Expanding the field of mRNA medicine

R&D day and business updates

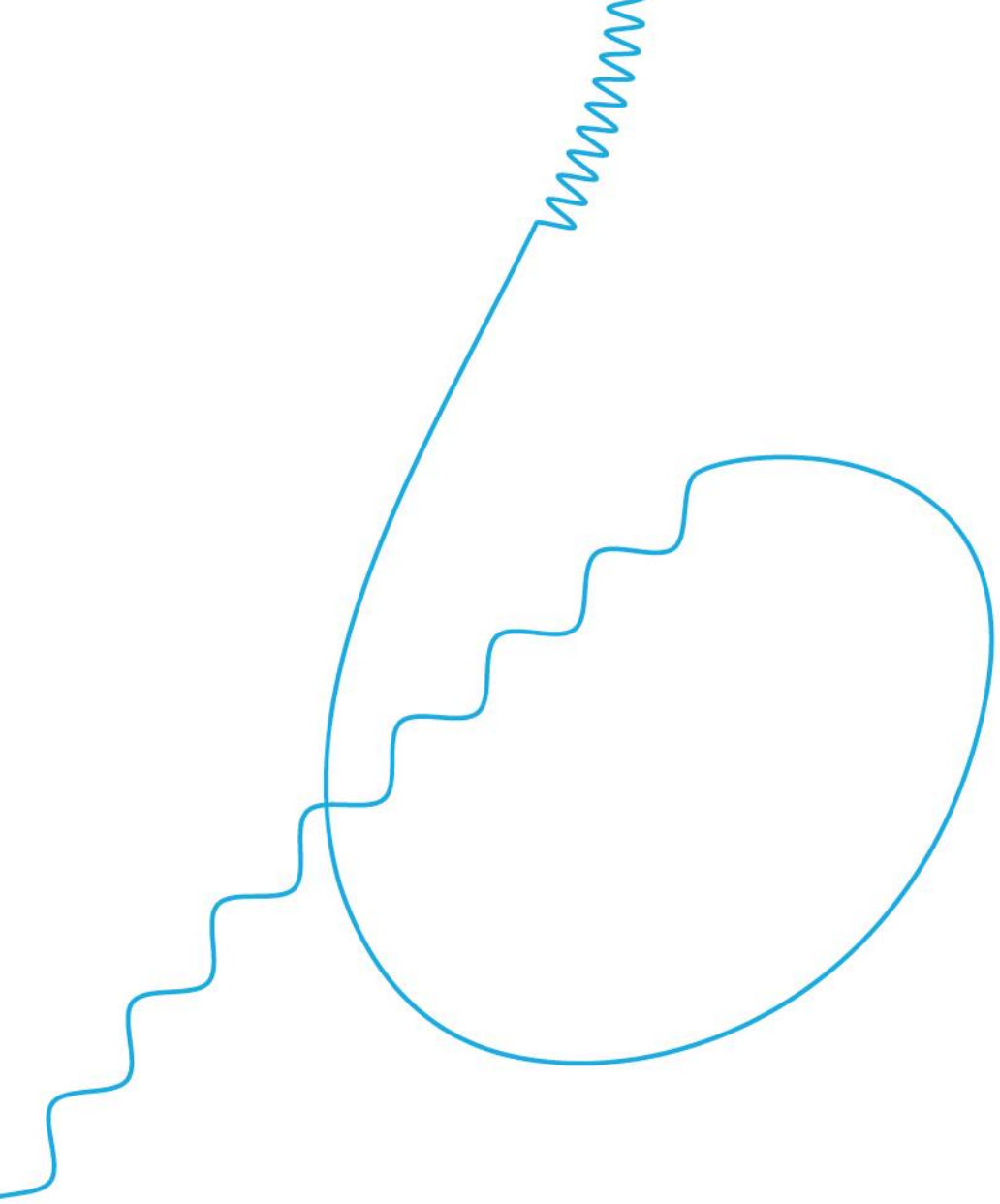
September 13, 2023

moderna

Forward-looking statements and disclaimer

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including statements regarding: the potential for Moderna to launch up to 15 products in the next 5 years, and advance new products into clinical studies; Moderna's discussions with regulators and the potential for accelerated, conditional or other product approvals in certain markets; the expectation that INT will begin a Phase 3 study in NSCLC in 2023, with more INT studies to be announced soon; clinical trial progress and results from Moderna's programs; Moderna's ability to develop combination vaccines and the anticipated benefits of those vaccines; the ability of Moderna's XBB.1.5 COVID-19 monovalent vaccine (mRNA-1283.815) to provide protection during the fall 2023/2024 season; Moderna's ability to develop updated vaccines to protect against evolving SARS-CoV-2 variants of concern; the safety and tolerability profile for Moderna's products; expected approvals for mRNA-1283.815 in various jurisdictions; Moderna's consultations with regulators on the licensure package for mRNA-1010; expectations regarding global regulatory approvals in 2024 for mRNA-1345 (RSV), and mRNA-1345's potential best-in-class profile; Moderna's ability to advance multiple generations of single-virus and combination respiratory vaccines to address unmet need; the size of the addressable markets being targeted by Moderna's pipeline, including for respiratory vaccines (COVID-19, RSV and flu), latent vaccines and rare disease therapeutics; the 2023 fall vaccine campaign, and Moderna's ability to increase market doses administered and solidify market share; the potential for Moderna to address the key challenges of developing a norovirus vaccine; Moderna's expectations for at least 4 rare disease product launches in the next 5 years; INT's potential to transform the continuum of cancer treatment, and the size of the oncology market; the anticipated financial and operational benefits associated with Moderna's franchises; the rate of success of Modena's platform; Moderna's expected R&D investment over the next 5 years; Moderna's ability to build a business that generates ~$20-30 billion of annual revenue; expectations regarding future COVID-19 vaccine sales; and Moderna's actions to accelerate gross margin expansion. The forward-looking statements in this presentation are neither promises nor guarantees, and you should not place undue reliance on these forward-looking statements because they involve known and unknown risks, uncertainties, and other factors, many of which are beyond Moderna's control and which could cause actual results to differ materially from those expressed or implied by these forward-looking statements. These risks, uncertainties, and other factors include, among others, those risks and uncertainties described under the heading "Risk Factors" in Moderna's Annual Report on Form 10-K for the fiscal year ended December 31, 2022, filed with the U.S. Securities and Exchange Commission (SEC), and in subsequent filings made by Moderna with the SEC, which are available on the SEC's website at www.sec.gov. Except as required by law, Moderna disclaims any intention or responsibility for updating or revising any forward-looking statements contained in this presentation in the event of new information, future developments or otherwise. These forward-looking statements are based on Moderna's current expectations and speak only as of the date of this presentation.

moderna



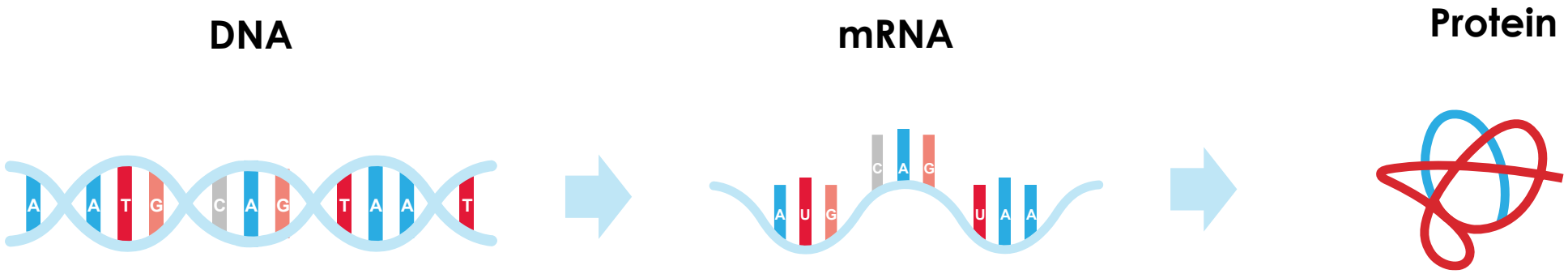
Introduction

Stéphane Bancel

Chief Executive Officer

moderna

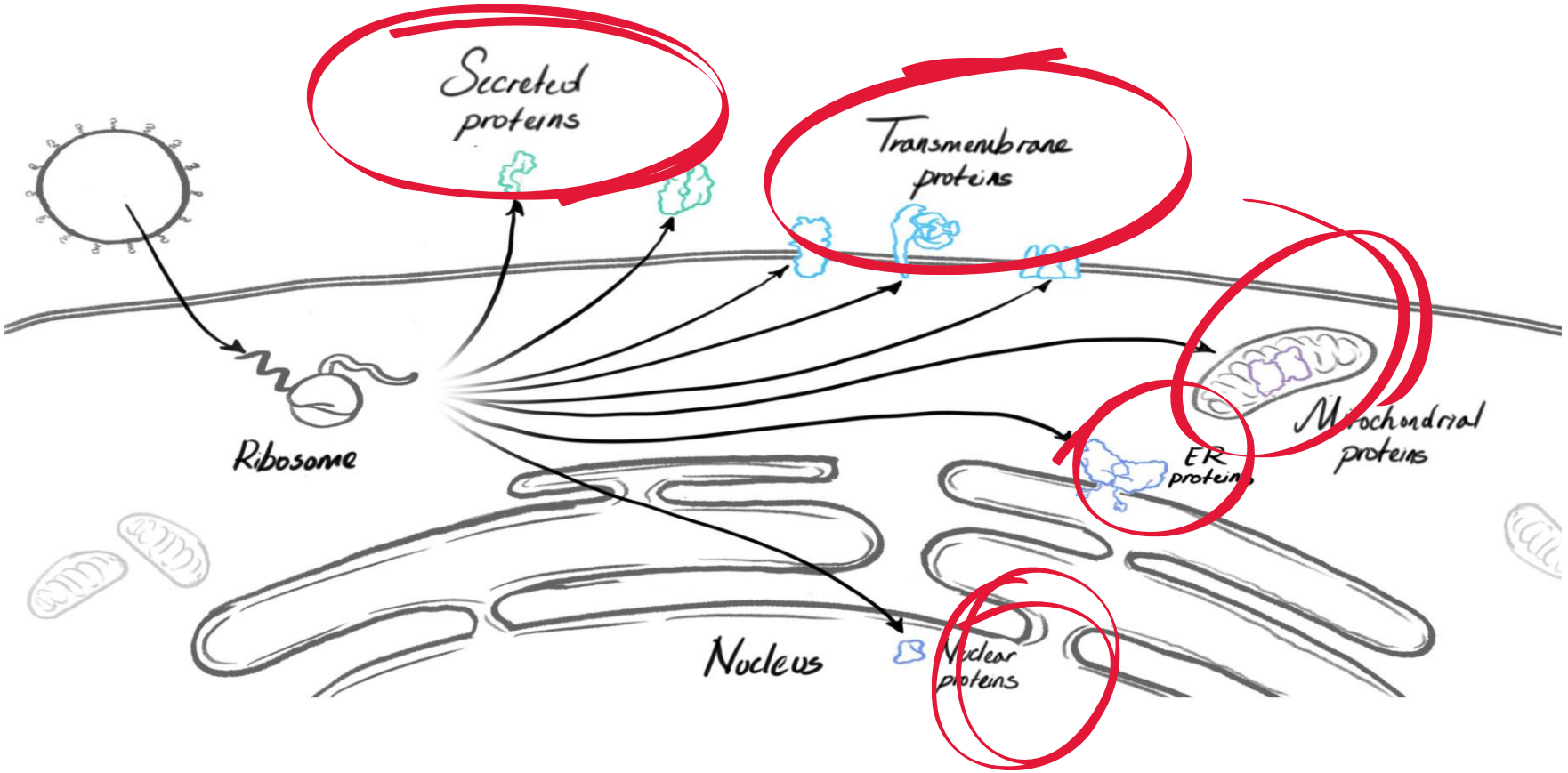
Moderna was founded and built to use nature's information molecule, mRNA, to treat and prevent disease



mRNA-based medicine could move at the pace of information by leveraging a common platform

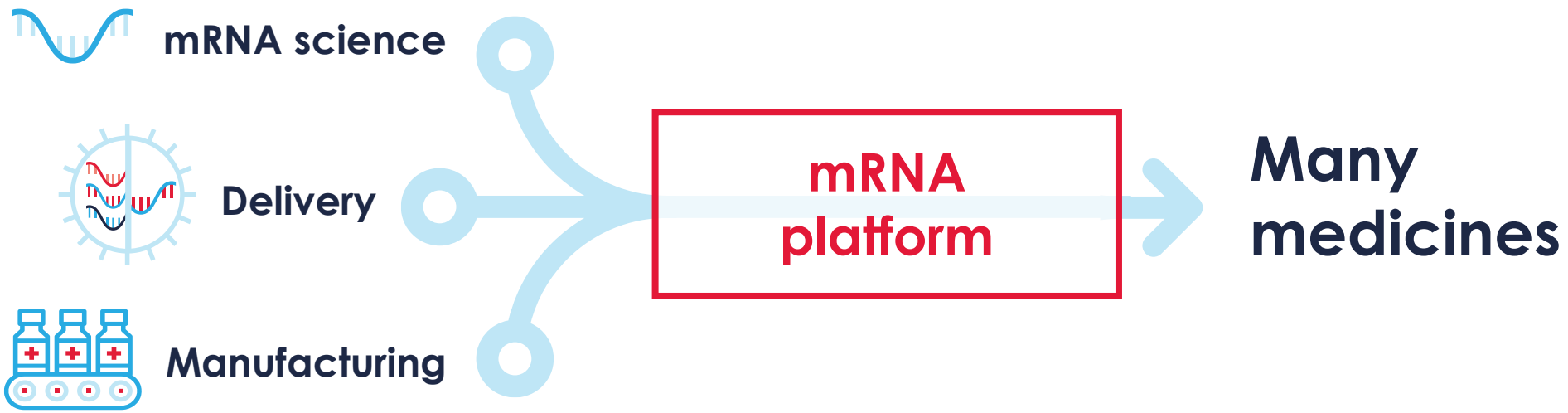
moderna

The promise of mRNA



1. Large opportunity to address unmet need
2. Higher efficiency in R&D
3. Rapid development
4. Greater capital efficiency

Investing in a platform to deliver on the promise of mRNA



Our platform incorporates the advancements and inventions we've made and continue to make in mRNA science, delivery technologies and manufacturing processes

Moderna's platform for harnessing the power of mRNA is being realized

Respiratory vaccines

3/3 positive Phase 3 programs

- **COVID:** Approved
- **RSV:** Filed
- **Flu:** Positive Phase 3 data

Latent + other vaccines

CMV: Phase 3 fully enrolled in adults

Oncology therapeutics

- **INT:** Positive Phase 2 data
- **INT:** Phase 3 in adjuvant melanoma enrolling
- **INT:** Phase 3 in NSCLC to begin in 2023

Rare disease therapeutics

3/3 programs with positive clinical signals

PA, MMA & GSD1a: Encouraging early data and preparing to move towards registrational studies

moderna

We are beginning to deliver great impact with our mRNA medicines

Anticipating up to 15 launches in the next 5 years[1]

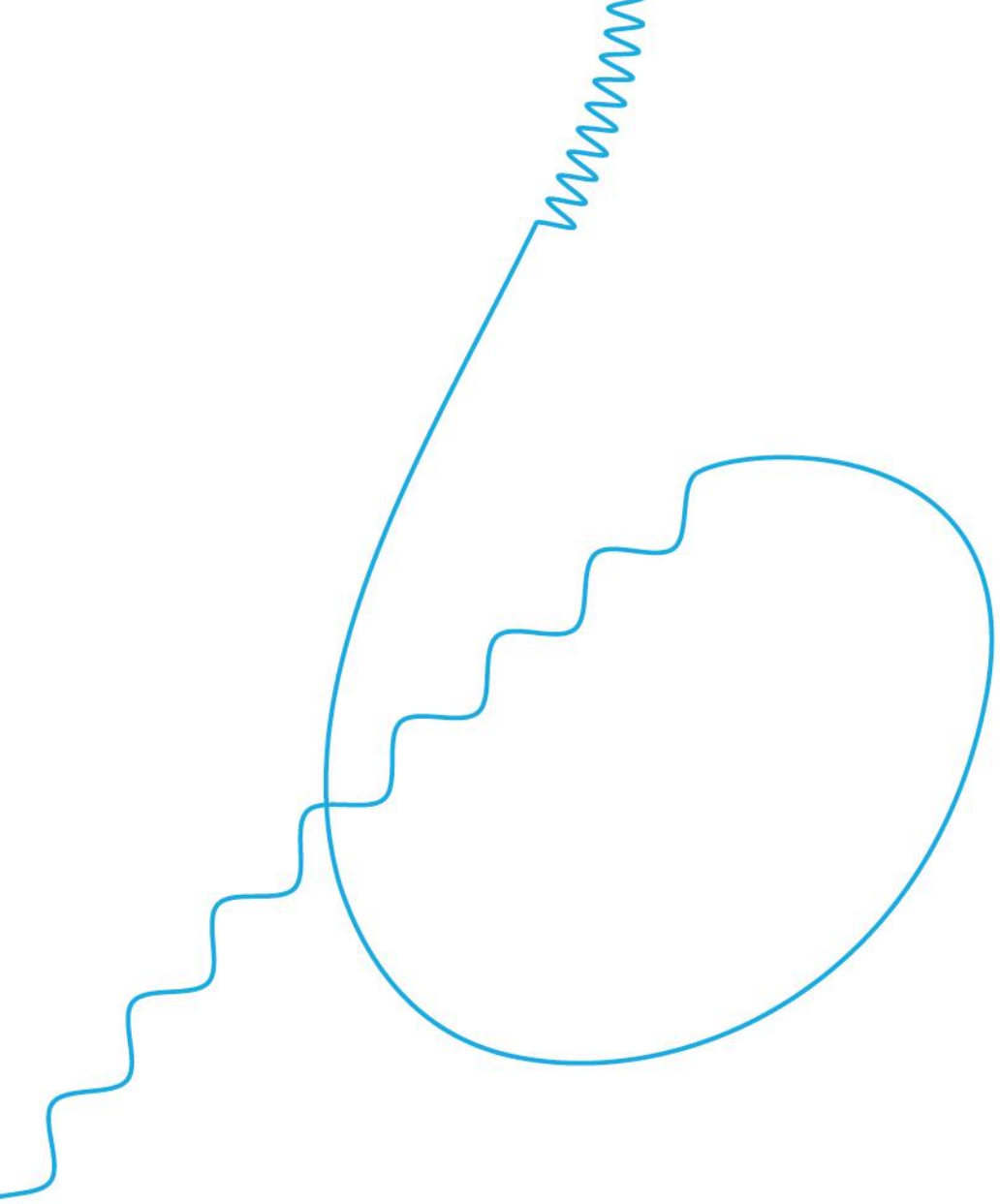
	Respiratory vaccines	Latent/other vaccines	Oncology	Rare disease
by 2025	**RSV** (older adults) mRNA-1345 **Seasonal Flu** mRNA-1010 **Flu/COVID** mRNA-1083 **NextGen COVID** mRNA-1283			
by 2028	**Flu/COVID/RSV** NextGen **RSV/hMPV** (older adults) mRNA-1365 **RSV** 2-18Y mRNA-1345 **Pandemic Flu** mRNA-1018 **NextGen Flu** mRNA-1011/-1020 **Endemic hCOV** mRNA-1287	**CMV** mRNA-1647 **Norovirus** (older adults) mRNA-1403/-05 **EBV (IM)** mRNA-1189 **Lyme** mRNA-1975/-82 **VZV** mRNA-1468 **HSV** mRNA-1608	*Subject to regulatory discussions[2]* **INT** (adjuvant melanoma) mRNA-4157 **INT** (undisclosed indication) mRNA-4157 **INT** (adjuvant NSCLC) mRNA-4157	**MMA** mRNA-3705 **PA** mRNA-3927 **PKU** mRNA-3210 **GSD1a** mRNA-3745

1 Subject to positive clinical data and regulatory discussions/approvals
2 Subject to future regulatory discussions, there may be potential for accelerated or conditional approvals in some markets

R&D Day Agenda

Introduction	**Stéphane Bancel**, *Chief Executive Officer*
Development Strategy	**Stephen Hoge, M.D.**, *President*
Respiratory Franchise	**Jacqueline Miller, M.D., Darin Edwards, Ph.D, Raffael Nachbagauer, M.D., Ph.D., Arpa Garay**, *Chief Commercial Officer*
Latent and Other Franchise	**Jacqueline Miller, M.D., Arpa Garay**
Coffee Break	
Rare Disease Franchise	**Kyle Holen, M.D., Geoff Rezvani M.D., Arpa Garay**
Oncology Franchise	**Kyle Holen M.D., Michelle Brown M.D. Ph.D, Arpa Garay**
Franchise Financials	**Jamey Mock**, *Chief Financial Officer*
Conclusion	**Stéphane Bancel**
General Q&A	**Stéphane Bancel, Stephen Hoge, Arpa Garay, Jamey Mock, Jacqueline Miller, Kyle Holen**

moderna



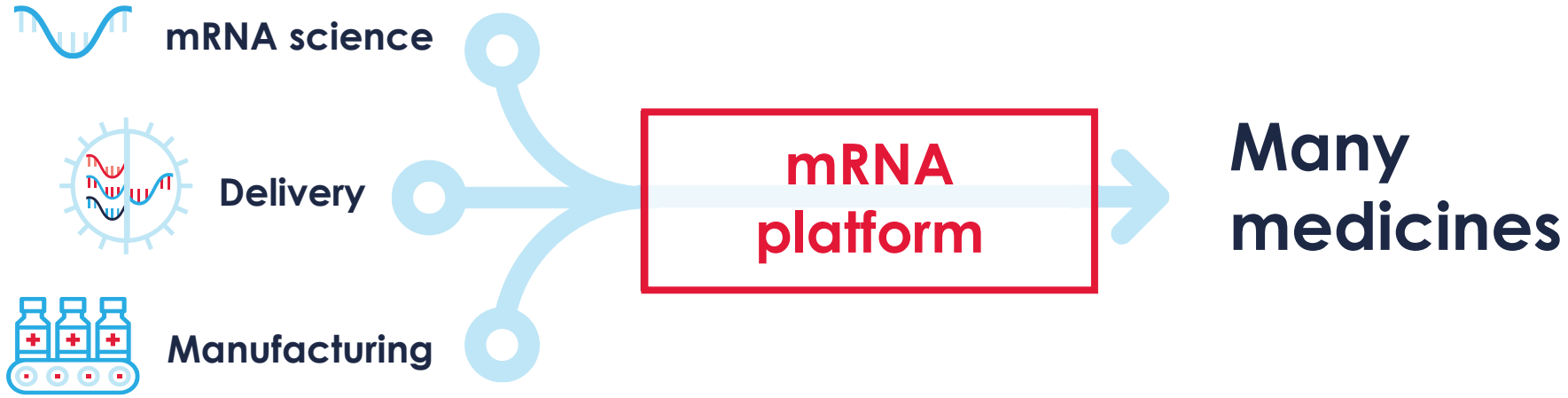
R&D strategy

Stephen Hoge, M.D.
President

moderna

Moderna was founded and built as a mRNA platform company

10 years of investment creating a singular platform



moderna

We leverage our mRNA platform to create modalities

mRNA science

Delivery

Manufacturing

mRNA platform

Infectious disease vaccines

Proof-of-concept
- COVID
- RSV
- Flu

Cancer therapeutics

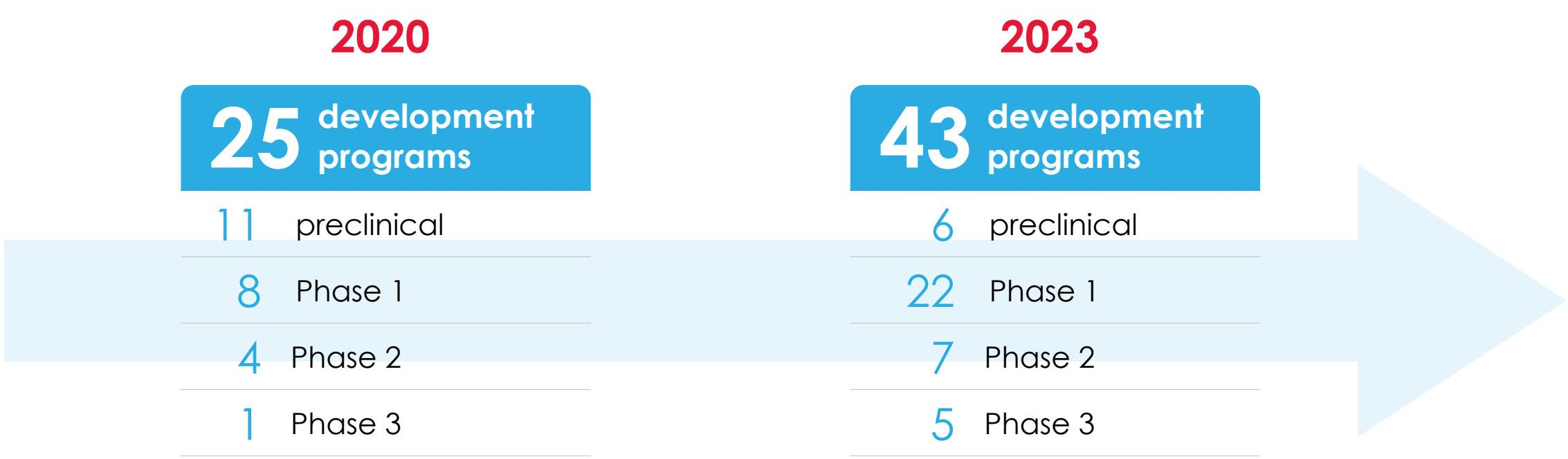
Proof-of-concept
- INT in adjuvant melanoma

Rare disease intracellular therapies

Proof-of-concept
- PA
- MMA
- GSD1a

moderna

Our platform has allowed us to double our pipeline in 3 years

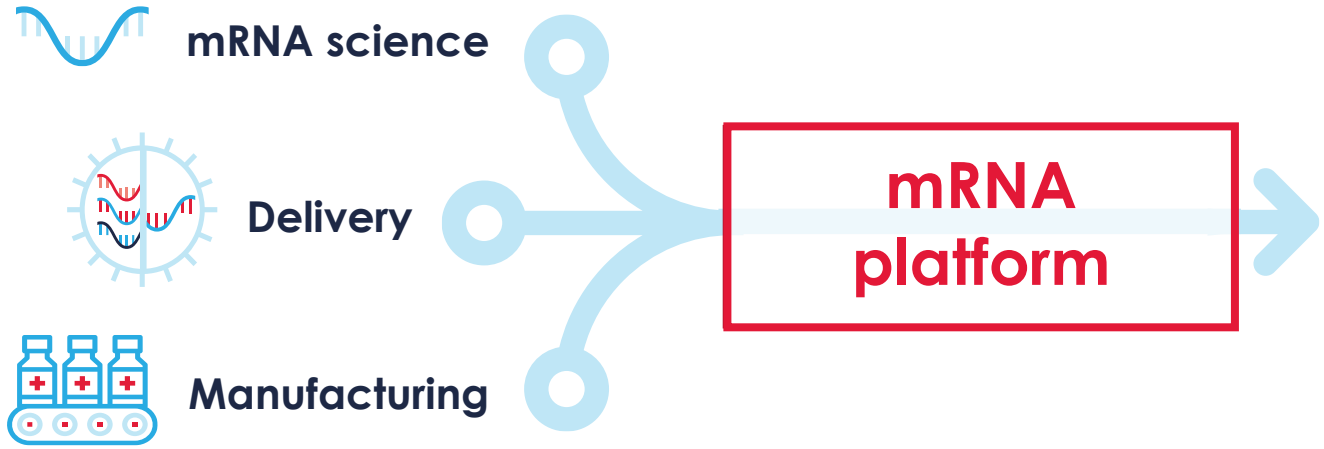


Note: numbers do not total as 2020 includes 1 commercial stage program, and 2023 includes 3 commercial stage programs

moderna

Moderna was founded and built as a mRNA platform company

We will continue to invest to expand our platform and deliver new medicines

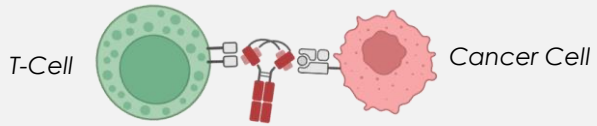


moderna

Expanding the frontiers of mRNA medicine (Oncology)

Our partnerships in oncology connect our mRNA platform to external collaborators who are pioneers in their fields, accelerating the advancement of innovative cancer medicines to patients

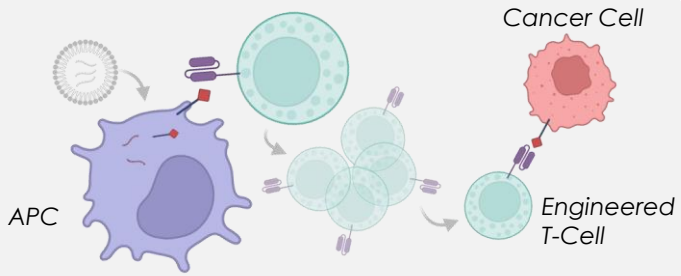
Novel proteins



T-cell Engagers

Expression of pMHC targeted T-cell engaging bispecific antibodies

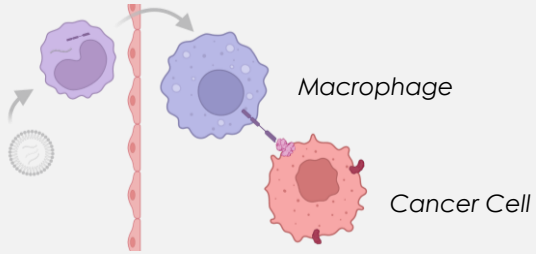
Cancer Vaccines



Cell Therapy Enhancing Vaccines

Vaccine for cognate antigen to boost CAR-T and TCR-T cells

Myeloid Cell Therapy



In vivo CAR-M

Expression of chimeric antigen receptors (CARs) in myeloid cells

Expanding the frontiers of mRNA medicine (Moderna Genomics)

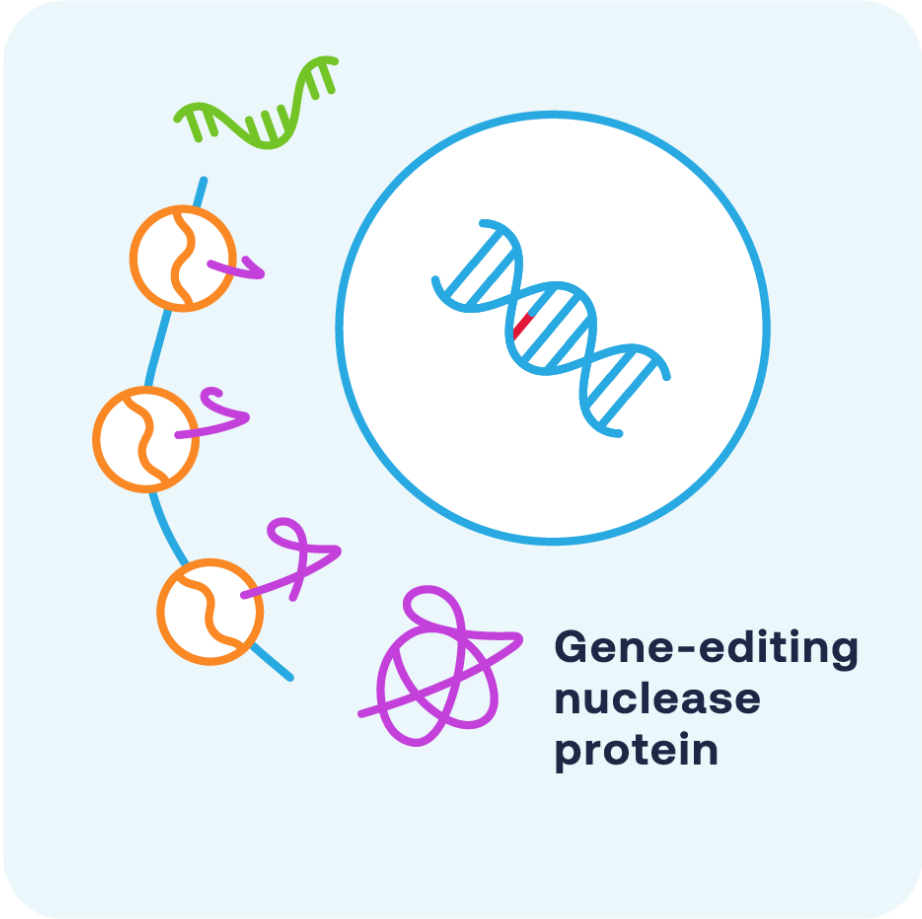
Investing in our mRNA platform and partnerships with gene editing leaders to deliver for patients suffering from rare genetic diseases

Expanding the frontier of mRNA to deliver the promise of gene-editing through Moderna Genomics (mGx)

Medicines will target genetic mutations specific to a patient's genome

life edit® an elevatebio company

Metagenomi



moderna

Prioritization of our pipeline when needed

Announced discontinuation of four clinical programs today

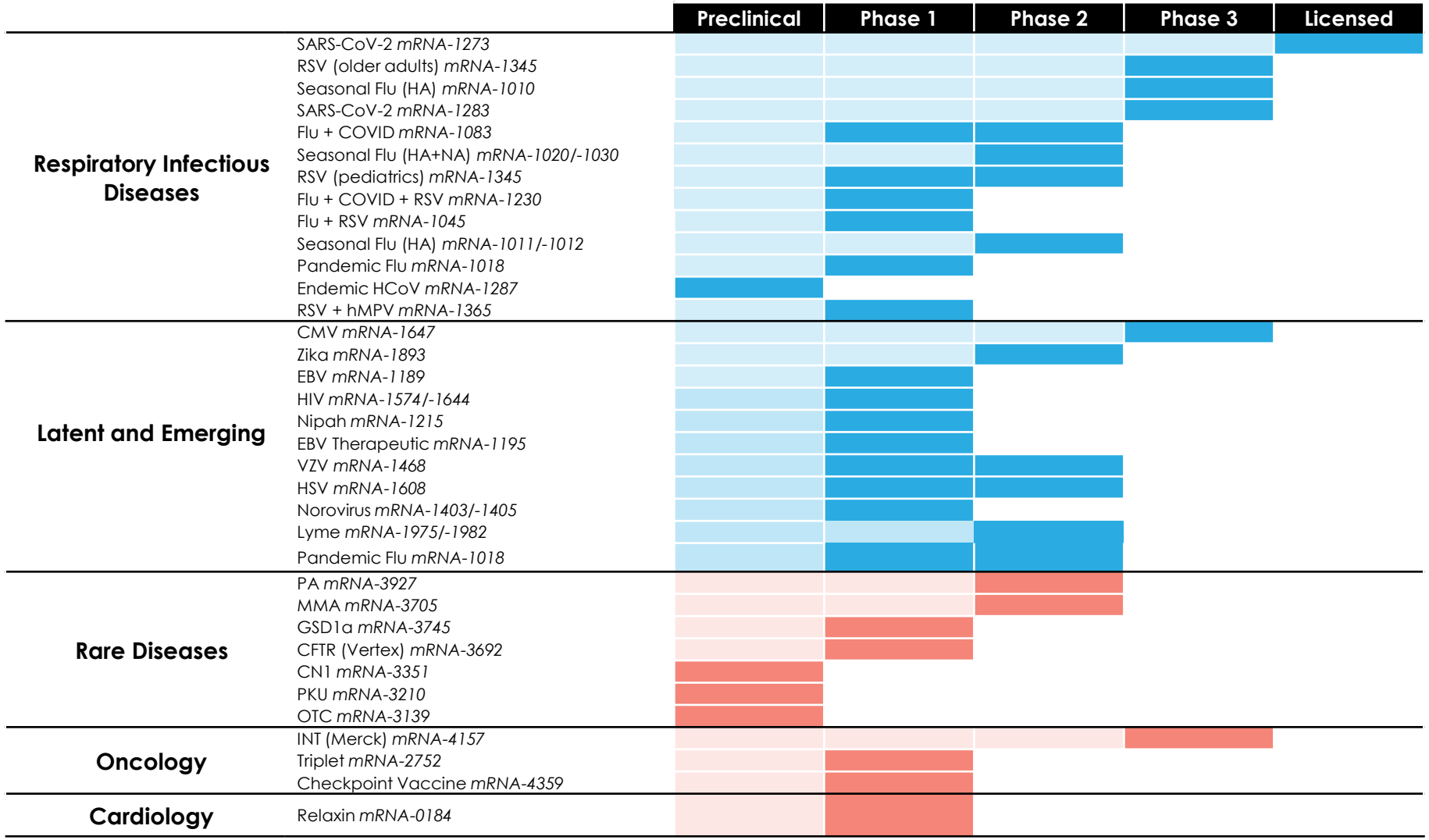
VEGF-A
AZD8601

IL-12
MEDI1191

Pediatric hMPV + PIV3
mRNA-1653

COVID + flu combo (first generation)
mRNA-1073

Moderna has a broad portfolio of mRNA medicines



moderna

Anticipating up to 15 product launches over the next 5 years

Our mRNA platform is delivering across cancer, rare disease, and infectious diseases

	Respiratory vaccines	Latent/other vaccines	Oncology	Rare disease
by 2025	**RSV** (older adults) mRNA-1345 **Seasonal Flu** mRNA-1010 **Flu/COVID** mRNA-1083 **NextGen COVID** mRNA-1283			
by 2028	**Flu/COVID/RSV** NextGen **RSV/hMPV** (older adults) mRNA-1365 **RSV** (2-18Y) mRNA-1345 **Pandemic Flu** mRNA-1018 **NextGen Flu** mRNA-1011/-1020 **Endemic hCOV** mRNA-1287	**CMV** mRNA-1647 **Norovirus** (older adults) mRNA-1403/-05 **EBV (IM)** mRNA-1189 **Lyme** mRNA-1975/-82 **VZV** mRNA-1468 **HSV** mRNA-1608	*Subject to regulatory discussions*[1] **INT** (adjuvant melanoma) mRNA-4157 **INT** (undisclosed indication) mRNA-4157 **INT** (adjuvant NSCLC) mRNA-4157	**MMA** mRNA-3705 **PA** mRNA-3927 **PKU** mRNA-3210 **GSD1a** mRNA-3745

Note: Subject to positive clinical data and regulatory discussions/approvals
1 Subject to future regulatory discussions, there may be potential for accelerated or conditional approvals in some markets

Focus of today's update

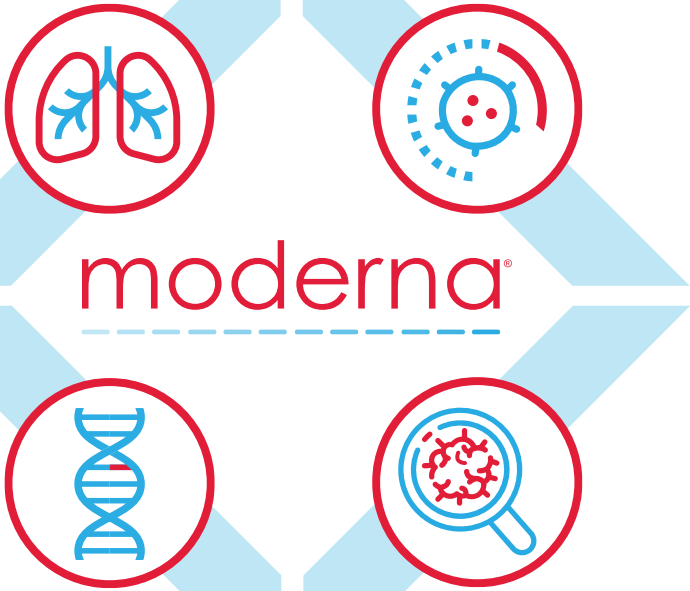
Respiratory vaccines

COVID-19

Seasonal Flu

Latent + other vaccines

Cytomegalovirus (CMV)



Rare disease therapeutics

Propionic acidemia (PA)

Methylmalonic acidemia (MMA)

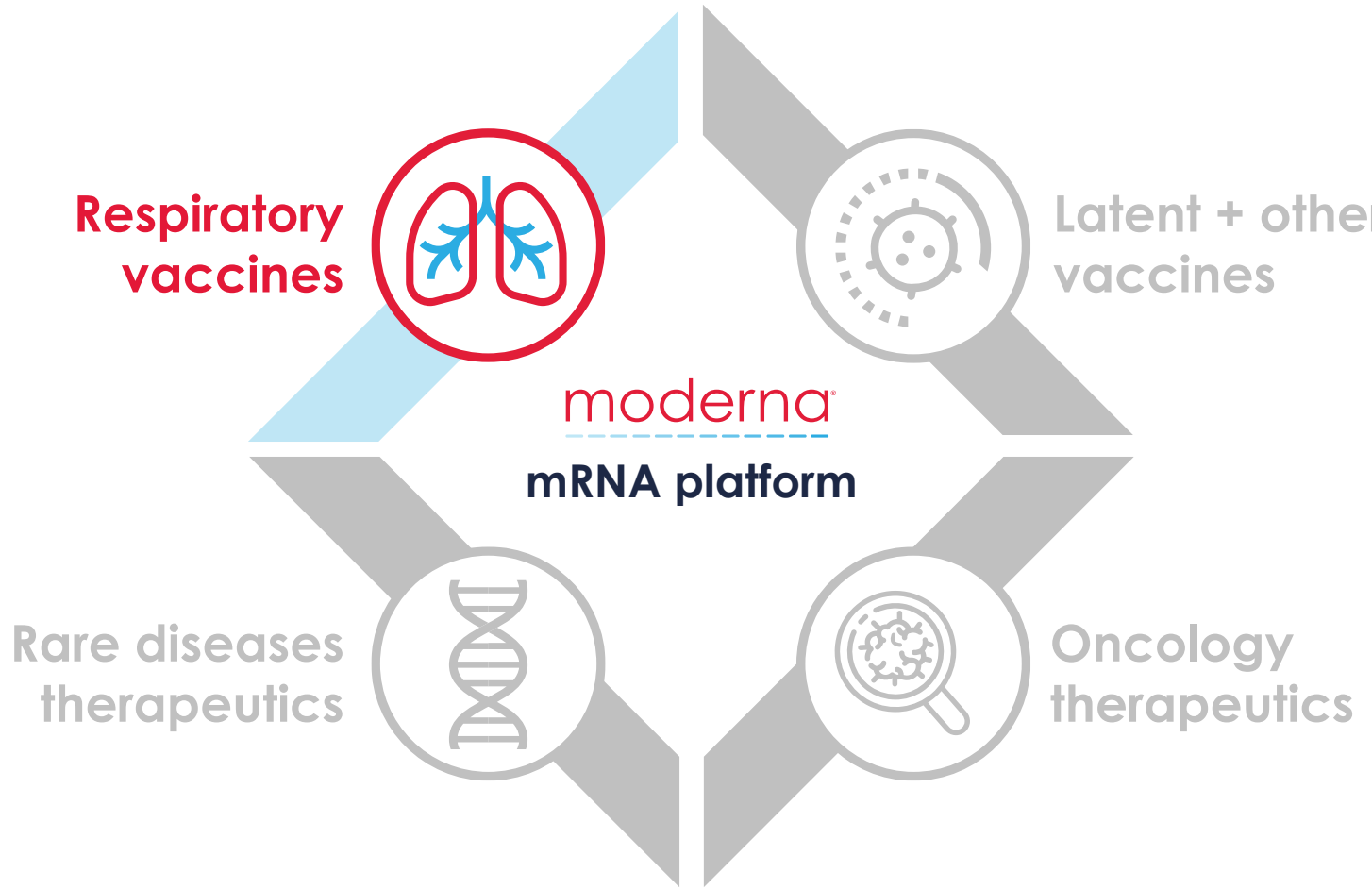
Phenylketonuria (PKU)

Oncology therapeutics

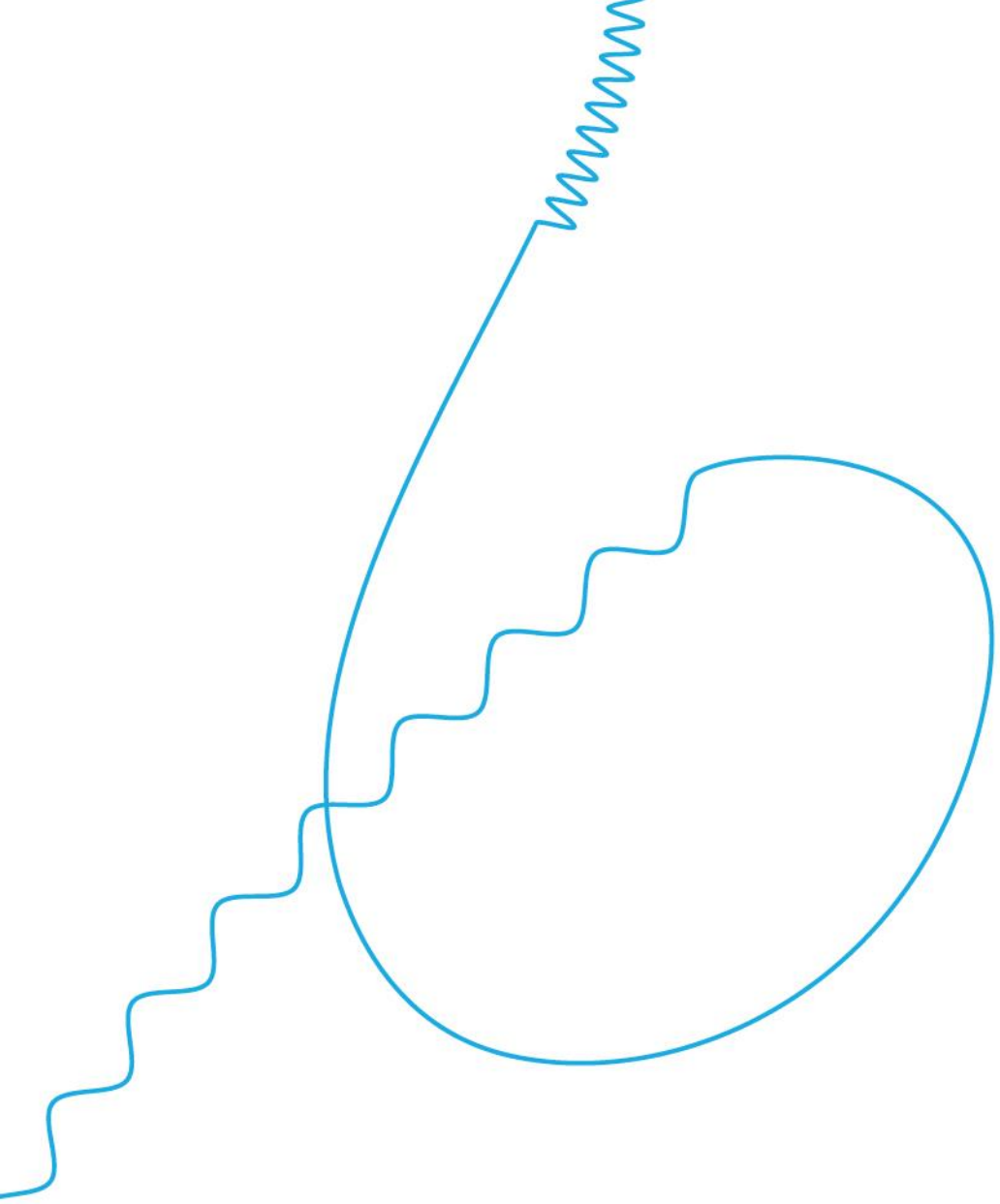
INT in multiple indications

moderna

Respiratory vaccines



moderna



Respiratory vaccines
Development

Jacqueline Miller, M.D.
SVP, Head of Development,
Infectious Diseases,
Research & Development

moderna

Respiratory vaccines pipeline overview

Commercial and Phase 3 programs

PC | Ph. 1 | Ph. 2 | Ph. 3 | Comm.

COVID-19 (mRNA-1273.222/.815)

PC | Ph. 1 | Ph. 2 | Ph. 3 | Comm.

Older adults RSV (mRNA-1345)

PC | Ph. 1 | Ph. 2 | Ph. 3 | Comm.

Flu (mRNA-1010)

Next-gen programs

PC | Ph. 1 | Ph. 2 | Ph. 3 | Comm.

COVID-19 next-gen booster (mRNA-1283)

PC | Ph. 1 | Ph. 2 | Ph. 3 | Comm.

Flu (mRNA-1011/-1012)

PC | Ph. 1 | Ph. 2 | Ph. 3 | Comm.

Flu (mRNA-1020/-1030)

Combination programs

PC | Ph. 1 | Ph. 2 | Ph. 3 | Comm.

Flu + COVID-19 (mRNA-1083)

PC | Ph. 1 | Ph. 2 | Ph. 3 | Comm.

Flu + COVID-19 + RSV (mRNA-1230)

PC | Ph. 1 | Ph. 2 | Ph. 3 | Comm.

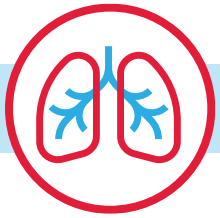
Flu + RSV (mRNA-1045)

PC | Ph. 1 | Ph. 2 | Ph. 3 | Comm.

RSV + hMPV (mRNA-1365)

moderna

Common characteristics for vaccine development in the respiratory viruses

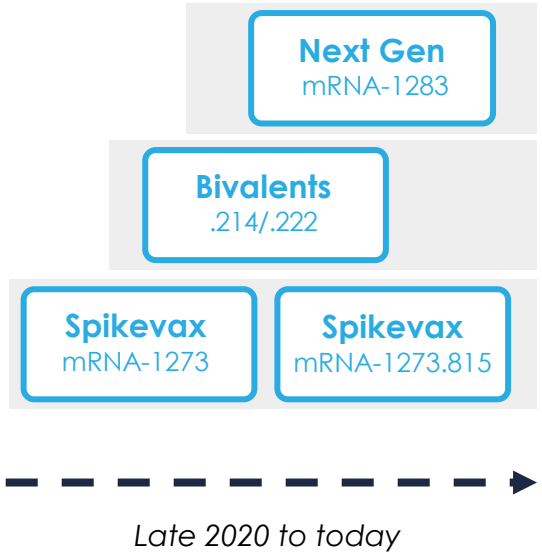


Respiratory vaccines franchise

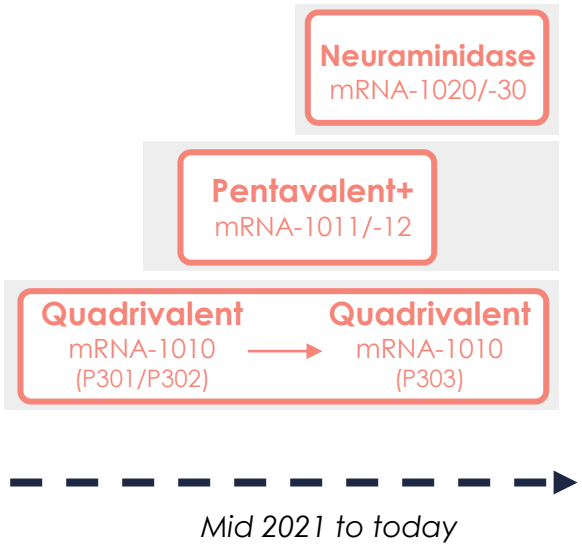
- SARS-CoV-2, RSV and influenza data are proof that this platform can effectively address respiratory pathogens
- Highest burden in older adults, young children and immunocompromised
- The successful implementation of bivalent COVID-19 suggests that the combination of multiple antigens should be technically feasible

Our platform has allowed us to rapidly create a diverse respiratory franchise

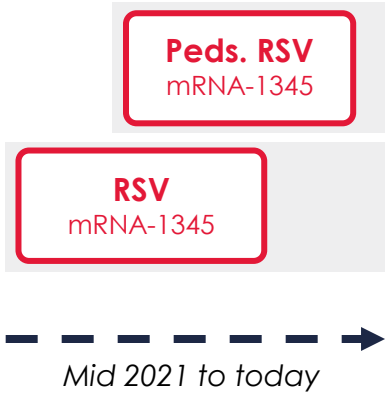
COVID: Rapid updates to meet endemic market needs



Influenza: Rapid iteration of additional antigens to try to address unmet needs



RSV: Rapid development of novel vaccine

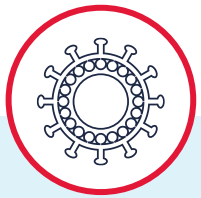


moderna

Today we will be presenting new data from our respiratory programs

COVID-19

- mRNA-1283 data: mRNA1283.222 vs. mRNA1273.222
- mRNA-1273.815: nAbs against emerging variants



Flu

mRNA-1010 P303 safety and immunogenicity

moderna

mRNA-1283.222 and mRNA-1273.222 were evaluated in a Phase 1/2 clinical study

- mRNA-1283 is a refrigerator-stable mRNA vaccine that will facilitate distribution and administration by healthcare providers
- mRNA-1283 encodes for the portions of the SARS-CoV-2 spike protein critical for neutralization, specifically the Receptor Binding Domain (RBD) and N-terminal Domain (NTD)

Design
Randomized, observer-blind, active-controlled study

Number of participants
~50 per vaccine and age group

Vaccination schedule
Single dose of mRNA-1283.222 or mRNA-1273.222

Duration: 6 months
Enrollment period: April–May 2023

Study participants will be followed up for 6 months

Site location
US

Phase 1/2 clinical study

Ages 18 to < 65

mRNA-1283.222
N~50

mRNA-1273.222
N~50

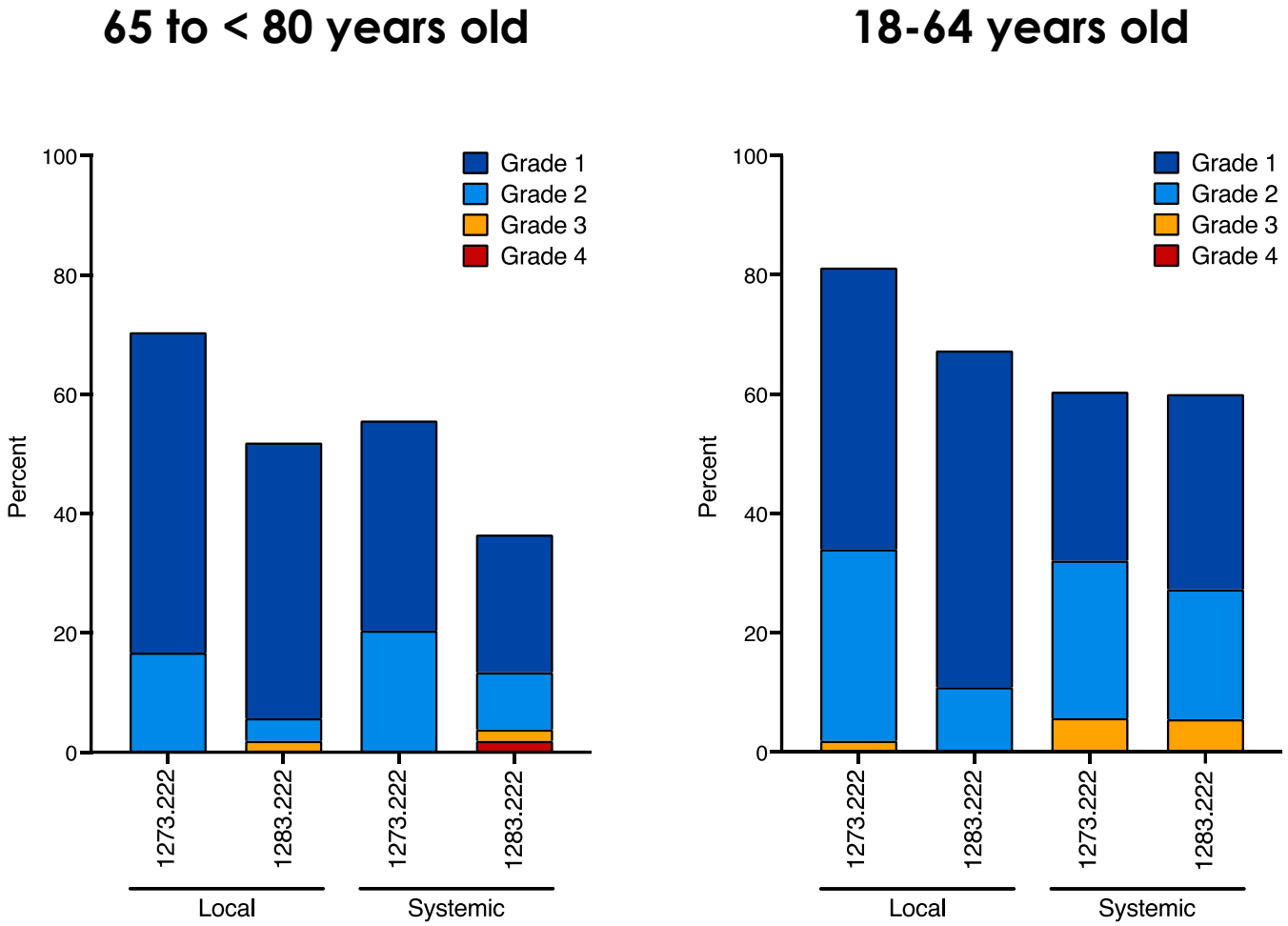
Ages 65 to < 80

mRNA-1283.222
N~50

mRNA-1273.222
N~50

Reactogenicity profile of mRNA-1283 is similar to mRNA-1273 in a Phase 1/2 study

- A booster dose of mRNA-1283.222 vs. mRNA-1273.222
- Approximately 50 participants in each study arm

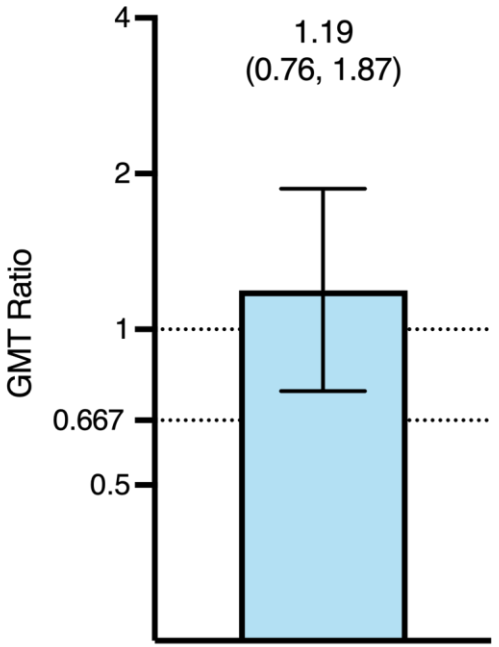


*Reported grade 4 fever in mRNA-1283 arm later verified as a reporting error and confirmed with subject

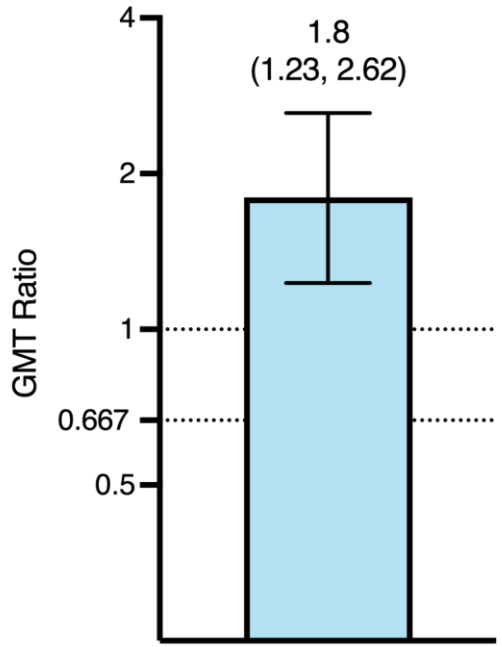
mRNA-1283.222 elicited higher titers against BA.4/5 compared to mRNA-1273.222 in a Phase 1/2 study

- Geometric mean titer (GMT) ratio of mRNA-1283.222 was compared to mRNA-1273.222 against BA.4/BA.5 in a Phase 1/2 study
- Approximately 50 participants in each study arm
- Titers were numerically higher for mRNA-1283 across both age groups

65 to < 80 years old



18-64 years old



moderna

mRNA-1283 pivotal Phase 3: primary endpoint of immunogenicity is expected in 4Q 2023

The Phase 3 was designed to test the immunogenicity, safety and relative vaccine efficacy of mRNA -1283.222 against mRNA-1273.222 in participants 12+ years of age

Design
Randomized 1:1, observer-blind, active-controlled study

Number of participants
11,500 medically stable adults ≥ 12 years old

Vaccination schedule
Single dose of mRNA-1283.222 or mRNA-1273.222

Duration: 12-months
Enrollment period: April–August 2023

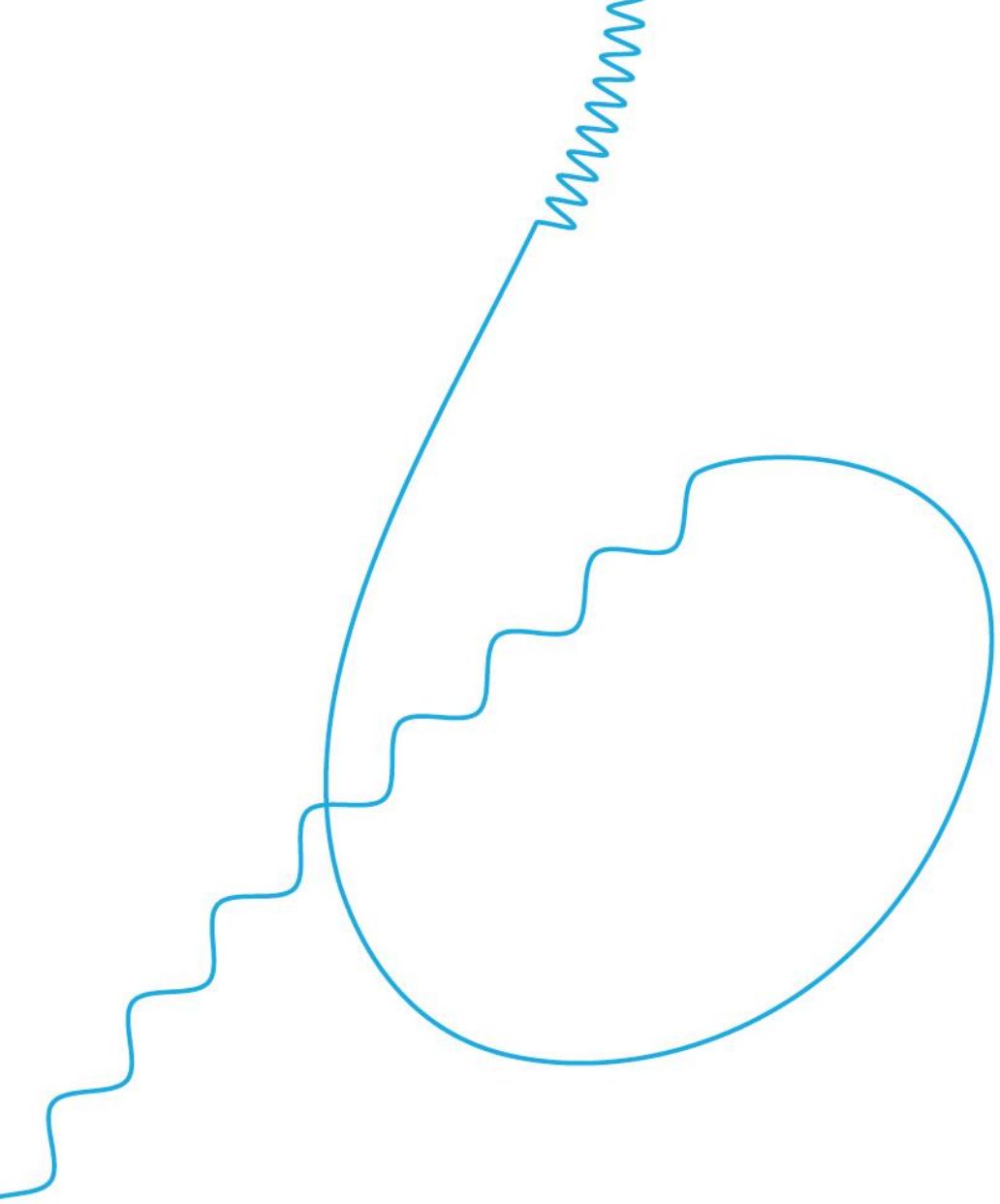
Study participants will be followed up for 12 months after study injection

Site location
US, UK and Canada

Total N = 11,500
Randomization Ratio = 1:1

mRNA-1283.222
N~5750

mRNA-1273.222
N~5750



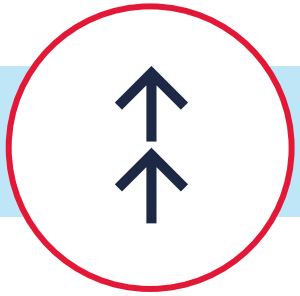
COVID-19

Darin Edwards, PhD

Executive Director, COVID Vaccines Program Leader

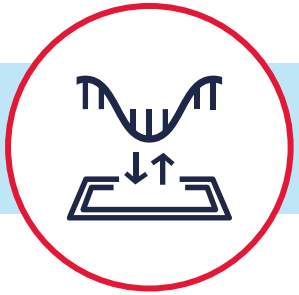
moderna

Moderna's variant monitoring and seasonal update process



Preparation for strain selection

- Moderna performs continuous epidemiological monitoring and risk assessment of variants throughout the year
- Updated variant vaccine candidates were prepared and assessed in animals and humans



Seasonal strain selection

- New variant vaccines were assessed in animals and humans
- Results informed on strain selection for the 2023/24 season
  - XBB.1.5 monovalent vaccine was selected as the 2024 vaccine composition

Continued monitoring / assessment

- Assessment of Spikevax 2023/24 clinical participants against new variants as they emerge
- Emerging variants with human and animal sera

moderna

Moderna's variant monitoring and seasonal update process

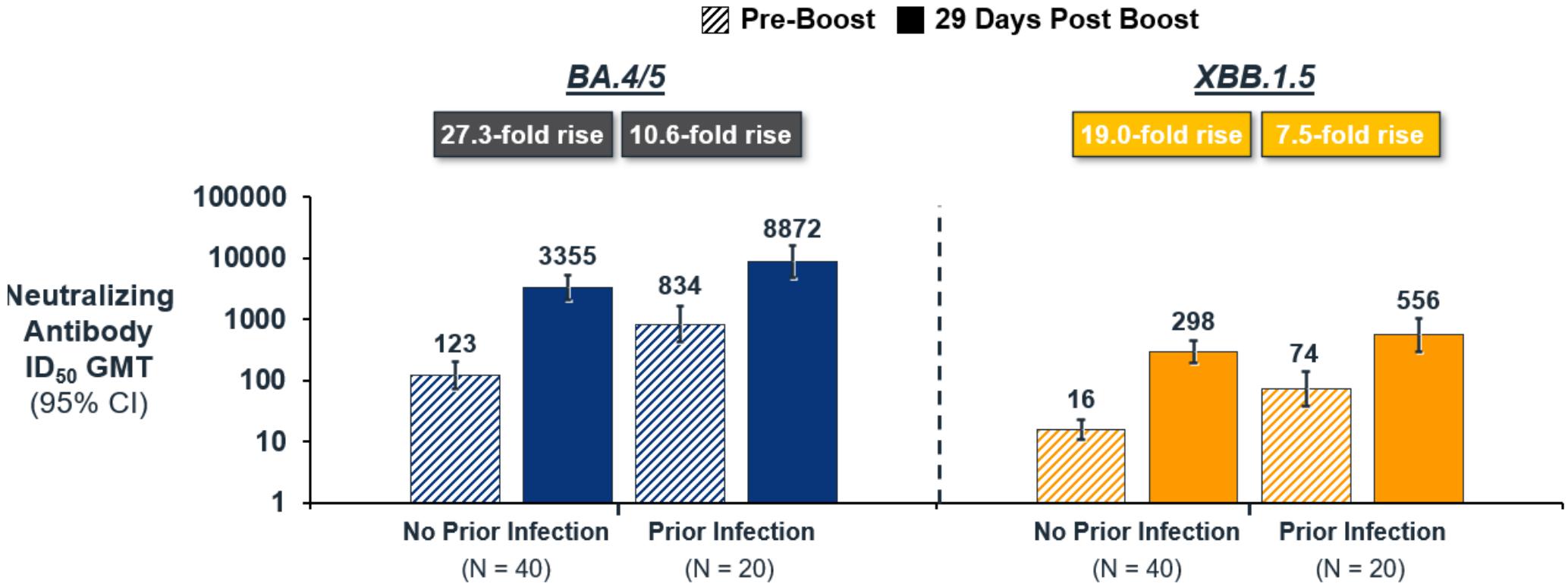
Preparation for Strain Selection

- Moderna performs continuous epidemiological monitoring and risk assessment of variants throughout the year
- Develop new candidate vaccines compositions
- Updated variant vaccine candidates were prepared and assessed in animals and humans

What are the new mutations versus Wuhan and other subvariants? Are the mutations found in key sites of known neutralization?

		339	346	356	368	371	373	375	376	405	408	417	440	444	445	446	452	460	477	478	484	486	490	493	496	498	501	505
	Wuhan-Hu-1	G	R	K	L	S	S	S	T	D	R	K	N	K	V	G	L	N	S	T	E	F	F	Q	G	Q	N	Y
	BA.1	D	R	K	L	L	P	F	T	D	R	N	K	K	V	S	L	N	N	K	A	F	F	R	S	R	Y	H
	BA.2	D	R	K	L	F	P	F	A	N	S	N	K	K	V	G	L	N	N	K	A	F	F	R	G	R	Y	H
BA.5 family	BA.4/5	D	R	K	L	F	P	F	A	N	S	N	K	K	V	G	R	N	N	K	A	V	F	Q	G	R	Y	H
BA.5 family	BQ.1.1	D	T	K	L	F	P	F	A	N	S	N	K	T	V	G	R	K	N	K	A	V	F	Q	G	R	Y	H
	BA.2.75	H	R	K	L	F	P	F	A	N	S	N	K	K	V	S	L	K	N	K	A	F	F	Q	G	R	Y	H
BA.2.75 family	BA.2.75.2	H	T	K	L	F	P	F	A	N	S	N	K	K	V	S	L	K	N	K	A	S	F	Q	G	R	Y	H
BA.2.75 family	BN.1	H	T	T	L	F	P	F	A	N	S	N	K	K	V	S	L	K	N	K	A	F	S	Q	G	R	Y	H
	XBB.1	H	T	K	I	F	P	F	A	N	S	N	K	K	P	S	L	K	N	K	A	S	S	Q	G	R	Y	H
XBB family	XBB.1.5	H	T	K	I	F	P	F	A	N	S	N	K	K	P	S	L	K	N	K	A	P	S	Q	G	R	Y	H

Neutralization capacity of previously authorized BA.4/5 vaccine considerably lower against XBB.1.5

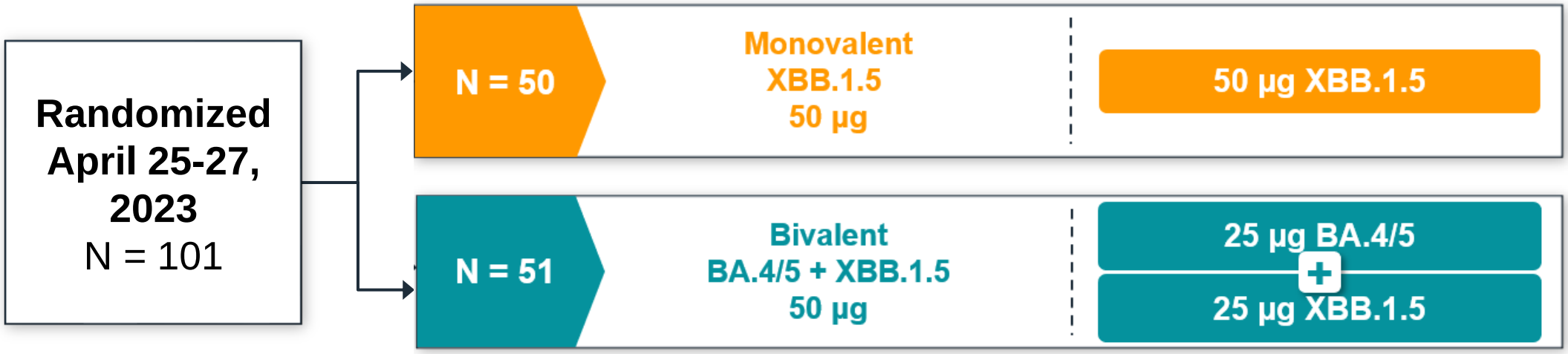


Cross-Neutralization at Day 29 Following Omicron BA.4/5 Bivalent Booster Study 205H, Per-Protocol Immunogenicity Set

Chalkias et al., *medRxiv*, 2022

moderna

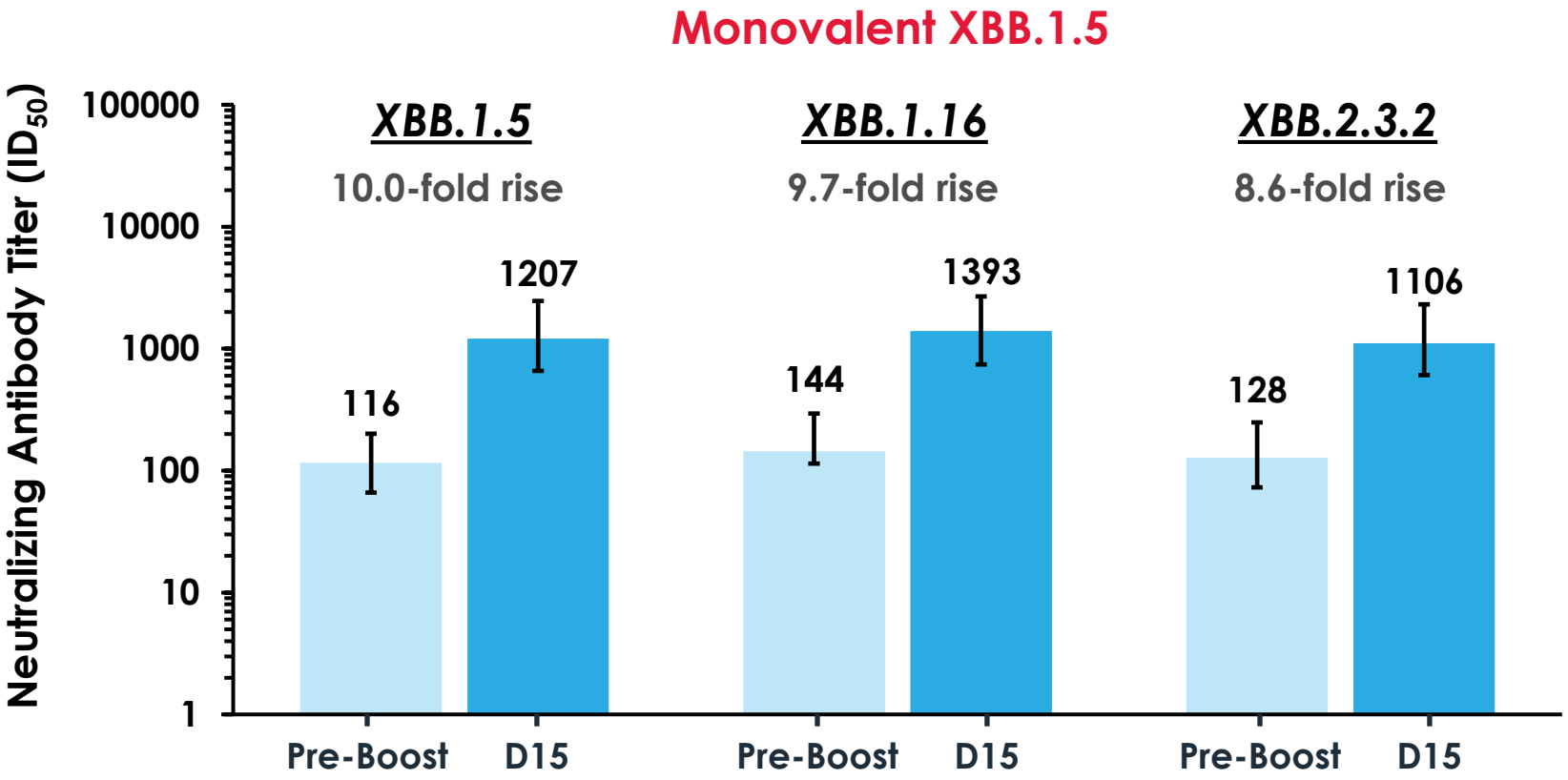
Monovalent and bivalent vaccines containing new variant were prepared and clinical studies were conducted



- Participants previously received 4 doses of COVID-19 vaccine (primary series and booster of -mRNA-1273 + booster of BA.4/BA.5 vaccine)
- **Focus of today's will be on the monovalent XBB.1.5 vaccine selected for 2023-2024 season**
- All analyses are descriptive

https://clinicaltrials.gov/ct2/show/NCT04927065

Clinical data from our Phase 2/3 study with a monovalent XBB.1.5 vaccine (mRNA-1273.815) demonstrated potent neutralization and cross-reactivity



XBB.1.5, XBB.1.16, and XBB.2.3.2 Neutralizing Antibodies After 5th Dose (3rd Booster) of Monovalent XBB.1.5 Vaccine in Adults Study 205J, Subset Analysis (N = 20)

XBB.1.5 monovalent vaccine approved for fall 2023/2024 season with broad ACIP recommendation

Strain selection and vaccine approvals

Strain selection

- Moderna's new variant vaccine human clinical results were presented to FDA VRBPAC on June 15th
  - Unanimous vote in favor of an update to an XBB.1.5 monovalent vaccine

Approvals and recommendations

- FDA approval (12+) and authorization (6m-11yrs) granted on September 11th, Japan and Canada approval on September 12th
  - Approvals in Europe, Taiwan and others expected this week
- U.S. CDC ACIP met on September 12th resulting in broad recommendation for all authorized and approved groups (6 months and above)

Continuous monitoring and new variant assessments after strain selection and approval

Continued monitoring / assessment

Moderna remains committed to

- Monitoring the continued evolution of the virus
- Assessing and reporting on the impact of new variants against the fall 2023/2024 vaccine composition, XBB.1.5 monovalent

This commitment includes assessment of variants that become globally dominant AND those variants that show potential for immune escape from this season's vaccine composition

moderna

New variants that have emerged since the fall 2023 vaccine strain selection meeting

EG.5.1, FL.1.5.1, and BA.2.86 variants have met our criteria for assessment

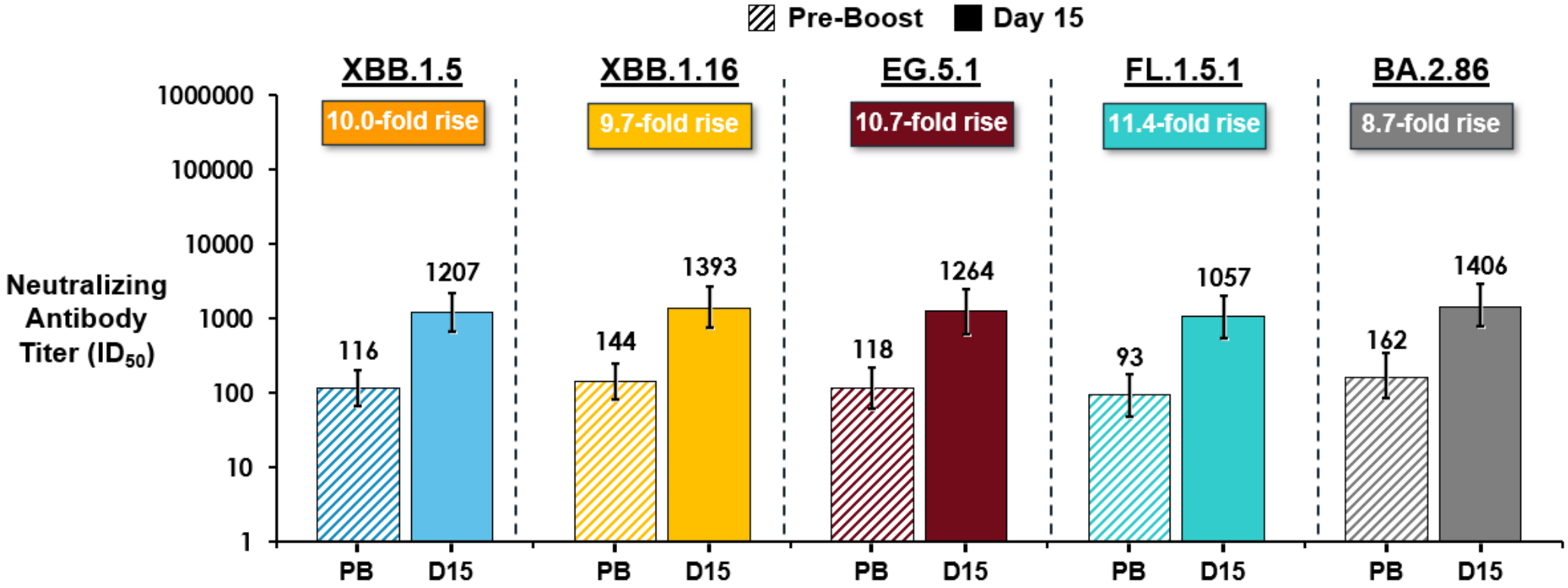
RBD mutations relative to Wuhan-Hu-1

	332	339	346	356	368	371	373	375	376	403	405	408	417	440	445	446	450	452	456	460	477	478	481	483	484	486	490	498	501	505	521
Wuhan-Hu-1	I	G	R	K	L	S	S	S	T	R	D	R	K	N	V	G	N	L	F	N	S	T	N	V	E	F	F	Q	N	Y	P
XBB.1.5	I	H	T	K	I	F	P	F	A	R	N	S	N	K	P	S	N	L	F	K	N	K	N	V	A	P	S	R	Y	H	P
XBB.1.9.1	I	H	T	K	I	F	P	F	A	R	N	S	N	K	P	S	N	L	F	K	N	K	N	V	A	P	S	R	Y	H	P
XBB.1.16	I	H	T	K	I	F	P	F	A	R	N	S	N	K	P	S	N	L	F	K	N	R	N	V	A	P	S	R	Y	H	P
XBB.2.3.2	I	H	T	K	I	F	P	F	A	R	N	S	N	K	P	S	N	L	F	K	N	K	N	V	A	P	S	R	Y	H	S
EG.5.1	I	H	T	K	I	F	P	F	A	R	N	S	N	K	P	S	N	L	L	K	N	K	N	V	A	P	S	R	Y	H	P
FL.1.5.1	I	H	T	K	I	F	P	F	A	R	N	S	N	K	P	S	N	L	L	K	N	R	N	V	A	P	S	R	Y	H	P
BA.2.86	V	H	R	T	L	F	P	F	A	K	N	S	N	K	H	S	D	W	F	K	N	K	K	-	K	P	F	R	Y	H	P

EG.5.1 & FL.1.5.1 (Growth example): ***Currently a leading variant globally, and growing in proportion, necessitating testing***
Predicted to have minimal immune escape potential (<2 Fold) against XBB.1.5-containing monovalent vaccine (mRNA-1273.815)

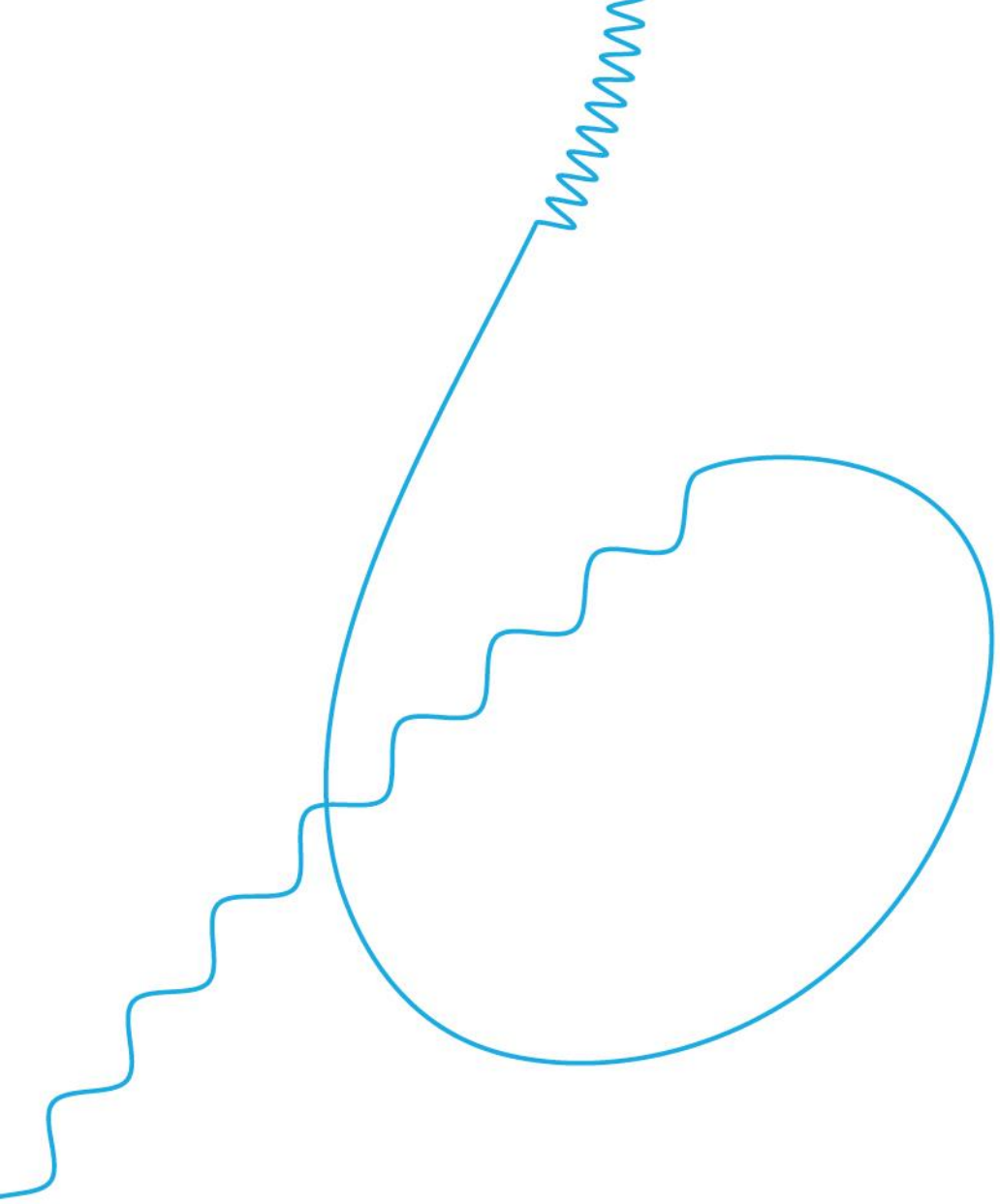
BA.2.86 (potential for immune escape example): ***Currently circulating in very low numbers***
Highly mutated relative to Wuhan-Hu-1 and has several mutations versus XBB.1.5, the strain in the updated mRNA-1273.815 monovalent vaccine for the 2023/2024 season

Human data demonstrate consistent cross neutralization for newer variants in Moderna assay, including BA.2.86



Cross Neutralization Results (Day 15) After XBB.1.5 Vaccine in Adults
Study 205J, Subset Analysis (N = 20)

moderna



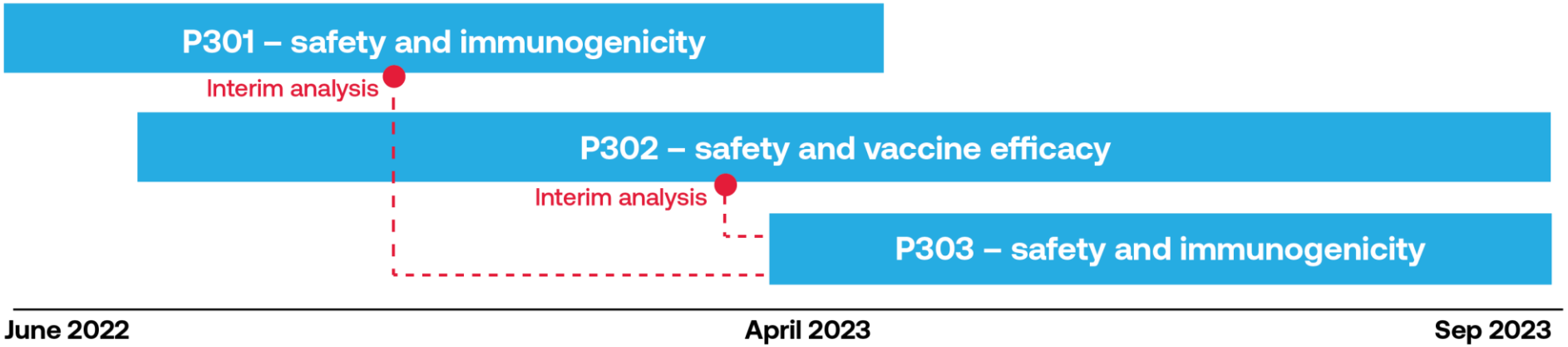
Influenza

Raffael Nachbagauer, M.D., Ph.D.

Executive Director, Influenza Portfolio Lead

moderna

mRNA-1010 has made rapid progress in 15 months



P301
Southern Hemisphere

- Immunogenicity study met each of its endpoints for influenza A strains, including superiority for H3N2
- Did not meet non-inferiority for influenza B strains

P302
Northern Hemisphere

- End of season efficacy analysis did not accrue target number of cases (only 282 total cases; +48 since Vaccines Day update)
- Did not demonstrate protocol defined statistical non-inferiority

P303
Northern Hemisphere

- Made improvements to mRNA-1010 to increase immune responses in our P303 study
- mRNA-1010 met all 8 primary immunogenicity endpoints. GMT titers were higher compared to standard dose vaccine

mRNA-1010 Phase 3 P303 study overview

P303 was designed to test the immunogenicity and safety of an optimized composition of mRNA-1010

Design
Randomized, observer-blind, active-controlled study

Number of participants
2,416 medically stable adults ≥ 18 years old

Vaccination schedule
Single dose of mRNA-1010 or Fluarix

Duration: 6 months
Enrollment period: April-May 2023

Study participants will be followed for 6 months after study injection

Site location
Northern Hemisphere (United States)

Total N = 2,416
Randomization Ratio = 1:1

mRNA-1010 (50 µg)
N=1227

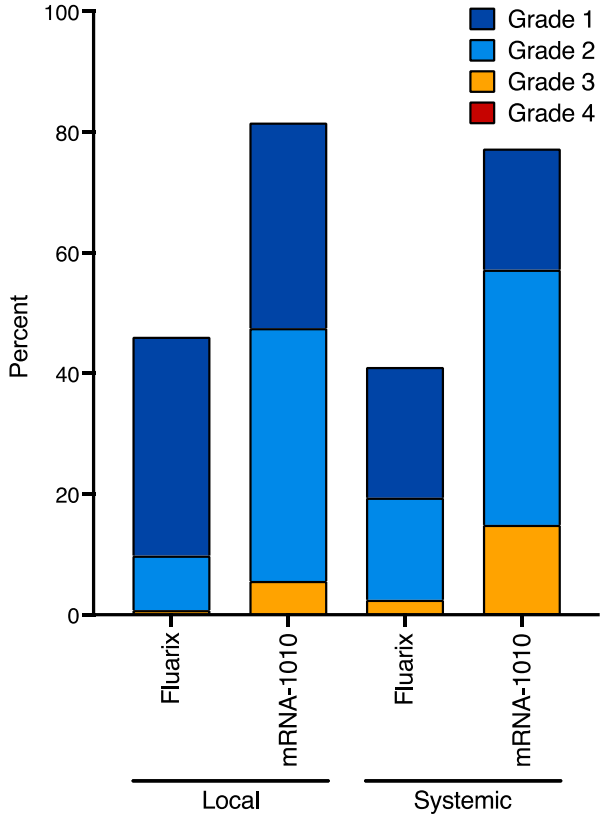
Fluarix
N=1189

moderna

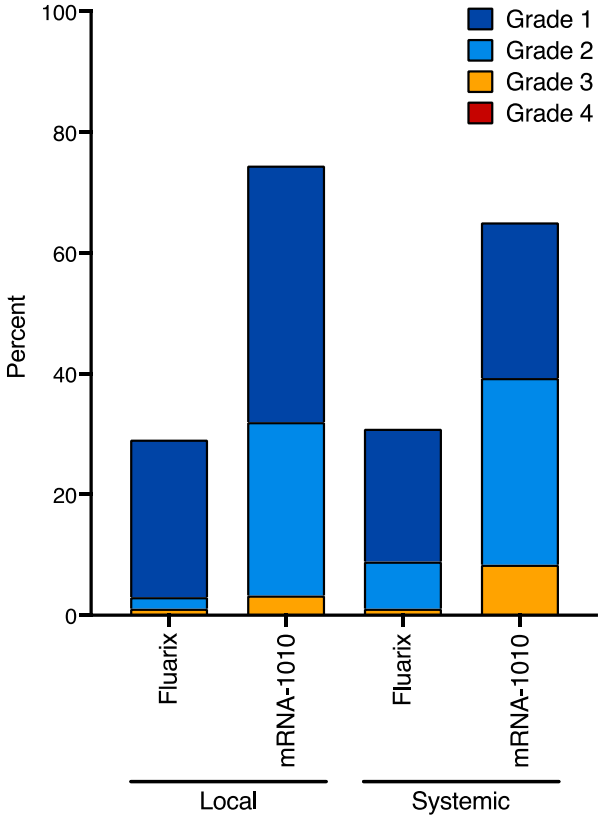
Reported rates of local and systemic reactogenicity after mRNA-1010 compared to standard dose influenza vaccine

- Safety profile was in line with prior clinical studies for mRNA-1010
- mRNA-1010 showed an acceptable reactogenicity profile, with the majority of solicited adverse reactions reported as grade 1 or 2 in severity
- Reactogenicity was higher in mRNA-1010 recipients compared to standard dose influenza vaccine recipients
- Reactogenicity in older adults was lower compared to younger age groups.

Adult 18 years and older

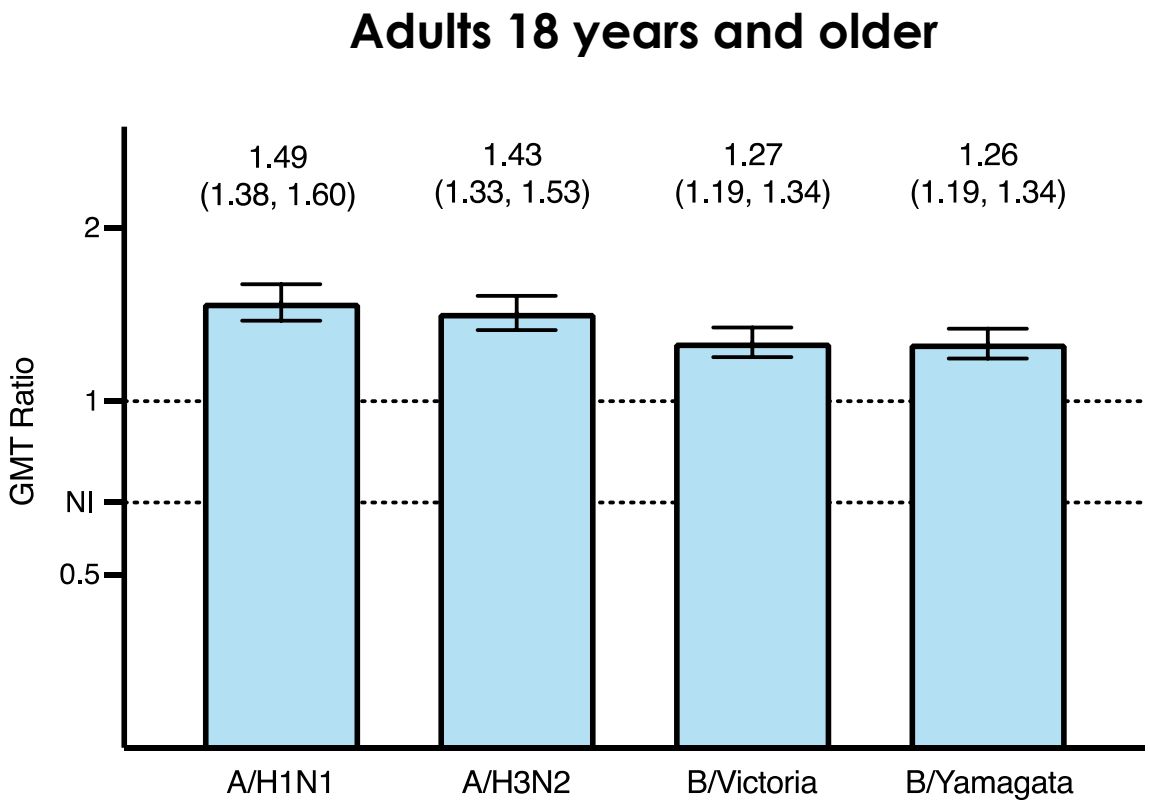


Adults 65 years and older



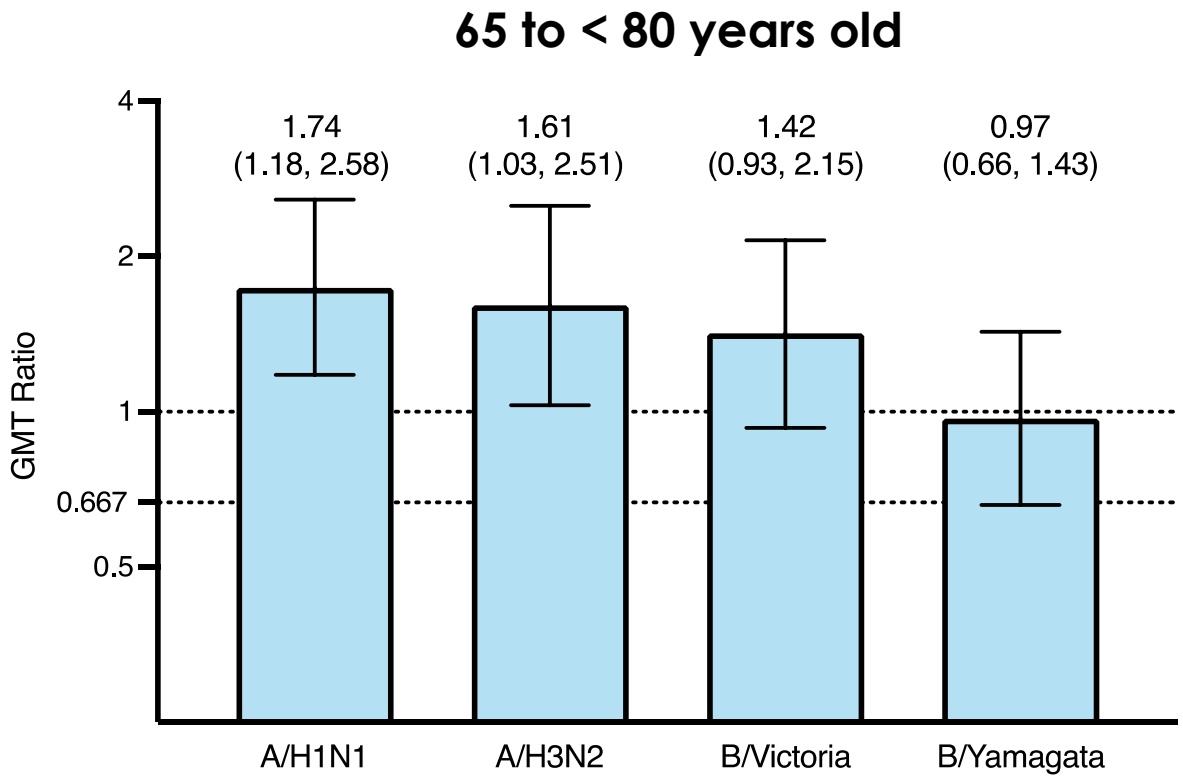
mRNA-1010 met all primary immunogenicity endpoints in P303

- Immunogenicity criteria for licensure according to regulatory guidance were met for all 8 co-primary endpoints
  - GMR
  - Seroconversion rates
- Higher GMTs and seroconversion rates were observed for mRNA-1010 for all four strains in P303 study
- Higher immunogenicity relative to standard dose influenza vaccine was consistently observed across age groups



mRNA-1010 elicited similar or numerically higher titers compared to Fluzone® HD in a Phase 1/2 study

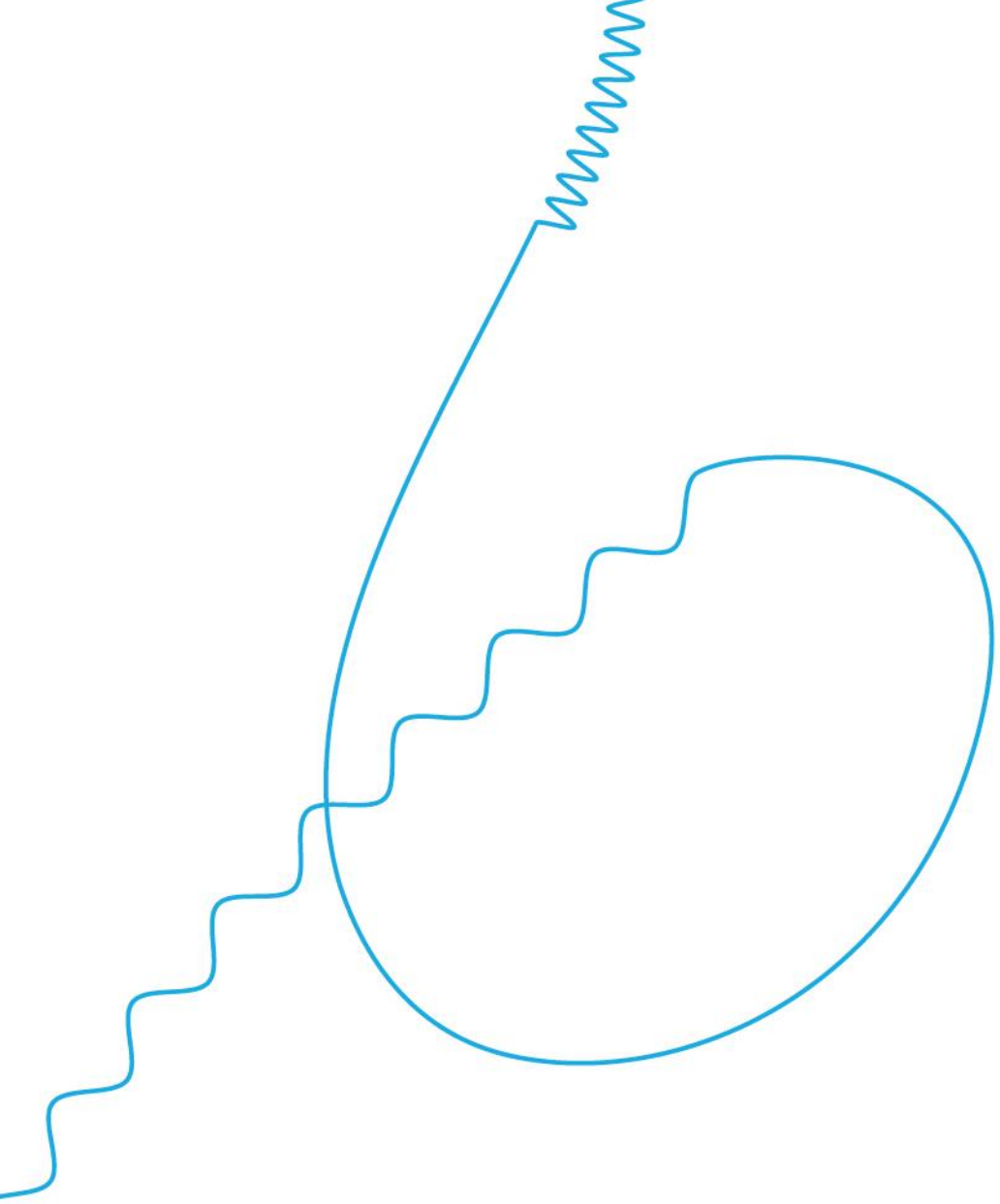
- mRNA-1010 was compared to a preferentially recommended enhanced vaccine for older adults (Fluzone® HD) in a clinical study
- Approximately 50 participants in each study arm
- Titers were similar or numerically higher than Fluzone® HD
- Supports future Phase 3 studies to formally compare immune responses to enhanced influenza vaccines



mRNA-1010 summary and next steps

- mRNA-1010 demonstrated a consistently acceptable safety and tolerability profile across three Phase 3 trials
- In the most recent Phase 3 trial (P303), mRNA-1010 has met all immunogenicity endpoints, demonstrating higher titers compared to a licensed vaccine, consistent with criteria for licensure according to regulatory guidance
- mRNA-1010 has also shown higher or comparable titers compared to an enhanced vaccine (Fluzone HD) in a separate Phase 1/2 study
- Rapid progress of the mRNA-1010 program in the last year, <2.5 years from IND filing, demonstrates the power of the mRNA platform to drive continuous innovation and improvement
- Consultations with regulators have begun on submission package for licensure of mRNA-1010

moderna



Respiratory portfolio
Additional updates

Jacqueline Miller

SVP, Head of Development,
Infectious Diseases,
Research & Development

moderna

Respiratory vaccines pipeline overview

Commercial and Phase 3 programs

PC | Ph. 1 | Ph. 2 | Ph. 3 | Comm.

COVID-19 (mRNA-1273.222/.815)

PC | Ph. 1 | Ph. 2 | Ph. 3 | Comm.

Older adults RSV (mRNA-1345)

PC | Ph. 1 | Ph. 2 | Ph. 3 | Comm.

Flu (mRNA-1010)

Next-gen programs

PC | Ph. 1 | Ph. 2 | Ph. 3 | Comm.

COVID-19 next-gen booster (mRNA-1283)

PC | Ph. 1 | Ph. 2 | Ph. 3 | Comm.

Flu (mRNA-1011/-1012)

PC | Ph. 1 | Ph. 2 | Ph. 3 | Comm.

Flu (mRNA-1020/-1030)

Combination programs

PC | Ph. 1 | Ph. 2 | Ph. 3 | Comm.

Flu + COVID-19 (mRNA-1083)

PC | Ph. 1 | Ph. 2 | Ph. 3 | Comm.

Flu + COVID-19 + RSV (mRNA-1230)

PC | Ph. 1 | Ph. 2 | Ph. 3 | Comm.

Flu + RSV (mRNA-1045)

PC | Ph. 1 | Ph. 2 | Ph. 3 | Comm.

RSV + hMPV (mRNA-1365)

moderna

RSV: mRNA-1345 older adult regulatory submissions completed in multiple countries; expecting global regulatory approvals in 2024

U.S. regulatory submission

Filed for a Biologics License Application (BLA) with the FDA, with a Priority Review Voucher (PRV)

Global regulatory submissions

Regulatory applications submitted in Europe (EMA), Switzerland (Swissmedic), Australia (TGA) and United Kingdom (MHRA)

FDA: U.S. Food and Drug Administration
EMA: European Medicines Agency
TGA: Therapeutic Goods Administration
MHRA: Medicines and Healthcare products Regulatory Agency

moderna

mRNA-1345 Phase 3 in older adults – summary of primary analysis and next steps

Efficacy

- 83.7% and 82.4% vaccine efficacy against RSV-LRTD with ≥2 and ≥ 3 signs/symptoms, respectively
- Secondary analysis was performed according to the presence/absence of medical comorbidities for RSV-LRTD with ≥2 symptoms
  - VE for RSV-LRTD with no comorbidity was 81.6%
  - VE for RSV-LRTD with ≥ 1 comorbidity was 88.4%

Safety

- Pain was the most frequently reported local solicited symptom
- Headache, fatigue, myalgia and arthralgia were the most frequently reported systemic solicited symptoms
- Most solicited adverse reactions were grade 1 or grade 2
- No cases of GBS or ADEM have been reported in mRNA-1345 Phase 3 study
- No safety concerns identified

Next steps

- Expecting regulatory action as early as 2Q 2024

RSV-LRTD: Respiratory Syncytial Virus Lower Respiratory Tract Disease
GBS: Guillain-Barré Syndrome
ADEM: Acute demyelinating encephalomyelitis
*Medical comorbidities included COPD, asthma, chronic respiratory disease, diabetes, CHF, advanced liver disease, or advanced renal disease

Our strategy is to advance multiple generations of single-virus and combination respiratory vaccines to address unmet need

Evolution of target portfolio profile

1st generation single-virus vaccines

Advance vaccines that provide **the highest protection** against seasonal respiratory viruses **for those most at risk**

2nd generation single-virus vaccines

Enhance single-virus vaccines with **improved product attributes**, such as higher efficacy, improved tolerability, product image, storage

Combination vaccines

Deliver **diverse portfolio of 1st and 2nd generation-based combination vaccines,** ideally with non-inferior profiles to single-virus vaccines and improved convenience (patient) and value (payor/system)

moderna

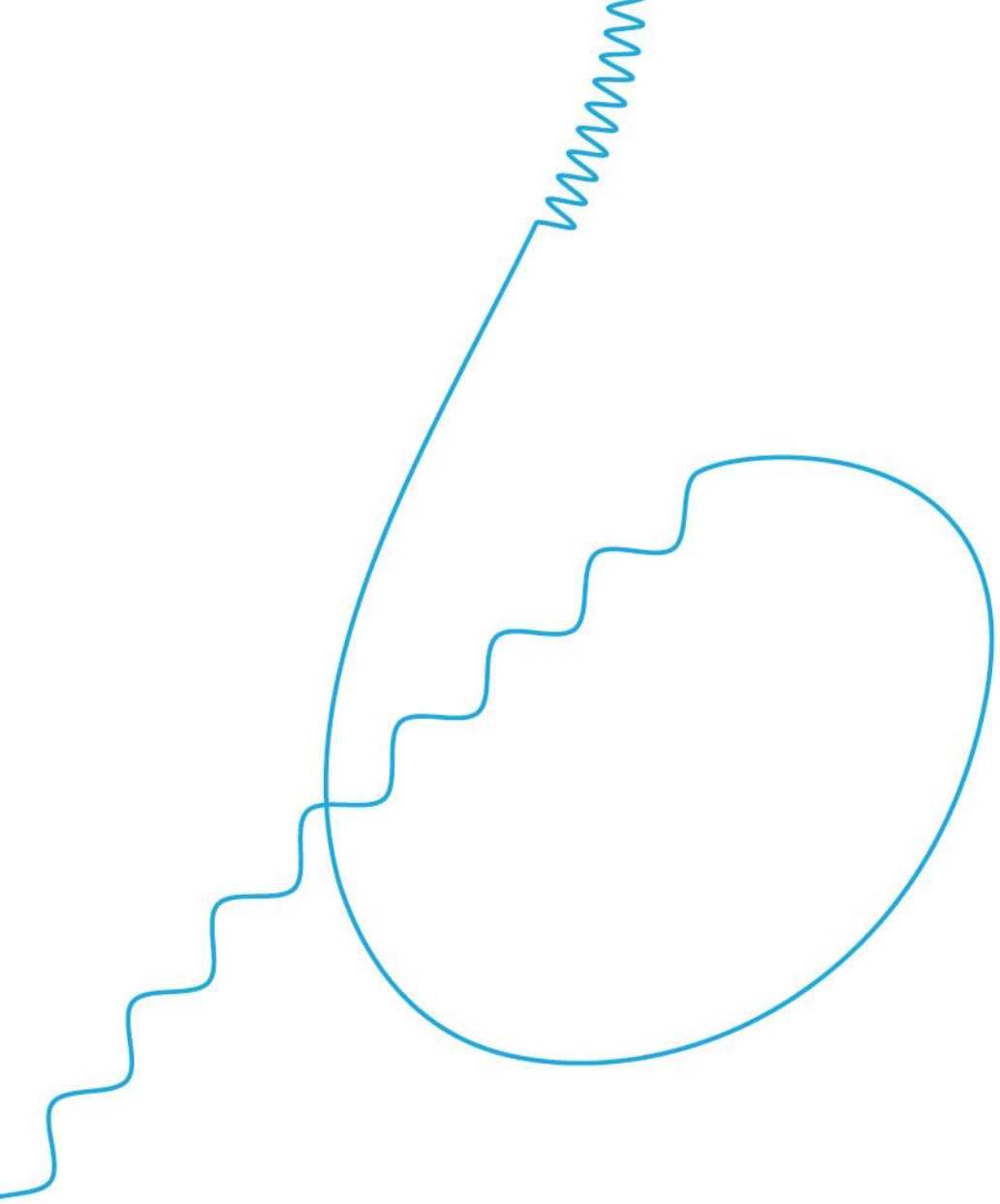
Our development strategy for combination vaccines can provide substantial public health benefits

Flu/COVID **mRNA-1083** *mRNA-1283/mRNA-1010*	Phase 1/2 enrollment complete
Flu/RSV **mRNA-1045** *mRNA-1010/mRNA-1345*	Phase 1 enrollment complete
Flu/RSV/COVID **mRNA-1230** *mRNA-1273/mRNA-1010/mRNA-1345*	Phase 1 enrollment complete
RSV/hMPV **mRNA-1365** *mRNA-1345/hMPV mRNA*	Phase 1 enrollment ongoing

Benefits of combination vaccines

- Higher compliance
- Better uptake
- Larger benefit to healthcare systems
- Consumer convenience

moderna

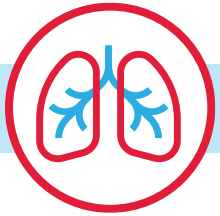


Respiratory vaccines
Commercial opportunity

Arpa Garay
Chief Commercial Officer

moderna

Common commercial characteristics for the respiratory vaccines franchise



Respiratory vaccines

- Same contracting & selling season
- Similar customer base
- Potential portfolio contracting opportunities

moderna

Moderna's current pipeline is targeting large addressable markets

Respiratory vaccines
(COVID-19, RSV, flu, combinations)

~$30b+

COVID

Based on disease burden and vaccine effectiveness, COVID has the potential to be **~$15 billion market**

RSV

Potential to be **~$10 billion market**

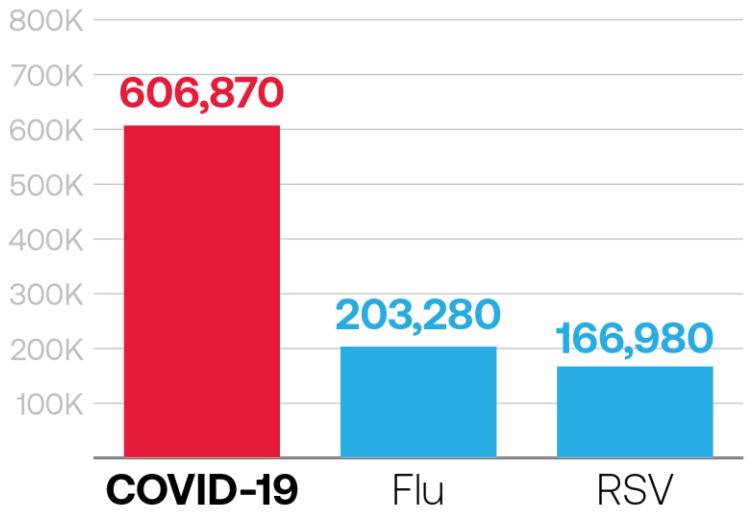
Flu

Current influenza market ~$6 billion; market could grow to **~$9 billion** in 2028, with rise in more effective vaccines

moderna

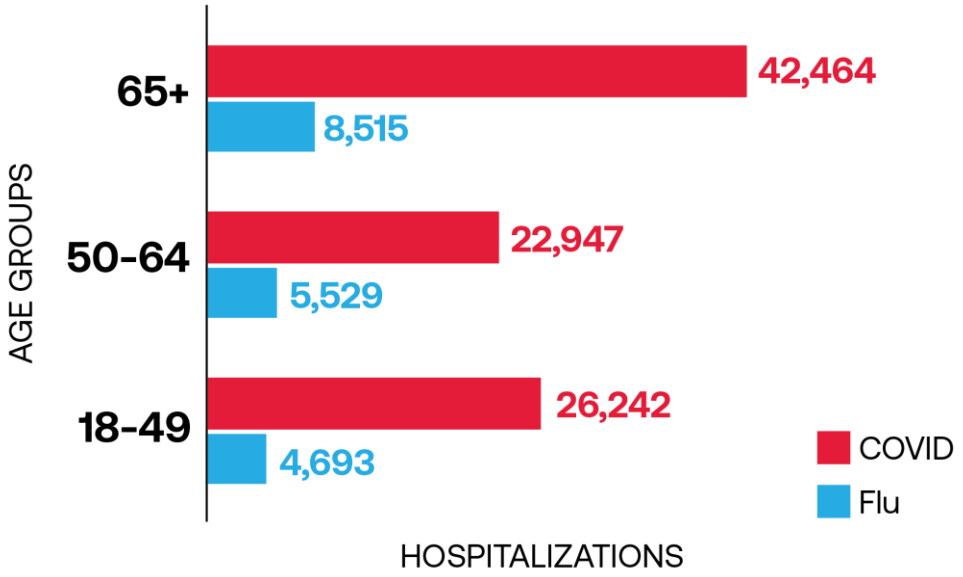
During the 2022/2023 season COVID-19 remained a substantial health burden in the US

Total hospitalizations from October '22 through April '23 season (10/1/2022 – 4/16/2023)



SOURCE: RESP-NET – Respiratory Virus Hospitalizations Surveillance Network – CDC

COVID-19 and influenza hospitalizations by age group
N=110,390

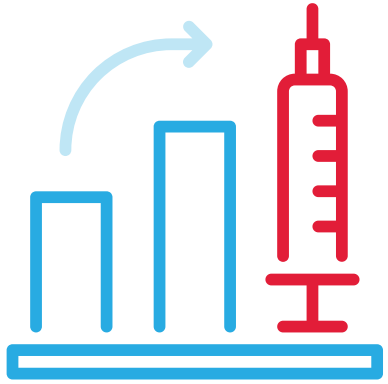


SOURCE: Comparison of COVID-19 and Influenza-Related Outcomes in the United States during Fall-Winter 2022-2023
Hagit Kopel, et al medRxiv 2023.09.08.23295262; doi: https://doi.org/10.1101/2023.09.08.23295262

2023 fall vaccine campaign focused on increasing market doses administered and solidifying Moderna's market share

First half **2023** Second half

Focus on securing contracts



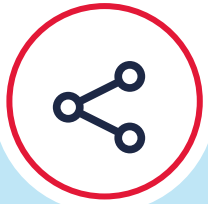
Focus on increasing vaccination rates

moderna

We are using a multi-pronged approach to increase urgency for COVID vaccination

Activate the medical community to proactively recommend the updated COVID vaccine to their patients this fall, especially 65+ and high risk

Support customers throughout the season, minimizing provider confusion, supporting patient outreach, and encouraging the extension of the immunization season



Re-engage the consumer with a focus on adults who receive their annual flu shots

Amplify voice of advocacy groups and major professional organizations to create credible messaging on need for updated COVID vaccine

moderna

Strong product profile for expected RSV 2024 launch

Only mRNA RSV investigational vaccine with positive Phase 3 data

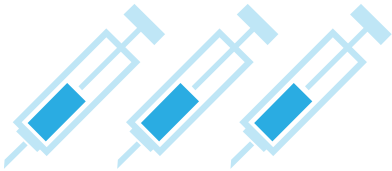
Vaccine efficacy against RSV-LRTD ≥2 symptoms was generally consistent in patients regardless of co-morbidities[1]

83.7% efficacy in overall study population

88.4% efficacy in participants with co-morbidities

Well-established safety and tolerability profile for mRNA vaccine technology

- Over 1 billion COVID-19 doses using same mRNA technology
- Most solicited adverse reactions were mild to moderate[1,2]
- No cases of Guillain-Barré Syndrome (GBS) have been reported with mRNA-1345 in Phase 3 RSV trial[2]



Ease of administration

- Single-dose prefilled syringe
- HCP customer convenience: only ready-to-use formulation, saving time and reducing administration errors[3,4]

1 Based of RSV LRTD with ≥2 symptoms; RSVVW data
2 As of April 30, 2023
3 www.ncbi.nlm.nih.gov/pmc/articles/PMC7846520/
4 www.ncbi.nlm.nih.gov/pmc/articles/PMC7913196/

moderna

Flu: opportunity to expand the market with next-generation premium vaccines

Current influenza market ~$6 billion

Market could grow to ~$9 billion in 2028[1], with rise in more effective vaccines

Market dynamics

Addressable population

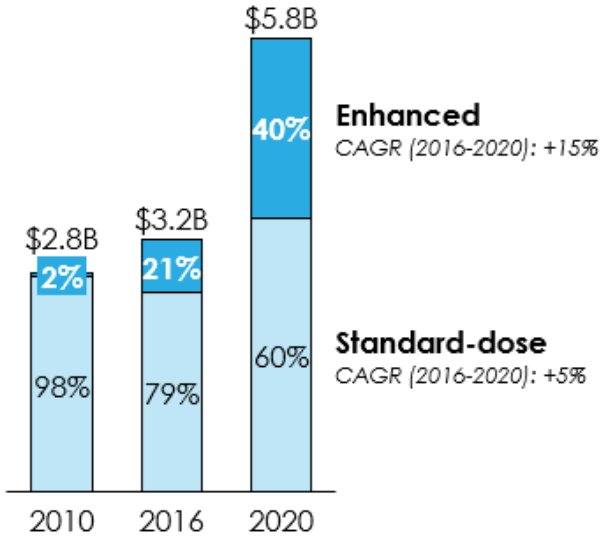
- Aim for recommendation in older adults (>65 years old)
- Adults 18+ eligible
- Explore pediatric indications

Enhanced vaccines

Premium vaccines with improved vaccine efficacy get a higher price (>$50/dose) and are growing at a faster rate[2]

Reported Global Influenza Vaccine Sales[3]

USD, billions



Source: EvaluatePharma, IQVIA MIDAS, Sanofi Vaccine Day (2021); High-dose products include Fluzone HD, Flublok, Fluad, total sales estimated

1. EvaluatePharma. Influenza vaccine : Worldwide | Overview
2. https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Part-B-Drugs/McrPartBDrugAvgSalesPrice/VaccinesPricing
3. EvaluatePharma, IQVIA MIDAS, Sanofi Vaccine Day (2021); High-dose products include Fluzone HD, Flublok, Fluad, total sales estimated

moderna

We believe combination vaccines will expand the current seasonal respiratory vaccine market [1]

Current annual global flu market

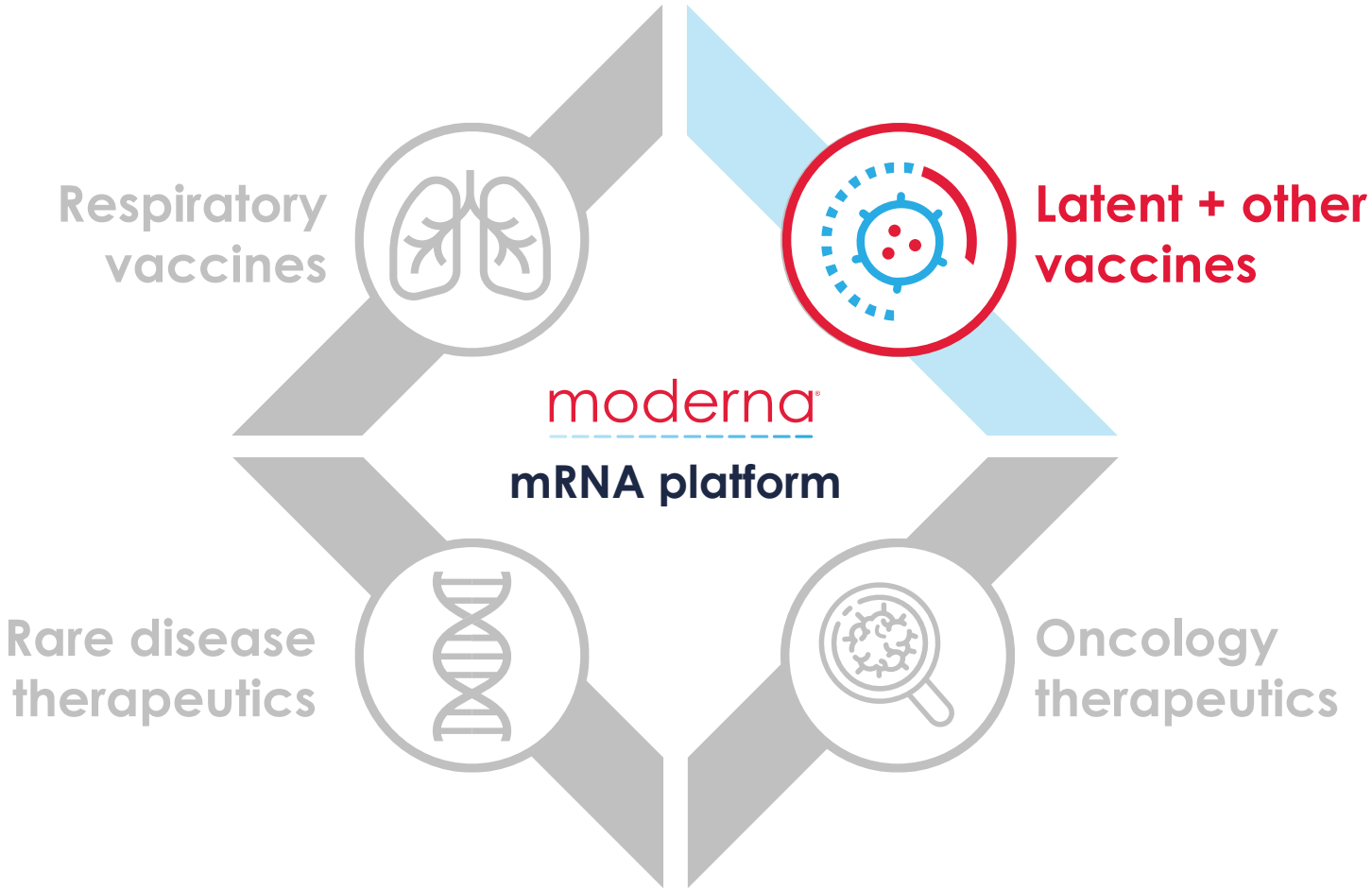
500-600m
doses
volume

- Increased vaccine value to health ecosystem
- Greater vaccination rates & compliance
- Market shift towards more effective vaccines

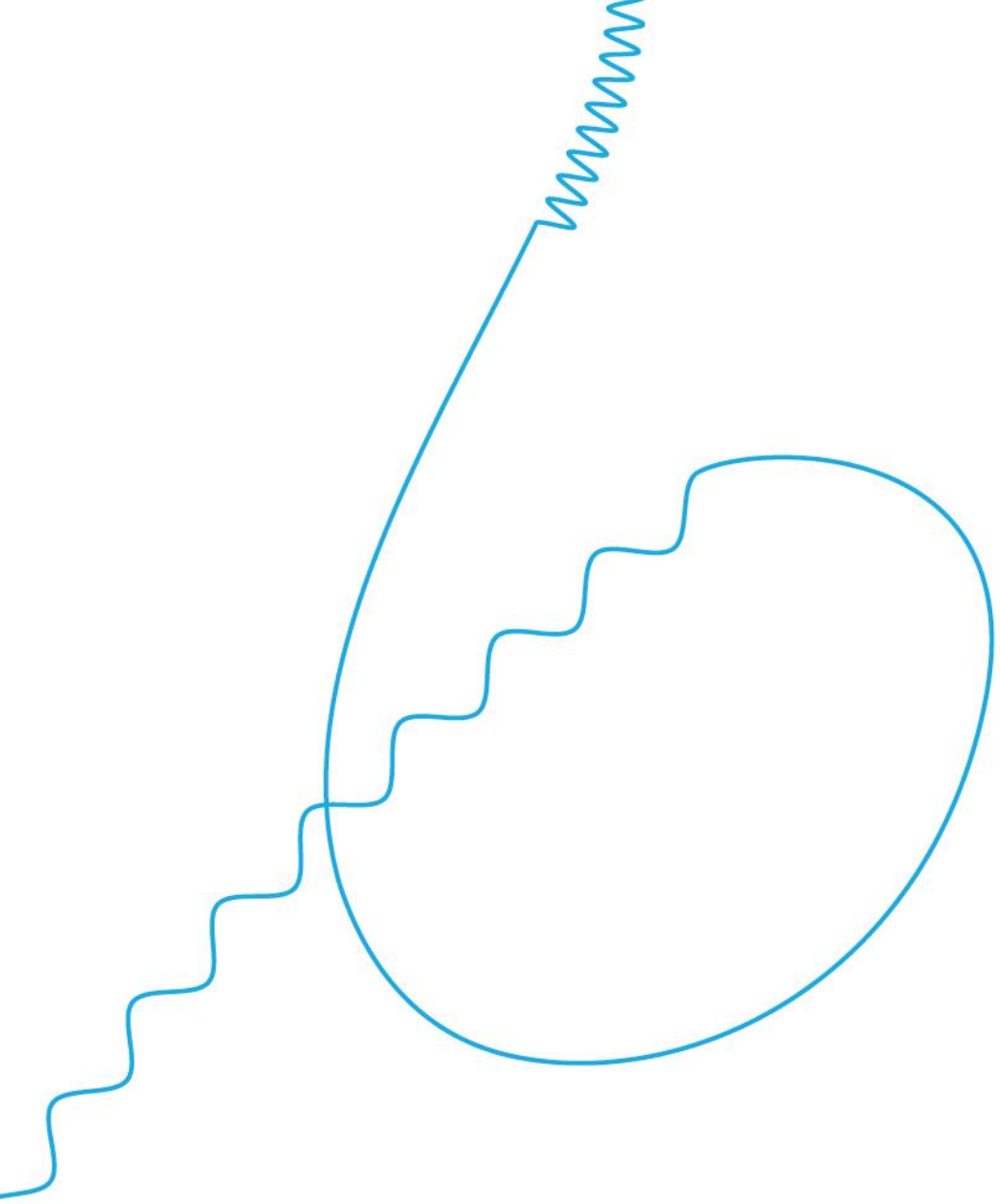
1. Seasonal respiratory vaccine market currently defined as influenza market

moderna

Latent + other vaccines



moderna



Latent + other vaccines

Development

Jacqueline Miller, M.D.

SVP, Head of Development, Infectious Diseases, Research & Development

moderna

We are advancing multiple programs to address significant unmet medical needs associated with latent and other virus infections

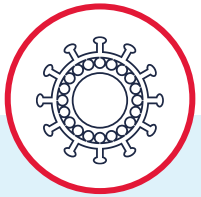
CMV mRNA-1647	Primary prevention to enable universal vaccination, in women of childbearing age	**Phase 3 ongoing**
EBV mRNA-1647 mRNA-1195	Prevention of infectious mononucleosis Prevention of longer-term sequelae of EBV infection	**Phase 1 enrollment ongoing**
VZV mRNA-1468	Prevention of herpes zoster (shingles) in older adults	**Phase 1/2 enrollment ongoing**
HSV mRNA-1608	Prevention of HSV-2 disease	**Phase 1/2 enrollment ongoing**
HIV mRNA-1644 mRNA-1574	Germline targeting approach Trimer approach	**Phase 1 ongoing**
Norovirus mRNA-1403 mRNA -1405	Prevention of norovirus acute gastroenteritis (AGE)	**Phase 1 ongoing**
Lyme mRNA-1982 mRNA -1975	Prevention of Lyme disease	**Phase 1/2 ongoing**

moderna

Today we will be discussing our CMV and Norovirus programs

CMV (mRNA-1647)

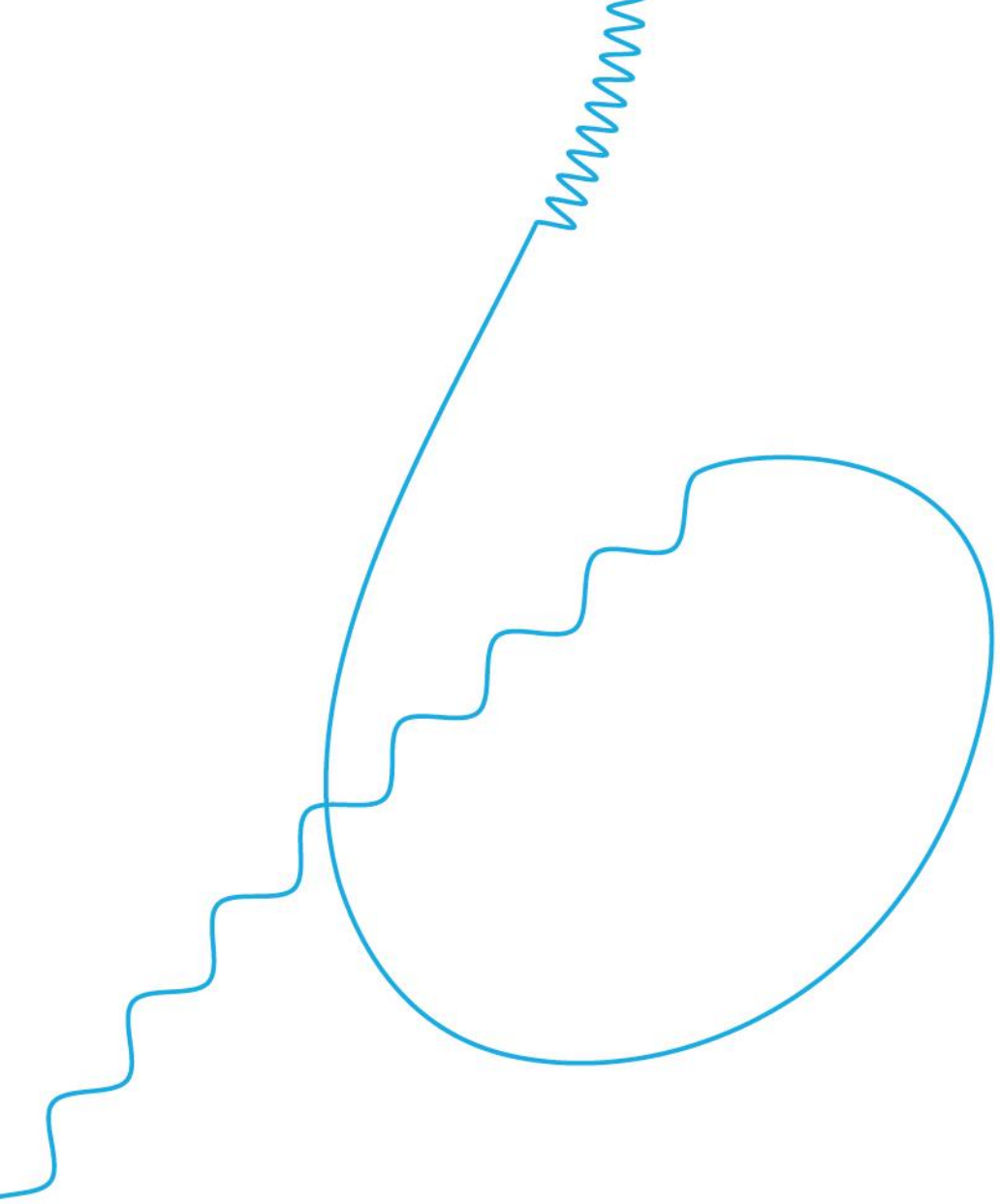
Phase 3 enrollment update



Norovirus (mRNA-1403/-1405)

Phase 1 is enrolling

moderna



Cytomegalovirus (CMV)

Cytomegalovirus (CMV) Overview

Most common cause of congenital infection worldwide

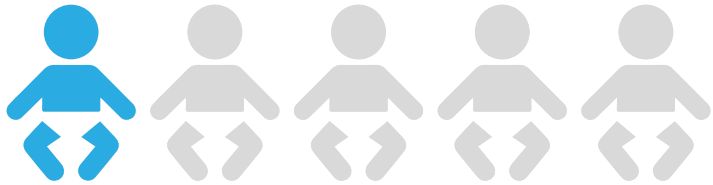
>$1B in annual healthcare costs[1]

Sequelae include:

- **At birth:** microcephaly, chorioretinitis, seizures, sensorineural hearing loss
- **Long term:** cognitive impairment, cerebral palsy, seizure disorder, sensorineural hearing loss

1 in 200

babies in the U.S. are born with a congenital CMV infection (CMV infection is present at birth)



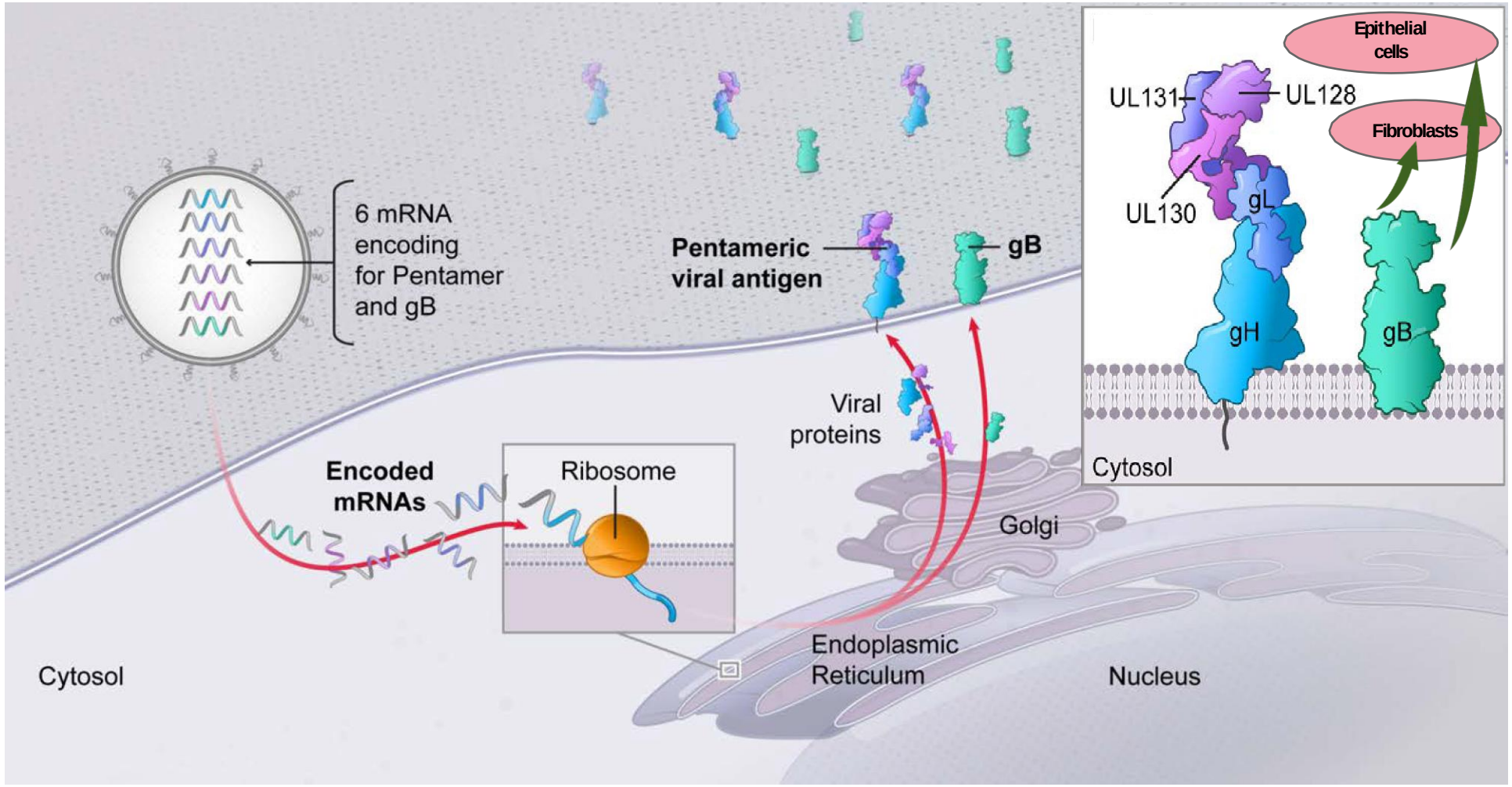
1 in 5

will have severe, life-altering health problems

(1) Grosse, Scott et al. "Economic assessments of the burden of congenital cytomegalovirus infection and the cost-effectiveness of prevention strategies," *Seminars in perinatology,* 2021, https://doi.org/10.1016/j.semperi.2021.151393

moderna

Our CMV vaccine (mRNA-1647) includes 6 mRNAs (five encode the pentamer, the 6th encodes for the gB antigen)



moderna

The CMV vaccine Phase 3 trial has fully enrolled the cohort of women over the age of 18

Randomized, observer-blind, placebo-controlled study to evaluate the **efficacy, safety and immunogenicity of mRNA-1647 to evaluate prevention of primary infection**

Enrollment is ongoing in the U.S. and internationally across 290 sites globally

Participants are at a higher risk of contracting CMV due to contact with young children

Enrollment of adolescent cohort **could be completed in 2023**

Primary efficacy analysis will be triggered based on accrual of primary infection cases

Phase 3 trial design

mRNA-1647 (100 µg) N=~3,650	**Placebo** N=~3,650

3 dose course: D1, D57, D169

CMVictory

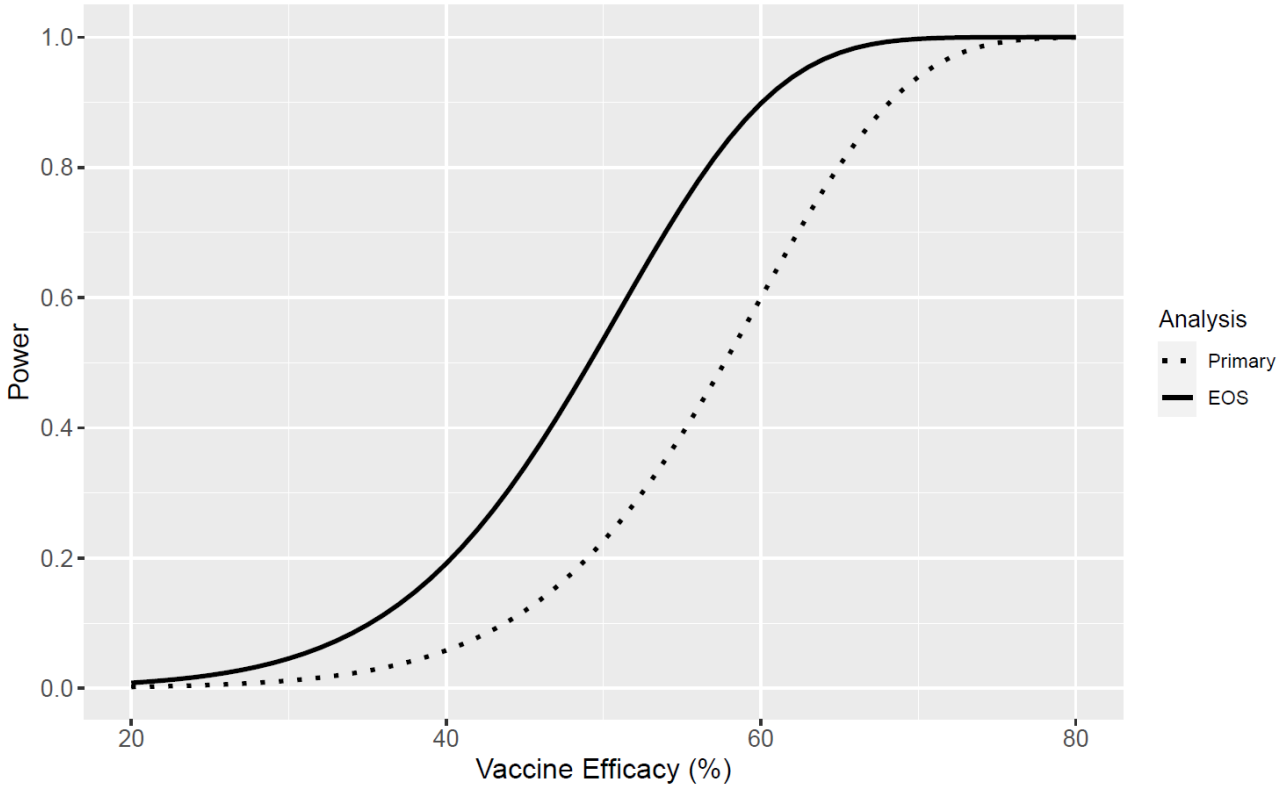
moderna

Overview of primary efficacy endpoint

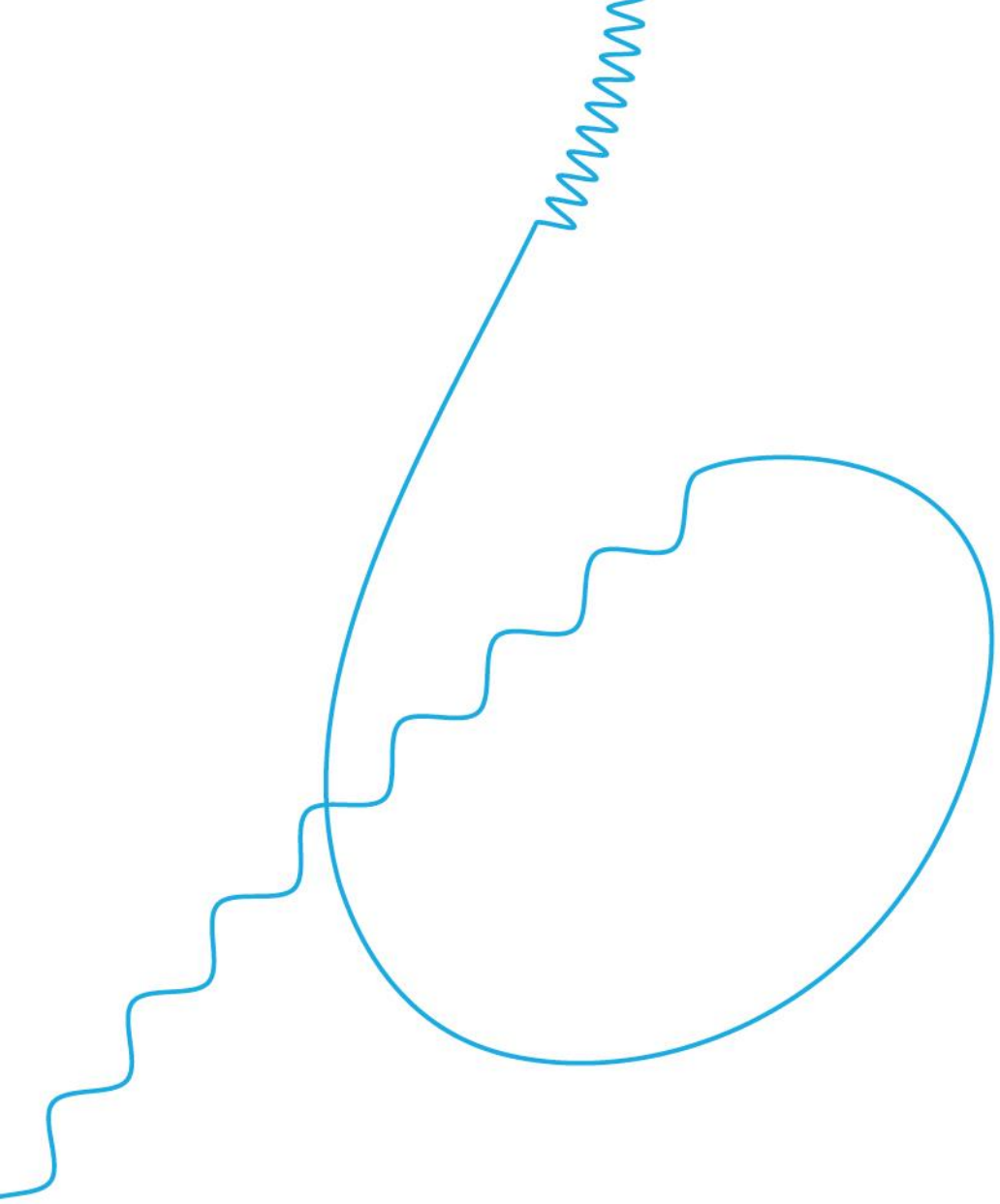
CMVictory

Efficacy Boundaries with Alpha-allocation between 2 Planned Analyses

	Approximate # of Cases	One-sided Alpha	VE: Efficacy Bound
Primary Analysis	81	0.5%	~ 57.7%
End of Study (EOS) Analysis	112	2.0%	~ 49.1%



moderna



Norovirus

moderna

Among enteric viruses, norovirus is a leading cause of diarrheal disease globally resulting in substantial health care burden

Norovirus is associated with 18% of all acute gastroenteritis worldwide[1]

The **highest incidence is in children**; morbidity and mortality greatest in children in low-income countries

In high-income countries, **older adults and immunocompromised patients are at highest risk of severe outcomes**, including death

The **burden of norovirus among older adults is expected to rise** along with societal aging and an increased need for institutionalized care

	United States (per year)[2]	Global (per year)[3,4]
Infections	**~20M** infections	**~685M** infections
Deaths and hospitalizations	**~900** deaths (mostly older adults) **~100K** hospitalizations	**~200K** deaths (~50K among children)
Societal costs	**~$2B** in healthcare costs and lost productivity	**~$60B** in healthcare costs and lost productivity

1. Ahmed, S.M., et al., Global prevalence of norovirus in cases of gastroenteritis: a systematic review and meta-analysis. Lancet Infect Dis, 2014.
2. https://www.cdc.gov/norovirus/trends-outbreaks/burden-us.html
3. https://www.cdc.gov/norovirus/trends-outbreaks/worldwide.html
4. https://www.who.int/teams/immunization-vaccines-and-biologicals/diseases/norovirus

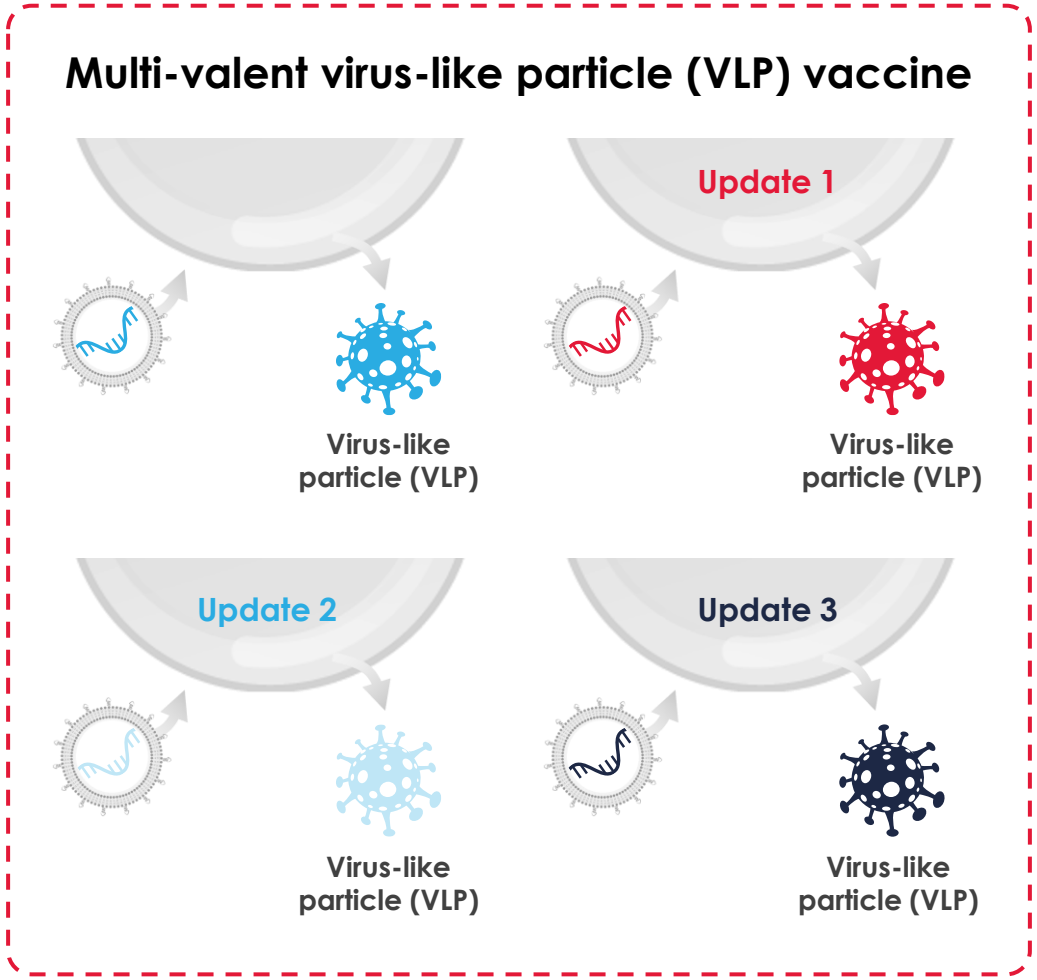
moderna

mRNA vaccine technology provides the ability to make multivalent VLPs that can be quickly updated

mRNA vaccines allow for intracellular production of virus-like particles (VLPs)

These VLPs are structurally similar to native virions and mimic major antigenic features including the display of critical epitopes

mRNA platform provides the ability to make multivalent compositions that can quickly be updated based on real world data from ongoing epidemiologic surveillance

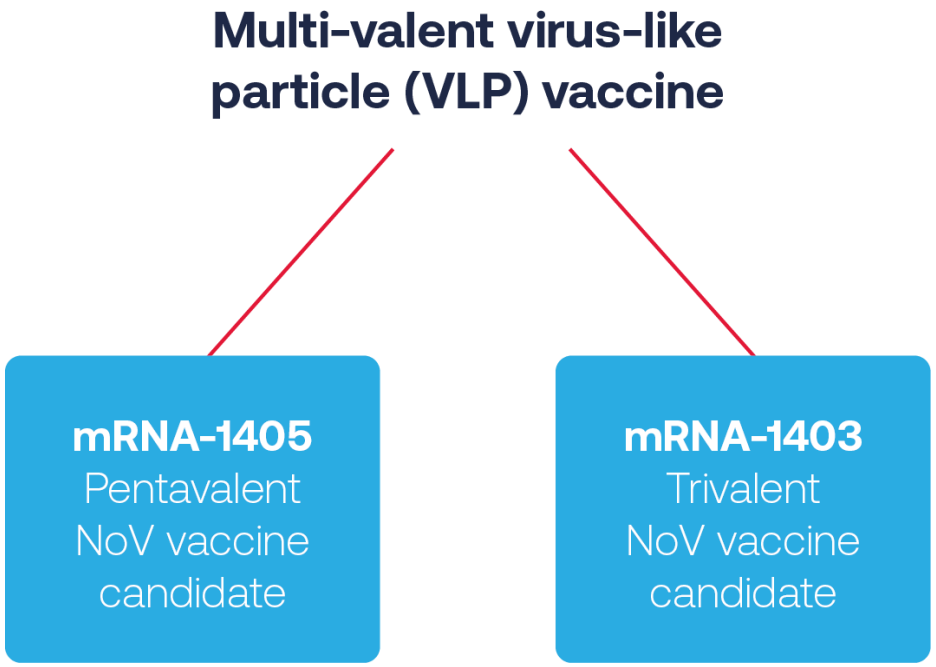


moderna

Moderna has two vaccine candidates that tackle key challenges of norovirus genotypic diversity and variability

mRNA-1403 and mRNA-1405 for Norovirus, multi-valent virus-like particle (VLP) vaccines for the prevention of acute gastroenteritis (AGE) from the most prevalent norovirus genotypes in young children and older adults

This intramuscular vaccine **uses the same LNP technology** as our respiratory vaccines



Our mRNA-1403/-1405 Phase 1 study is enrolling participants

Design
Randomized, observer-blind, placebo-controlled study

Number of participants
660 medically stable adults ages 18-49 & 60-80

Vaccination schedules
- 2 doses at Day 1 and 29
- 1 dose at Day 29 (with placebo on Day 1)

Duration: 12 months
Enrollment period: initiated enrollment September 2023

Study participants will be followed up for 12 months after the last study injection

Site location
Multiple US sites

Ph 1 safety and immunogenicity trial design

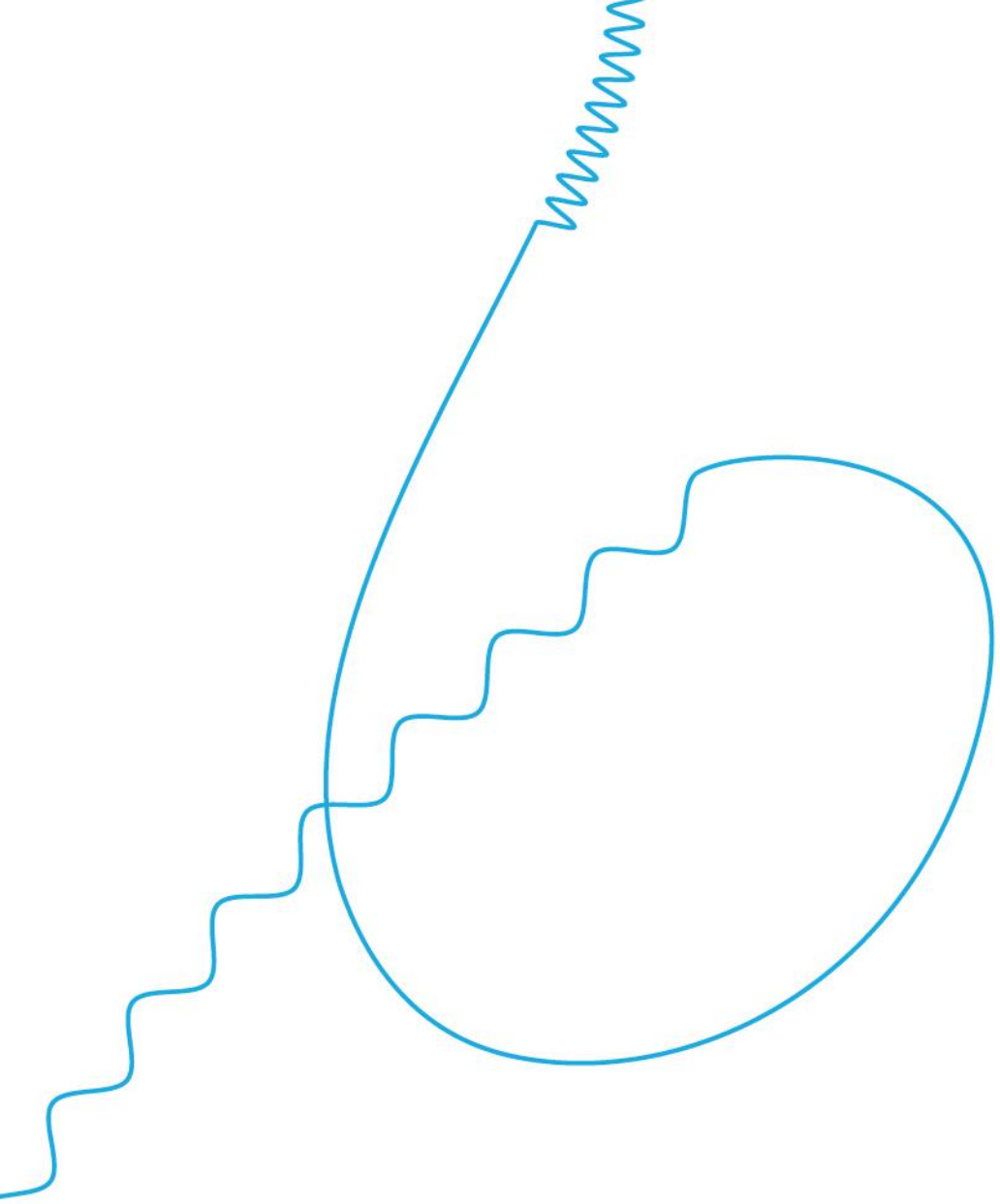
mRNA-1403
2 doses at 4 dose levels
1 dose at 1 dose level

mRNA-1405
2 doses at 4 dose levels
1 dose at 1 dose level

Placebo

NOVA

moderna



Latent + other vaccines

Commercial opportunity

Arpa Garay

Chief Commercial Officer

moderna

Common commercial characteristics for the latent + other vaccines franchise

Latent + other vaccines

- No seasonal pattern for sales, demand more constant throughout year
- Market increases by expanding eligible populations
- Similar vaccine procurement and contracting

moderna

Moderna's current pipeline is targeting large addressable markets

Latent + other vaccines
(CMV, EBV, HSV, VZV, HIV, Norovirus)

~$10-25b+

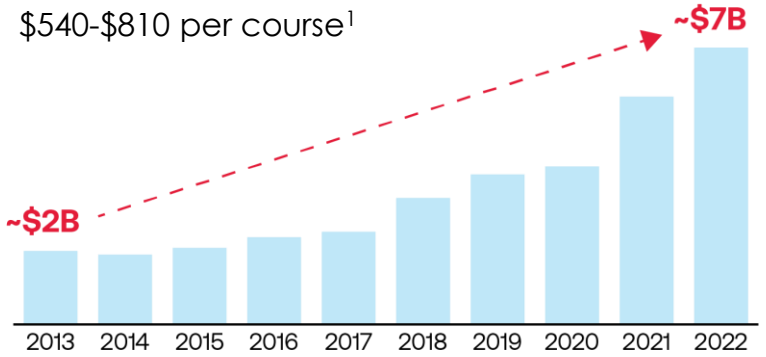
moderna

Moderna's latent vaccine development candidates have potential to address multi billion-dollar markets

Latent and other vaccines	Moderna Program
Cytomegalovirus (CMV)	mRNA-1647
Epstein-Barr virus (EBV)	mRNA-1189 mRNA-1195
Herpes simplex virus (HSV)	mRNA-1608
Varicella zoster virus (VZV)	mRNA-1468
Human immunodeficiency virus (HIV)	mRNA-1644 mRNA-1574

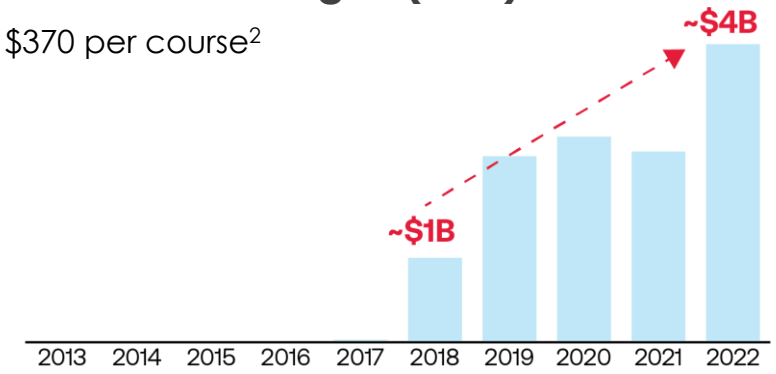
Worldwide Gardasil (HPV) Sales

$540-$810 per course[1]



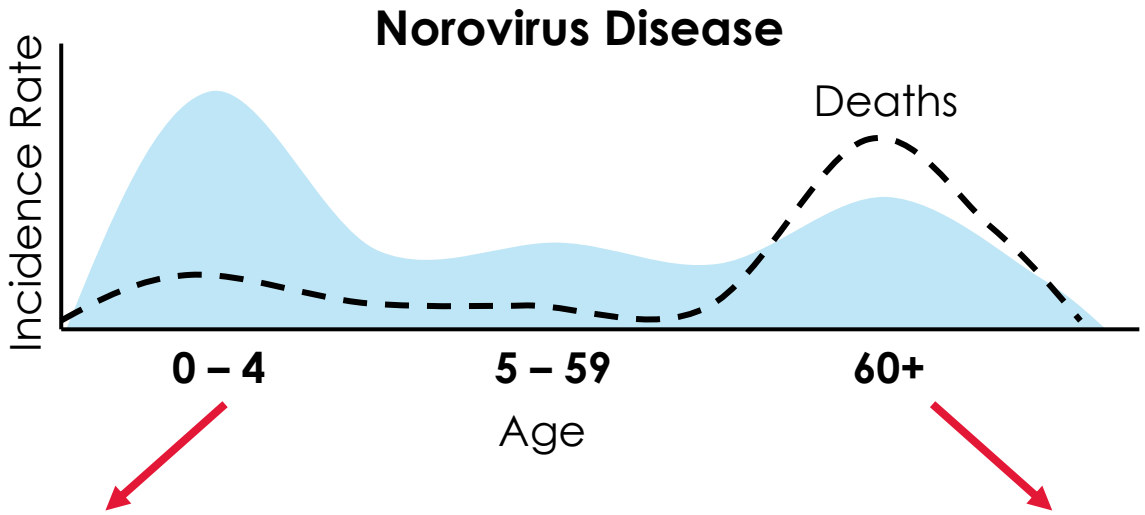
Worldwide Shingrix (VZV) Sales

$370 per course[2]



1. Gardasil is a registered trademark of Merck Sharpe & Dohme Corp. Revenue: Evaluate Pharma estimates; Price. Annual report
2. Shingrix is a registered trademark of GlaxoSmithKline Biologicals, S.A. Revenue: Evaluate Pharma estimates; Price. Annual report

Norovirus disease burden in the US is similar in scale to other high value vaccine market diseases



U.S. Disease Burden in Children <5

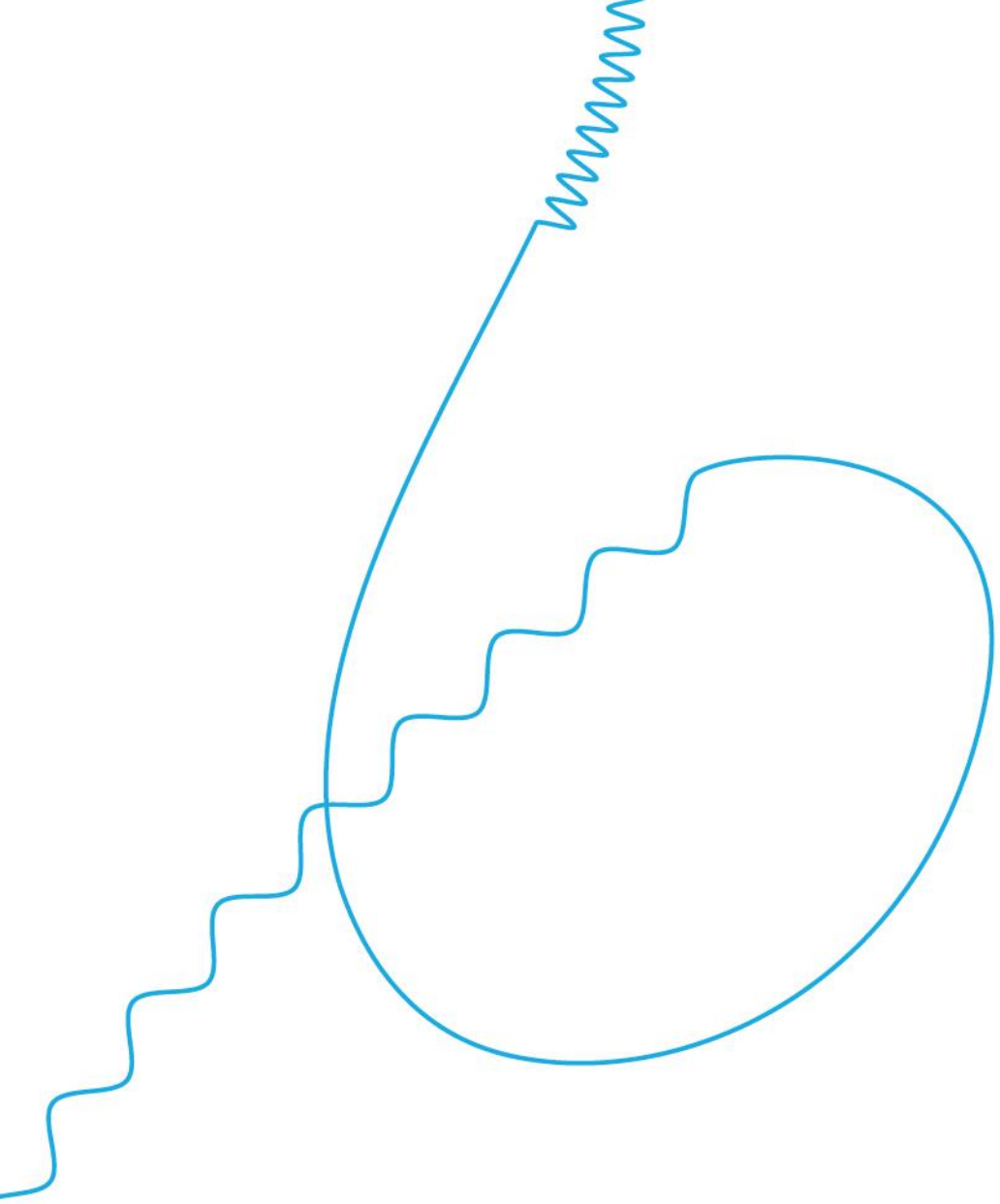
	Norovirus current day	Rotavirus pre-vaccine era
Cases	~4.2 M	~2.7 M
Outpatient visits	~815 K	~410 K
ED visits	~130 K	200 – 270 K
Hospitalizations	~25 K	55 – 70 K
Deaths	~40	20 – 60

U.S. Disease Burden in Adults 60+

	Norovirus current day	RSV pre-vaccine era
Cases	~3.5 M	2.5 – 3 M
Outpatient visits	~625 K	~1.4 M
ED visits	~95 K	~120 K
Hospitalizations	~50 K	100 – 150 K
Deaths	~1 K	8 – 12 K

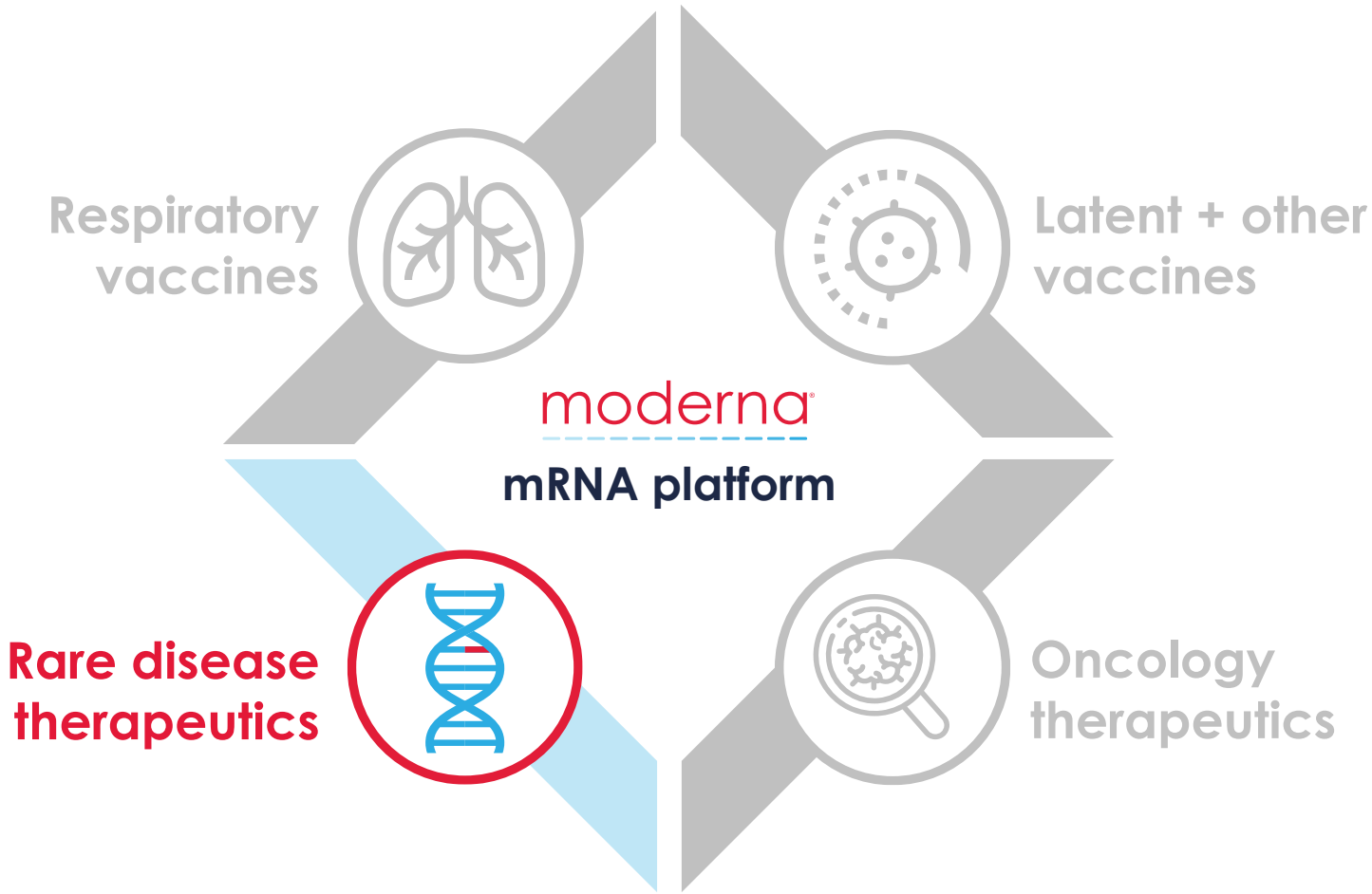
* Cost-effective price estimate for Norovirus, current vaccine prices for Rotavirus and RSV

Cortese et al. MMWR; February 6, 2009 / 58(RR02);1-25. Bartsch et al. Am J Prev Med 2021;60(3):360–368. Burke et al. Clin Infect Dis 2021;73(1):e1–e8. Savic et al. Influenza Other Respir Viruses 2023 Jan;17(1):e13031. McLaughlin et al. Open Forum Infect Dis 2022 Jun 17;9(7):ofac300. CDC. ACIP Meeting; Feb 23 2023.

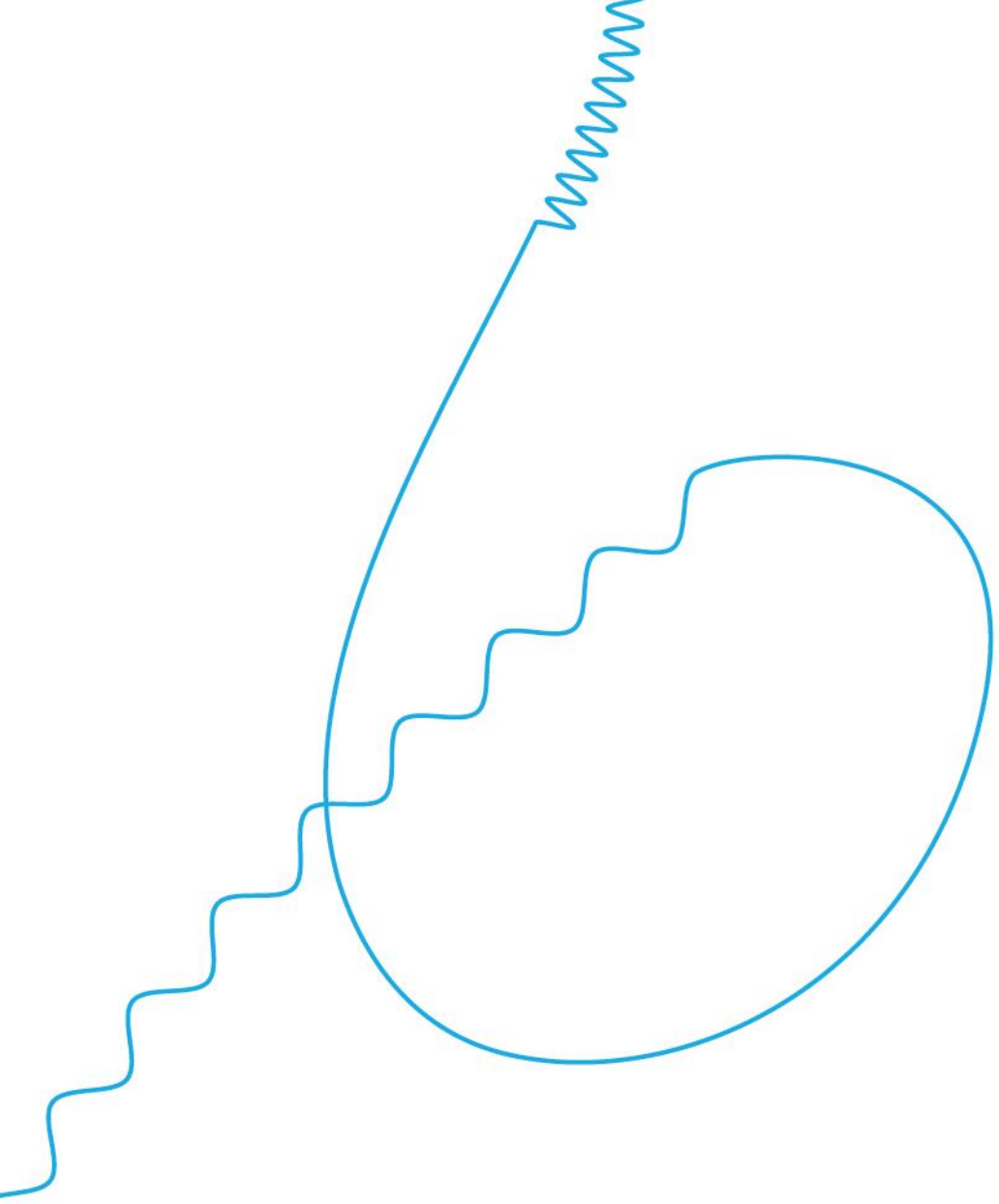


Break

Rare disease therapeutics



moderna



Rare disease therapeutics

Development

Kyle Holen, M.D.

SVP, Head of Development, Therapeutics and Oncology, Research & Development

moderna

Common characteristics for therapeutic development in rare diseases

Rare diseases

- Matching LNPs to specific indications (in liver and lung)
- Leveraging use of data within a common LNPs
- Similar trial design elements

moderna

Rare disease therapeutics pipeline

Rare Disease

PA (mRNA-3927)

MMA (mRNA-3705)

GSD1a (mRNA-3745)

CF (VX-522)

OTC, PKU, CN-1
(mRNA-3139/-3210/-3351)

moderna

Announcing clinical data and new development programs in rare diseases

MMA (mRNA-3705)

Phase 1/2 preliminary safety and efficacy data

PKU (mRNA-3210)

Open IND

PA (mRNA-3927)

Phase 1/2 update

moderna

Clinical evidence with shared components over our rare disease portfolio are de-risking future programs

Component	Indications	Data	Will inform
LNP 1	PA, MMA	• Cumulative 29.6 years of patients dosing experience • Generally well-tolerated • Encouraging signs of clinical benefit	PKU
LNP 2	GSD1a	• Well-tolerated with no dose limiting toxicities observed to date • Encouraging signs of clinical benefit	OTC

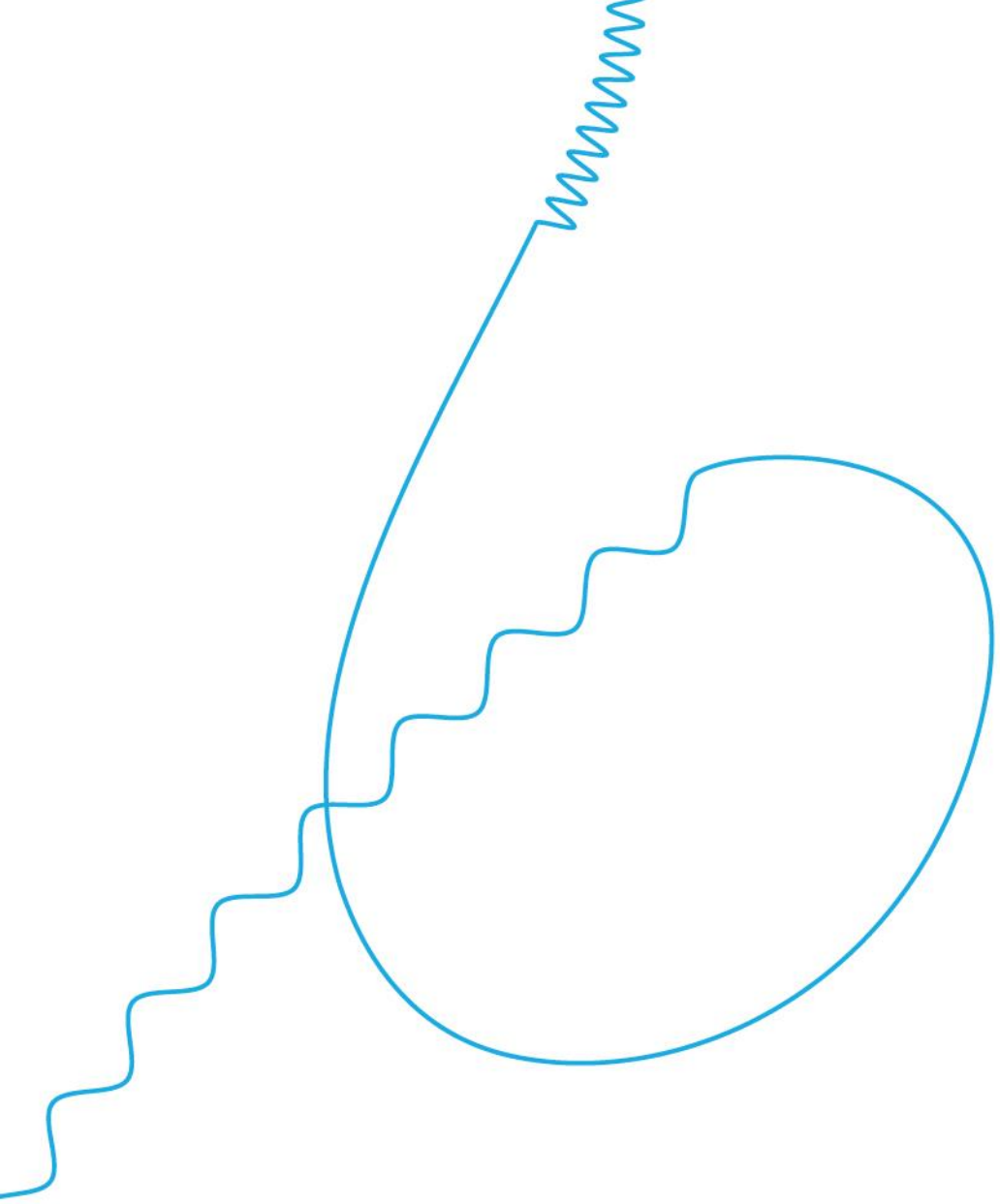
moderna

Expecting up to 4 rare disease product launches in the next 5 years

- Propionic Acidemia (PA)
- Methylmalonic Acidemia (MMA)
- Phenylketonuria (PKU)
- Glycogen Storage Disease (GSD1a)

Others to be announced

moderna



Propionic Acidemia (PA)

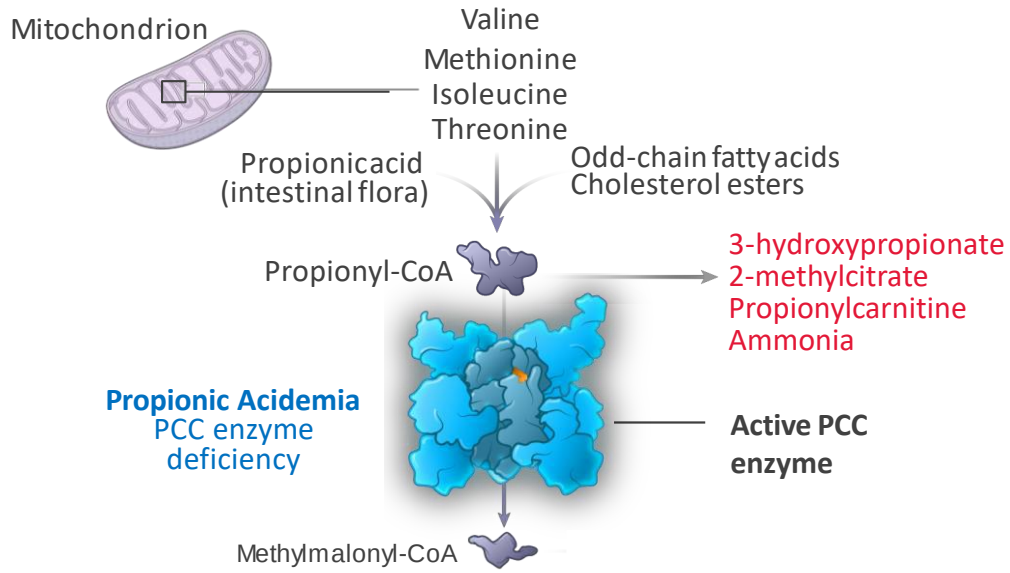
Geoffrey Rezvani, M.D.

Program Leader, CV/Emerging Therapeutics and Oncology

moderna

PA therapy (mRNA-3927) encodes for an intracellular enzyme

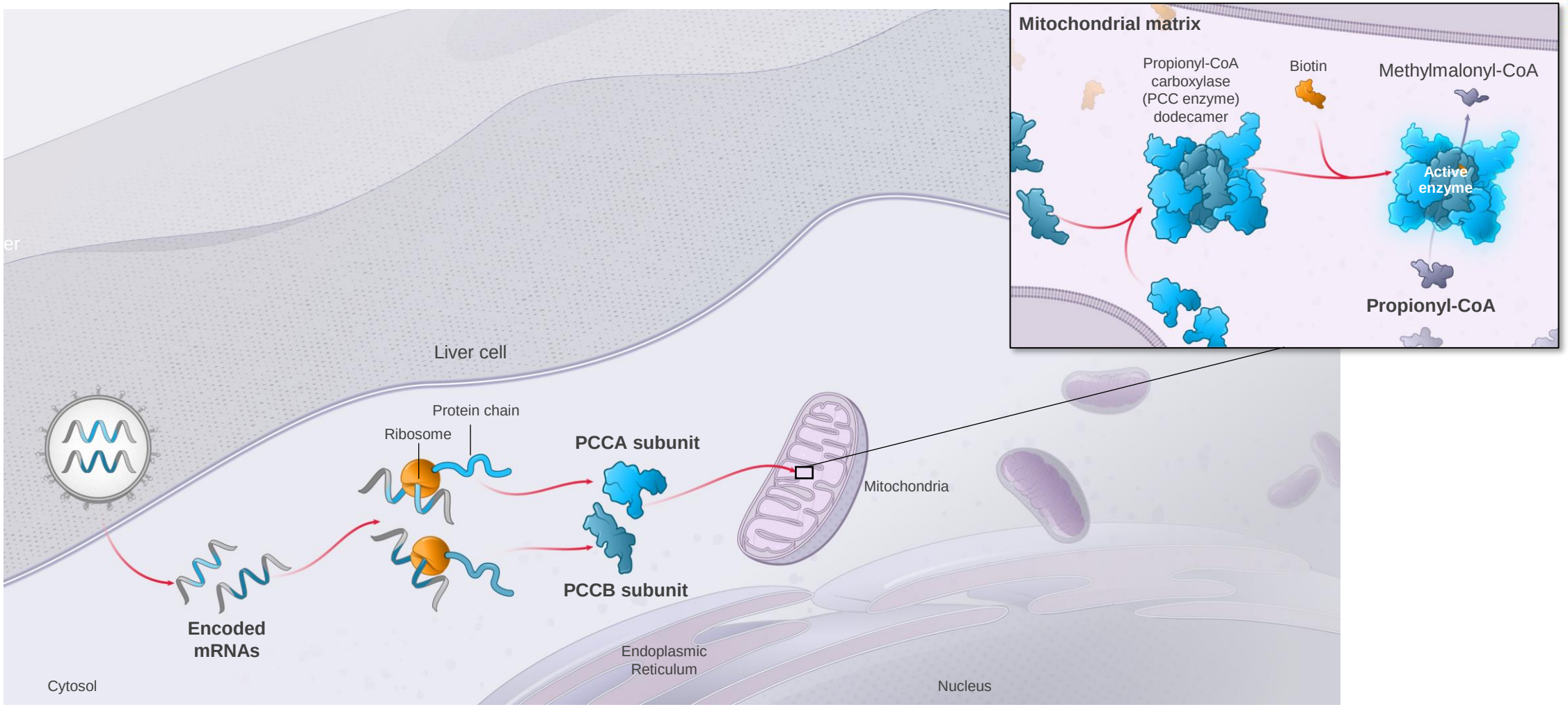
Moderna's mRNA therapy for PA (mRNA-3927) encodes for two proteins that form the deficient enzyme



PA biology

- **Changes in the *PCCA* and *PCCB* genes cause propionic acidemia**
  - These genes provide instructions for making two parts (subunits) of the propionyl-CoA carboxylase enzyme
  - Change in the *PCCA* or *PCCB* genes affect the normal function of the PCC enzyme and prevent the normal breakdown of propionyl-CoA
- As a result, propionyl-CoA and other **harmful compounds** accumulate causing acute **metabolic decompensation** events and **damage to the brain** and other organs, causing the serious health problems associated with propionic acidemia

mRNA-3927 encodes for PCCA and PCCB subunit proteins to form an active PCC enzyme



Ongoing Phase 1/2 Study designed to evaluate safety and pharmacology of mRNA-3927 in participants with PA

First study testing an mRNA therapeutic for intracellular protein replacement

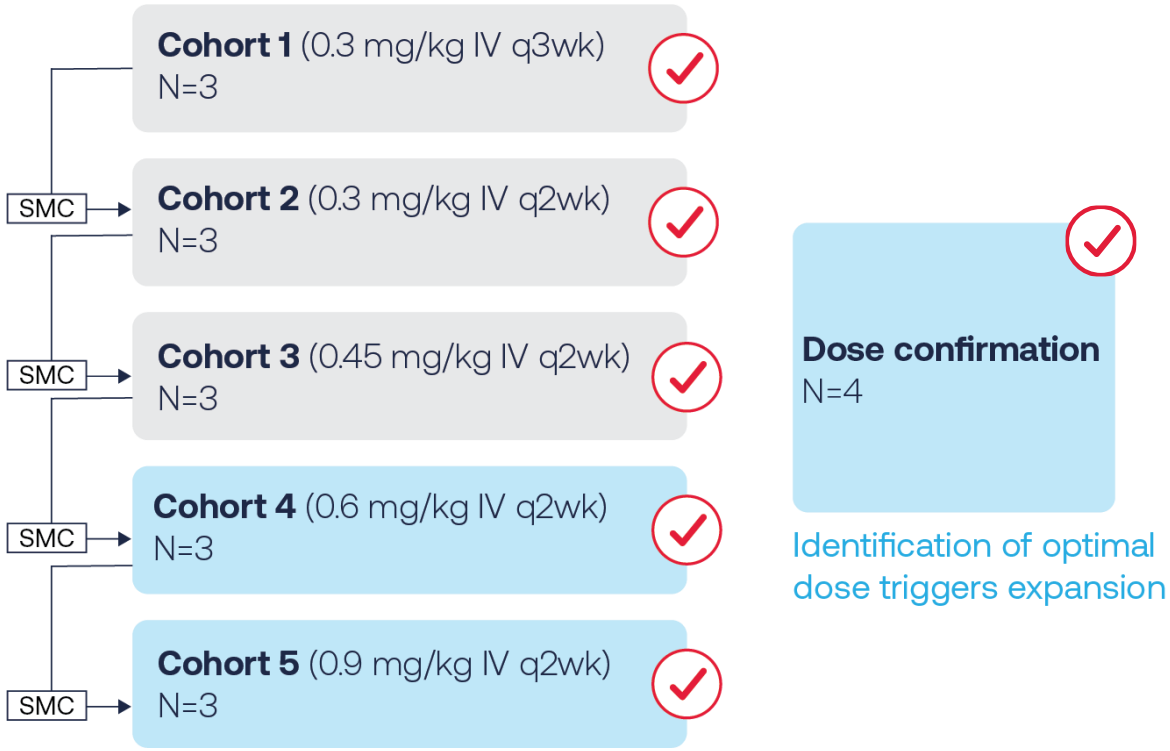
Primary endpoints: Safety and PK/PD

Secondary endpoints: Incidence and severity of adverse events and change in plasma biomarkers (Hydroxypropionic acid (3-HP) and methylcitric acid (2-MC))

Exploratory clinical endpoints: Metabolic decompensations events (MDE), cardiac function, quality of life

Current demographics: Participants aged 1-26 have been enrolled; 13 participants have completed the study

Phase 1/2 Trial Design (3 + 3 design)



Overall Phase 1/ 2 clinical experience

As of August 25, 2023, twenty participants have been dosed

- Twelve participants have >1 year of dosing
- 19.1 cumulative patient-years of experience on study drug
- Longest duration of treatment is 2.4 years and median duration 0.9 years
- Over 433 intravenous doses administered
- Study is ongoing; independent safety monitoring committee approved moving to fifth cohort (0.9 mg/kg)

- The majority of participants have elected to continue on Open Label Extension (OLE) Study
- Generally well-tolerated to date
- No dose limiting toxicities
- Three cases of drug related serious adverse events reported in two participants (Vascular device infection Grade 2, Infusion site erythema Grade 2, and Pancreatitis Grade 3[1])
- Mild to moderate infusion related reactions were reported in <10% of doses administered

1 Patient had a history of recurrent pancreatitis prior to enrollment

moderna

Metabolic decompensation events (MDEs) are serious, clinically significant events in organic acidemias

Presentation of MDEs in PA and MMA

- PA & MMA are characterized by intermittent life-threatening **MDEs**
- Patients with PA & MMA commonly present with an MDE soon after birth
- MDEs are a major contributor to mortality and long-term irreversible sequelae, such as brain damage

Identification and measurement of MDEs

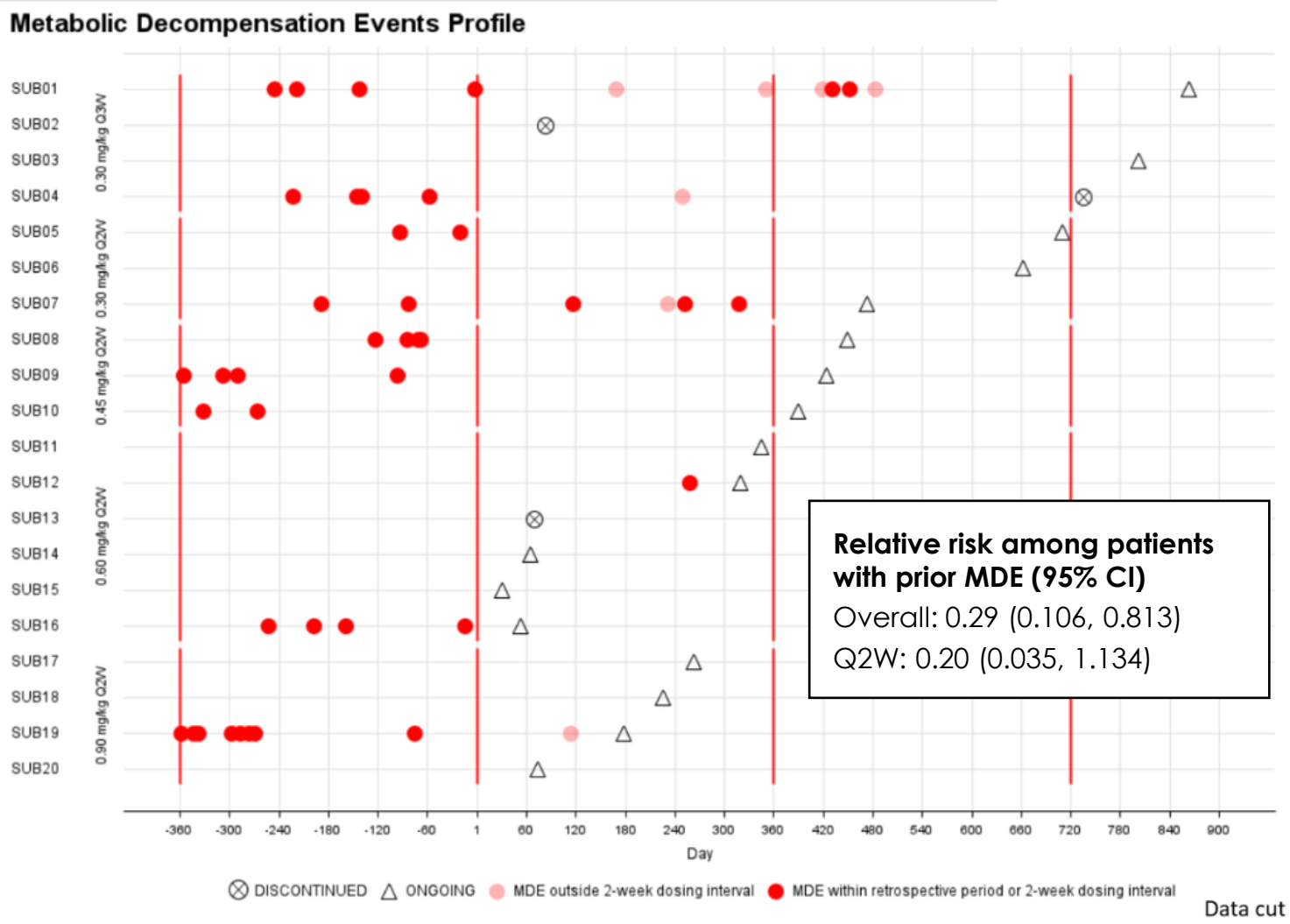
MDEs can be objectively identified in a patient with clinical deterioration and:

- Signs or symptoms, including vomiting, anorexia, lethargy, or seizure
- Metabolic acidosis (pH <7.35)and in many cases high ammonia
- Needs acute medical care (ER or hospitalization)

- **Regulators have provided initial support for MDE as a clinically meaningful endpoint measure for therapeutic trials in patients with Propionic Acidemia**
- **Discussions with key regulators for MMA are on-going**

moderna

Summary of metabolic decompensation events (MDEs)



Relative risk among patients with prior MDE (95% CI)

Overall: 0.29 (0.106, 0.813)

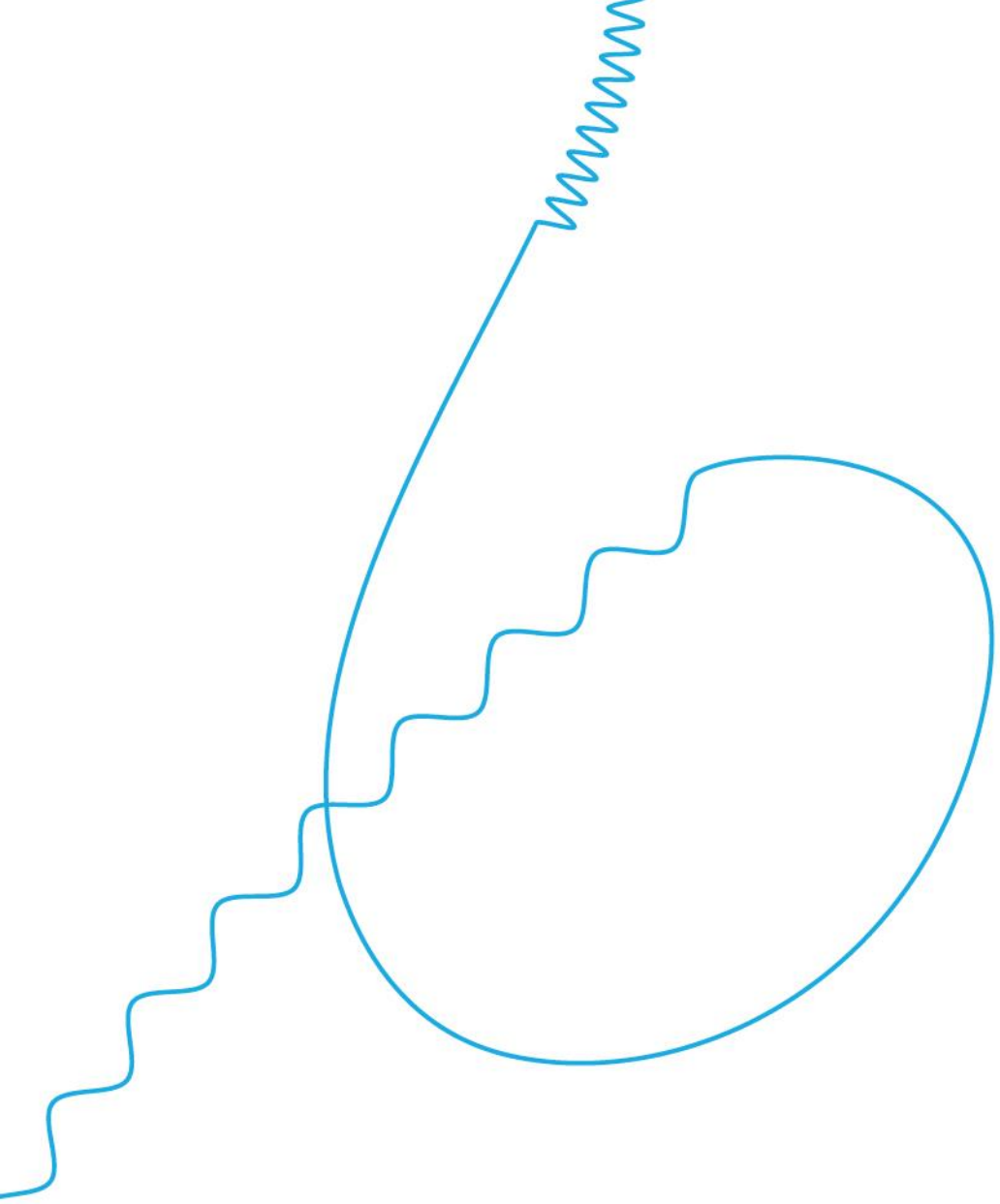
Q2W: 0.20 (0.035, 1.134)

Data cut 25 Aug 2023

moderna

Summary

- **Expanding clinical experience:** Cumulative treatment duration of over 19.1 patient years
- **Safety:** Generally well-tolerated to date with no events meeting protocol-defined dose-limiting toxicity criteria
- **Clinical endpoints:** Early results suggest potential decreases in annualized MDE frequency and PA-related hospitalizations compared to pre-treatment
- **Open label extension study:** Majority of patients have elected to continue on open label extension study
- **Next steps:** Continue study enrollment and identify an optimal dose while engaging with global regulators on a path to registration



Methylmalonic Acidemia (MMA)

moderna

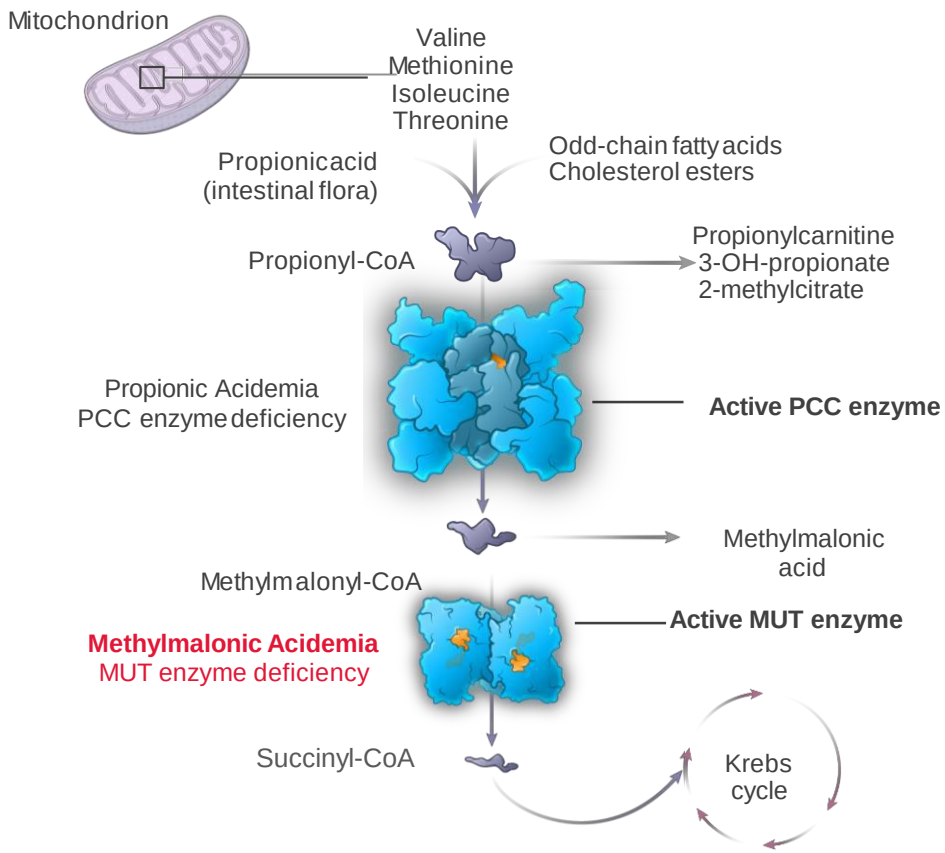
Overview of Methylmalonic Acidemia (MMA) due to MUT deficiency

Methylmalonic acidemia (MMA) refers to a rare, autosomal recessive acidemia

It is caused by a defective or missing MUT enzyme (methylmalonic CoA mutase)

Changes in the *MMUT gene* causes methylmalonic acidemia

- Gene provides instructions for making an enzyme called methylmalonyl CoA mutase
- Changes in the gene disrupt the function of the enzyme and prevent the normal breakdown of molecules



Methylmalonic acidemia (MMA) has no approved therapies

Primarily a pediatric disease with onset in early infancy; significant mortality and morbidity

Treatment: There is no approved therapy for MMA

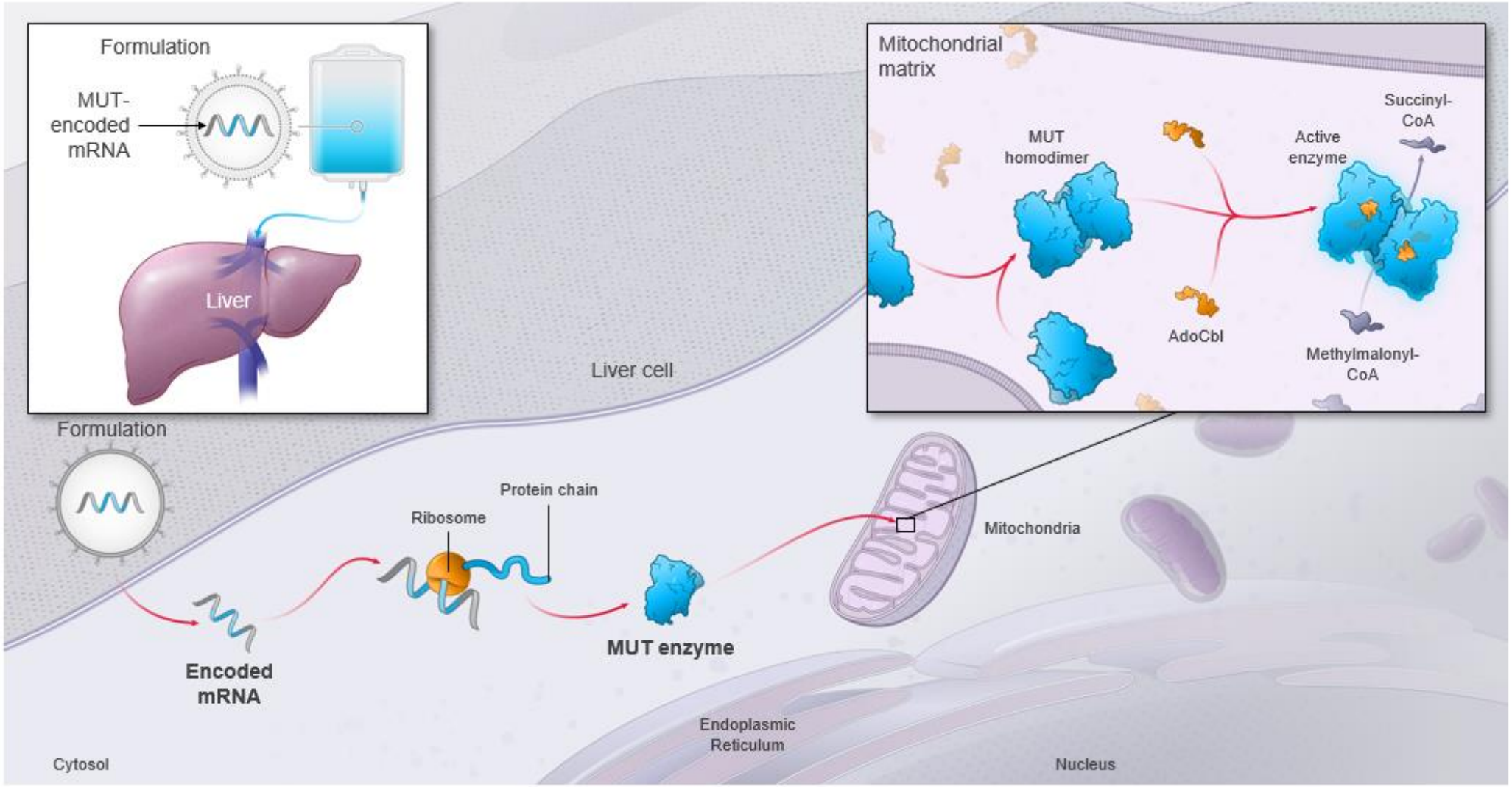
Current interventions include:

- Protein-restricted diet, carnitine supplementation
- Carbaglu® approved for the treatment of hyperammonemia
- Liver and/or kidney

MMA Clinical Manifestations

- Recurrent episodes of **life-threatening metabolic decompensations**
- **Progressive multi-organ damage**
  - Brain damage
  - Seizures
  - Intellectual disability
  - Severe vision problems
  - Inflammation of the pancreas (pancreatitis)
  - Chronic renal failure
  - Heart failure (cardiomyopathy); heart rhythm problems
  - Increased risk of having a metabolic stroke as early as a few weeks of age
  - Osteoporosis which can lead to fractures
  - Hematologic: reduced number of cells in blood (anemia, leukopenia, thrombocytopenia, pancytopenia)
  - Growth retardation

mRNA-3705 encodes the intracellular MUT enzyme



Note: AdoCbl = cofactor adenosylcobalamin

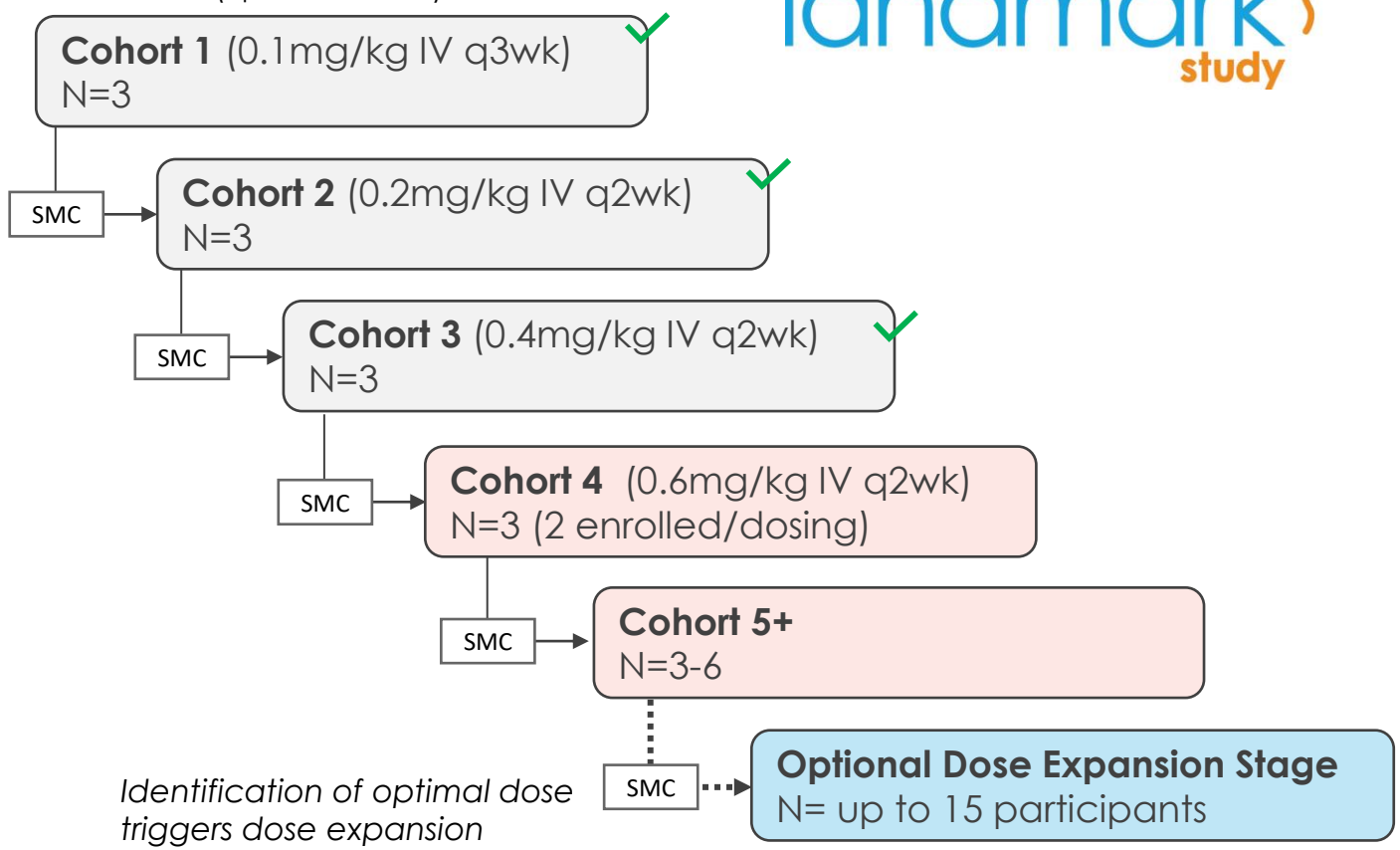
moderna

Ongoing Phase 1/2 Study designed to evaluate safety and pharmacology of mRNA-3705 in participants with MMA

Dose Optimization Stage Endpoints:

- **Primary endpoints:** safety and tolerability
- **Secondary endpoints:** Pharmacokinetic parameters and change in blood methylmalonic acid and 2-methylcitrate (2-MC)
- **Exploratory clinical endpoints:** Include metabolic decompensation events (MDEs), MMA-related hospitalizations, patient-centered outcome measures

Treatment period is 10 doses, after which participants may enter an extension study



landmark study

SMC: safety monitoring committee
✓: Fully enrolled

moderna

mRNA-3705-P101: summary of demographics and baseline characteristics

	Cohort 1 0.1 mg/kg Q3W (N=3)	Cohort 2 0.2 mg/kg Q2W (N=3)	Cohort 3 0.4 mg/kg Q2W (N=3)	Cohort 4 0.6 mg/kg Q2W (N=2)	Total (N=11)
Age at enrollment, median (years)	12.17	2.67	7.83	11.54	7.83
Min, Max	4.5, 14.4	2.5, 39.5	5.8, 16.0	4.3, 18.8	2.5, 39.5
Age at disease onset, median (months)	0	0	3	58.5	0
Min, Max	0	0, 1	0, 10	0, 117	0, 117
Sex, n					
Male	1	1	1	2	5
Female	2	2	2	0	6
Weight					
Weight at baseline, median (kg)	25.70	13.40	22.50	38.55	22.50
Min, Max	19.5, 41.4	12.3, 58.0	16.6, 54.9	16.5, 60.6	12.3, 60.6
Phenotype					
Mut0	3	3	3	1	10
Mut-	0	0	0	1	1

moderna

mRNA-3705-P101: clinical experience to date

As of August 25, 2023*:

- Eleven participants have been dosed, with a total of 221 doses administered
- Total cumulative treatment duration among all participants is ~10.5 patient-years
  - Median treatment duration among all participants is 1.02 patient-years
  - Maximum participant treatment duration is 1.95 patient-years
- Study is ongoing; final participant in Cohort 4 expected to be enrolled soon
- Generally well-tolerated to date with no discontinuations due to safety and no events meeting protocol-defined dose-limiting toxicity criteria
- All participants who have completed the treatment period of the main study have opted to enter a long-term extension study

*Data include both on-going mRNA-3705-P101 and Extension studies

moderna

Safety in mRNA-3705-P101: overall Summary to date

As of August 25, 2023:

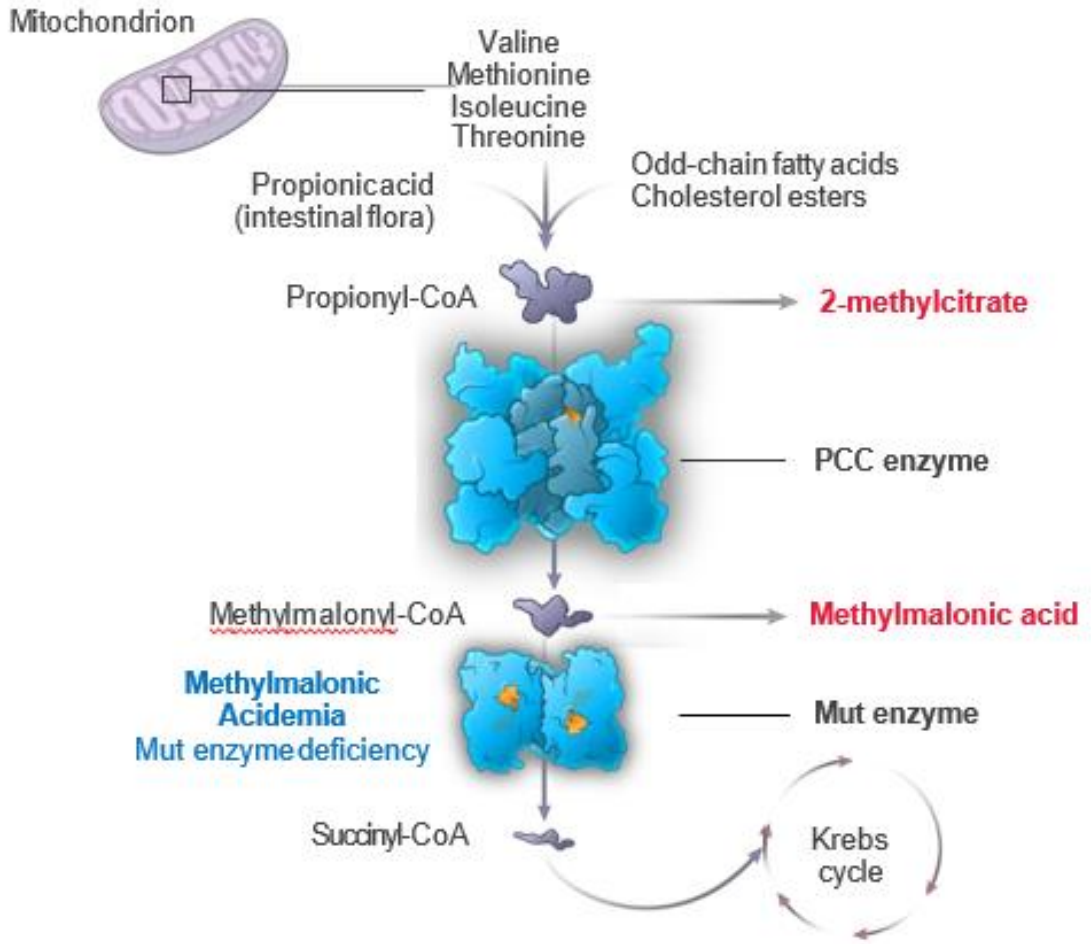
- No deaths or discontinuations due to safety-related reasons
  - One discontinuation in the extension for non-safety reasons
- No events meeting dose-limiting toxicity criteria have been observed
- 1 Serious AE assessed as related to mRNA-3705 by the Investigator:
  - Event of "body temperature increased" (CTCAE grade 2, resolved). Patient has continued on treatment
- Drug related adverse events were mostly mild or moderate (CTCAE grade 1 or 2)
- Most common adverse events (AEs) are pyrexia (n=4) and upper respiratory tract infection (n=4)
- Less than 5% of administered doses associated with infusion-related reactions

Biomarkers to evaluate pharmacodynamics of mRNA-3705

Methylmalonic acid and 2-methylcitrate represent **primary biomarkers** proximal to the enzyme deficiency

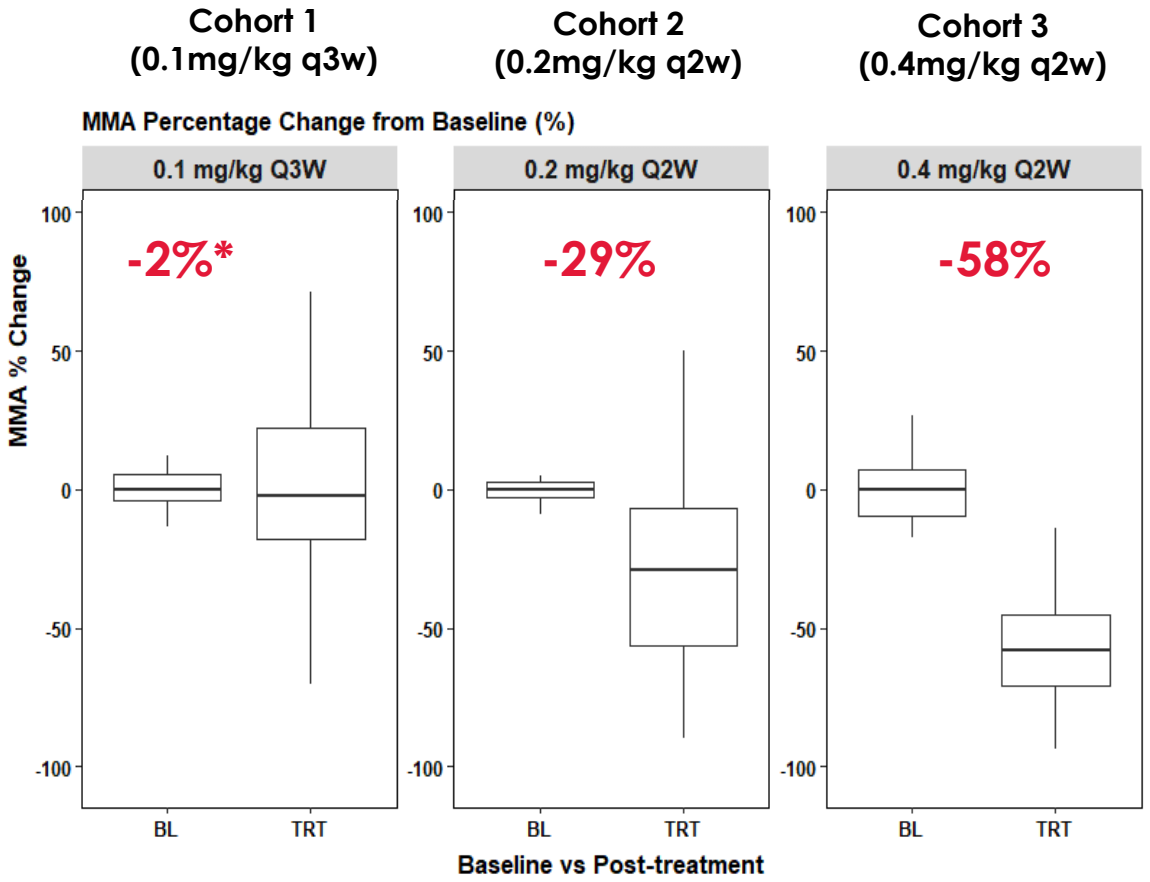
Changes in concentrations of methylmalonic acid generally **correlate with disease severity** and natural history data suggest that changes in methylmalonic acid may be associated with clinical events

There are **no clinically validated** biomarkers for MMA

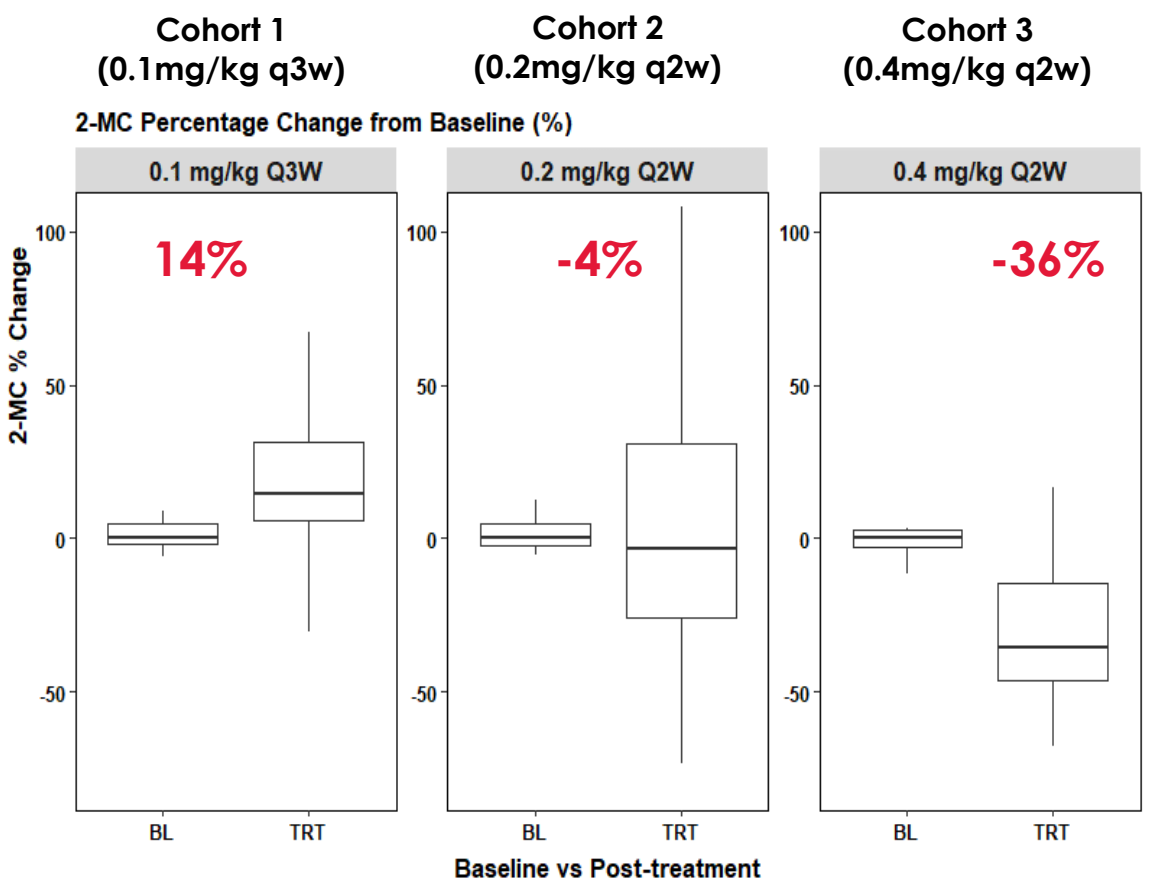


mRNA-3705-P101: dose-dependent changes in key biomarkers

Methylmalonic Acid



2-Methylcitrate

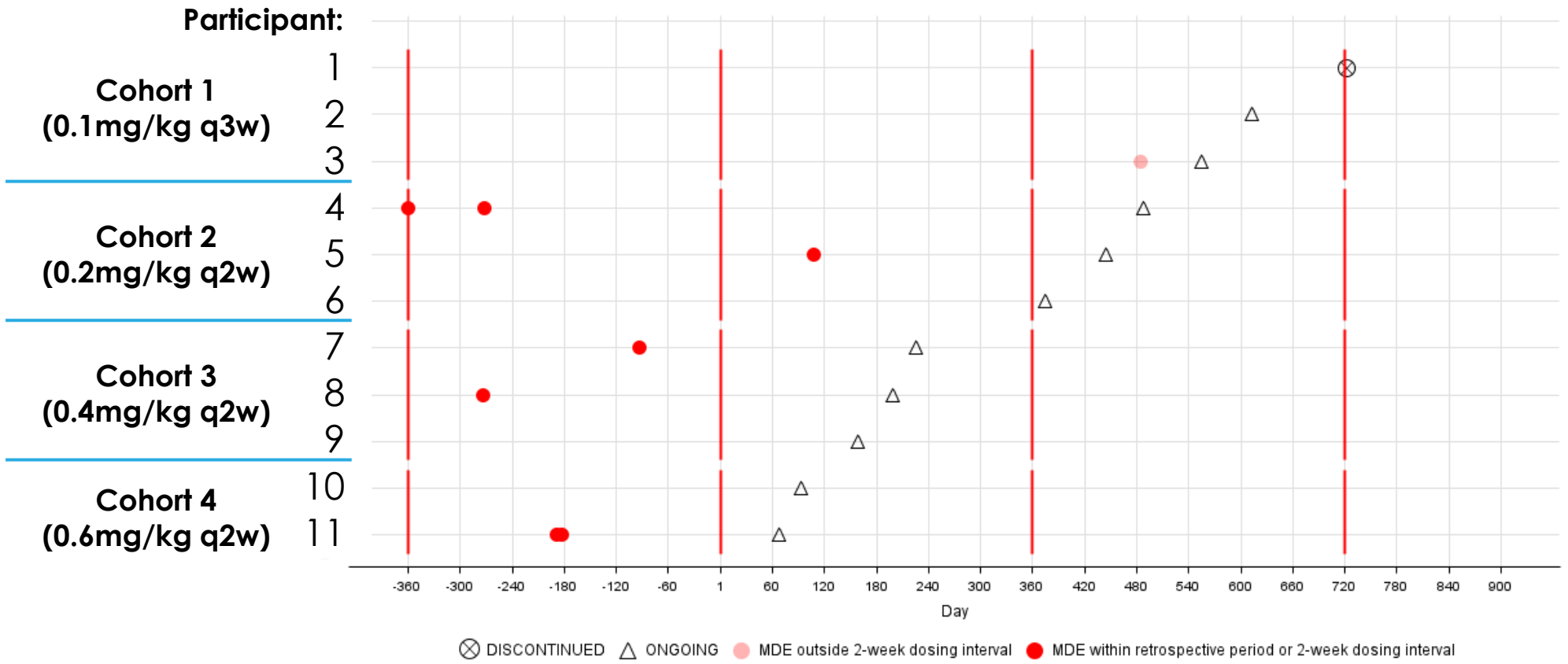


*Overall percent change from pre-treatment median baseline is shown for each cohort

Cohort 4 Update

- Recently initiated dosing in cohort 4, two patients enrolled, small number of doses per patient
- Safety and tolerability consistent with prior cohorts but continuing to follow
- The cohort includes the first patient with a Mut $^{-}$
- We've not yet observed decreases in the MMA levels, however it is early in the course of their treatment
- We will continue to enroll in this cohort and make a determination on further dose escalation

mRNA-3705-P101: Promising initial data on clinical endpoints



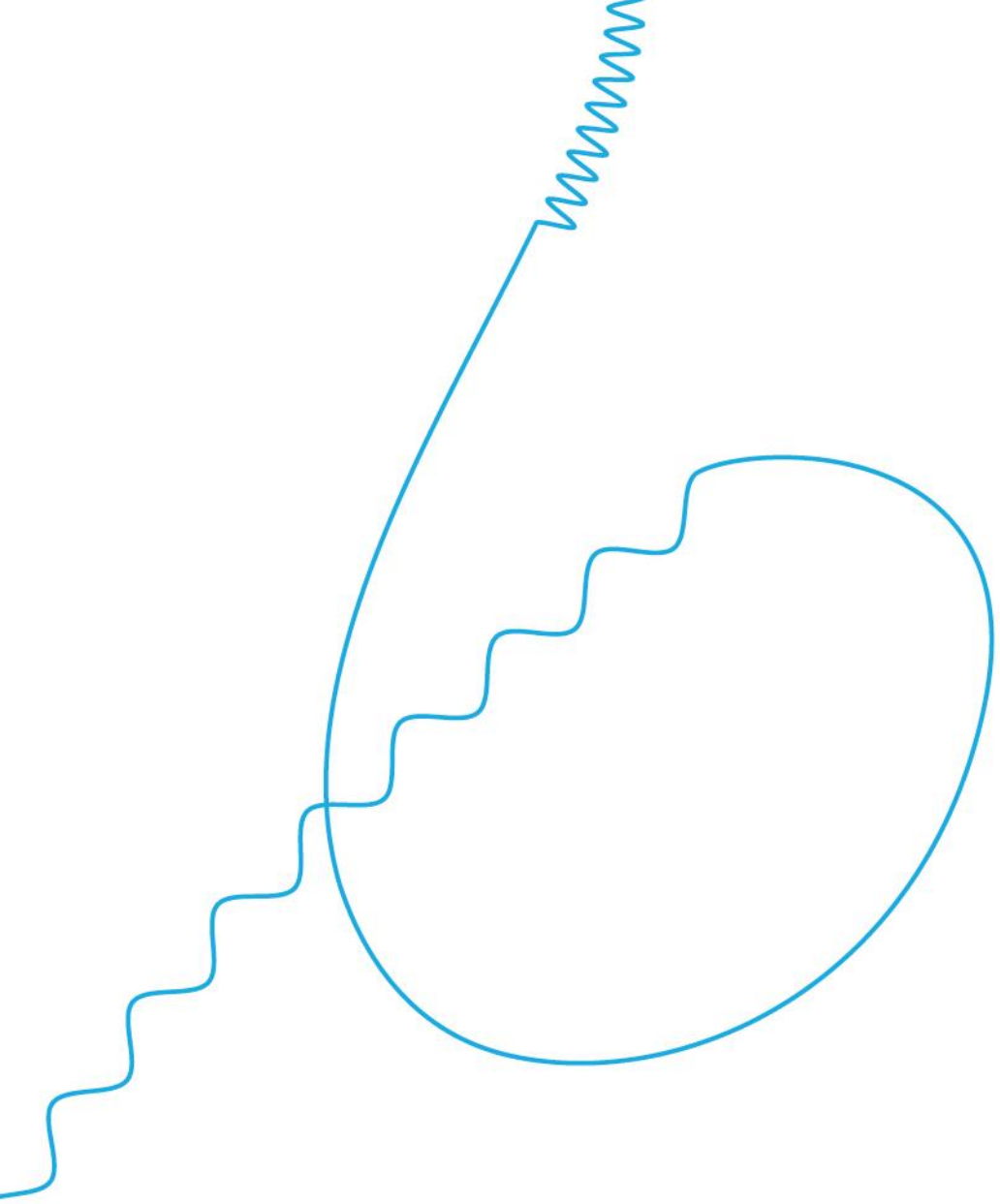
Comparing pre- to post-treatment, initial data:
To date no MDEs observed at expected efficacious dose levels (0.4mg/kg and above)

Data as of 25Aug2023

Summary

- **Expanding clinical experience:** Cumulative treatment duration of over 10.5 patient years
- **Safety:** Generally well-tolerated to date with no discontinuations due to safety and no events meeting protocol-defined dose-limiting toxicity criteria
- **Encouraging initial pharmacodynamic data:** Dose-dependent reductions in methylmalonic acid in Cohorts 2 and 3
- **Clinical endpoints:** Early results suggest potential decreases in annualized MDE frequency and MMA-related hospitalizations compared to pre-treatment
- **Next steps:** Continue study enrollment and identify an optimal dose while engaging with global regulators on a path to registration

moderna



Phenylketonuria (PKU)

moderna

Phenylketonuria (PKU) is a rare and serious metabolic disease with a high unmet need

PKU is a rare inherited metabolic disease resulting from a deficiency in the metabolism of phenylalanine, or PHE, due to mutations within the enzyme phenylalanine hydroxylase, PAH; typically identified by newborn screening

Disease burden: PKU affects brain growth and development[1]; progressive mental disability from tyrosine deprivation; severity of symptoms is strongly related to the degree and timing of exposure to high Phe levels[2]

Target population: Incidence of ~1:25K live births in the US and EU5

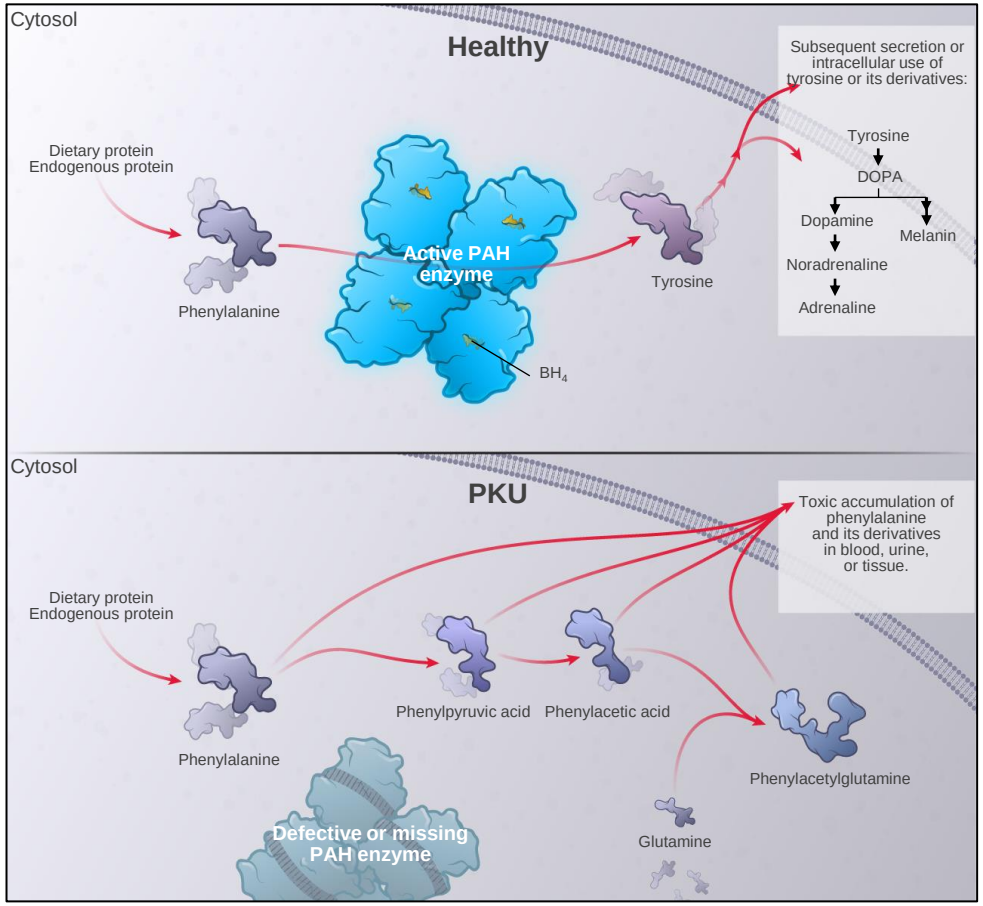
- ~40,000 patients in the US and EU5

Approved therapies include:

- There are 2 approved drugs to treat PKU: sapropterin (Kuvan®) with limited responsiveness, and pegvaliase (Palynziq™), which may be associated with severe adverse effects (including anaphylaxis)

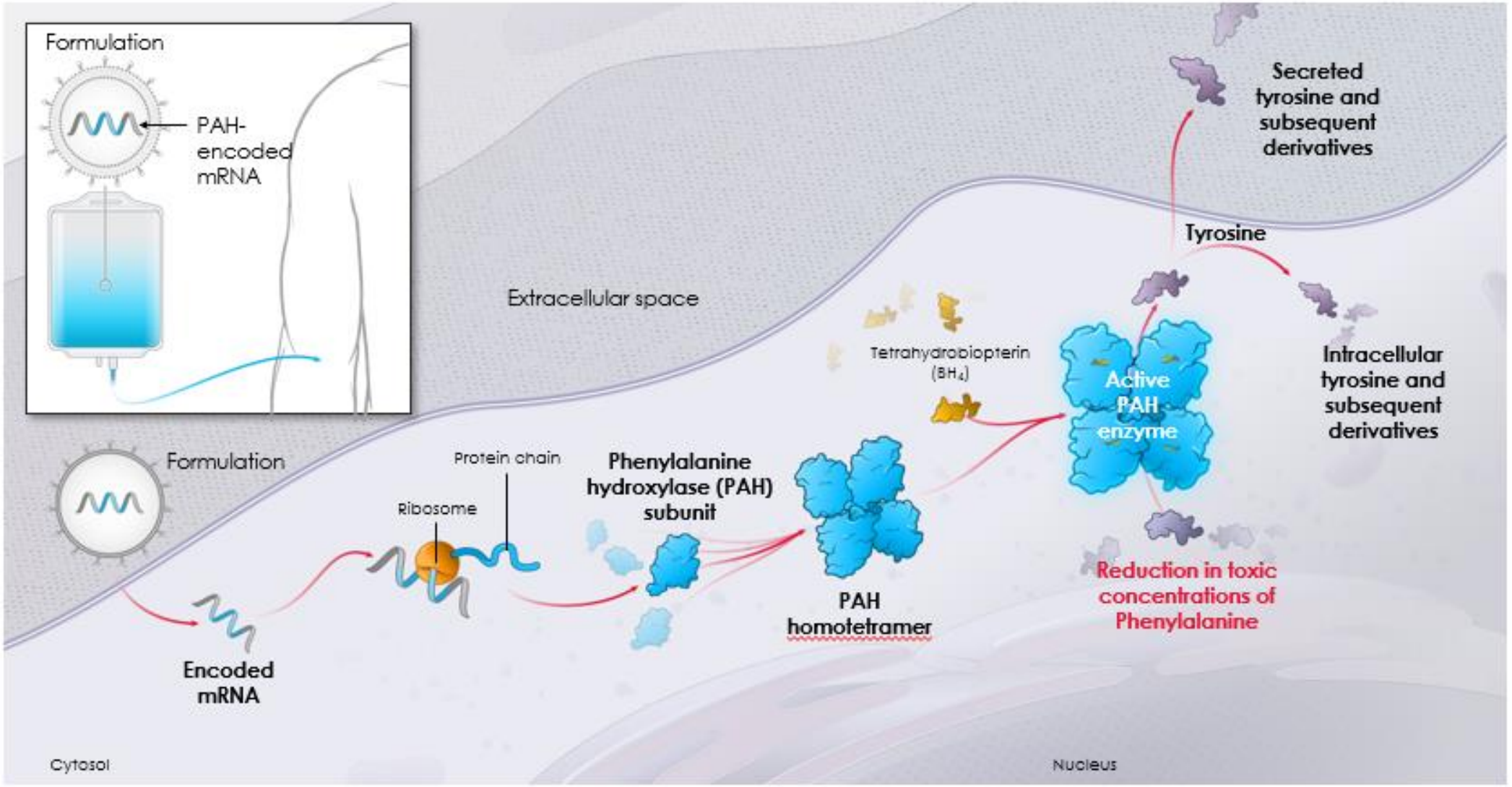
Early and continuous treatment throughout life is fundamental to prevent the development of irreversible neuropsychiatric outcomes[3]:

- Adherence to a lifelong Phe-restricted diet is challenging and decrease by age[4]

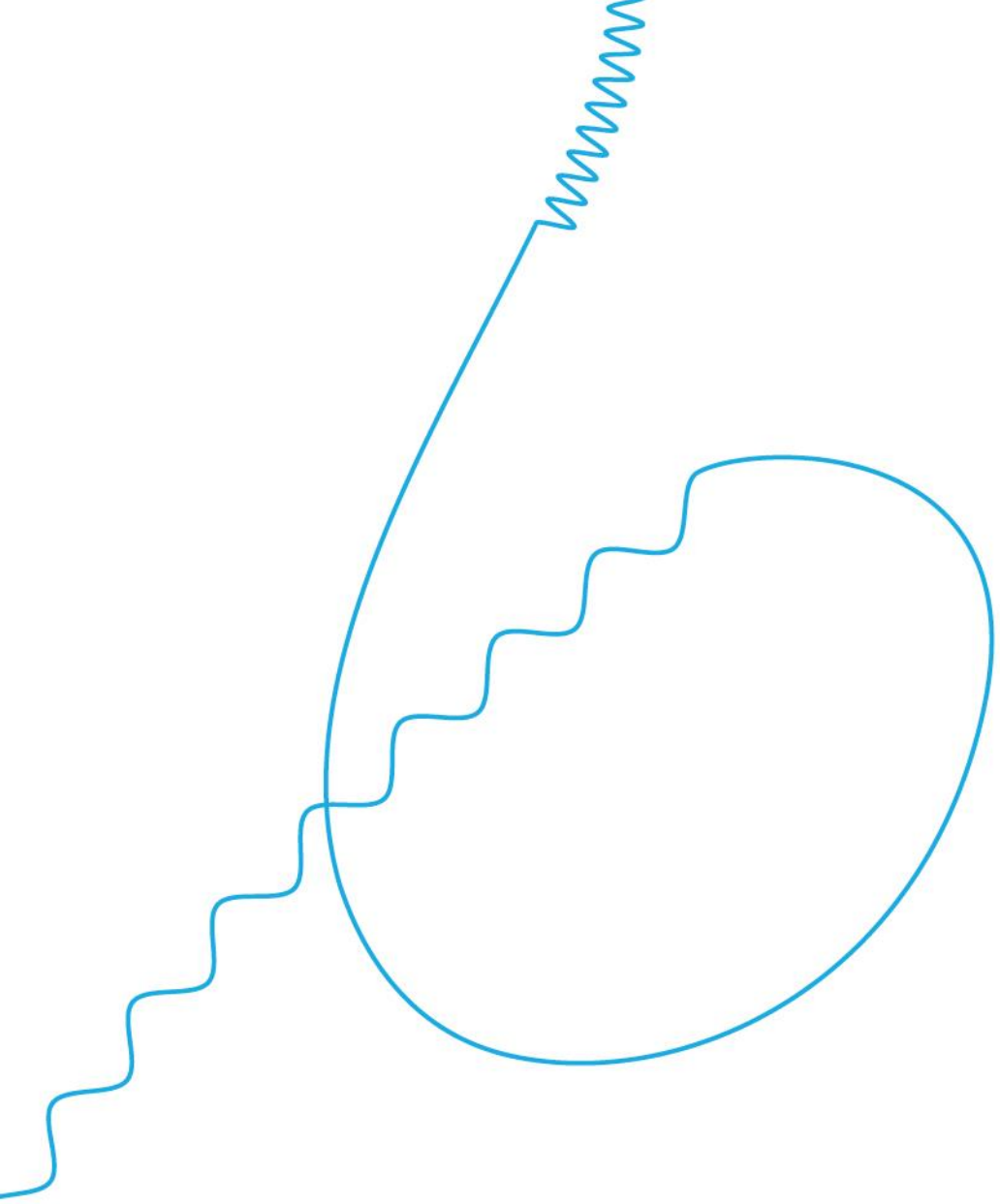


Phe: phenylalanine, Tyr: tyrosine [1] *Molecular Genetics and Metabolism 139 (2023) 107583* [2] Front. Psychiatr. 10 (2019) 561 [3] Genet Med. 2014 Feb;16(2):188-200 [4] *J Hum Nutr Diet. 2022;35:1016–1029*

mRNA-3210 encodes for the PAH enzyme



moderna



Rare disease franchise

Commercial opportunity

Arpa Garay

Chief Commercial Officer

moderna

Common commercial characteristics for the rare disease therapeutics franchise

Rare disease therapeutics

- High unmet medical need
- Increased awareness and prevalence after treatment
- High compliance with chronic, life-saving therapies
- Concentrated prescriber base

moderna

Moderna's current pipeline is targeting large addressable markets

Rare disease therapeutics

~10b+

moderna

Moderna's intracellular rare metabolic pipeline may address a multi-billion-dollar market

Intracellular Rare Metabolic Total Addressable Market

		Estimated US Prevalence
PA	Propionic acidemia	500 to 1,500
MMA	Methylmalonic acidemia	800 to 1,000
GSD1a	Glycogen storage disorder type 1a	2,000 to 4,000
PKU	Phenylketonuria	10,000 to 20,000
OTC	Ornithine transcarbamylase deficiency	1,000 to 2,000

Potential peak sales opportunities of intracellular rare metabolic disease of ~$500m-1B

Opportunity to expand into additional indications where we have potential to improve long-term patient outcomes

Internal Moderna estimates based on public sources

moderna

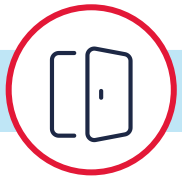
Attractive commercial opportunity in Rare Disease

High value medicines

Chronic, life-saving therapies

Increased patient identification and access drives diagnosis

Epidemiology estimates often understated for rare diseases with no treatment options



Efficient go-to-market model

Concentrated base of patients through patient advocacy groups

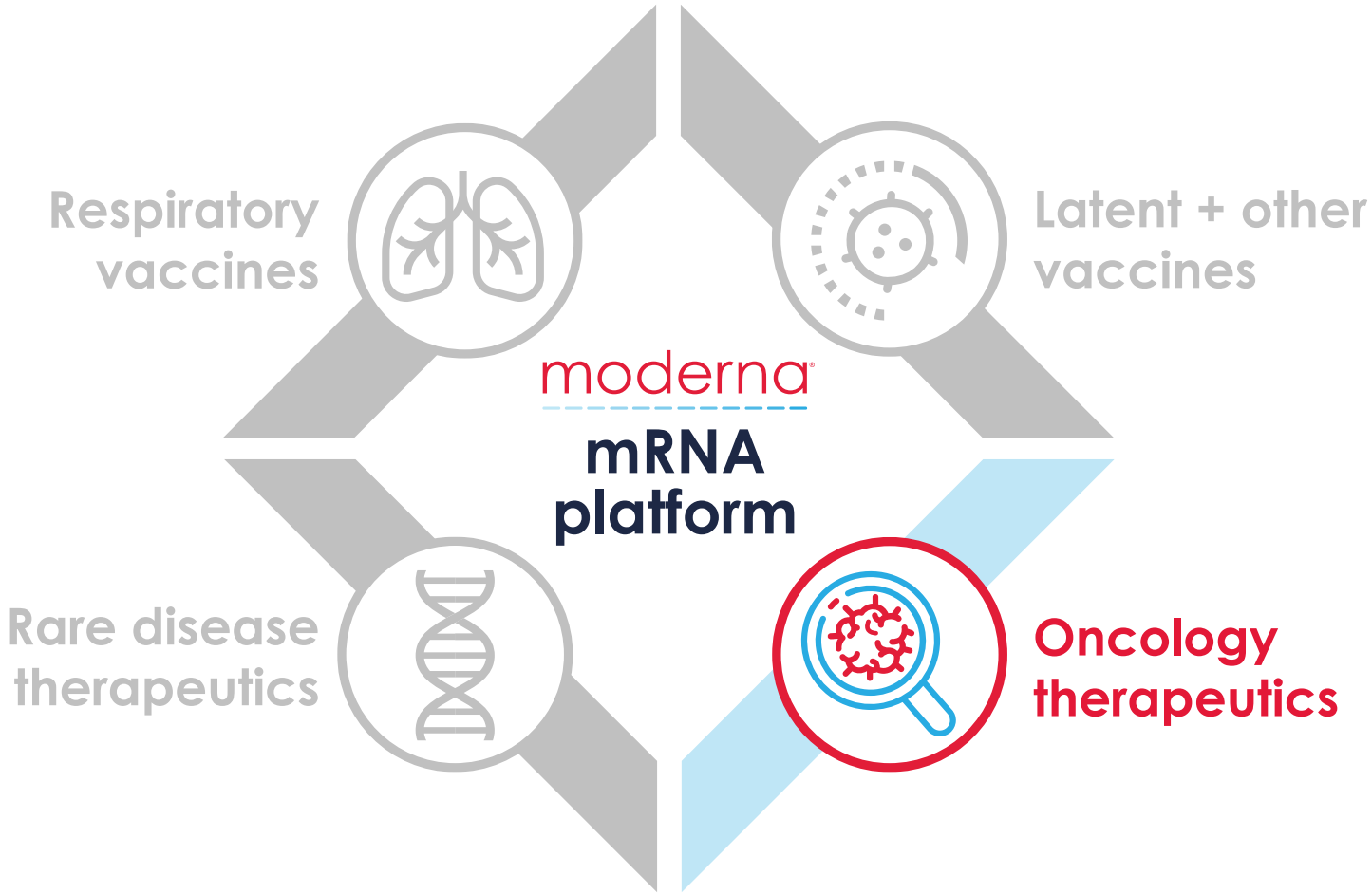
Unique regulatory benefits

High unmet need allows for accelerated timelines and regulatory incentives

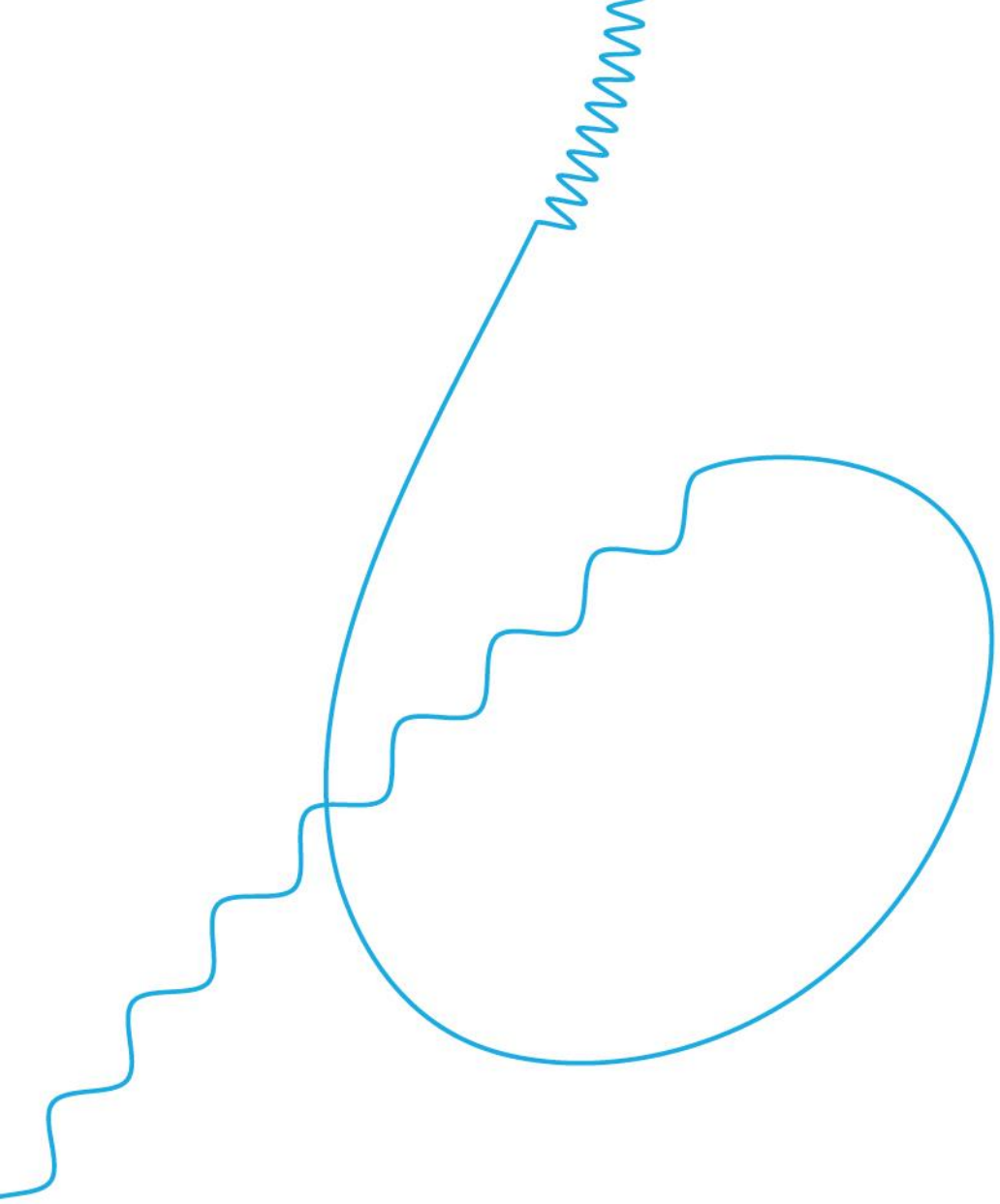
IP and competition

moderna

Oncology therapeutics



moderna



Oncology
Development

Kyle Holen, M.D.

SVP, Head of Development, Therapeutics and Oncology, Research & Development

moderna

Common characteristics for therapeutic development in the oncology franchise

Oncology therapeutics

- Elicit specific T-cell responses
- Robust safety data on delivery mechanism
- Low-grade, self-limited safety profile distinct from traditional oncology therapies

moderna

Oncology therapeutics

Programs

PC | Ph. 1 | Ph. 2 | Ph. 3 | Comm.

Individualized Neoantigen Therapy (INT) (mRNA-4157)

- Phase 3 adjuvant melanoma & NSCLC
- Additional indications

PC | Ph. 1 | Ph. 2 | Ph. 3 | Comm.

Triplet (mRNA-2752)

- Phase 1 ongoing

PC | Ph. 1 | Ph. 2 | Ph. 3 | Comm.

Checkpoint vaccine (mRNA-4359)

- Phase 1 ongoing

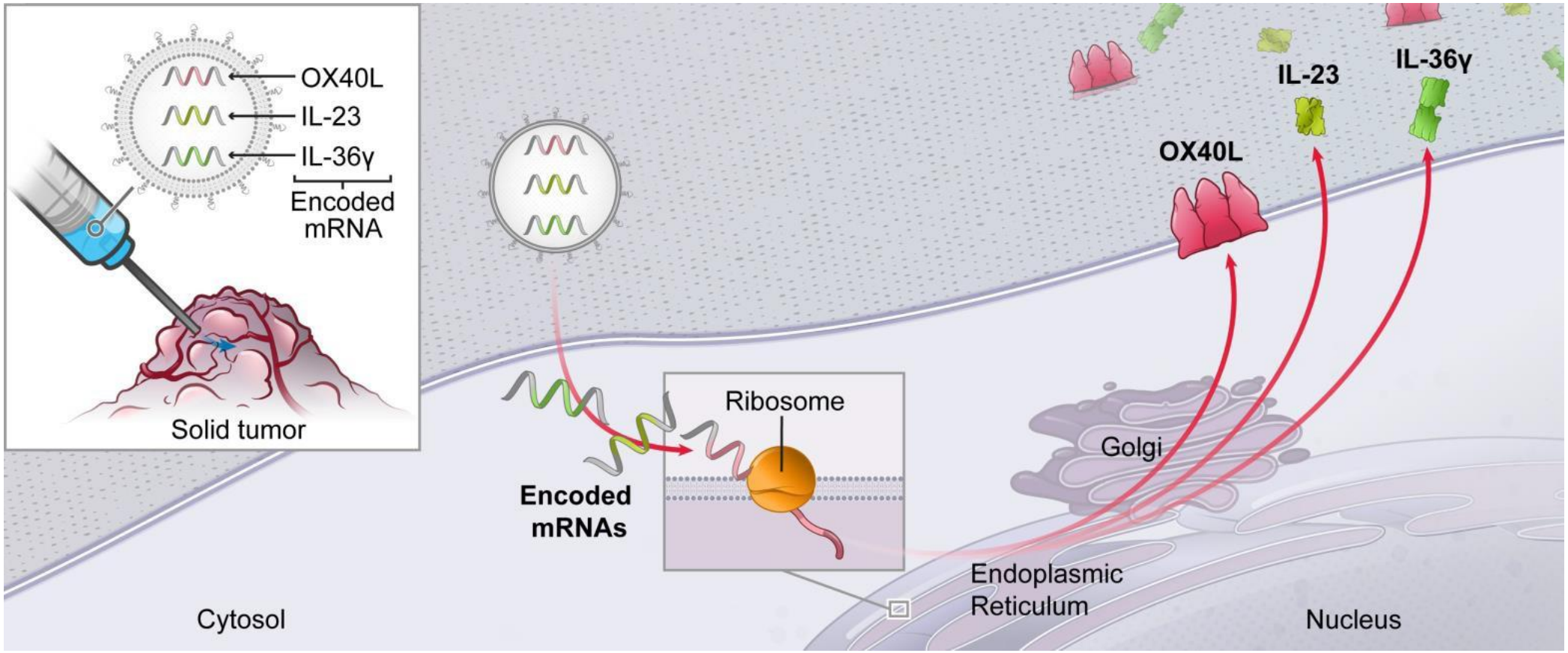
Partnerships

Expanding the reach of mRNA in oncology treatments

moderna

Triplet (OX40L/IL-23/IL-36γ) (mRNA-2752) overview

Moderna's technology enables novel combinations of targets



Intratumoral delivery may enable delivery of targets locally that are too toxic systemically

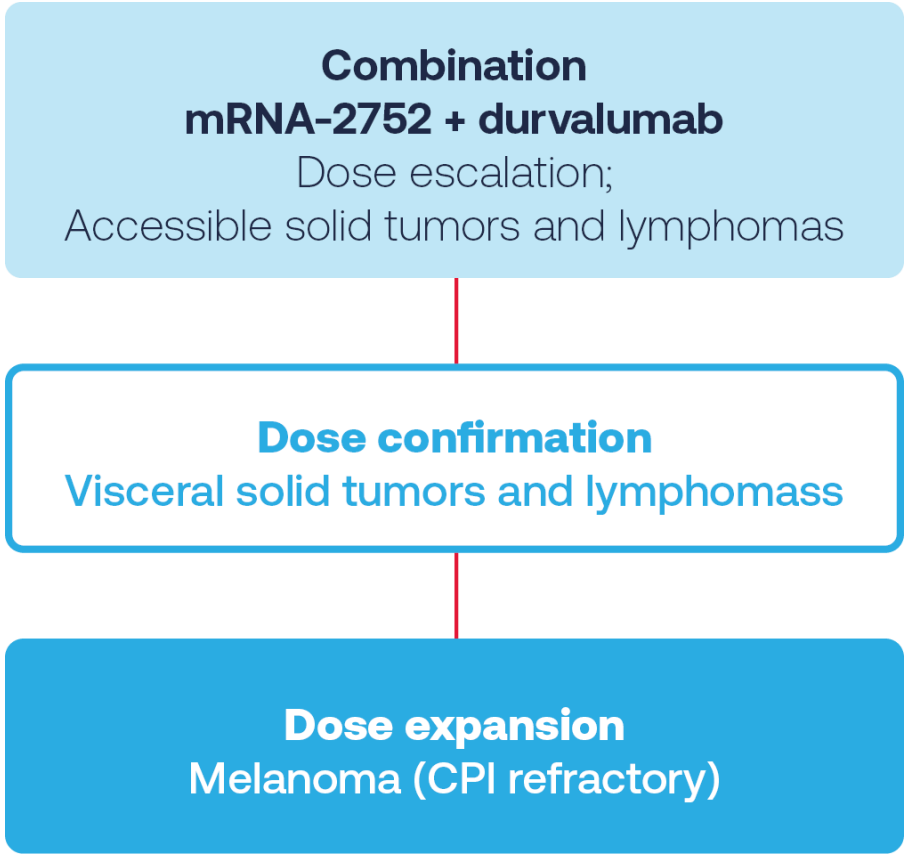
Triplet (mRNA-2752) is ongoing in a Phase 1; patients dosed in combination with durvalumab

Key Objectives

Evaluate safety and tolerability of mRNA-2752 administered alone and in combination with PD-L1 inhibitor

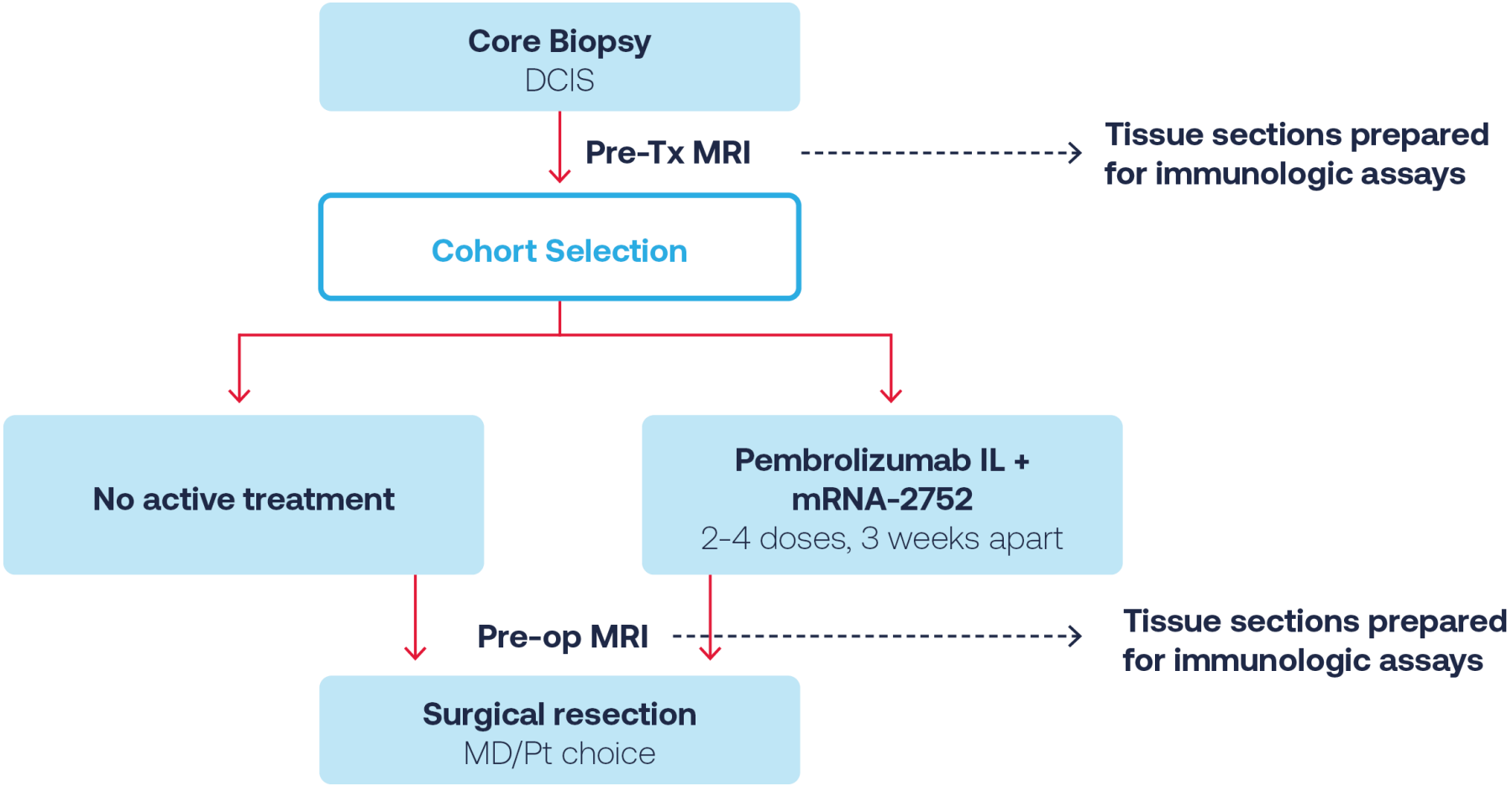
Define maximum tolerated dose (MTD) and recommended dose for expansion for mRNA-2752 alone and in combination with durvalumab

Secondary Objectives: (1) Anti-tumor activity, (2) Protein expression in tumors and (3) Pharmacokinetics



moderna

Investigator sponsored ductal carcinoma in situ (DCIS) study with Triplet (OX40L/IL-23/IL-36γ) (mRNA-2752)



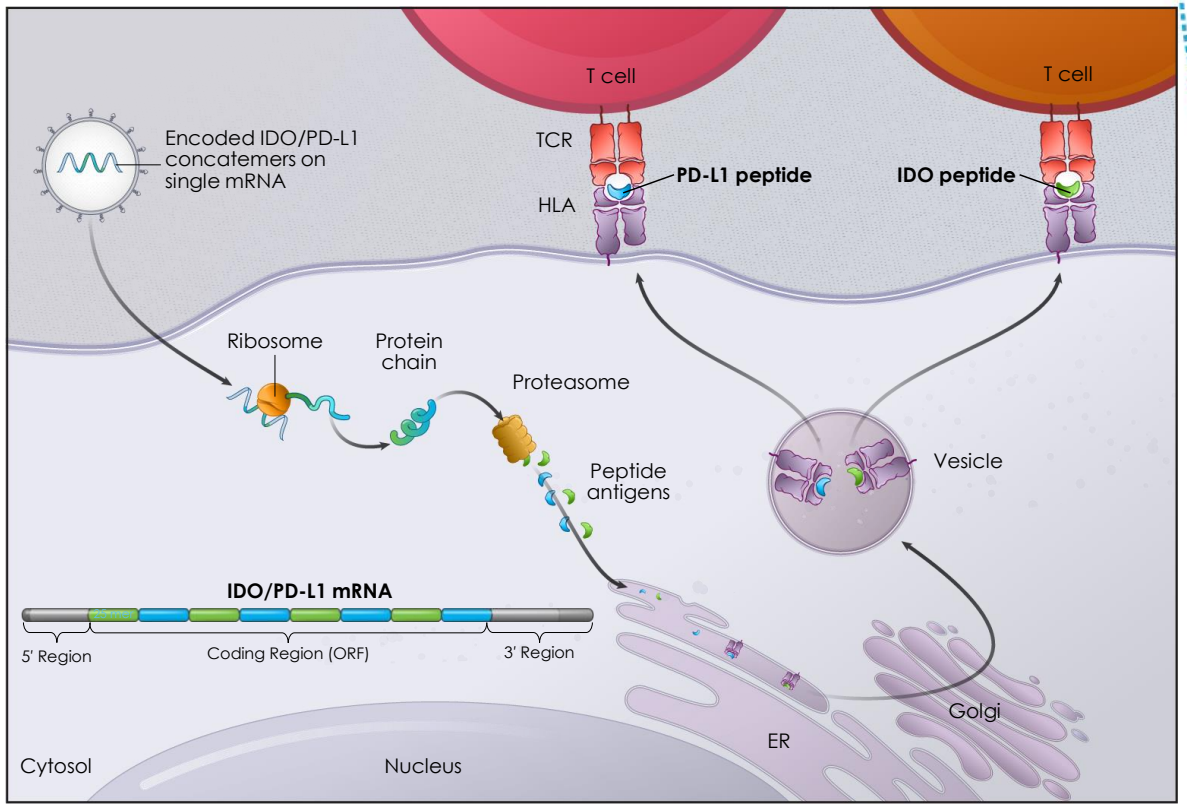
Checkpoint vaccine (mRNA-4359) aims to promote anti-checkpoint T-cell responses

Program objective: Stimulate effector T cells that target and kill suppressive immune and cancer cells that express high levels of target checkpoint antigens:

- Pre-existing IDO- and PD-L1 specific T cells have been identified in cancer patients
- IDO- and PD-L1-specific T cells can kill immunosuppressive (regulatory) immune cells and cancer cells that overexpress IDO and PD-L1 checkpoints
- Our vaccine can expand IDO- and PD-L1 specific T cells in pre-clinical models
- Vaccine induced direct tumor killing can facilitate recognition of tumor-associated antigens by other cytotoxic T cells leading to more tumor killing
- Systemic PD-1/PD-L1 blockade may further amplify the effect

Initial indications: 1L cutaneous melanoma stage IIIB+ and 1L NSCLC

Phase 1 study ongoing



moderna

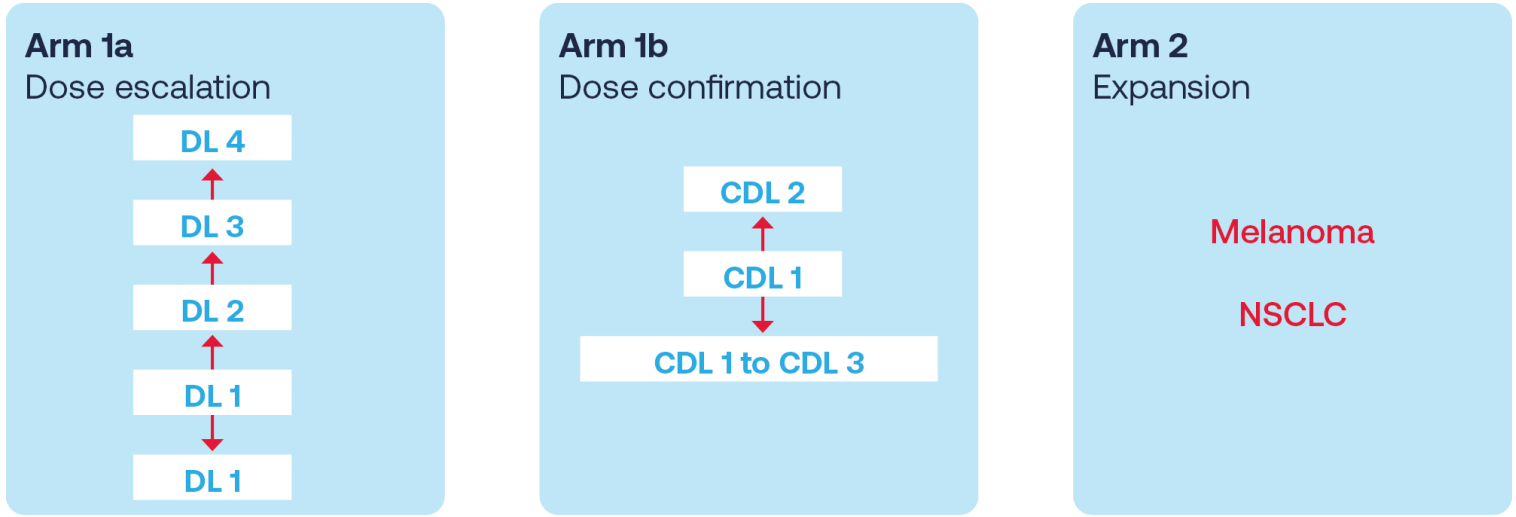
Checkpoint vaccine Phase 1 study objectives and endpoints

Primary objective

To assess the safety and tolerability of mRNA-4359 administered alone and in combination with pembrolizumab

Secondary objective

- To assess the antitumor activity of mRNA-4359 alone and in combination with pembrolizumab
- To measure and assess T-cell profile changes in both the periphery and in the tumor after the administration of mRNA-4359 with or without pembrolizumab



Estimated enrollment: 194 patients

Oncology therapeutics

Programs

PC | Ph. 1 | Ph. 2 | Ph. 3 | Comm.

Individualized Neoantigen Therapy (INT) (mRNA-4157)

- Phase 3 adjuvant melanoma & NSCLC
- Additional indications

PC | Ph. 1 | Ph. 2 | Ph. 3 | Comm.

Triplet (mRNA-2752)

- Phase 1 ongoing

PC | Ph. 1 | Ph. 2 | Ph. 3 | Comm.

Checkpoint vaccine (mRNA-4359)

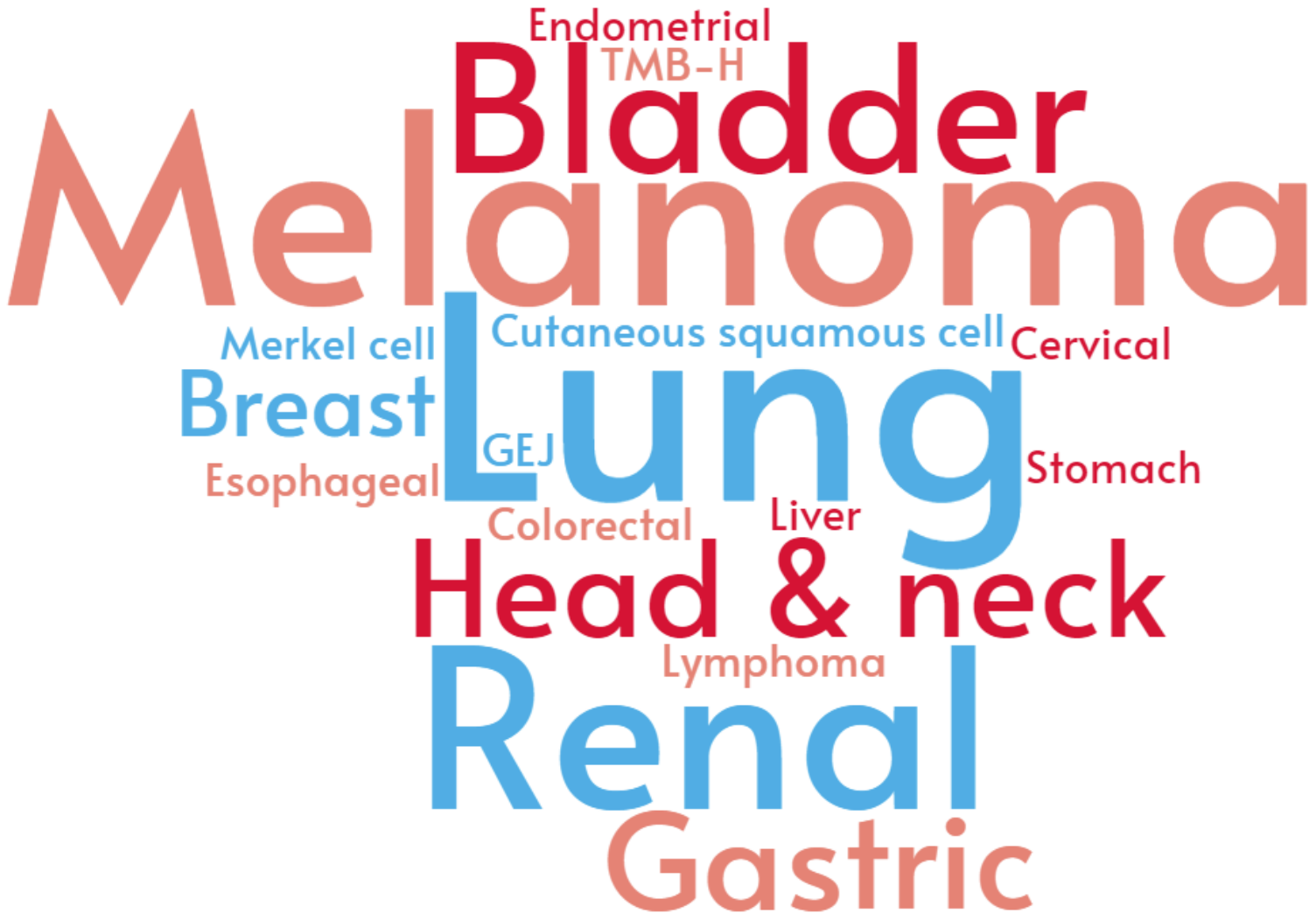
- Phase 1 ongoing

Partnerships

Expanding the reach of mRNA in oncology treatments

moderna

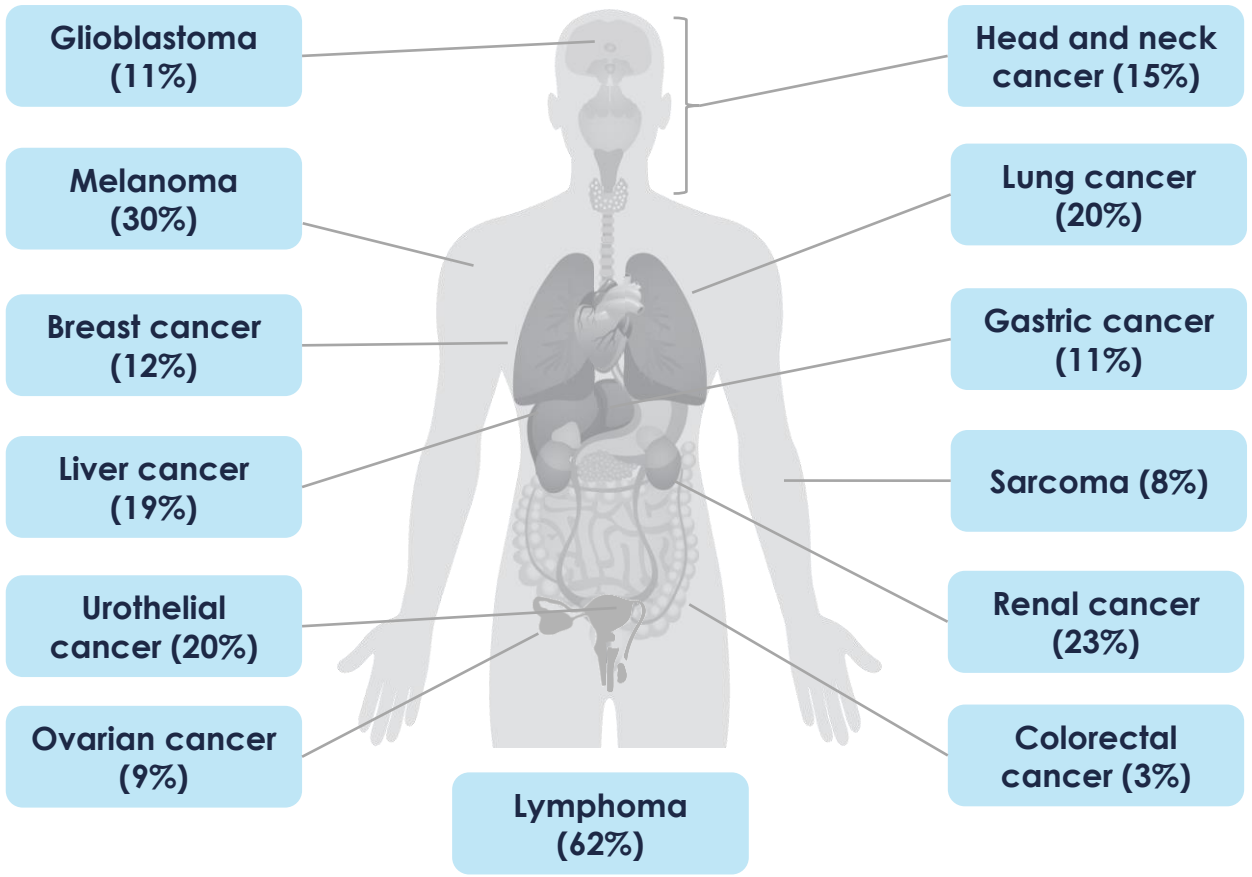
Non-specific therapies like checkpoint inhibitors set the standard for immuno-oncology treatment



moderna

Despite success with checkpoint inhibitors, unmet medical need exists

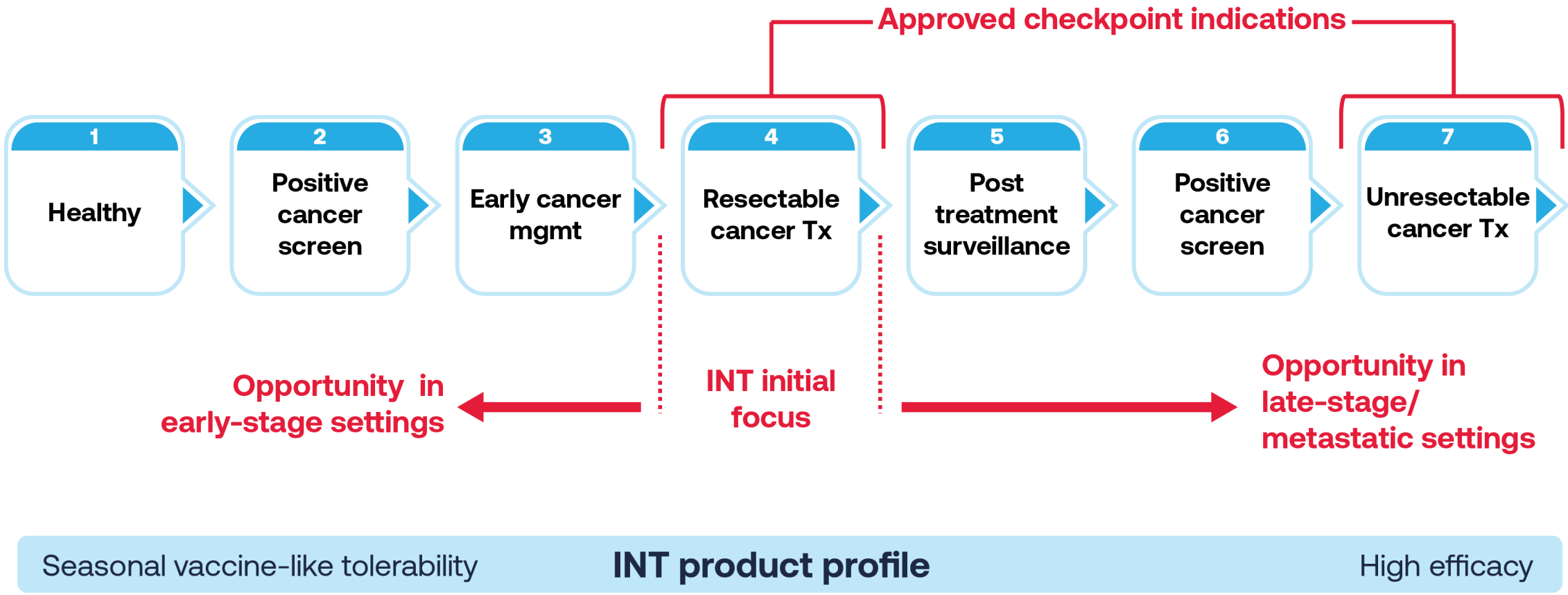
Anti-PD-L1/PD-1 response rates among various tumor types[1]



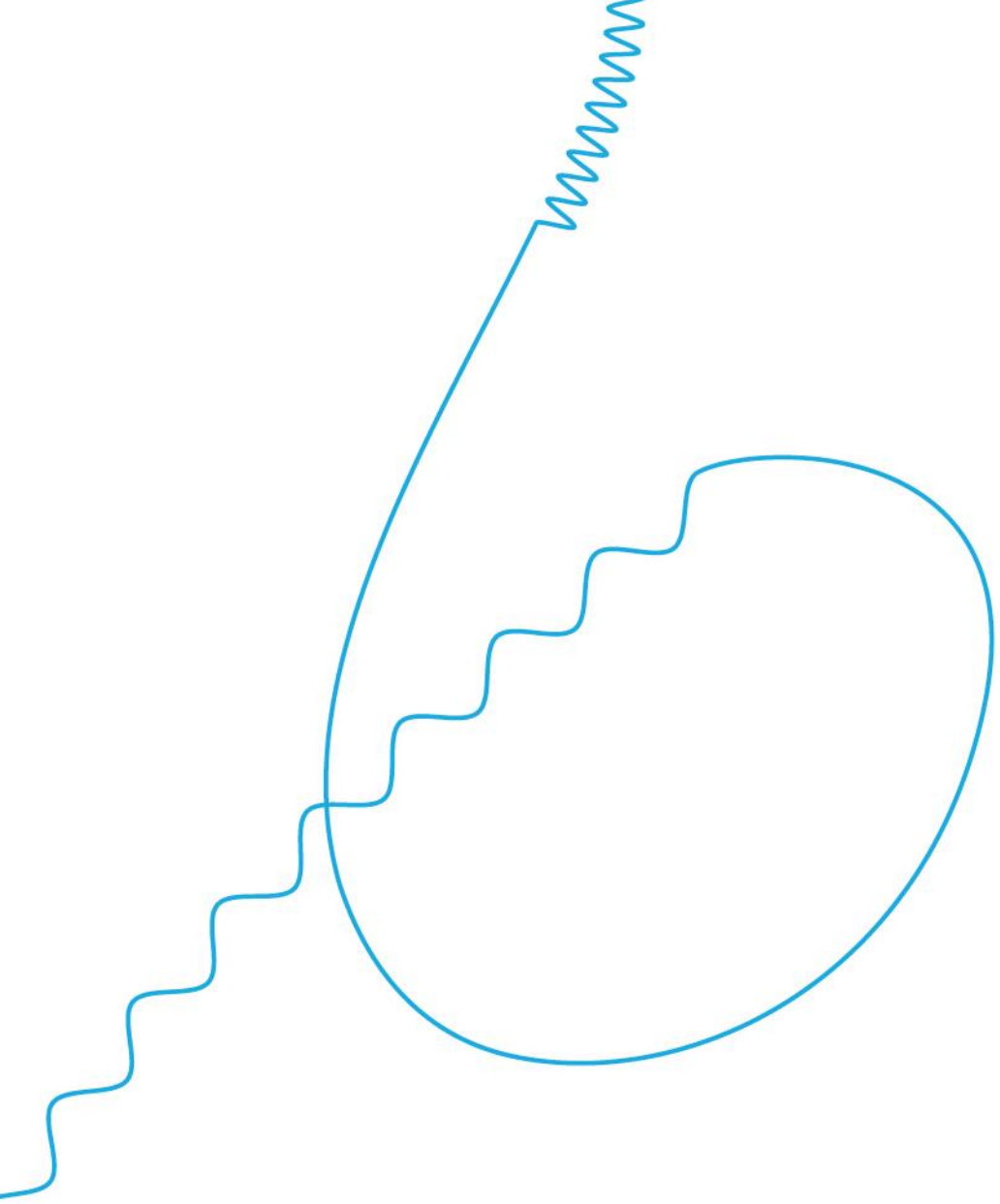
Response rates to ICIs typically range from 10% to 30% depending on the tumor type[1-3]

1. Zhao B, et al. *Ther Adv Med Oncol.* 2020;12:1–22; 2. Sun JY, et al. *Biomark Res.* 2020;8:35; 3. Zhang T, et al. *Oncotarget.* 2016;7(45):73068–73079.

INT has the potential to transform the continuum of cancer treatment by specifically harnessing T-cells



moderna



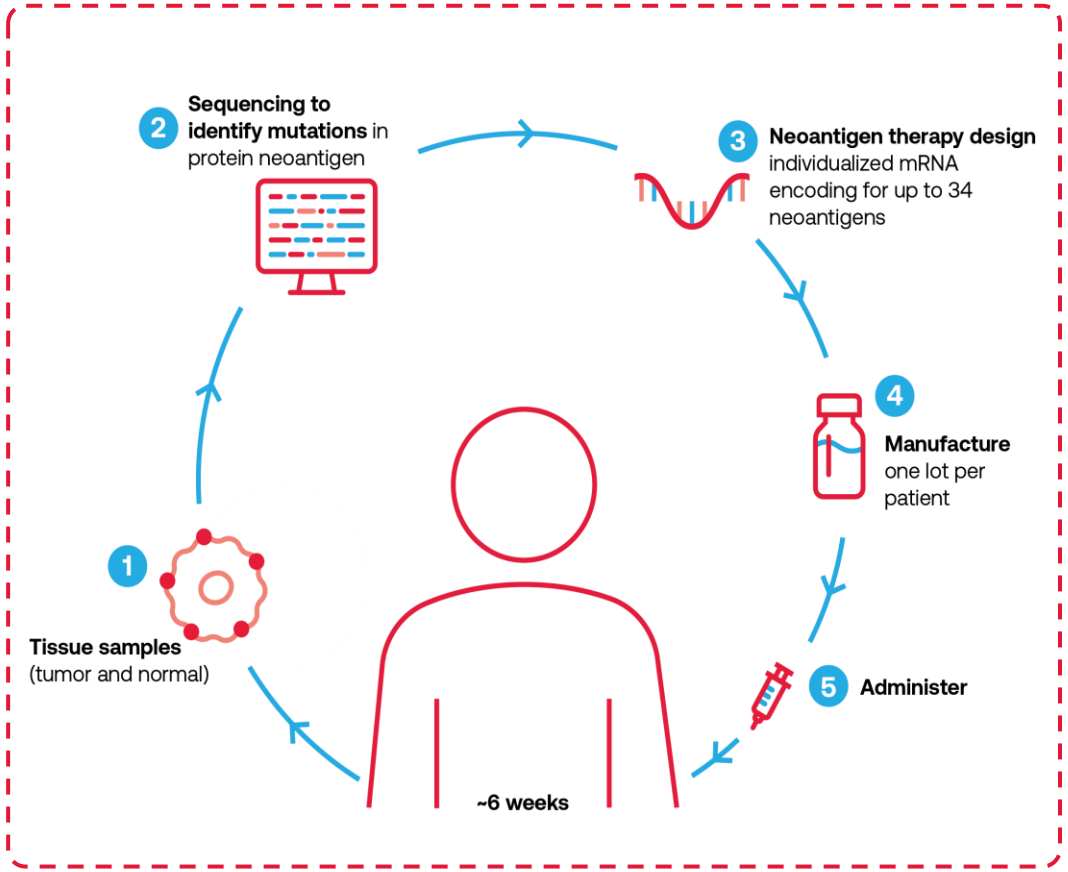
Oncology
Clinical update

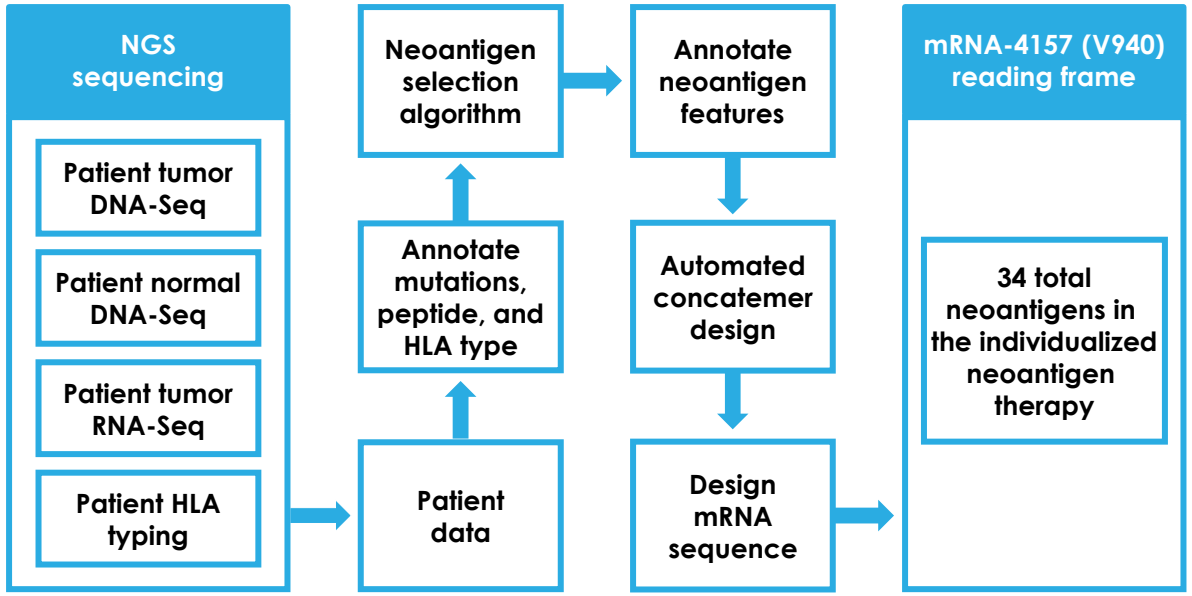
Michelle Brown, M.D., Ph.D.
VP, Portfolio Leadership, INT Therapeutics and Oncology

moderna

mRNA-4157 (V940): An Individualized Neoantigen Therapy (INT)

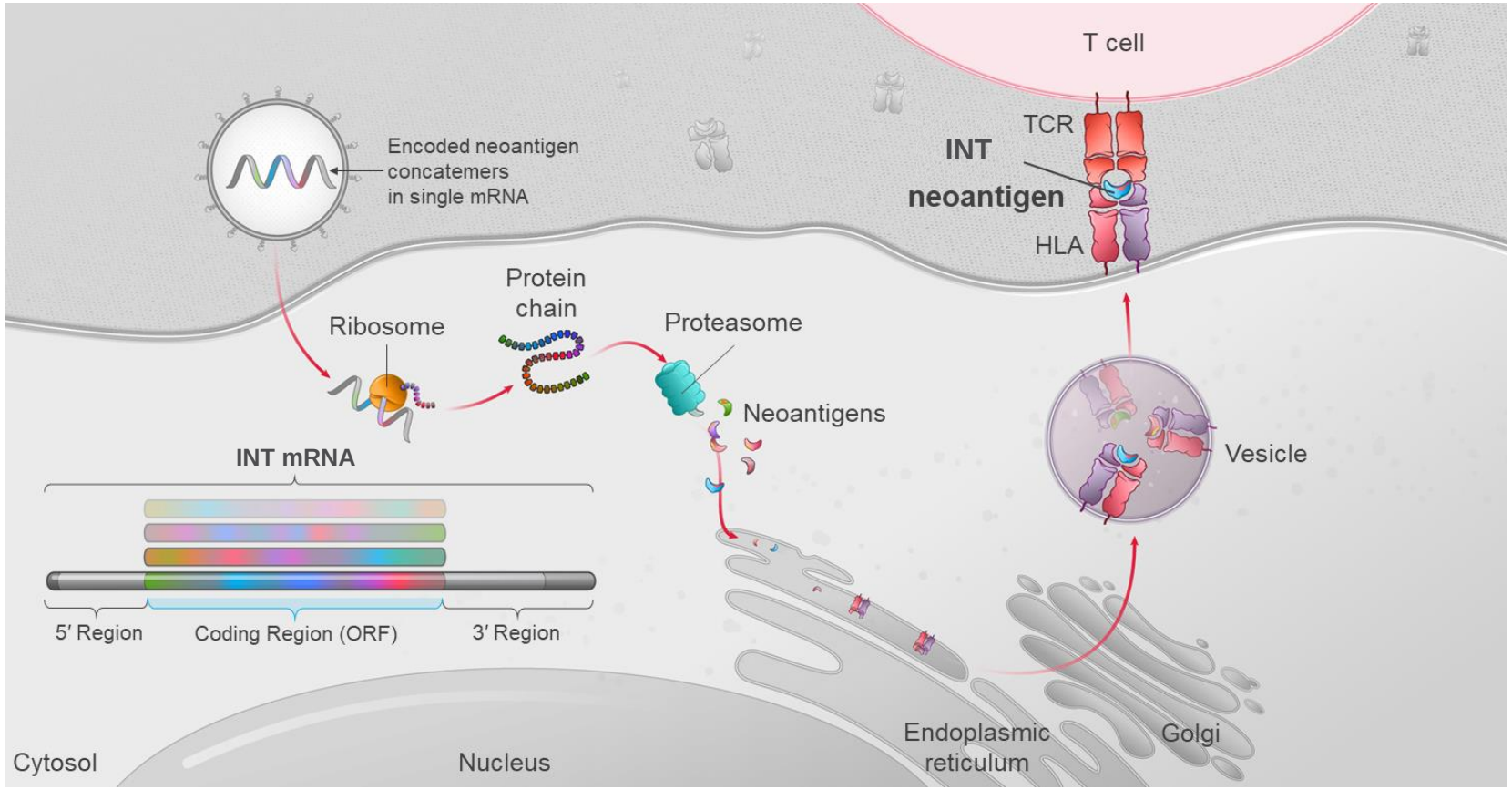
Our individualized neoantigen therapy designed to target an individual patient's unique tumor mutations and encodes up to 34 neoantigens





DNA-Seq, DNA sequencing: HLA, human leukocyte antigen; mRNA, messenger RNA; NGS, next-generation sequencing; RNA-Seq, RNA sequencing.

mRNA-4157 (V940) Mechanism of Action



Therapies targeting neoantigens can increase endogenous **neoantigen T-cell responses and induce epitope spreading** to novel antigens with the ability **to drive antitumor responses** and **maintain memory** with cytolytic properties, potentially **producing long-term disease control** for patients[1-5]

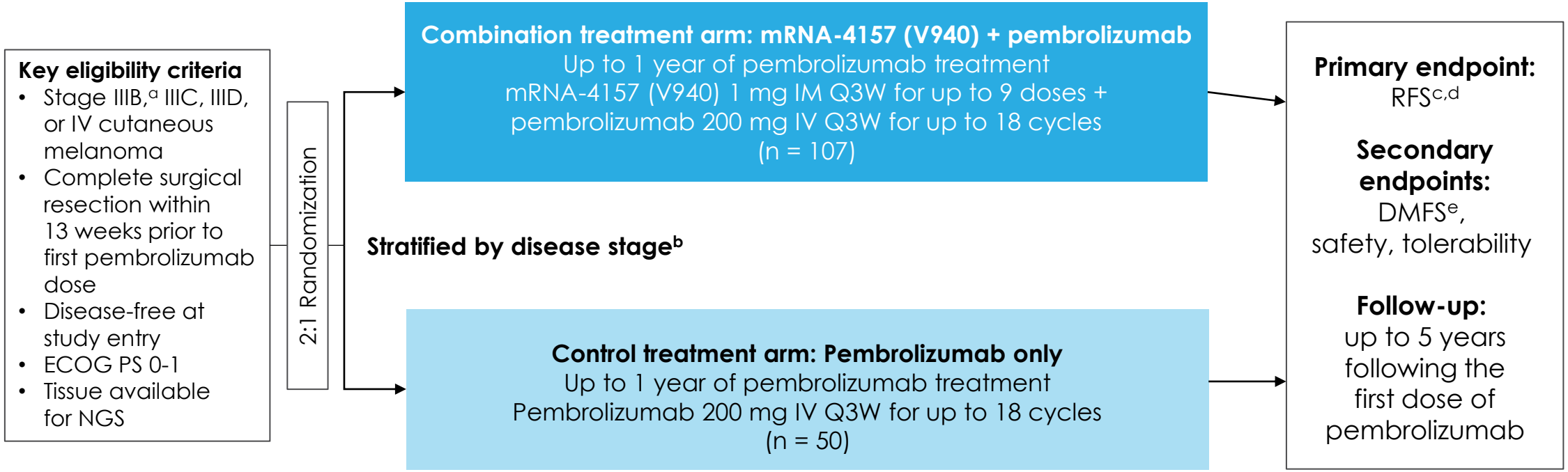
HLA, human leukocyte antigen; INT, individualized neoantigen therapy; ORF, open reading frame.

1. Wirth TC, Kühnel F. *Front Immunol.* 2017;8:1848. 2. Ott PA, et al. *Nature*. 2017;547:217-221. 3. Hu Z, et al. *Nat Med.* 2021;27:515-525. 4. Ott PA, et al. *Cell*. 2020;183:347-362. 5. Palmer CD, et al. *Nat Med*. 2022;28:1619-1629.

moderna

mRNA-4157-P201/KEYNOTE-942 (NCT03897881) Study Design

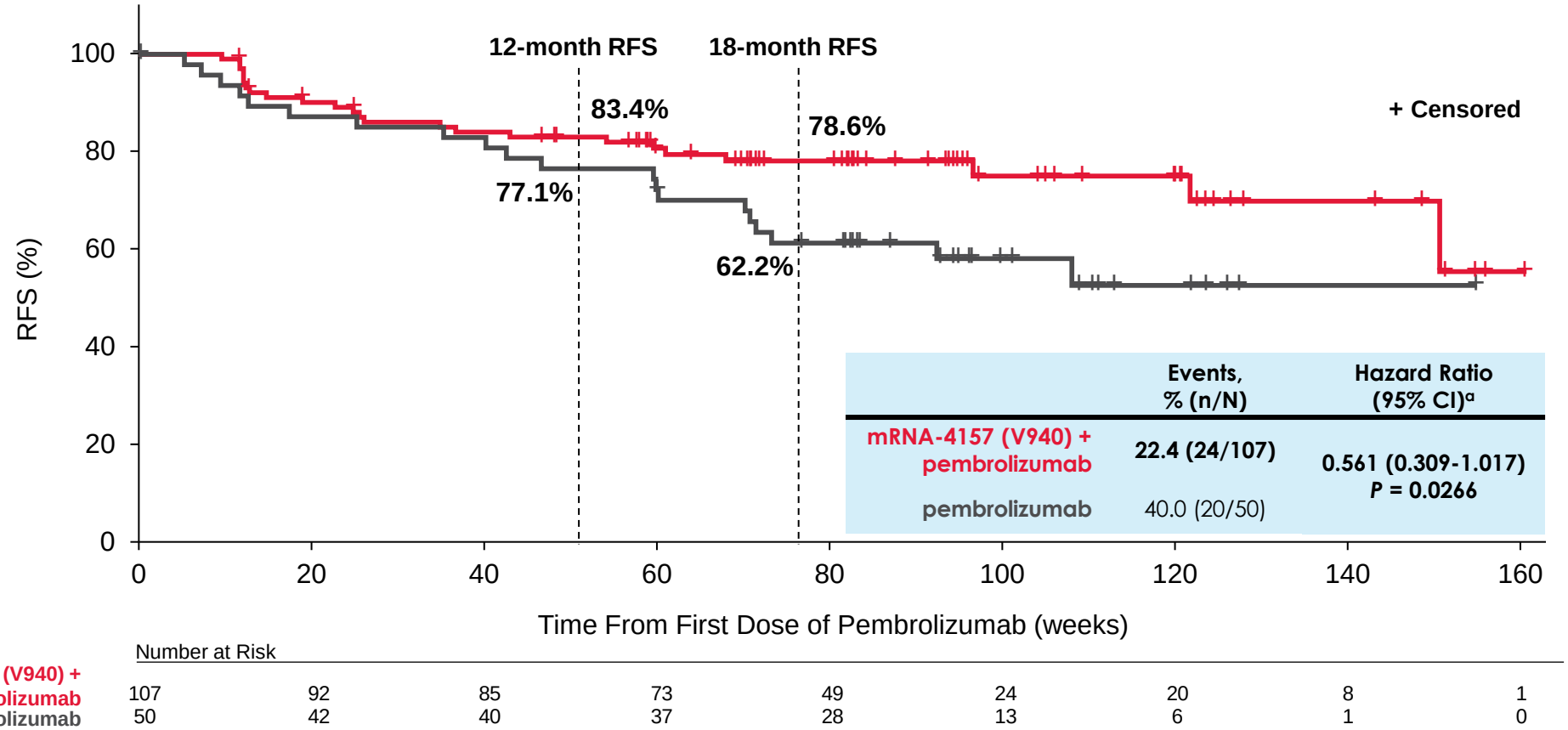
Randomized, Phase 2, open-label study in adjuvant resected melanoma patients at high risk of recurrence



Designed with 80% power to detect an HR of 0.5 with ≥40 RFS events (with a 1-sided alpha of 0.1)
DMFS analysis was prespecified for testing following positive RFS in the ITT population[f]
Median follow-up: 23 months for mRNA-4157 (V940) + pembrolizumab
24 months for pembrolizumab only
Time of database cutoff was November 14, 2022

Khattak A, et al. Presented at the American Association for Cancer Research® (AACR) Annual Meeting; April 14-19, 2023; Orlando, FL, USA. Oral presentation CT001
DMFS, distant metastasis-free survival; ECOG PS, Eastern Cooperative Oncology Group performance status; HR, hazard ratio; IM, intramuscular; IV, intravenous; mRNA, messenger RNA; NGS, next-generation sequencing; Q3W, every 3 weeks; RFS, recurrence-free survival.
[a]Patients with stage IIIB disease were eligible only if relapse occurred within 3 months of prior surgery of curative intent. [b]According to the 8th edition of the American Joint Committee on Cancer staging manual. [c]The primary endpoint was investigator-assessed RFS (defined as the time from first dose of pembrolizumab until the date of first recurrence [local, regional, or distant metastasis], a new primary melanoma, or death from any cause) in the intention-to-treat population. [d]The primary analysis for RFS was specified to occur after all patients completed ≥12 months on study and ≥40 RFS events were observed. [e]Investigator-assessed DMFS was defined as the time from first dose of pembrolizumab until the date of first distant recurrence or death from any cause. [f]The stratified log-rank test was used for comparison. [g]Time of database cutoff was November 14, 2022.

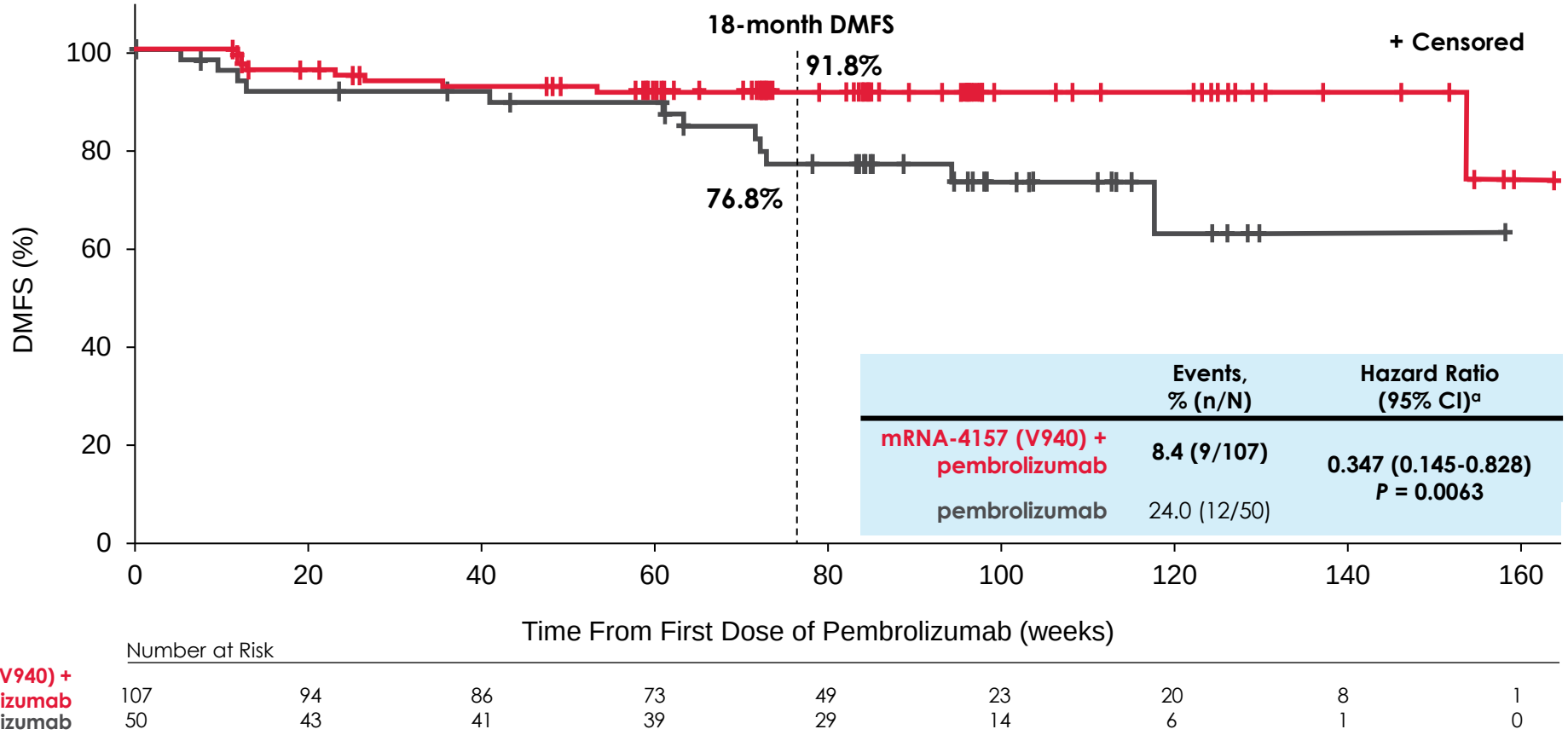
INT: mRNA-4157 (V940) in combination with pembrolizumab reduced the risk of recurrence or death by 44% compared to pembrolizumab alone



1. Khattak A, et al. Presented at the American Association for Cancer Research® (AACR) Annual Meeting; April 14-19, 2023; Orlando, FL, USA. Oral presentation CT001. 2. Khattak A, et al. Presented at the American Society of Clinical Oncology (ASCO) Annual Meeting; June 2-6, 2023; Chicago, IL, USA. Oral presentation

CI, confidence interval; mRNA, messenger RNA; RFS, recurrence-free survival.
[a]The hazard ratio and 95% CI for mRNA-4157 (V940) plus pembrolizumab versus pembrolizumab is estimated using a Cox proportional hazards model with treatment group as a covariate, stratified by disease stage (stages IIIB or IIIC or IIID vs stage IV) used for randomization. The *P* value is based on a 1-sided log-rank test stratified by disease stage (stages IIIB or IIIC or IIID vs stage IV) used for randomization.

INT: mRNA-4157 (V940) in combination with pembrolizumab reduced the risk of distant metastasis or death by 65% compared to pembrolizumab alone



1. Khattak A, et al. Presented at the American Association for Cancer Research® (AACR) Annual Meeting; April 14-19, 2023; Orlando, FL, USA. Oral presentation CT001. 2. Khattak A, et al. Presented at the American Society of Clinical Oncology (ASCO) Annual Meeting; June 2-6, 2023; Chicago, IL, USA. Oral presentation

[a]The hazard ratio and 95% CI for mRNA-4157 (V940) plus pembrolizumab versus pembrolizumab is estimated using a Cox proportional hazards model with treatment group as a covariate, stratified by disease stage (stages IIIB or IIIC or IIID vs stage IV) used for randomization. The *P* value is based on a 1-sided log-rank test stratified by disease stage (stages IIIB or IIIC or IIID vs stage IV) used for randomization. At 18-months, the estimated DMFS rates were 91.8% (95% CI, 84.2-95.8) versus 76.8% (95% CI, 61.0-86.8) in the combination and monotherapy arm, respectively.

mRNA-4157-P201/KEYNOTE-942 Safety and Tolerability[1]

	mRNA-4157 (V940) + pembro (n = 104)		pembro (n = 50)	
Event, n (%)	**Any grade**	**Grade ≥3**	**Any grade**	**Grade ≥3**
Any AE	104 (100.0)	36 (34.6)	47 (94.0)	18 (36.0)
Any treatment-related AE	104 (100.0)	26 (25.0)	41 (82.0)	9 (18.0)
Serious AE[a]	**15 (14.4)**	**13 (12.5%)**	**5 (10.0)**	**4 (8.0%)**
mRNA-4157 (V940) or combination-related AEs[b] occurring in >20% of patients				
Any	98 (94.2)	**12 (11.5)**	-	-
Fatigue	63 (60.6)	5 (4.8)	-	-
Injection site pain	58 (55.8)	0	-	-
Chills	52 (50.0)	0	-	-
Pyrexia	50 (48.1)	1 (1.0)	-	-
Headache	33 (31.7)	0	-	-
Injection site erythema	33 (31.7)	0	-	-
Influenza-like illness	32 (30.8)	0	-	-
Nausea	26 (25.0)	0	-	-
Myalgia	22 (21.2)	1 (1.0)	-	-
Pembro or combination related AEs[c] occurring in >20% of patients				
Any	101 (97.1)	24 (23.1)	41 (82.0)	9 (18.0)
Fatigue	72 (69.2)	6 (5.8)	20 (40.0)	0
Diarrhea	31 (29.8)	2 (1.9)	5 (10.0)	0
Pruritus	30 (28.8)	0	10 (20.0)	0
Nausea	23 (22.1)	0	5 (10.0)	0
Chills	22 (21.2)	0	1 (2.0)	0
Pyrexia	22 (21.2)	0	0	0

Safety analyses were conducted in the safety population, which was defined as all randomly assigned patients who received ≥1 dose of treatment. Grading per National Cancer Institute Common Terminology Criteria for Adverse Events version 5.0. [a]Serious AEs included grade 1 fever, attributed to mRNA-4157 (V940), and grade 3 muscular weakness and grade 3 autoimmune nephritis, attributed to both mRNA-4157 (V940) and pembrolizumab. [b]mRNA-4157 (V940) treatment-related AEs included events attributed by the investigator to mRNA-4157 (V940) alone as well as events attributed to both mRNA-4157 (V940) and pembrolizumab. [c]AEs related to pembrolizumab include events attributed by the investigator to pembrolizumab alone and events attributed to both pembrolizumab and mRNA-4157 (V940)..

1. Khattak A, et al. Presented at the American Association for Cancer Research® (AACR) Annual Meeting; April 14-19, 2023; Orlando, FL, USA. Oral presentation CT001.

mRNA-4157-P201/KEYNOTE-942 Safety and Tolerability

All-cause immune-mediated AEs	mRNA-4157 (V940) + pembro (n = 104)		pembro (n = 50)	
Event, n (%)	**Any grade**	**Grade ≥3[a]**	**Any grade**	**Grade ≥3[b]**
Any	**37 (35.6)**	**11 (10.6)**	**18 (36.0)**	**7 (14.0)**
Adrenal insufficiency	5 (4.8)	4 (3.8)	2 (4.0)	1 (2.0)
Colitis	6 (5.8)	3 (2.9)	2 (4.0)	0
Hepatitis	1 (1.0)	0	1 (2.0)	1 (2.0)
Hyperthyroidism	6 (5.8)	0	3 (6.0)	1 (2.0)
Hypophysitis	1 (1.0)	0	0	0
Hypothyroidism	21 (20.2)	0	8 (16.0)	0
Myositis	0	0	1 (2.0)	1 (2.0)
Nephritis	3 (2.9)	3 (2.9)	1 (2.0)	0
Pancreatitis	0	0	1 (2.0)	1 (2.0)
Pneumonitis	4 (3.8)	1 (1.0)	0	0
Sarcoidosis	0	0	1 (2.0)	0
Severe skin reaction	3 (2.9)	0	1 (2.0)	0
Thyroiditis	0	0	2 (4.0)	1 (2.0)
Type 1 diabetes mellitus	0	0	1 (2.0)	1 (2.0)
Uveitis	1 (1.0)	0	1 (2.0)	0

Safety analyses were conducted in the safety population, which was defined as all randomly assigned patients who received ≥1 dose of treatment. Grading per National Cancer Institute Common Terminology Criteria for Adverse Events version 5.0. [a]Includes grade 4 adrenal insufficiency and colitis (n = 1 each), attributed to pembro only and not mRNA-4157 (V940); no grade 5 events occurred. [b]No grade 4 or 5 events occurred.

moderna

INT adjuvant melanoma

Summary

- mRNA-4157-P201/KEYNOTE-942 is the **first randomized trial** to **demonstrate improvement** in recurrence-free survival and distant metastasis-free survival with **an individualized neoantigen therapy approach**
- mRNA-4157 (V940) and pembrolizumab demonstrated a **clinically significant improvement in RFS and DMFS** compared to standard of care pembrolizumab in high-risk resected melanoma, with a **44% reduction in the risk of recurrence or death** and a **65% reduction in the risk of distant metastasis or death** with a median of 2 years of follow-up
- mRNA-4157 (V940) in combination with pembrolizumab was **well-tolerated without an increase in immune-mediated AEs** compared with pembrolizumab monotherapy
- mRNA-4157 (V940) in combination with pembrolizumab received **Breakthrough Therapy Designation** from FDA in February 2023 and **PRIME Designation** from EMA in April 2023

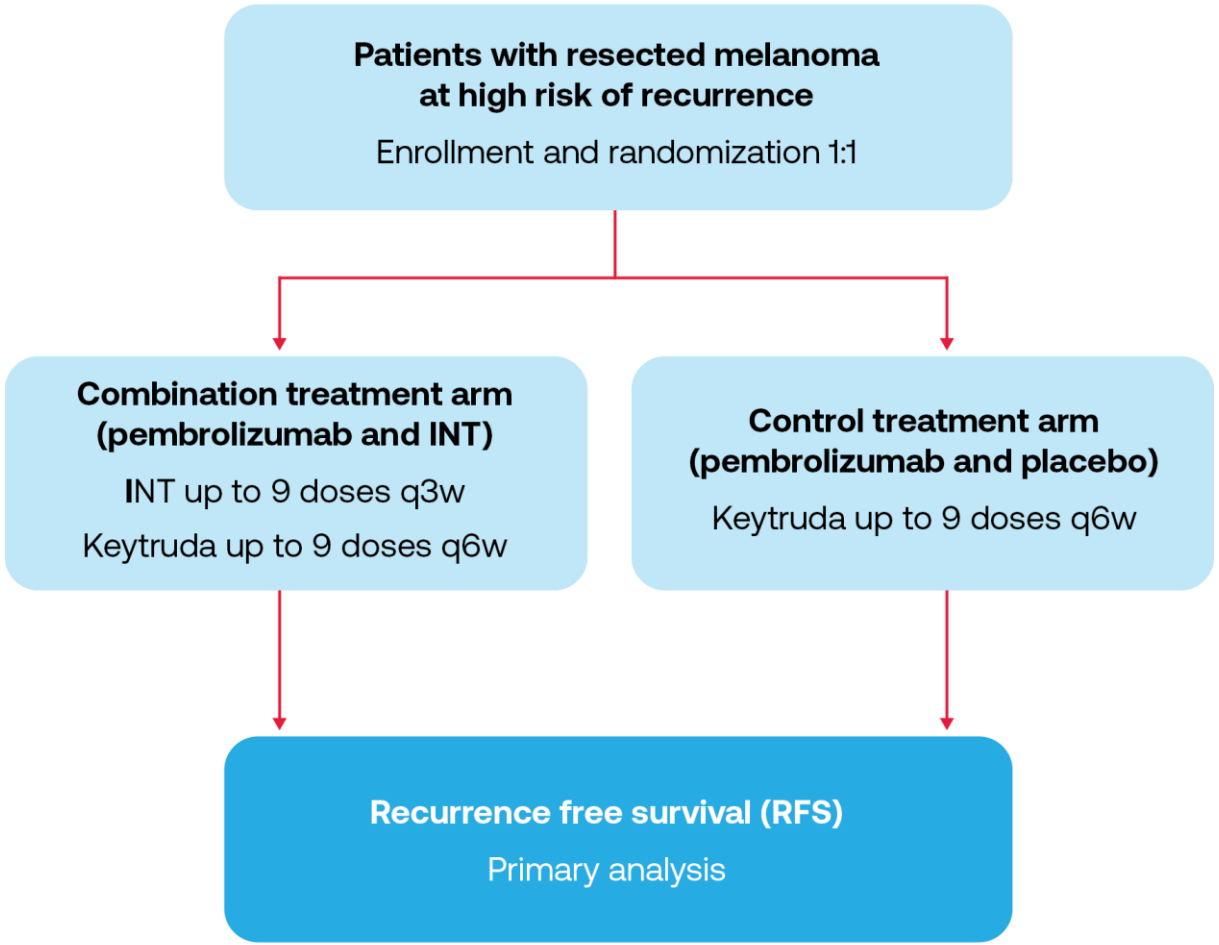
INT adjuvant melanoma

Next steps

- Additional analyses to include RFS/DMFS according to the statistical analysis plan to evaluate durability
- Translational assessments including immunogenicity plan to be conducted on newly enrolled participants
- Path for approval under discussion with regulators
- Continue to enroll Phase 3 study

Adjuvant melanoma Phase 3 (V940-001) trial is now enrolling

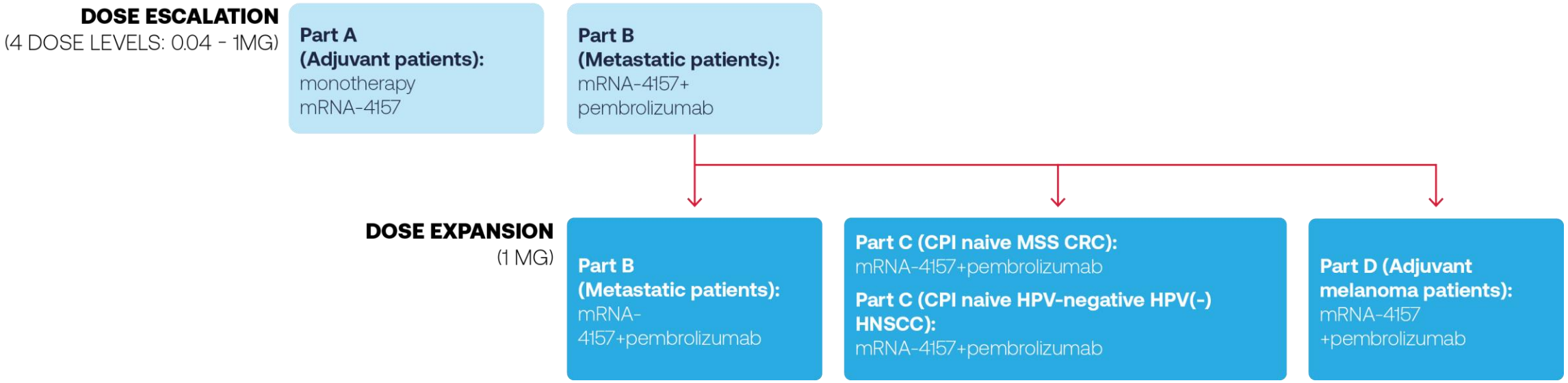
Primary endpoint is recurrence free survival compared to pembrolizumab



NCT05933577

- Randomized, double-blind placebo controlled, INT + pembrolizumab (KEYTRUDA®) vs. placebo + pembrolizumab (1:1)
- Resected melanoma patients: stage IIB or IIC, III, IV
- Primary endpoint: recurrence free survival (RFS)
- Secondary endpoints: Distant Metastasis-Free Survival (DMFS), Overall-Survival (OS)
- Number of participants: ~1,089

mRNA-4157-P101/KEYNOTE-603 Phase 1 study provided data on multiple tumor types



Part A histologies (adjuvant)

- Melanoma
- MSI High/MMR Deficient
  - Colorectal carcinoma
- Non-small cell lung cancer

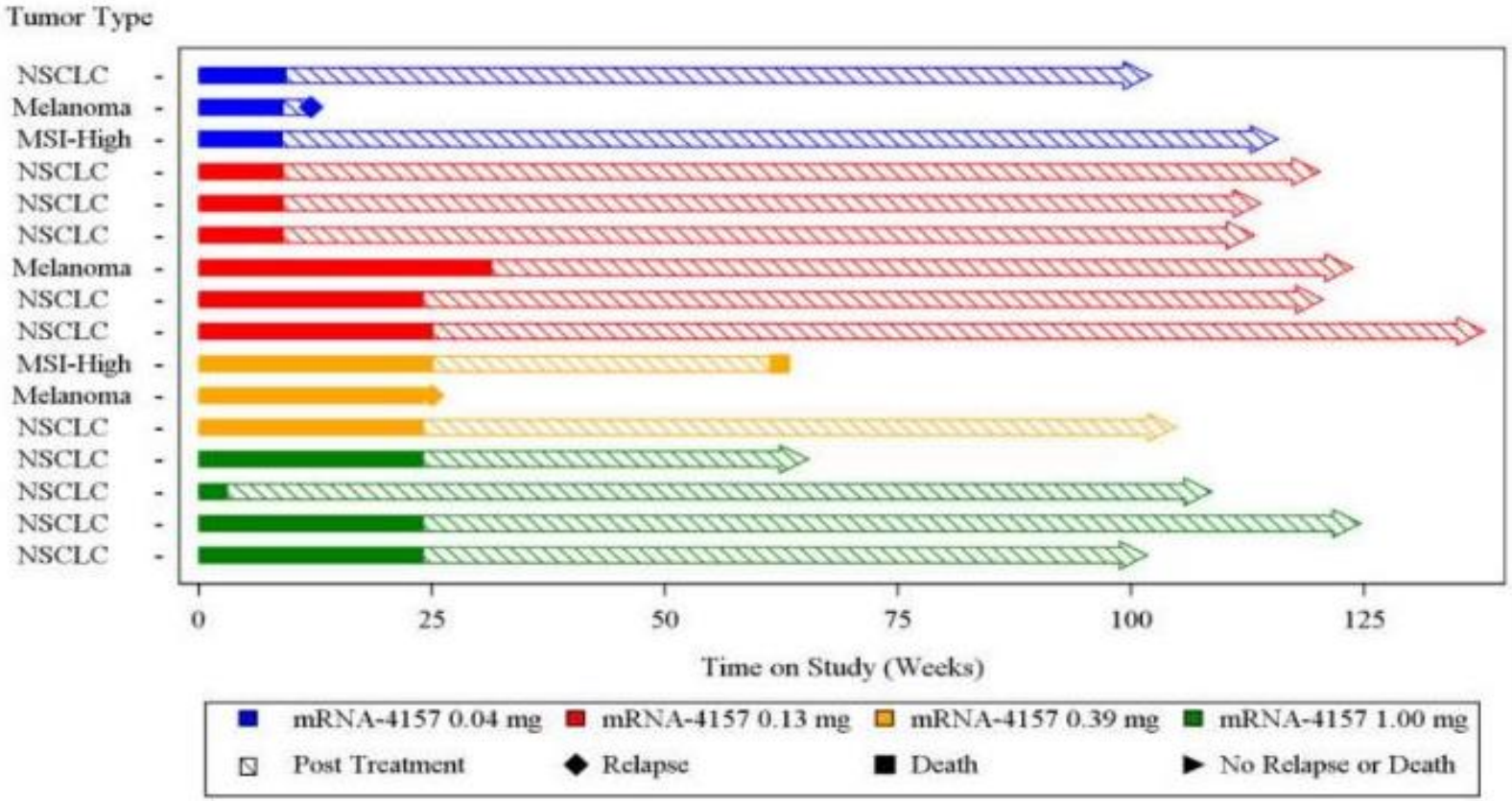
Part B histologies (metastatic)

- TMB High Malignancies
- Bladder Urothelial carcinoma
- HNSCC
- Melanoma
- MSI High/MMR Deficient Malignancies
- Non-small cell lung cancer
- Small cell lung cancer

1. ClinicalTrials.gov Identifier: NCT03313778. Updated Feb 24, 2023. https://clinicaltrials.gov/ct2/show/NCT03313778. Accessed May 26, 2023.

INT monotherapy in adjuvant suggests encouraging clinical activity in early disease setting

Part A: Adjuvant patients receiving mRNA-4157 monotherapy



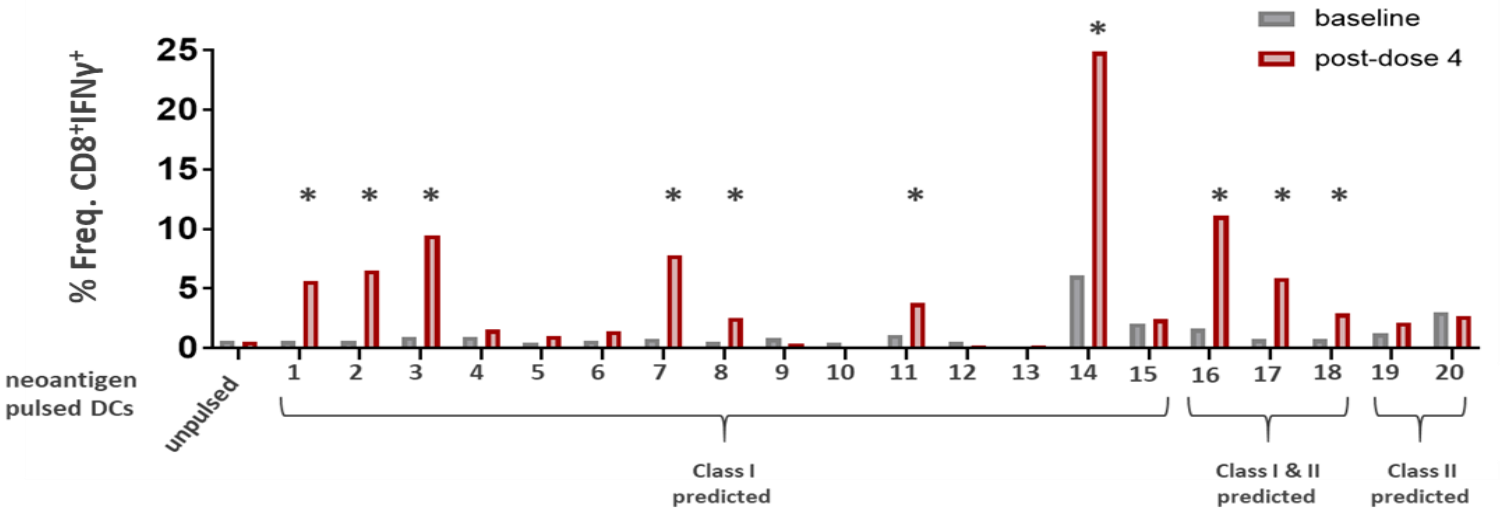
Positive outcomes for patients treated with mRNA-4157 monotherapy

n= 11 early stage (1A-IIB) NSCLC patients showed potential benefit compared to historical studies, aligned with Ph2 melanoma results

moderna

Phase 1 study demonstrates INT induces CD8 T-cell proliferation against selected neoantigens

Immunogenicity profile of an adjuvant NSCLC patient



CD8 T cell responses to individual neoantigens were measured in in vitro stimulated (IVS, expanded) T cells
Flow cytometry plots show increases in % freq. of CD8 cells producing IFNγ 7d post 4th vaccine dose to multiple neoantigens
** Is greater than 3x increased in neoantigen specific CD8 T-cells post treatment*

Previously shared at ASCO 2019

Greater than 3x increases in neoantigen specific CD8 T-cells were detected post 4th dose against 10 out of 18 class I targeted neoantigens

All positive CD8 T-cell responses post vaccination were to **neoantigens with high predicted binding affinity of < 500 nm**

Burris H.A., et al. Presented at the American Society of Clinical Oncology(ASCO) Annual Meeting; May 31-June 4, 2019; Chicago, IL, USA. Abstract 93

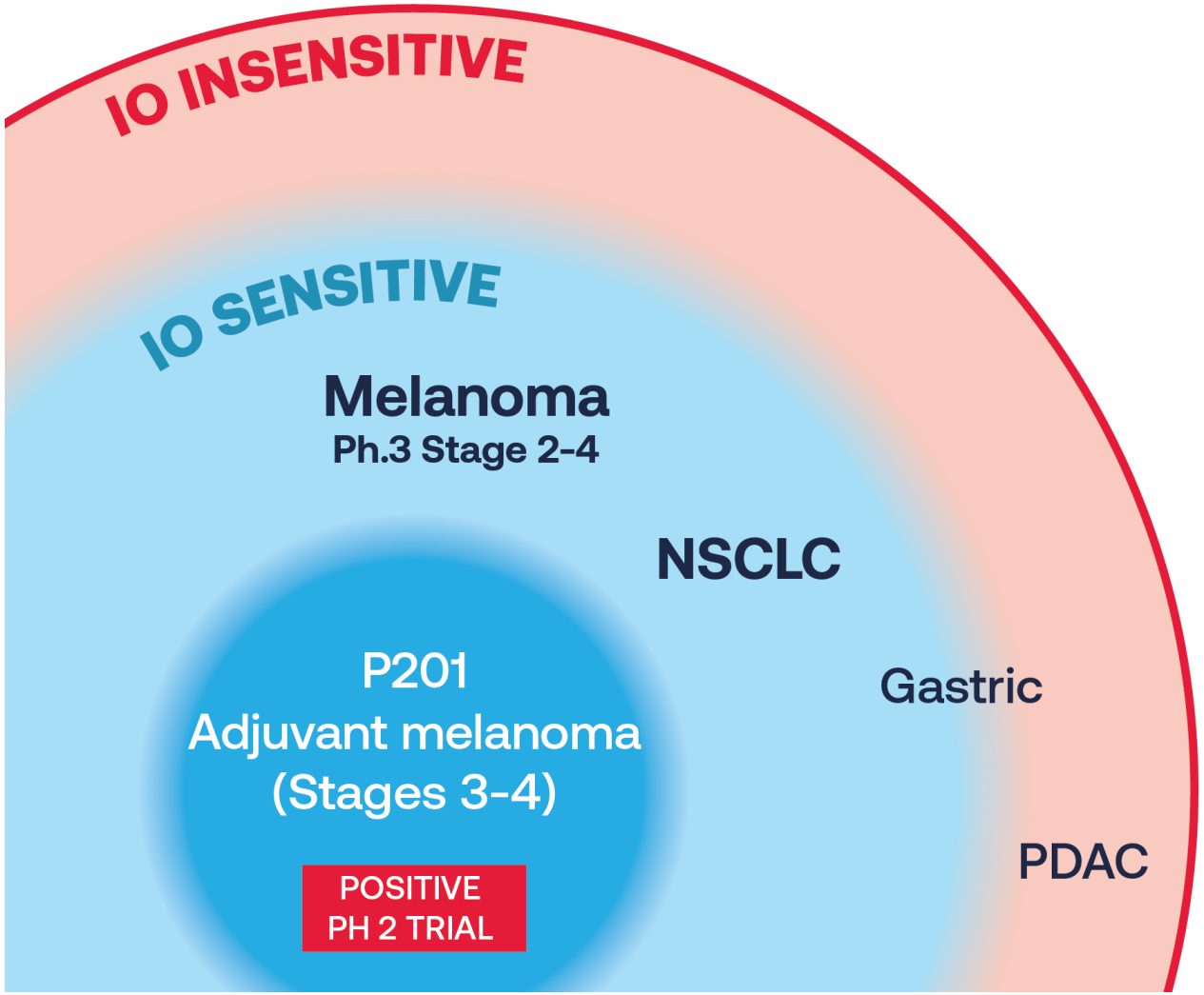
moderna

INT summary – NSCLC Ph1 Data and adjuvant Phase 3

- Non-small cell lung cancer (NSCLC) is one of the most common cancers in the world and remains an area of high unmet medical need with 5-year overall survival (OS) rates for patients with surgically treated NSCLC ranging from approximately 10% (Stage IIIB) to 65% (Stage I)
- NSCLC can be regarded as a direct biological adjacency to melanoma, whereby increasing neoantigen presentation may produce clinically superior outcomes over checkpoint blockade alone
- Treatment with mRNA-4157 monotherapy resulted in induction of T cell responses to selected INT neoantigens
- 11 of 11 participants with early stage NSCLC treated with mRNA-4157 monotherapy remained recurrence event free throughout the Phase 1 study
- Phase 3 study in adjuvant NSCLC is planned for initiation

moderna

Potential INT indications



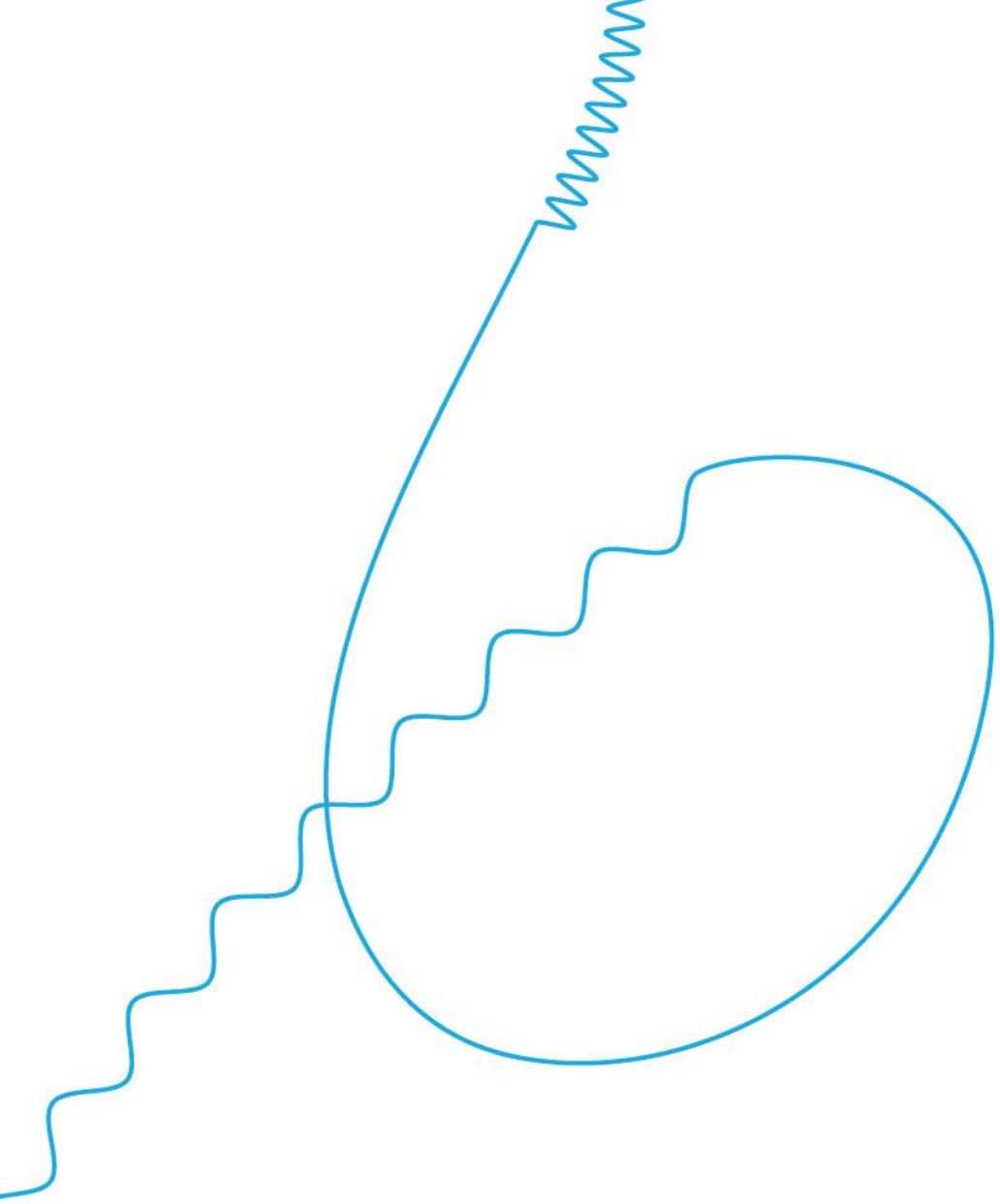
Pivotal Studies

- Adjuvant melanoma (open)
- Adjuvant NSCLC (planned)

Signal Seeking (opening)

- Adjuvant Pancreatic
- Peri-Operative NSCLC
- Peri-Operative Gastric

moderna



Franchise financial opportunity

Jamey Mock
Chief Financial Officer

moderna

Franchises leverage commonalities across programs, resulting in financial and operational benefits

Research

- Similar processes and technologies across programs
- Expertise within biology areas

Development

- Higher probability of success
- Rapid and iterative
- Leveraging clinical trial infrastructure

Commercial

- Similar customer base
- Shared sales force
- Brand recognition and loyalty

Financial and Operational Benefits

- Large sales opportunities with recurring revenue streams
- Optimized manufacturing; shared manufacturing facility and process
- More efficient R&D investment

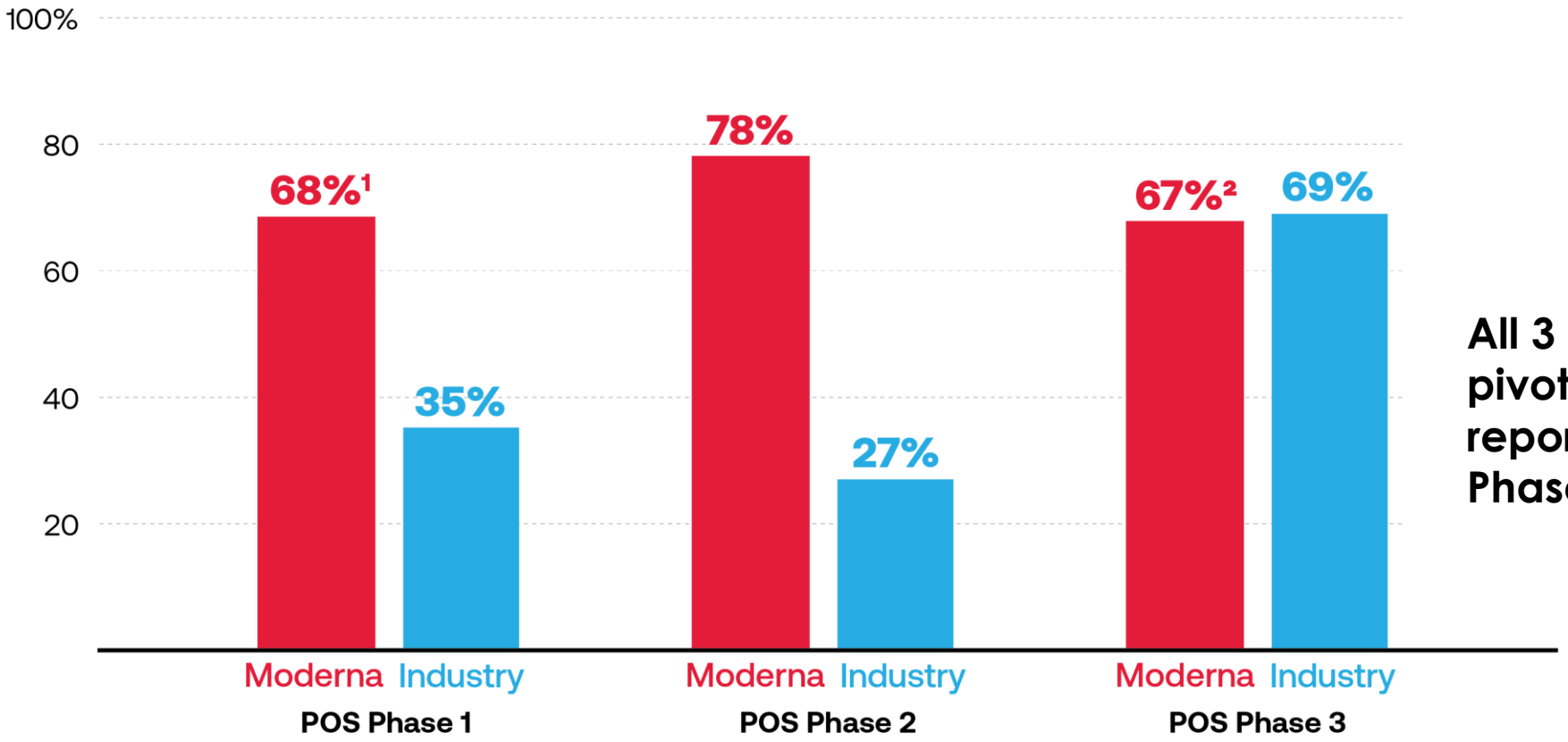
moderna

Financial and operational benefits of our franchises

	Respiratory	Latent +	Oncology	Rare disease
Large sales opportunity				
High value medicines	✓	✓	✓	✓
Innovation driven value	✓	✓	✓	✓
Annual recurring revenue stream	✓		✓	✓
Optimized manufacturing				
Low capital intensity beyond initial investment	✓	✓		✓
Economies of scale	✓	✓		
Flexible manufacturing utilization		✓		✓
More efficient R&D investment				
Limited R&D expense after initial Phase 3 investment	✓	✓	✓	✓
Shared research expense			✓	
Small clinical studies				✓

moderna

Moderna's rate of success with our platform technology is higher than industry standard



All 3 of our pivotal programs reported positive Phase 3 results

Note: Includes (Phase 1: 19 programs; Phase 2: 9 programs ; Phase 3: 6 programs). Assumes 85% of successful Phase 3 programs are approved
1. Early trials establishing platform technology not intended for commercialization excluded from count.
2. Includes failures from P301 and P302, but program is successful overall (Phase 1: 18 programs; Phase 2: 9 programs ; Phase 3: 6 programs)
3. Wong et al., biostatistics (2019) 20, 2 , pp273-286
4. Assumes industry 85% probability for a successful phase 3 program to get approved

We expect to invest a total of ~$25B in R&D over the next five years as we continue to build our franchises

Spend Drivers

	2024	2025	2026	2027	2028
#1	Respiratory	Respiratory	Latent & other ID	Latent & other ID	Latent & other ID
#2	Latent & other ID	Latent & other ID	Respiratory	Oncology	Oncology
#3	Oncology	Oncology	Oncology	Rare Disease	Rare Disease
#4	Rare Disease	Rare Disease	Rare Disease	Respiratory	Respiratory
#5	Platform investments				

Diversified spending across all franchises and platform research

R&D investments lead to the potential launch of up to 15 products over the next 5 years

Franchise specific investment varies over time

Ability to flex spending

Consistent level of investment in platform and research for future pipeline

moderna

Building a business that generates ~$20-30B of revenue annually

Respiratory

2027 revenue of

~$8-15B



Latent + other vaccines, oncology therapeutics, rare disease therapeutics

Revenue 5-years post launch

~$10-15B

Note: Non-risk adjusted revenues

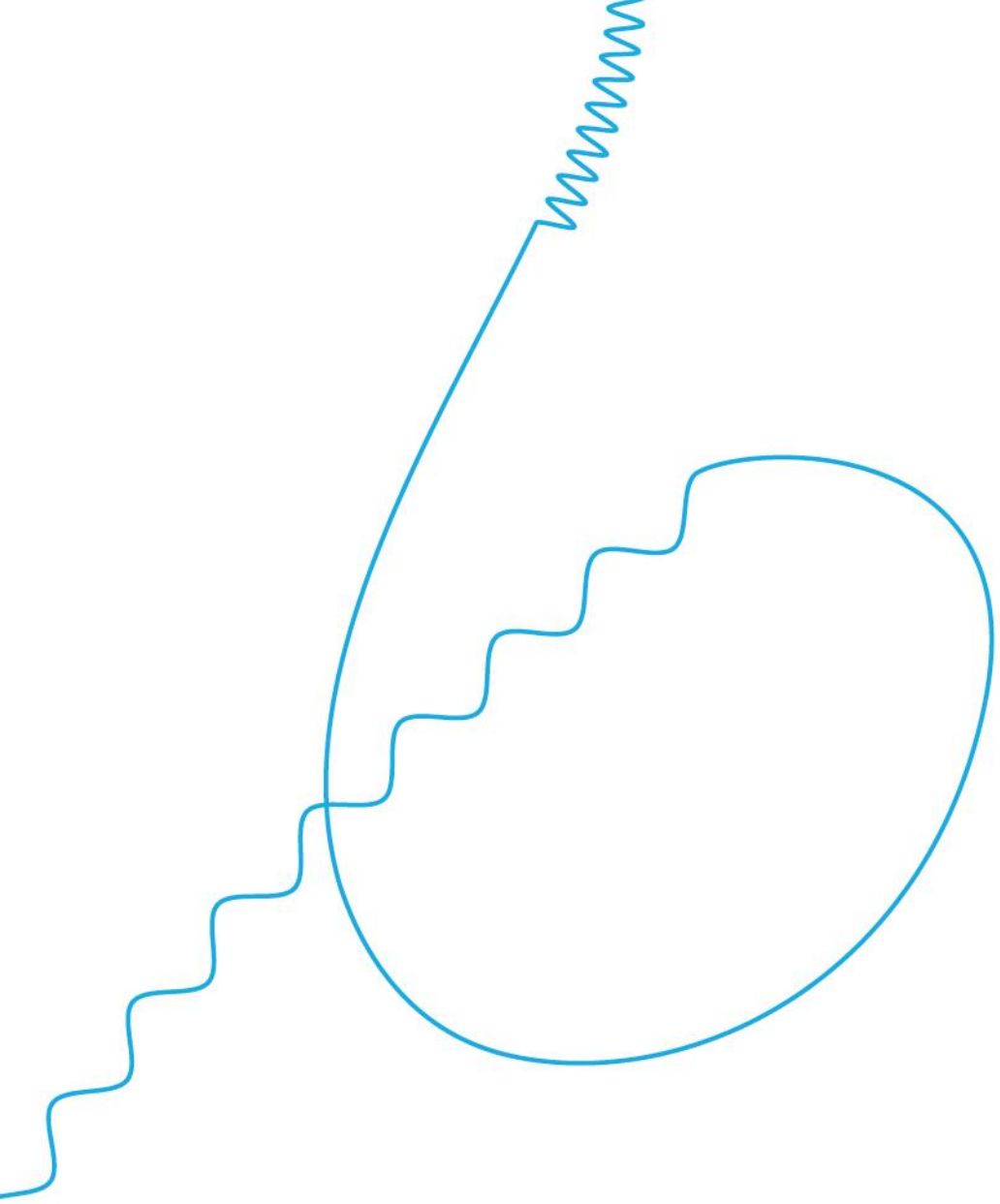
moderna

Transforming COVID business to generate significant cash flow in the endemic setting

Continue to expect 2023 COVID-19 sales of $6-8 billion, dependent on U.S. vaccination rates

The company is currently resizing its manufacturing footprint and supply base to accelerate gross margin expansion towards its longer-term target of 75-80%

moderna



Conclusion

Stéphane Bancel

Chief Executive Officer

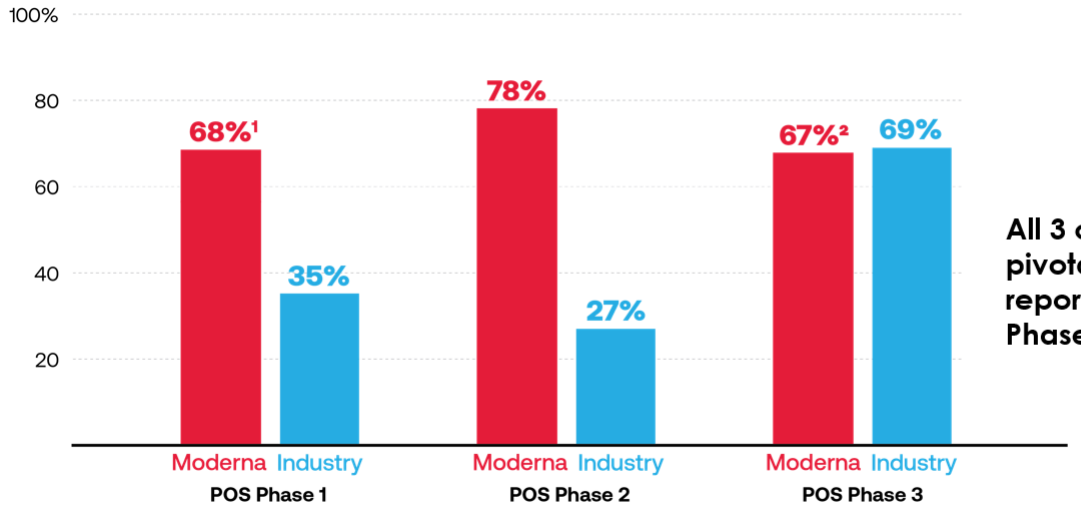
moderna

Moderna's platform is delivering and high rates of success promise additional future products

Our mRNA platform is delivering across vaccines and therapeutics, leading to the formation of our franchises

Three modalities with positive late-stage clinical data, filed marketing/regulatory applications or commercial products establish the power of the platform

Moderna's success rate for clinical drug development is higher than industry benchmarks



All 3 of our pivotal programs reported positive Phase 3 results

moderna

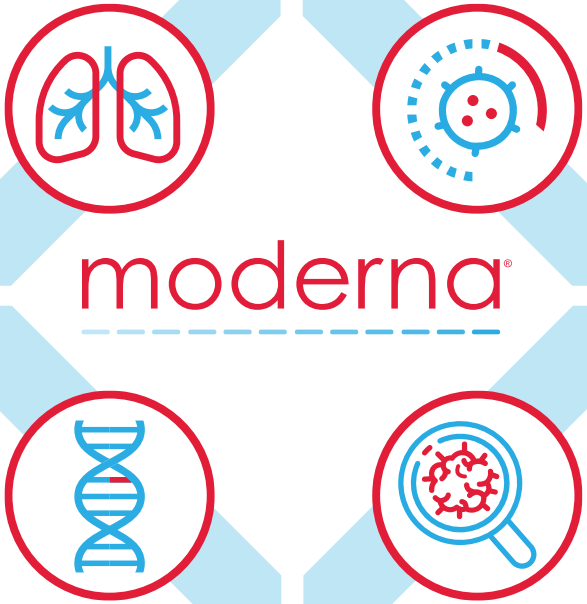
Moderna's four franchises provide foundation for future growth

Respiratory vaccines

- COVID-19
- RSV
- Seasonal Flu
- Combination vaccines
- Next-gen COVID-19
- Next-gen Flu

Latent + other vaccines

- Cytomegalovirus (CMV)
- Epstein Barr Virus (EBV)
- Varicella zoster virus (VZV)
- HIV
- Norovirus



Rare disease therapeutics

- Propionic acidemia (PA)
- Methylmalonic acidemia (MMA)
- Glycogen storage disease type 1a (GSD1a)

Oncology therapeutics

- INT in multiple indications
- Checkpoint
- Triplet

moderna

The next few years look really exciting

	Respiratory vaccines	Latent/other vaccines	Oncology	Rare disease
by 2025	**RSV** (older adults) mRNA-1345	**Seasonal Flu** mRNA-1010		
	Flu/COVID mRNA-1083	**NextGen COVID** mRNA-1283		
by 2028	**Flu/COVID/RSV** NextGen	**RSV/hMPV** (older adults) mRNA-1365	**CMV** mRNA-1647	**Norovirus** (older adults) mRNA-1403/-05
	RSV 2-18Y mRNA-1345	**Pandemic Flu** mRNA-1018	**EBV (IM)** mRNA-1189	**Lyme** mRNA-1975/-82
	NextGen Flu mRNA-1011/-1020	**Endemic hCOV** mRNA-1287	**VZV** mRNA-1468	**HSV** mRNA-1608

Subject to regulatory discussions[1]

INT (adjuvant melanoma) mRNA-4157

INT (undisclosed indication) mRNA-4157

INT (adjuvant NSCLC) mRNA-4157

MMA mRNA-3705

PKU mRNA-3210

PA mRNA-3927

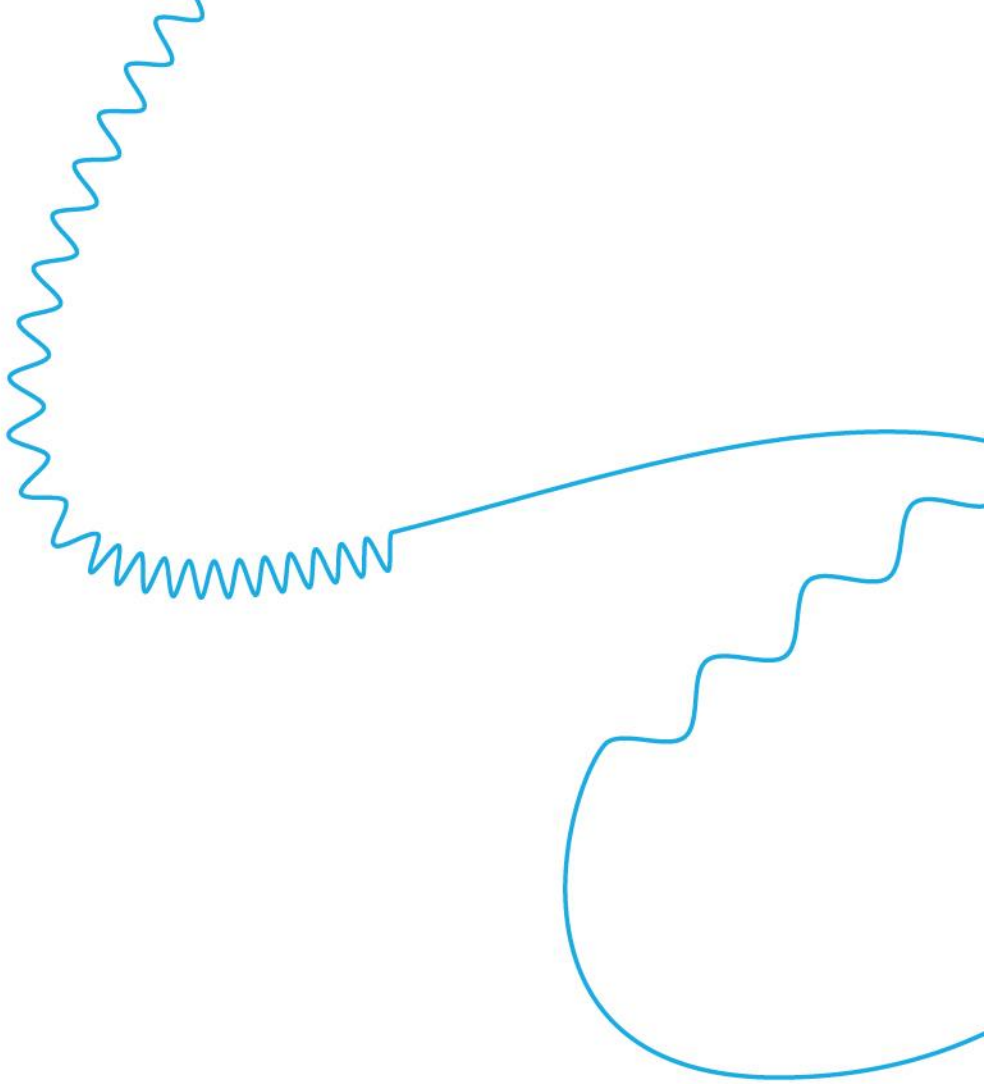
GSD1a mRNA-3745

Note: Subject to positive clinical data and regulatory discussions/approvals
1 Subject to future regulatory discussions, there may be potential for accelerated or conditional approvals in some markets

moderna

Q&A

Thank you



moderna