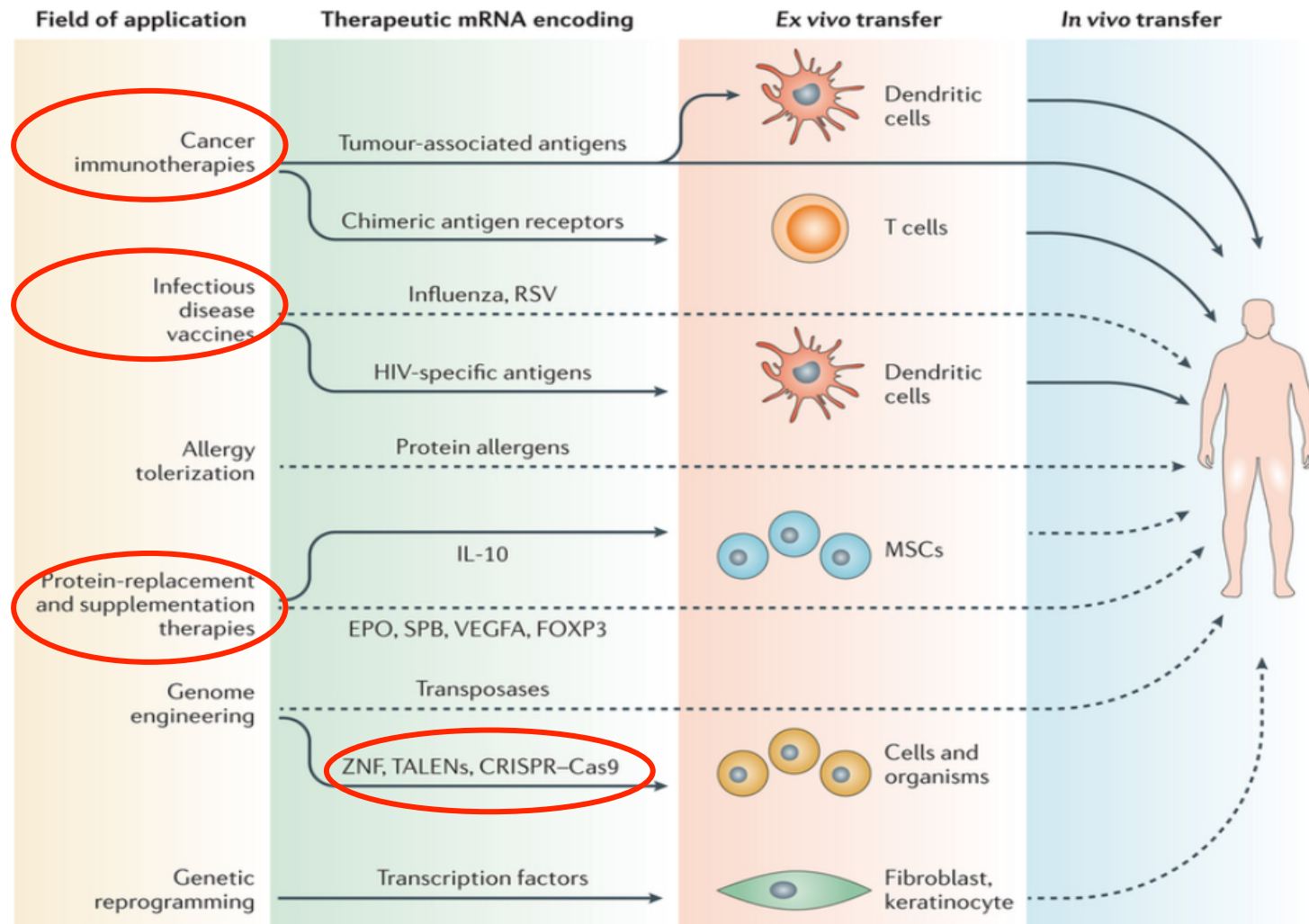
- No risk of random genome integration
- Introduce protein into the cytoplasm **without** the need for **nuclear entry**
- mRNA can **rapidly express protein** immediately after being introduced into the cells
- **Transient and regulatable** effects

### Conventional drugs:

- Encoding for intracellular proteins in **compartments unreachable by injected drugs**
- „Simple“ and **cost effective production** compared to complex proteins
- **Better immune response** as antigens are produced cell-> presentation through MHC I and II, inducing CD4+ (humoral) and CD8+ (cellular) response
- Treatment with mRNA can be **personalized**
- Easily enabled **combinations**
- **Speed:** relevant DNA sequence is characterized -> vaccine production within weeks



# RNA BASED THERAPEUTICS IN VIVO & EX VIVO



Nature Reviews | Drug Discovery

Sahin et al., 2014

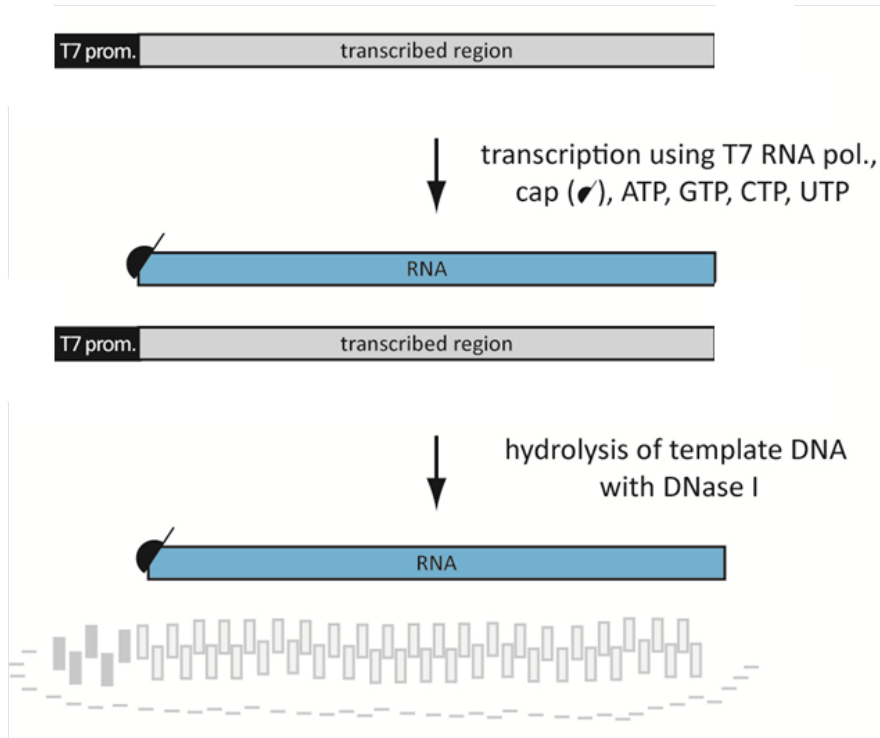
## PROCESS SET-UP AT BIONTECH IMFS

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- BNT IMFS was one the first GMP sites worldwide dedicated to the manufacturing of mRNA
- The initial set-up, from project start to obtaining the manufacturing license, was performed in less than two years
- With >100 RNA batches manufactured (both for BioNTech-projects as well as for external customers), this is – to our knowledge – the most experience in mRNA manufacturing under GMP
- If required, new processes and/or capacities can be implemented in a short time frame to meet the needs of new projects
- Automation for individualized cancer vaccines established

# MANUFACTURING PROCESS OF mRNA → USP

In vitro transcription → completely cell-free process



linear template DNA

in vitro transcribed mRNA  
( > 500 copies per template DNA )  
with a yield of > 5 mg/ml

raw reaction mixture with mRNA and impurities  
(T7 RNA pol., remaining cap and NTPs,  
hydrolysed DNA, ...)

# MANUFACTURING PROCESS OF mRNA → DSP

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What to remove:

- process-related impurities (e.g. left-over NTPs, T7 RNA pol., template DNA)
- product-related impurities (e.g. break off transcripts, side products)

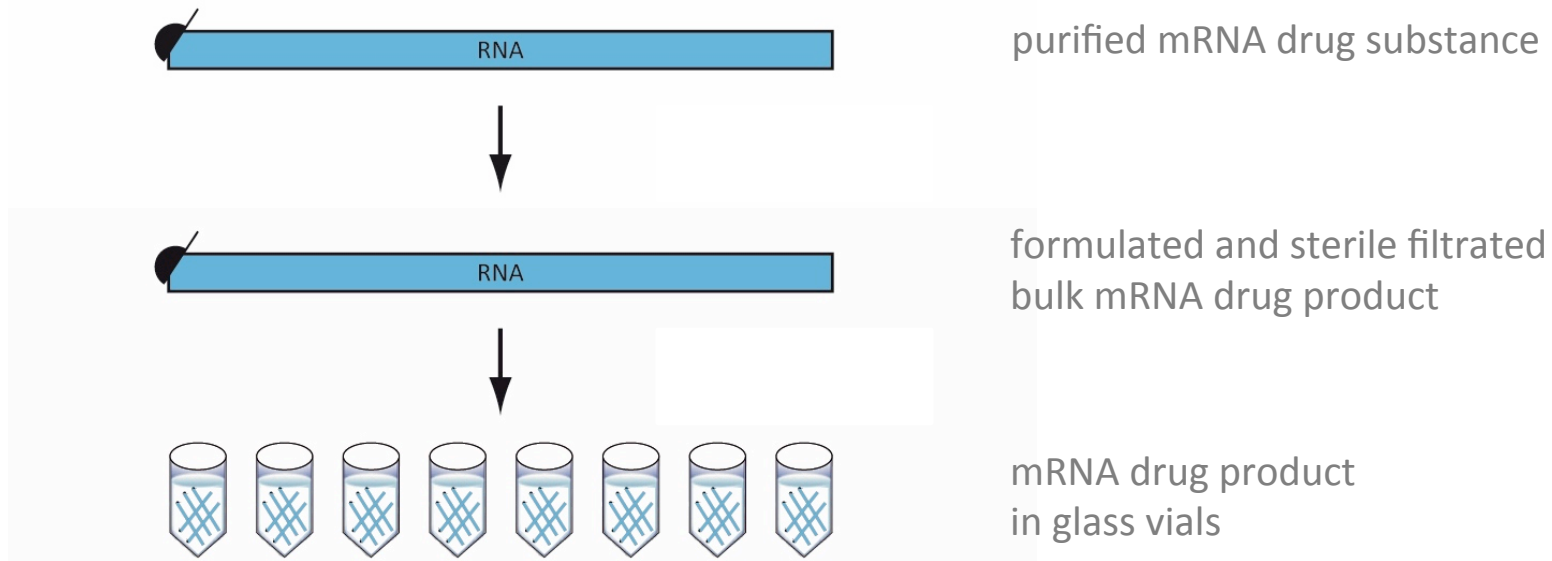
Challenges:

- highly charged and dynamic molecule
- RNA vs. DNA – removing the chemical cousin
- scalability of the purification process

Solution:

- establishment of two purification procedures:
  - for batch sizes up to 1 g
  - for batches of 1 to 10 g
- delivering mRNA with high purity and integrity

# MANUFACTURING PROCESS OF mRNA → DSP



USP: Transcription reaction

1d

DSP: mRNA purification reaction

1-2 days

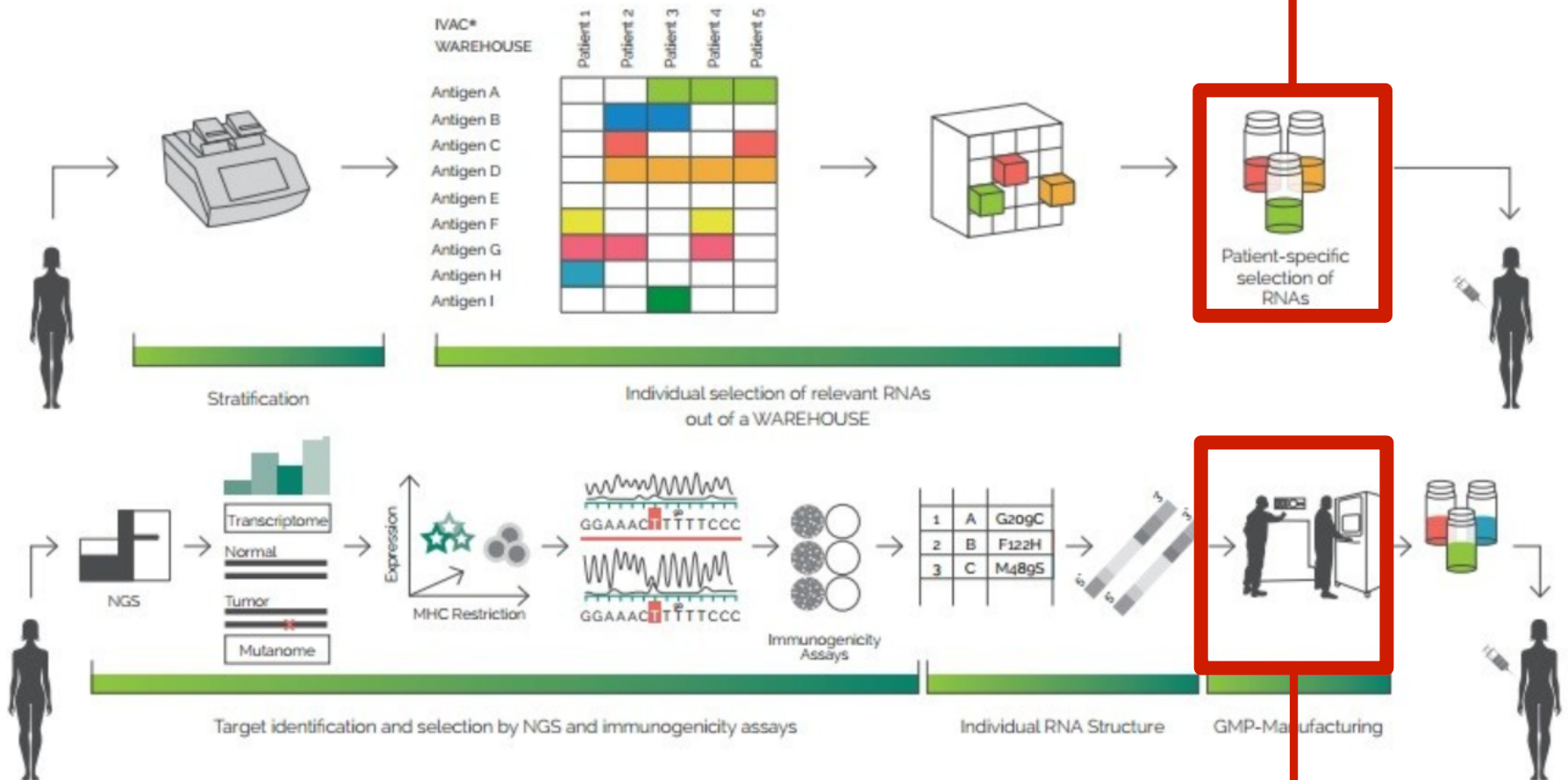
QC: comprehensive testing (inc. bioburden)

14d

Stability: general RNA stability for months (even years when frozen)

# AUTOMATED MANUFACTURING PROCESS

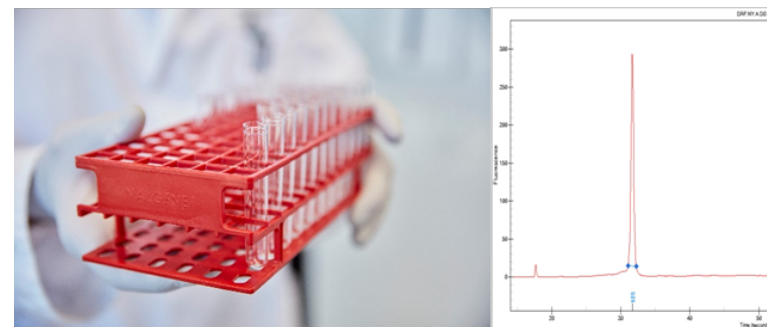
„standard mRNA“ -> manual mRNA production



„personalized mRNA“ IVAC -> automated mRNA production

# QUALITY CONTROL

- Separate quality control department ensuring compliant testing
- Expertise in qualification and validation of assays
- Testing each batch of mRNA for:
  - concentration
  - identity
  - Integrity
  - appearance (clear, colorless)
  - particles (visible/subvisible)
  - pH
  - osmolality
  - critical residuals
  - bioburden/sterility
  - potency
- Network of qualified contract laboratories
- Product release by inhouse QP





# BIONTECH IMFS' ADVANTAGES



Scientific excellence  
and technology  
leadership



Robust production  
process delivering  
best-in-class mRNA



One facility for  
different mRNA  
products with ability to  
scale-up/out

Platform approach allowing for rapid  
turn-over of new products and  
economies of scale



Time



Resources

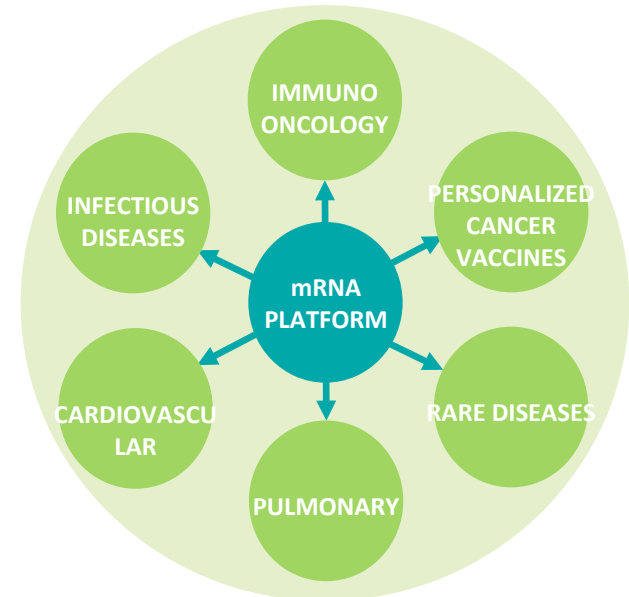


Costs

Time

Resources

Costs



# MANUFACTURING OF mRNA

## BioNTech IMFS' mRNA Services:

- Standardized production process for all mRNA constructs
- Minimal restrictions in construct length
- Yields up to 3 gr/batch
- Sterile filtration and final filling in up to 1200 glass vials
- Fast setup for new products
- Scale-up to industrial-scale manufacturing feasible
- Inhouse QP release





BioNTech IMFS -  
Experts in Cell & Gene  
Therapy Manufacturing

Vielen Dank!

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# APPROVED AND IN-DEVELOPMENT GENE THERAPIES (SELECTION)

