Innovation via New EU Pharma Legislation?

Platform Technologies and the Definition of Gene Therapies

Maren von Fritschen, PhD, Head Regulatory Policy Europe, Moderna

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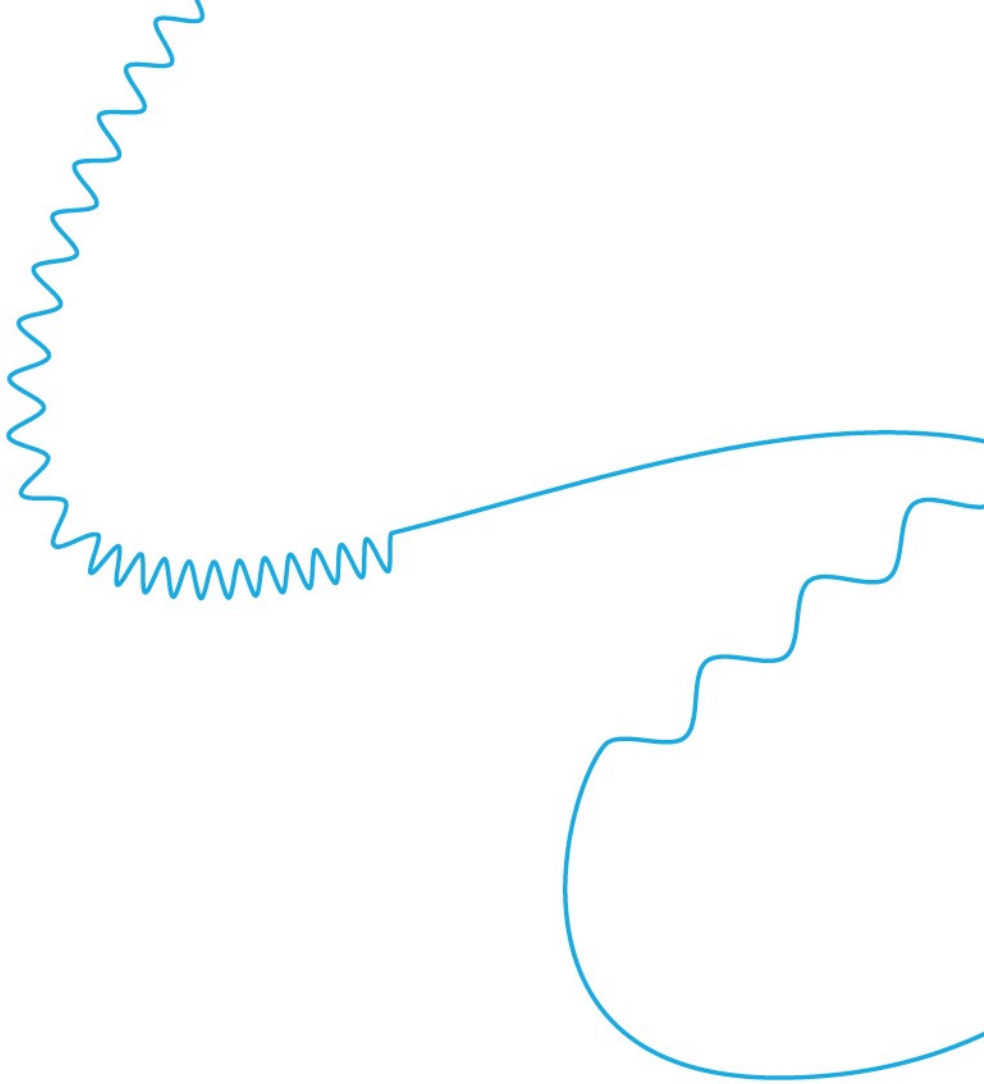
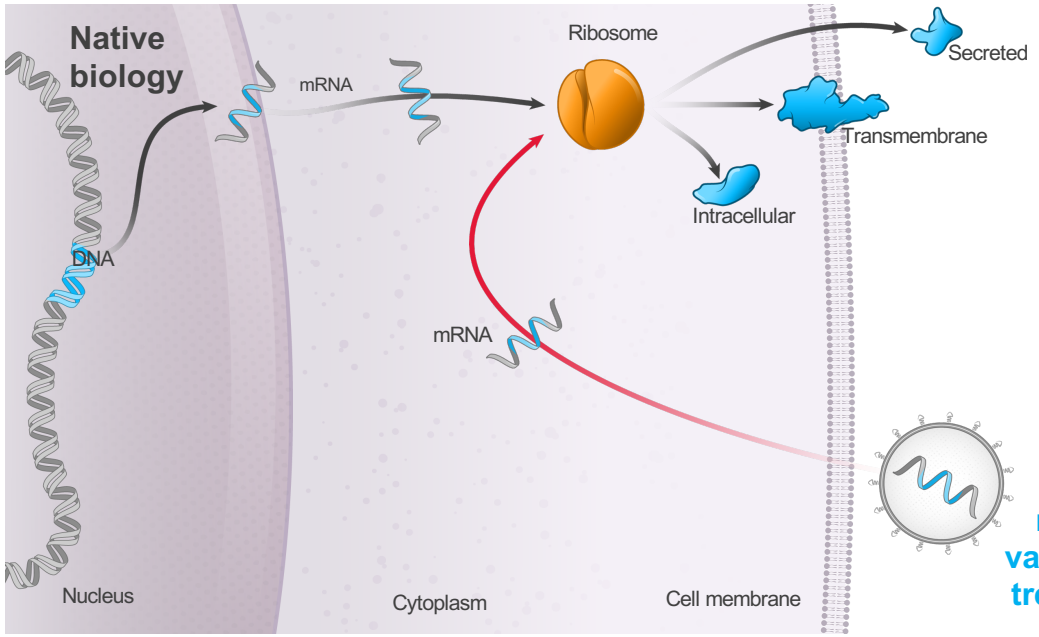
mRNA medicines



mRNA encodes for proteins to prevent or treat certain diseases

mRNA could encode for a variety of proteins that e.g. stimulate the immune systems or replace defective or missing proteins



mRNA vaccine or treatment

- mRNA is used by every cell to produce proteins as essential component of life
- Making proteins inside one's own cells mimics human biology – mRNA is a messenger
- Once its job is done, an mRNA is broken down by the body. It doesn't stick around for very long.
- mRNA has a simple and flexible chemical structure and classic pharmacological features

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mRNA is a unique opportunity to change medicine development

- mRNA is an **information molecule.**
- All **mRNA medicines start with identifying a protein** that is designed to prevent or treat.
- Then **an mRNA sequence** that **carries instructions** for this protein is designed.
- **Other parts** (non-coding regions) **of the mRNA are largely the same** in different products.
- The **same lipid nanoparticle technology** is used for different products.

The process of the development of mRNA vaccines and therapeutics is remarkably similar for very different diseases and conditions.

- **Knowledge** gained in one product can be applied to a different product
- use **existing knowledge** to accelerate development
- establishment of a **mRNA platform technology approach**

→ maximize impact for patients

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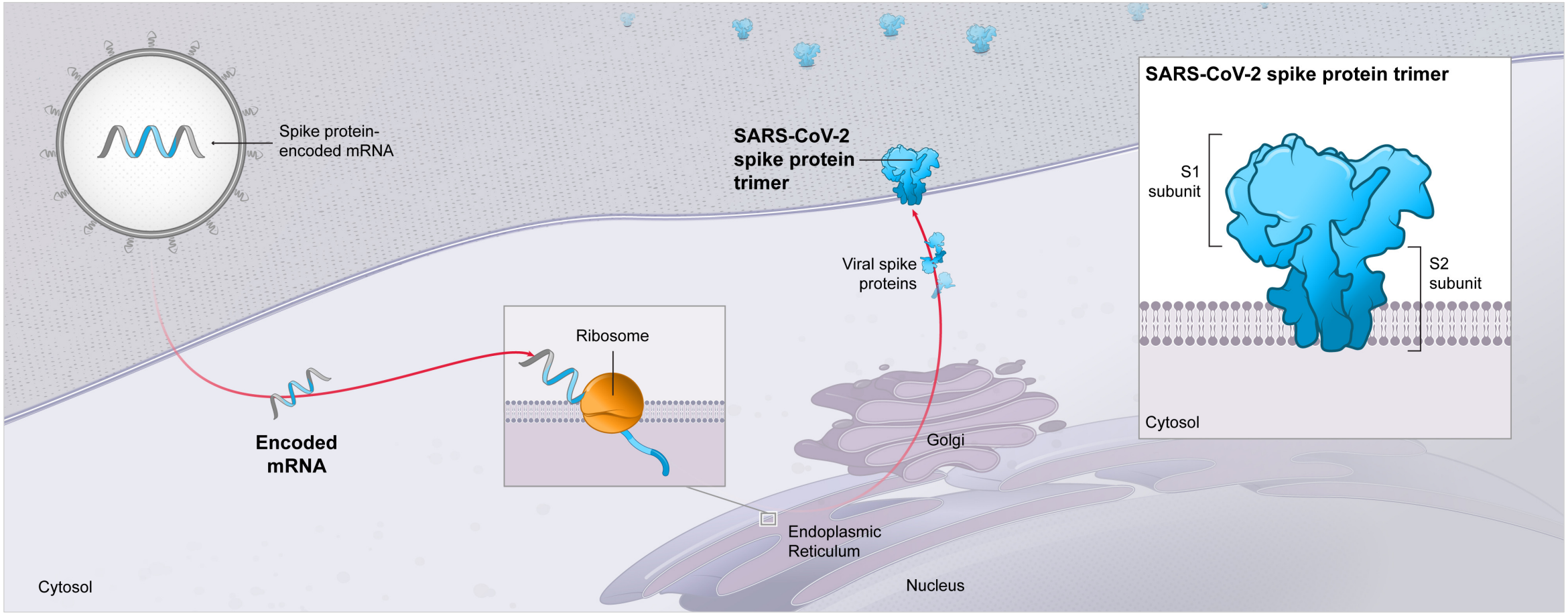
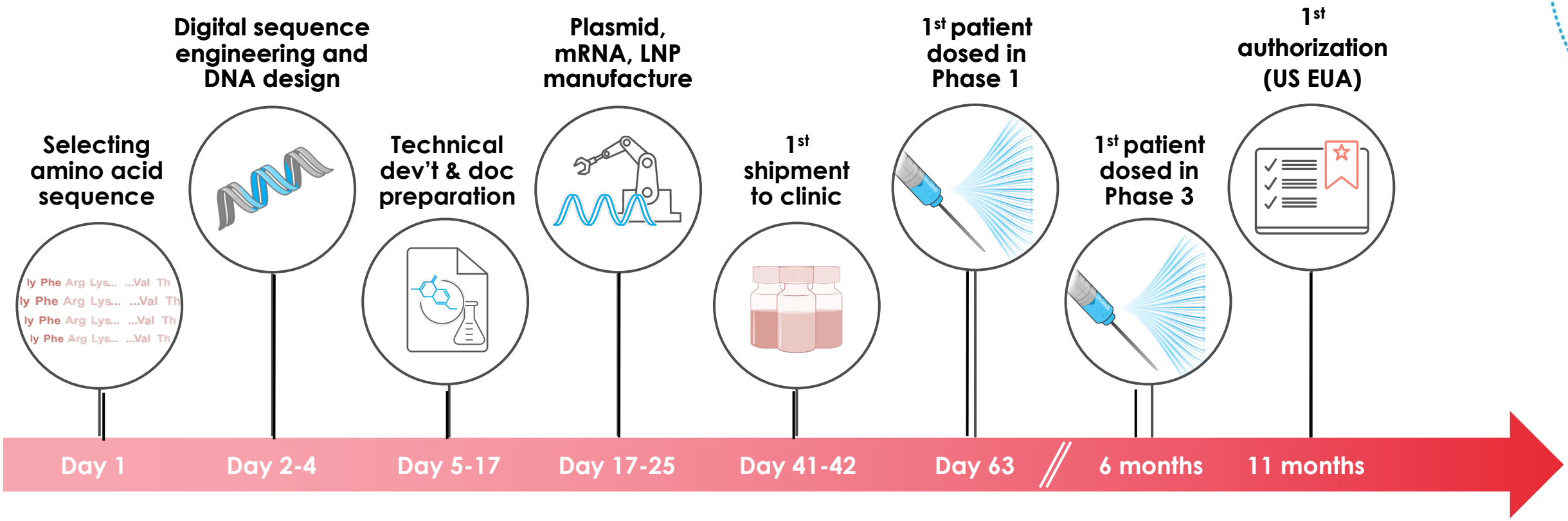
Example for an mRNA Vaccine for prevention



Example for an mRNA Vaccine for prevention

Accelerated timeline for mRNA-1273 (Spikevax)



Total Time: 11 MONTHS (compared to years to decades for current technologies)

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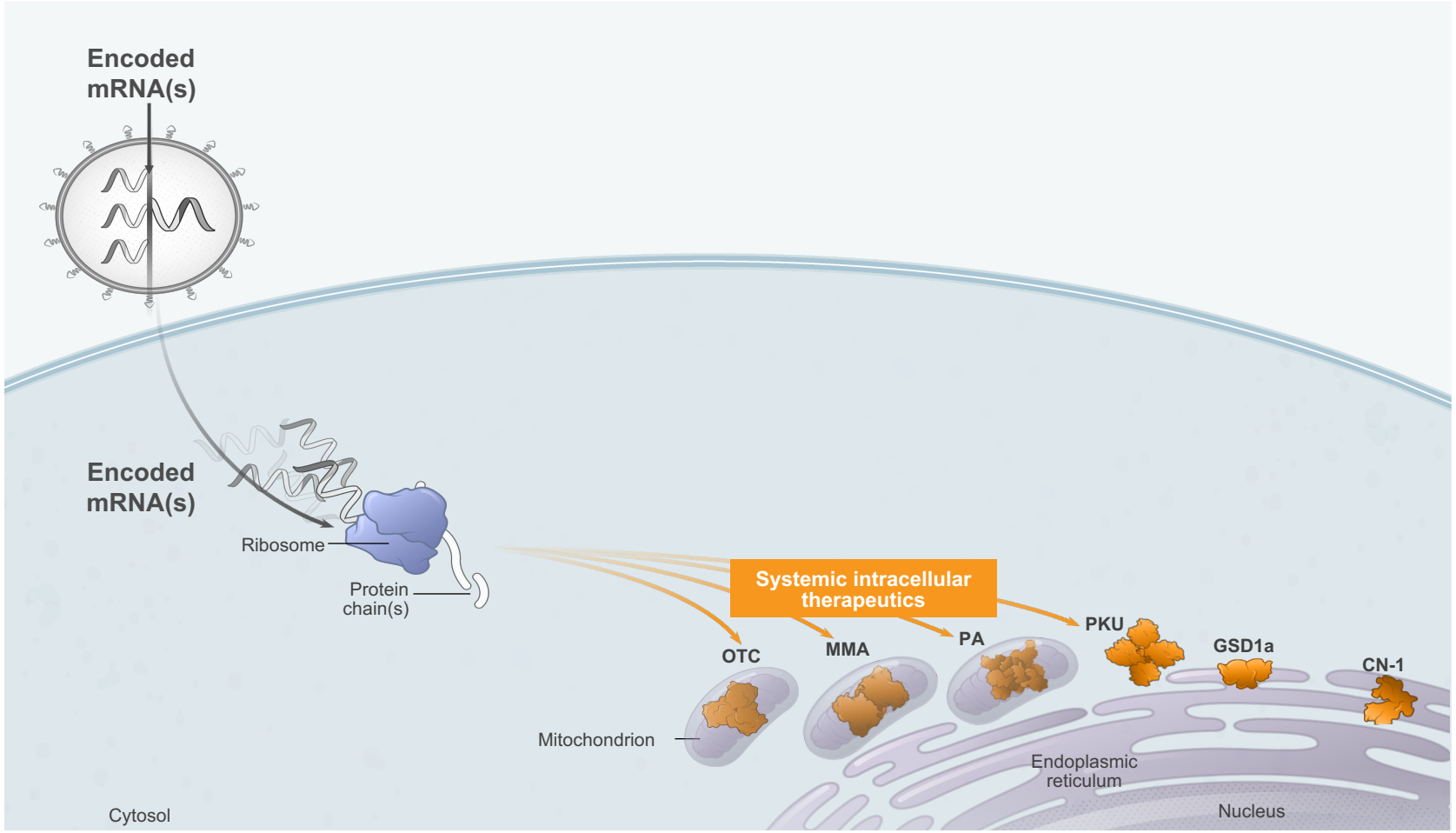
Example for a potential mRNA treatment

mRNA allows restoration of the physiologic process of metabolism in the liver / addressing the underlying defect



Prospective great impact of mRNA medicines for patience

2024 - 2025

Respiratory vaccines

- RSV
- Next-Gen COVID
- Flu
- Flu/COVID combo

2025 +

Latent + other vaccines

- CMV

Oncology therapeutics

- INT
- Adjuvant Melanoma
- Adjuvant NSCLC

Rare disease therapeutics

- PA
- MMA

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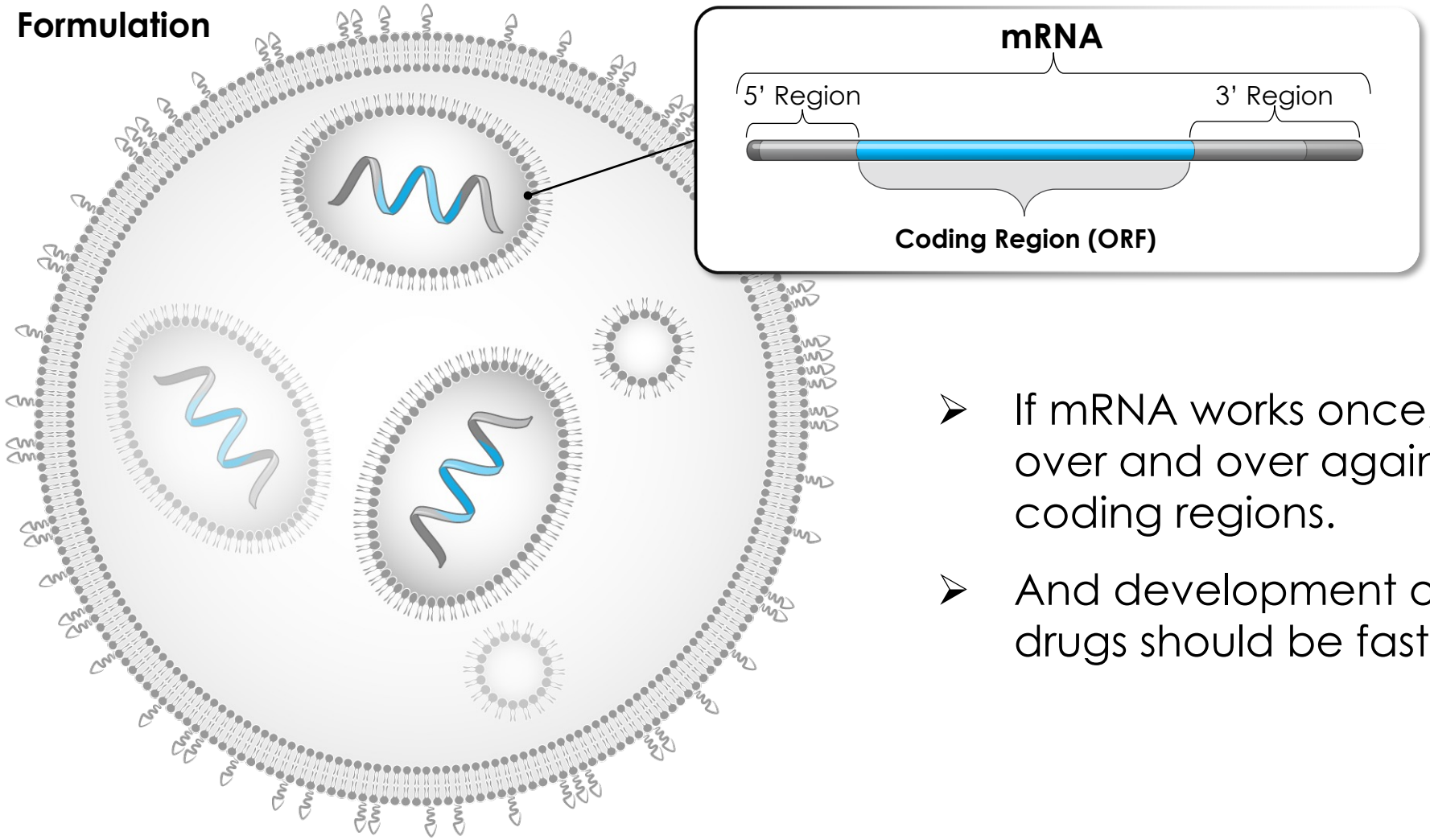
mRNA medicines constitute a platform technology

They act like software; only the coding region varies from mRNA drug to mRNA drug



- If mRNA works once, it should work over and over again for different coding regions.
- And development of new mRNA drugs should be fast.

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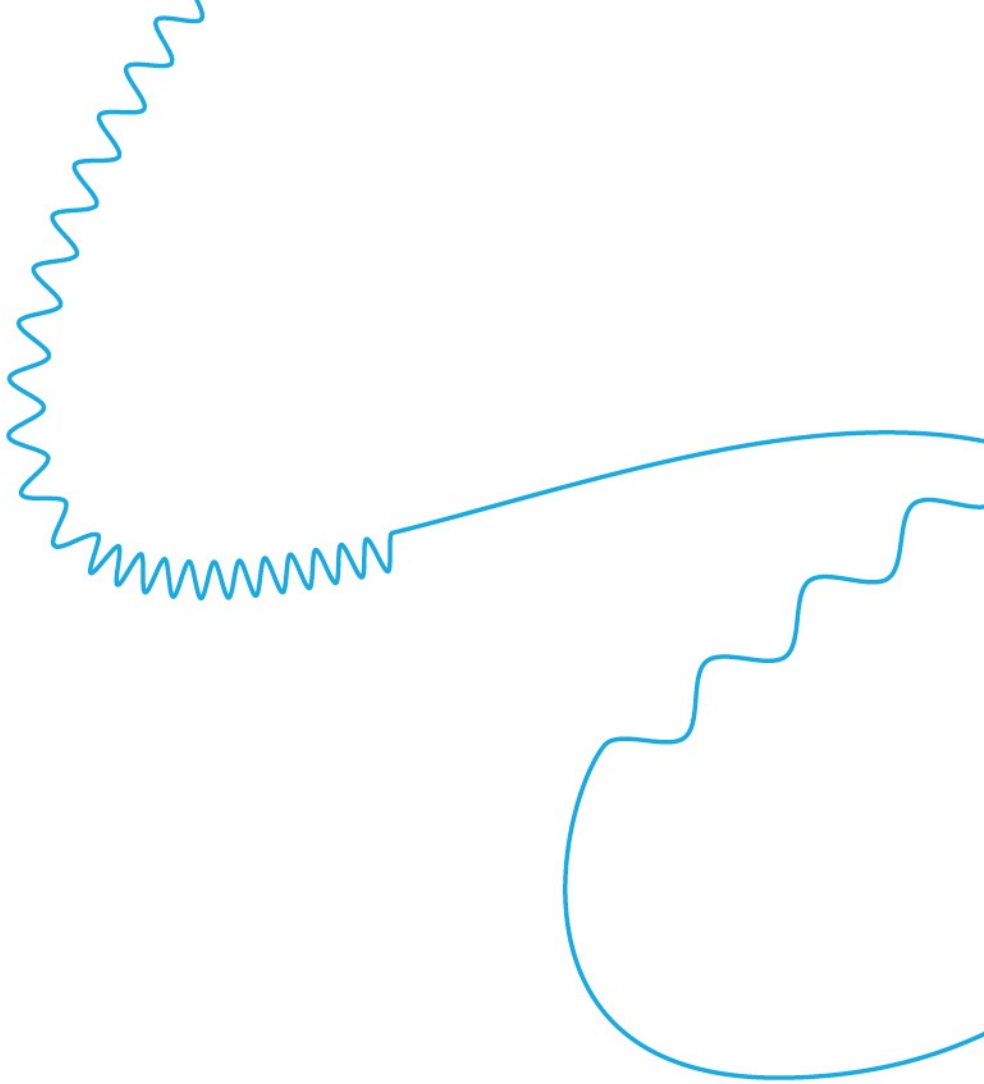
Platform technology approach for innovative medicines



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Advantages of an mRNA technology platform

Challenging the traditional R&D timelines paradigm

mRNA technology providing many potential advantages

Key characteristics & differentiation

Broad applicability

- Ability to include complex antigens
- Ability to develop combinations

Higher probability of success

- Understanding the vaccine mechanism of action (MOA)
- Induces both B-cell and T-cell responses

Accelerated R&D timelines

- Toxicology data consistent across platform
- Uniform process allows for fast scale up

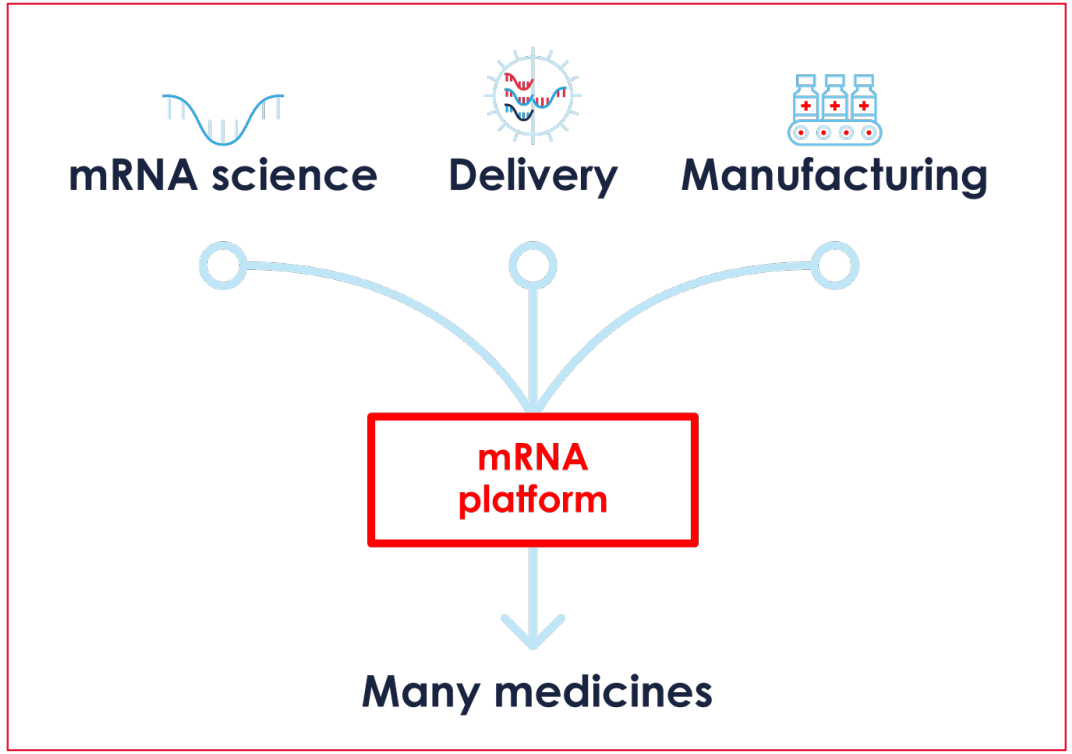
Flexible manufacturing

- Cell free manufacturing
- Non-product dedicated plants

The value of platform technology for mRNA products

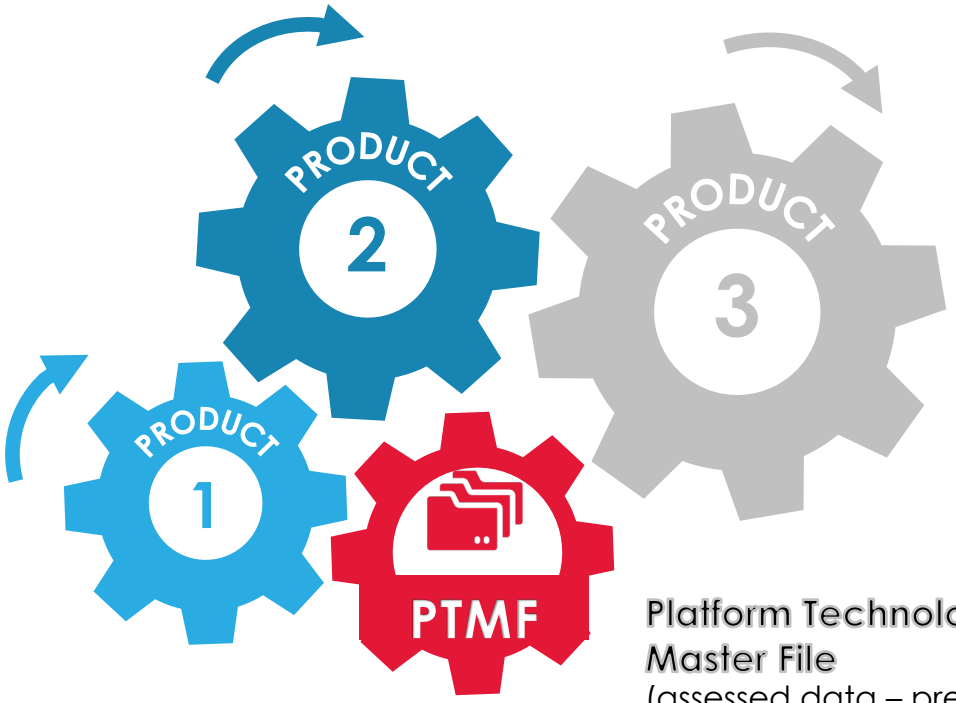
Transformative potential of mRNA platform technologies

- Platform Technology can **expedite patient provision** of innovative medicines through the **accelerated development** and review of drugs and vaccines, emerging infectious diseases, cancers, and rare genetic conditions.
- Platform technologies can consolidate **economic impact for health care systems** and minimize resources for regulators and developers.
- Utilization of platform technology is the morally and ethically appropriate approach to drug development, reducing patient burden and **unnecessary repetition** of non-clinical and clinical studies.



Legal options for enabling Platform Technology in the EU

High potential for disease prevention and treatment: Efficiency for drug development, manufacture and review



Platform Technology Master File
(assessed data – previous approval)

Safe and efficient re-use of data

- Platform Technology based on previous knowledge
- Increased data set with each subsequent application
- Increased confidence in new technology
- Ultimately earlier provision to patients.

Agile and flexible approach

- Efficiency in regulatory assessment, without altering criteria and standards for benefit-risk evaluation – addressing resource constraints
- Non-clinical and clinical testing to be included in definition to avoid unnecessary studies in animals (in line with 3Rs)* and humans

Definition of Platform Technologies
Need for clear & broad scope

Legal basis for Platform Technology Masterfile
And development of scientific guidance by the EMA

Global regulatory alignment:
Enabling patient access and ensuring increased confidence in mRNA technology

** Replacement, Reduction and Refinement*

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Master File approach in the EU – Platform Technology

Acknowledgment and further improvement of EC proposal to a PLATFORM TECHNOLOGY MASTER FILE

1.	"Active Substance Master File" (**ASMF**) concept (Art 25)	Legal basis for well-established concept for *chemical* active substances
2.	"Additional Quality Master File" (**AQMF**) concept (Art 26)	Broadening this concept to *Biologics*
3.	"Technology Platform" (Art 6 and recital 92)	recognition of technology platform for MAA
4.	"Platform Technology Master File" (**PTMF**) (new Art 26a)	Legal basis for "**PLATFORM TECHNOLOGY MASTER FILE**"

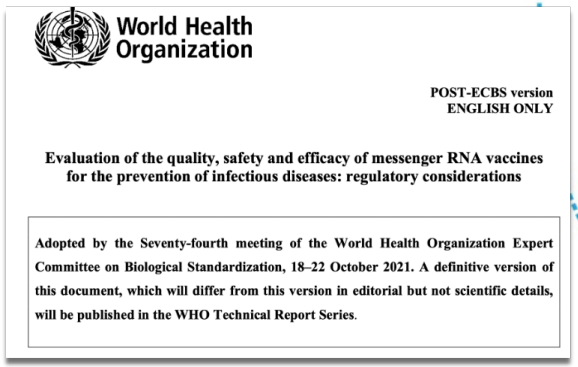
Regulatory landscape: platform approaches for medicines

The use of platform technology approaches is evolving

World Health Organization

"Evaluation of the quality, safety and efficacy of messenger RNA vaccines for the prevention of infectious diseases: regulatory considerations" (2021)

Platform technology: *a group of technologies used as a base upon which other applications, processes or technologies are developed*


World Health Organization

POST-ECBS version
ENGLISH ONLY

Evaluation of the quality, safety and efficacy of messenger RNA vaccines for the prevention of infectious diseases: regulatory considerations

Adopted by the Seventy-fourth meeting of the World Health Organization Expert Committee on Biological Standardization, 18–22 October 2021. A definitive version of this document, which will differ from this version in editorial but not scientific details, will be published in the WHO Technical Report Series.

FDA

"Omnibus Reform Act (FDORA - 2022)"

Platform Technologies at SEC. 506K

Draft Guidance for industry: Platform Technology Designation Program for Drug Development, June 2024


Platform Technology Designation Program for Drug Development
Guidance for Industry

EUROPEAN MEDICINES AGENCY

"Regulatory and scientific virtual conference on RNA-based medicines" (2023)

Recognised value of platform approach, "extrapolate" from earlier products to a new product

Recognised need for guidance, e.g. workshop


Regulatory and scientific virtual conference on RNA-based medicines

2 February 2023, 09:00 – 16:30 (CET)

Background and objectives

The European Medicines Agency (EMA) is convening a virtual conference on 2 February 2023 to promote the development of RNA-based medicines, with the following objectives:


EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

23 May 2024

Quality Innovation Group

Listen and Learn Focus Group meeting on platform technologies

19-20 November 2024

Call for case studies

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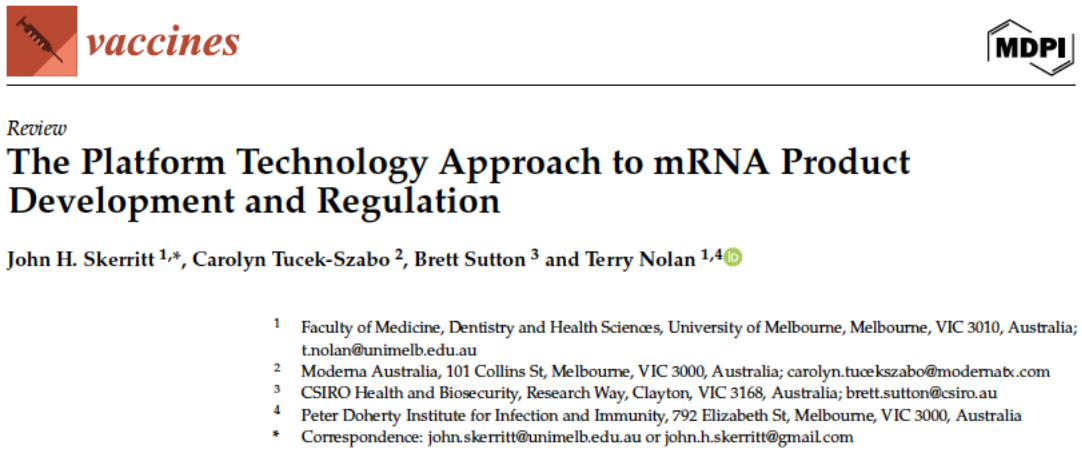
Platform approach to mRNA product development

Vaccines 2024, 12, 528. https://doi.org/10.3390/vaccines12050528



vaccines

MDPI

Review

The Platform Technology Approach to mRNA Product Development and Regulation

John H. Skerritt [1,*], Carolyn Tucek-Szabo [2], Brett Sutton [3] and Terry Nolan [1,4]

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[2] Moderna Australia, 101 Collins St, Melbourne, VIC 3000, Australia; carolyn.tucekszabo@modernatx.com
[3] CSIRO Health and Biosecurity, Research Way, Clayton, VIC 3168, Australia; brett.sutton@csiro.au
[4] Peter Doherty Institute for Infection and Immunity, 792 Elizabeth St, Melbourne, VIC 3000, Australia
* Correspondence: john.skerritt@unimelb.edu.au or john.h.skerritt@gmail.com

Experience with mRNA COVID variant vaccines has shown that use of a platform approach can **streamline regulatory review** without exposing the public to safety risks or efficacy concerns, increasing confidence in mRNA technology. With a number of other products either already submitted for regulatory review or in late-stage clinical trials, and the mRNA and LNP design of many of these products being heavily based on the COVID vaccines from the **same manufacturer**, it is feasible to utilise the platform approach for these products. The comparability and bridging studies required will **depend on the extent of difference** to the original vaccines.

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FDA Platform Technology Designation Guidance for Industry

Draft guidance published May 29th 2024 for public consultation with a 60-day deadline, ending on July 28.

Contains Nonbinding Recommendations

Draft — Not for Implementation

TABLE OF CONTENTS

Platform Technology Designation Program for Drug Development

Guidance for Industry

DRAFT GUIDANCE

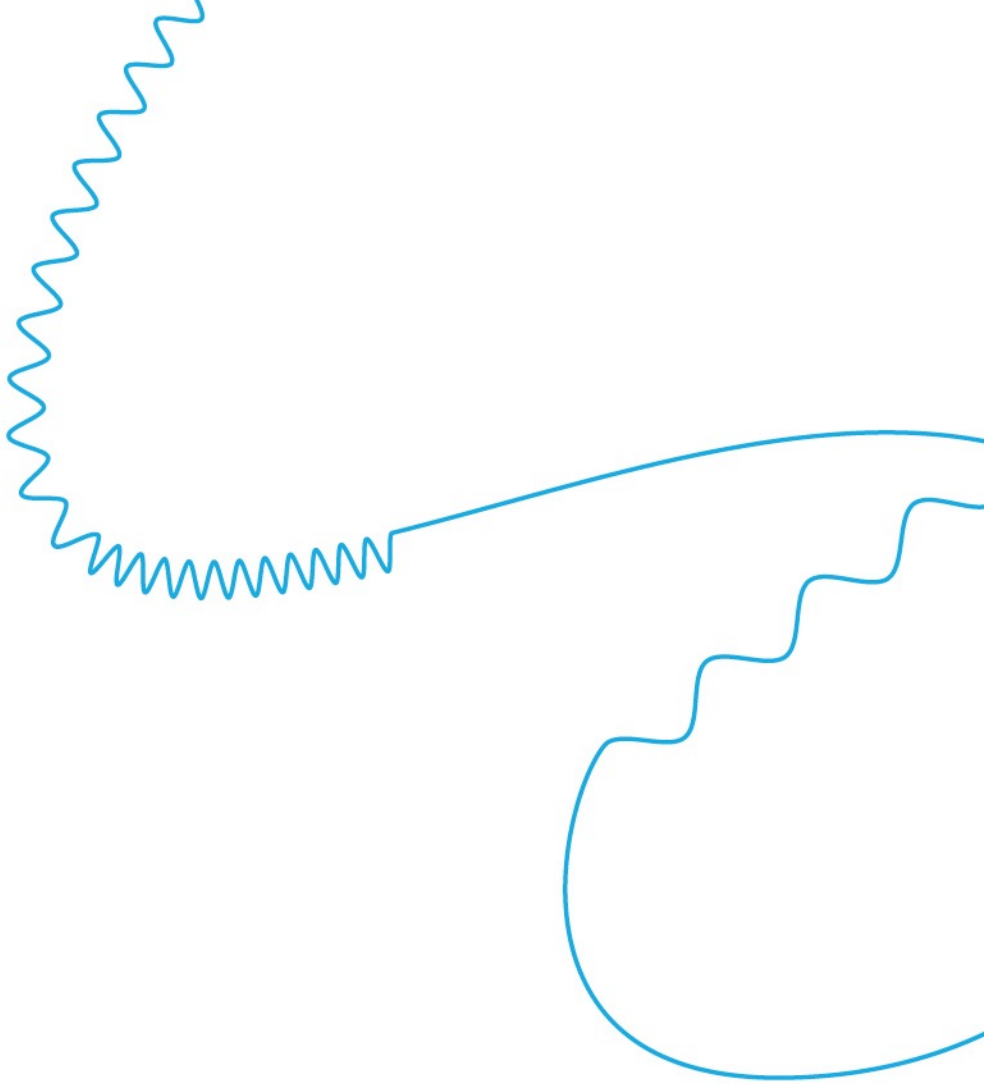
This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact (CDER) Melissa Furness at 240-402-8912, or (CBER) James Meyers at 240-402-7911.

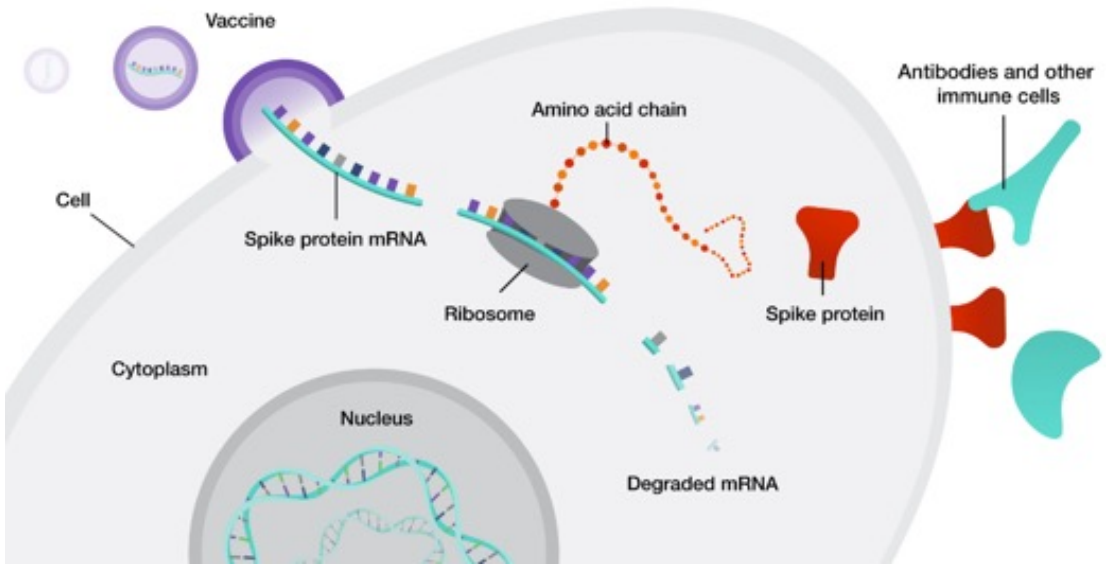
Details about the implementation of the platform technology designation program established by section 506K of the Federal Food, Drug, and Cosmetic Act

Gene Therapy definition



The value of a precise and more limited Gene Therapy definition

Current mRNA medicines do not alter the human genome



Example for mRNA based medicines for prevention or treatment from National Human Genome Research Institute (NHGRI); https://www.genome.gov/

mRNA Mode of action – scientific perspective

- Current mRNA medicines do not alter human genome
- Short persistence in the human body
- Well defined safety profile

Risk of imprecise definition of Gene Therapy

- Potential harm of misinformation and fake news
- May undermine confidence in the use of medicines for treatment or prevention

No change of high standards

- Clear definition of gene therapy does not change scientific standards for benefit-risk assessment or affect regulatory procedures.

Precise and Science-based Definition of Gene Therapy Medicinal Products
Need for scientifically correct and well understood term – avoid public misunderstanding

Maintaining high regulatory standards and requirements for mRNA medicines
The EMA to develop specific scientific guidelines

Public perception and misconceptions

2024 Edelman Trust Barometer

Trust in Healthcare dicereases -23 for Gene-based medicine (mRNA vaccines, gene splicing, gene therapy)

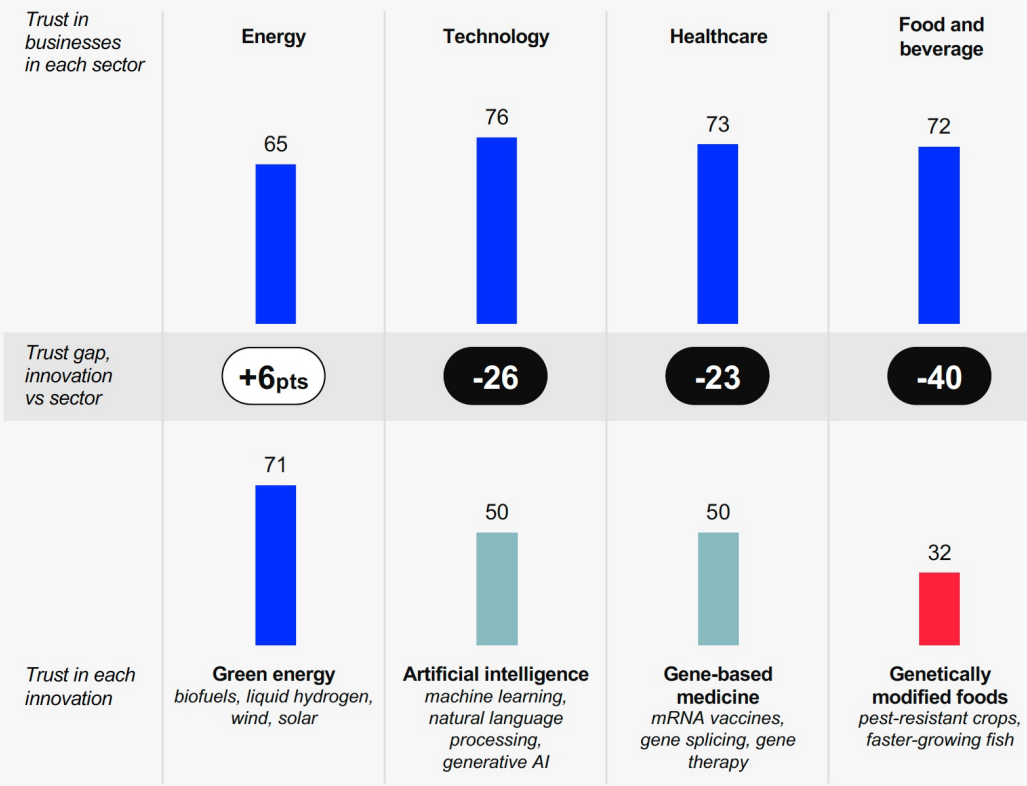
2024 Edelman Trust Barometer

Trust in Industry Sectors Does Not Guarantee Trust in Industry Innovations

Percent trust

GLOBAL 28

Distrust (1-49) | Neutral (50-59) | Trust (60-100)



2024 Edelman Trust Barometer. TRU_IND. Please indicate how much you trust businesses in each of the following industries to do what is right. 9-point scale; top 4 box, trust. Question asked of half the sample. TEC_TRU. How much do you trust each of these technologies? 9-point scale; top 4 box, trust. Question asked of half the sample. General population, 28-mkt avg.

High level of misunderstanding of mRNA

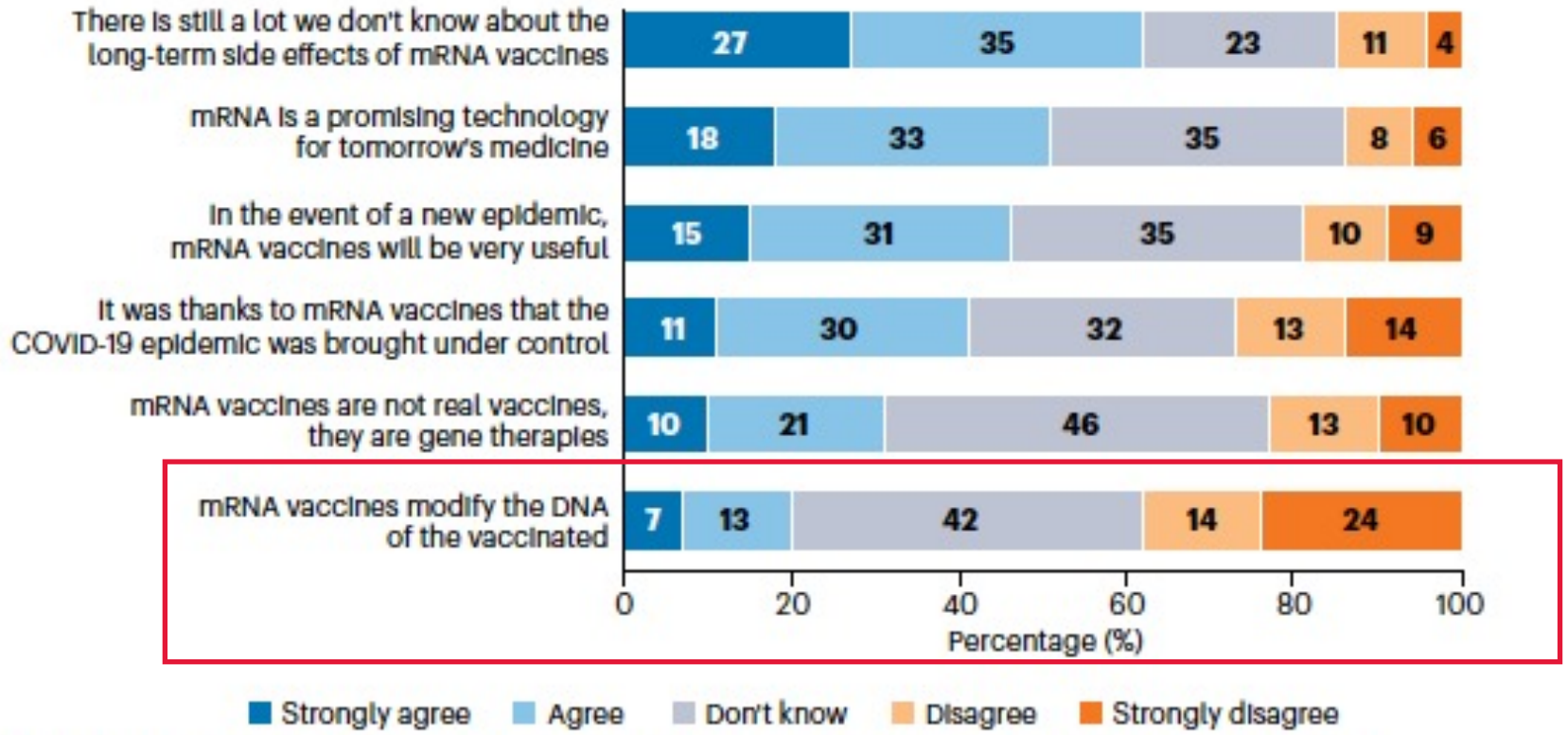


Fig. 1 | Opinions on mRNA vaccines. The ICOVAC1 survey was conducted online between 19 July and 14 August 2023 among a sample of 4,303 participants representative of the French mainland adult population, with a quota method on age, sex, profession, region and size of the area of residence.

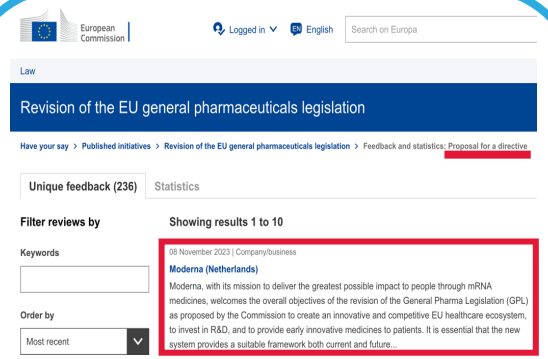
Source: nature medicine Volume 30 | April 2024 | 923–924 | 924

Defining Gene Therapy Medicinal Products in the EU

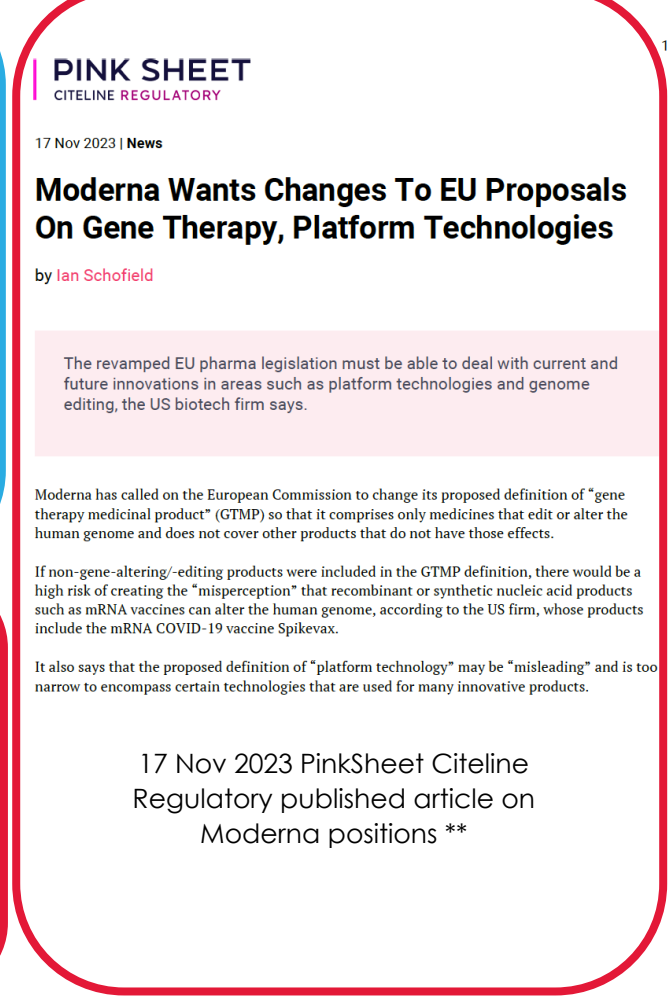
Proposed definition by the European Commission (EC) amended by the European Parliament (EP)

EC proposal, 26 April 2023	**“gene therapy medicinal product’ means a medicinal product, except vaccines against infectious diseases, that contains or consists of:**	
	a) a substance or a combination of substances intended to *edit the host genome* in a sequence-specific manner or that contain or consists of cells subjected to such modification; or	b) a recombinant or synthetic nucleic acid used in or administered to human beings with a view to regulating, replacing or adding a genetic sequence that mediates its effect by *transcription or translation* of the transferred genetic materials or that contain or consists of cells subjected to these modifications;”
EP amendment, 10 April 2024	**“gene therapy medicinal product” means a type 1 or type 2 medicinal product**	
	“type 1 gene therapy medicinal product” means a medicinal product, that contains or consists of a substance or a combination of substances that *edit the host genome* in a sequence-specific manner or that contain or consists of cells subjected to such modification;	“type 2 gene therapy medicinal product” means a medicinal product, except vaccines against infectious diseases, that contains or consists of a recombinant or synthetic nucleic acid used in or administered to human beings with a view to regulating, replacing or adding a genetic sequence that mediates its effect by *transcription or translation* of the transferred genetic materials or that contain or consists of cells subjected to these modifications;”

Scientific discussion initiated

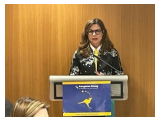


Moderna amendment to new Pharma Legislation (GPL) * among 254 others incl. EU trade associations



17 Nov 2023 PinkSheet Citeline Regulatory published article on Moderna positions **

1st Lunch Meeting 2024 at EU Parliament



Rapporteur MEP Pernille Weiss, DK

MEP Peter Liese, D

mRNA companies

DIA Global Forum publication March 2024

Defining Gene Therapy Medicinal Products in the EU: Scientific and Regulatory Perspectives

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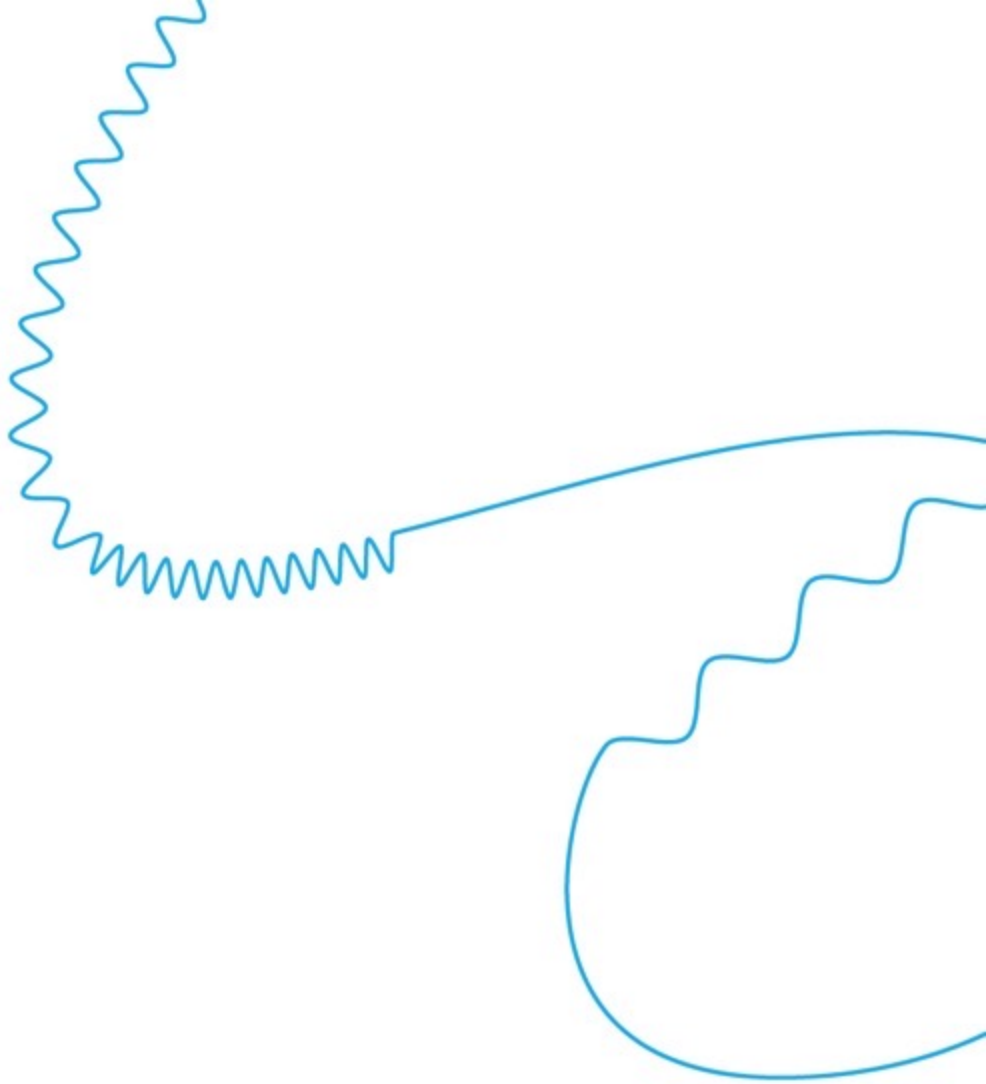
BIONTECH
CUREVAC
cencora PharmaLex

* https://ec.europa.eu/info/law/better-regulation/have-your-say/initiatives/12963-Revision-of-the-EU-general-pharmaceuticals-legislation/F3443091_en
** https://pink.citeline.com/PS149373/Moderna-Wants-Changes-To-EU-Proposals-On-Gene-Therapy-Platform-Technologies

*** Page 48ff - Art 26a Platform Technology Master File (PTMF)
Page 34f - Art 4 Definition (30a) Platform technology
Page 25 - Recital (149)

Thank you



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