Expanding the field of mRNA medicine

R&D day and business updates

September 13, 2023
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.
Introduction

Stéphane Bancel
Chief Executive Officer
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.
The promise of mRNA

1. Large opportunity to address unmet need
2. Higher efficiency in R&D
3. Rapid development
4. Greater capital efficiency
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
We are beginning to deliver great impact with our mRNA medicines
Anticipating up to 15 launches in the next 5 years \(^1\)

<table>
<thead>
<tr>
<th>respiratory vaccines</th>
<th>latent/other vaccines</th>
<th>oncology</th>
<th>rare disease</th>
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<tbody>
<tr>
<td>RSV (older adults) mRNA-1345</td>
<td>Seasonal Flu mRNA-1010</td>
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<tr>
<td>Flu/COVID mRNA-1083</td>
<td>NextGen COVID mRNA-1283</td>
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by 2025

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<td>Flu/COVID/RSV NextGen</td>
<td>RSV/hMPV (older adults) mRNA-1365</td>
<td>CMV mRNA-1647</td>
<td>Norovirus (older adults) mRNA-1403/-05</td>
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<td>RSV 2-18Y mRNA-1345</td>
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by 2028

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<td>MMA mRNA-3705</td>
<td>PA mRNA-3927</td>
<td>INT (undisclosed indication) mRNA-4157</td>
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<td>INT (adjuvant melanoma) mRNA-4157</td>
<td>PKU mRNA-3210</td>
<td>GSD1a mRNA-3745</td>
<td>INT (adjuvant NSCLC) mRNA-4157</td>
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\(^1\) 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

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## R&D Day Agenda

<table>
<thead>
<tr>
<th>Section</th>
<th>Responsible Party</th>
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<tbody>
<tr>
<td>Introduction</td>
<td>Stéphane Bancel, Chief Executive Officer</td>
</tr>
<tr>
<td>Development Strategy</td>
<td>Stephen Hoge, M.D., President</td>
</tr>
<tr>
<td>Respiratory Franchise</td>
<td>Jacqueline Miller, M.D., Darin Edwards, Ph.D., Raffael Nachbagauer, M.D., Ph.D., Arpa Garay, Chief Commercial Officer</td>
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<tr>
<td>Latent and Other Franchise</td>
<td>Jacqueline Miller, M.D., Arpa Garay</td>
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<td>Coffee Break</td>
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<td>Rare Disease Franchise</td>
<td>Kyle Holen, M.D., Geoff Rezvani M.D., Arpa Garay</td>
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<tr>
<td>Oncology Franchise</td>
<td>Kyle Holen M.D., Michelle Brown M.D. Ph.D, Arpa Garay</td>
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<tr>
<td>Franchise Financials</td>
<td>Jamey Mock, Chief Financial Officer</td>
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<tr>
<td>Conclusion</td>
<td>Stéphane Bancel</td>
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<tr>
<td>General Q&amp;A</td>
<td>Stéphane Bancel, Stephen Hoge, Arpa Garay, Jamey Mock, Jacqueline Miller, Kyle Holen</td>
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</tbody>
</table>
R&D strategy

Stephen Hoge, M.D.
President
Moderna was founded and built as a mRNA platform company

10 years of investment creating a singular platform

mRNA science
Delivery
Manufacturing

mRNA platform

Many medicines
We leverage our mRNA platform to create modalities

- **mRNA science**
- **Delivery**
- **Manufacturing**

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**mRNA platform**

**Proof-of-concept**
- COVID
- RSV
- Flu

**Infectious disease vaccines**

**Proof-of-concept**
- INT in adjuvant melanoma

**Cancer therapeutics**

**Proof-of-concept**
- PA
- MMA
- GSD1a

**Rare disease intracellular therapies**
Our platform has allowed us to double our pipeline in 3 years

2020

25 development programs

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<td>Phase 2</td>
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<td>Phase 3</td>
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2023

43 development programs

<table>
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<th>Count</th>
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<td>Phase 1</td>
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<td>Phase 3</td>
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Note: numbers do not total as 2020 includes 1 commercial stage program, and 2023 includes 3 commercial stage programs
Moderna was founded and built as a mRNA platform company

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

New modalities and new medicines
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
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
Modern has a broad portfolio of mRNA medicines

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<th>Phase 2</th>
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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

- **RSV (older adults)**
  - mRNA-1345
- **Flu/COVID**
  - mRNA-1083
- **NextGen COVID**
  - mRNA-1283

### Latent/other vaccines

- **Seasonal Flu**
  - mRNA-1010
- **RSV/nextGen RSV (older adults)**
  - mRNA-1345
- **RSV/hMPV (older adults)**
  - mRNA-1365
- **Pandemic Flu**
  - mRNA-1018
- **Endemic hCOV**
  - mRNA-1287
- **VZV**
  - mRNA-1468
- **HSV**
  - mRNA-1608
- **EBV (IM)**
  - mRNA-1189
- **Lyme**
  - mRNA-1975/82
- **CMV**
  - mRNA-1647
- **Norovirus (older adults)**
  - mRNA-1403/05
- **INT (adjuvant melanoma)**
  - mRNA-4157
- **INT (undisclosed indication)**
  - mRNA-4157
- **MMA**
  - mRNA-3705
- **PA**
  - mRNA-3927
- **PKU**
  - mRNA-3210
- **GSD1a**
  - mRNA-3745
- **VZV**
  - mRNA-1468
- **HSV**
  - mRNA-1608

### Oncology

- **INT (adjuvant melanoma)**
  - mRNA-4157
- **INT (adjuvant NSCLC)**
  - mRNA-4157

### Rare disease

- **RSV (2-18Y)**
  - mRNA-1345
- **NextGen Flu**
  - mRNA-1011/1020
- **NextGen COVID**
  - mRNA-1283

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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

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Focus of today’s update

Respiratory vaccines
- COVID-19
- Seasonal Flu

Latent + other vaccines
- Cytomegalovirus (CMV)
- INT in multiple indications

Rare disease therapeutics
- Propionic acidemia (PA)
- Methylmalonic acidemia (MMA)
- Phenylketonuria (PKU)

Oncology therapeutics
Respiratory vaccines
Development

Jacqueline Miller, M.D.
SVP, Head of Development,
Infectious Diseases,
Research & Development
Respiratory vaccines pipeline overview

### Commercial and Phase 3 programs

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>mRNA Code</th>
<th>Phases</th>
<th>Commercial</th>
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<td><strong>COVID-19</strong></td>
<td>mRNA-1273.222/0.815</td>
<td>PC, Ph. 1, Ph. 2, Ph. 3, Comm.</td>
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<td><strong>Older adults RSV</strong></td>
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### Next-gen programs

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<td><strong>Flu</strong></td>
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<td><strong>Flu</strong></td>
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### Combination programs

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<td><strong>Flu + COVID-19 + RSV</strong></td>
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<td><strong>RSV + hMPV</strong></td>
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<td>PC, Ph. 1, Ph. 2, Ph. 3, Comm.</td>
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</table>
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

- **Next Gen** mRNA-1283
- **Bivalents** .214/.222
- **Spikevax** mRNA-1273
- **Spikevax** mRNA-1273.815

**RSV:** Rapid development of novel vaccine

- **Peds. RSV** mRNA-1345

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

- **Neuraminidase** mRNA-1020/-30
- **Pentavalent+** mRNA-1011/-12
- **Quadrivalent** mRNA-1010 (P301/P302)
- **Quadrivalent** mRNA-1010 (P303)

**COVID:**

- Late 2020 to today

**Influenza:**

- Mid 2021 to today

**RSV:**

- Mid 2021 to today
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
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

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**Phase 1/2 clinical study**

<table>
<thead>
<tr>
<th>Group</th>
<th>Ages</th>
<th>Vaccine</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ages 18 to &lt; 65</td>
<td></td>
<td>mRNA-1283.222</td>
<td>N~50</td>
</tr>
<tr>
<td></td>
<td></td>
<td>mRNA-1273.222</td>
<td>N~50</td>
</tr>
<tr>
<td>Ages 65 to &lt; 80</td>
<td></td>
<td>mRNA-1283.222</td>
<td>N~50</td>
</tr>
<tr>
<td></td>
<td></td>
<td>mRNA-1273.222</td>
<td>N~50</td>
</tr>
</tbody>
</table>
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
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

<table>
<thead>
<tr>
<th>Group</th>
<th>N~5750</th>
</tr>
</thead>
<tbody>
<tr>
<td>mRNA-1283.222</td>
<td></td>
</tr>
<tr>
<td>mRNA-1273.222</td>
<td></td>
</tr>
</tbody>
</table>
COVID-19

Darin Edwards, PhD
Executive Director, COVID Vaccines Program Leader
Modernas 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’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?

<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>BA.1</td>
<td>D R K L F P T D R N K K V S L N N K A F F R S R Y H</td>
</tr>
<tr>
<td>BA.2</td>
<td>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</td>
</tr>
<tr>
<td>BA.4/5</td>
<td>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</td>
</tr>
<tr>
<td>BQ.1.1</td>
<td>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</td>
</tr>
<tr>
<td>BA.2.75</td>
<td>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</td>
</tr>
<tr>
<td>BA.2.75.2</td>
<td>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</td>
</tr>
<tr>
<td>BN.1</td>
<td>H 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</td>
</tr>
<tr>
<td>XBB.1</td>
<td>H T K L F P F A N S N K K P S L K N K A S S Q G R Y H</td>
</tr>
<tr>
<td>XBB.1.5</td>
<td>H T K L F P F A N S N K K P S L K N K A P S Q G R Y H</td>
</tr>
</tbody>
</table>
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
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

- 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 11\(^{\text{th}}\), Japan and Canada approval on September 12\(^{\text{th}}\)
  - Approvals in Europe, Taiwan and others expected this week
  - U.S. CDC ACIP met on September 12\(^{\text{th}}\) 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
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**

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)
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

<table>
<thead>
<tr>
<th>Group</th>
<th>Participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>mRNA-1010 (50 μg)</td>
<td>N=1227</td>
</tr>
<tr>
<td>Fluarix</td>
<td>N=1189</td>
</tr>
</tbody>
</table>
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.
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

**65 to < 80 years old**

<table>
<thead>
<tr>
<th></th>
<th>A/H1N1</th>
<th>A/H3N2</th>
<th>B/Victoria</th>
<th>B/Yamagata</th>
</tr>
</thead>
<tbody>
<tr>
<td>GMT Ratio</td>
<td>(1.18, 2.58)</td>
<td>(1.03, 2.51)</td>
<td>(0.93, 2.15)</td>
<td>(0.66, 1.43)</td>
</tr>
<tr>
<td>65 to &lt; 80 years old</td>
<td>1.74</td>
<td>1.61</td>
<td>1.42</td>
<td>0.97</td>
</tr>
</tbody>
</table>
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
Respiratory portfolio
Additional updates

Jacqueline Miller
SVP, Head of Development, Infectious Diseases, Research & Development
# Respiratory vaccines pipeline overview

## Commercial and Phase 3 programs

- **COVID-19** (mRNA-1273.222/.815)
- **Older adults RSV** (mRNA-1345)
- **Flu** (mRNA-1010)

## Next-gen programs

- **COVID-19 next-gen booster** (mRNA-1283)
- **Flu** (mRNA-1011/-1012)
- **Flu** (mRNA-1020/-1030)

## Combination programs

- **Flu + COVID-19** (mRNA-1083)
- **Flu + COVID-19 + RSV** (mRNA-1230)
- **Flu + RSV** (mRNA-1045)
- **RSV + hMPV** (mRNA-1365)
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

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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

**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

**Evolution of target portfolio profile**

**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)
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
Respiratory vaccines
Commercial opportunity

Arpa Garay
Chief Commercial Officer
Common commercial characteristics for the respiratory vaccines franchise

Respiratory vaccines

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

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

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

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
Focus on securing contracts

2023

Second half
Focus on increasing vaccination rates
We are using a multi-pronged approach to increase urgency for COVID vaccination

<table>
<thead>
<tr>
<th>Activate the medical community</th>
<th>Support customers</th>
<th>Re-engage the consumer</th>
<th>Amplify voice of advocacy groups and major professional organizations</th>
</tr>
</thead>
<tbody>
<tr>
<td>to proactively recommend the updated COVID vaccine to their patients this fall, especially 65+ and high risk</td>
<td>throughout the season, minimizing provider confusion, supporting patient outreach, and encouraging the extension of the immunization season</td>
<td>with a focus on adults who receive their annual flu shots</td>
<td>to create credible messaging on need for updated COVID vaccine</td>
</tr>
</tbody>
</table>
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 on RSV LRTD with ≥2 symptoms; [RSVVV data](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7846520/)

\(^2\) As of April 30, 2023

\(^3\) [www.ncbi.nlm.nih.gov/pmc/articles/PMC7913196/](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7913196/)

\(^4\) [www.ncbi.nlm.nih.gov/pmc/articles/PMC7913196/](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7913196/)
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

**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\(^3\)**

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>2010</td>
<td>$2.8B 98% 2%</td>
<td>$3.2B 79% 21%</td>
</tr>
<tr>
<td>2016</td>
<td>$4.0B 98% 2%</td>
<td>$5.8B 60% 40%</td>
</tr>
<tr>
<td>2020</td>
<td>$5.8B 98% 2%</td>
<td></td>
</tr>
</tbody>
</table>

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
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

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Latent + other vaccines

Respiratory vaccines

Rare disease therapeutics

Oncology therapeutics

Latent + other vaccines

mRNA platform
Latent + other vaccines
Development

Jacqueline Miller, M.D.
SVP, Head of Development,
Infectious Diseases,
Research & Development
We are advancing multiple programs to address significant unmet medical needs associated with latent and other virus infections

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

Sequelae include:

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

Most common cause of congenital infection worldwide

>$1B in annual healthcare costs\(^1\)

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

---

Our CMV vaccine (mRNA-1647) includes 6 mRNAs (five encode the pentamer, the 6th encodes for the gB antigen)
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
**Overview of primary efficacy endpoint**

### Efficacy Boundaries with Alpha-allocation between 2 Planned Analyses

<table>
<thead>
<tr>
<th>Analysis Type</th>
<th>Approximate # of Cases</th>
<th>One-sided Alpha</th>
<th>VE: Efficacy Bound</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Analysis</td>
<td>81</td>
<td>0.5%</td>
<td>~ 57.7%</td>
</tr>
<tr>
<td>End of Study (EOS) Analysis</td>
<td>112</td>
<td>2.0%</td>
<td>~ 49.1%</td>
</tr>
</tbody>
</table>

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Norovirus
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

---

<table>
<thead>
<tr>
<th>Infections</th>
<th>United States (per year)(^2)</th>
<th>Global (per year)(^3,4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>~20M infections</td>
<td>~685M infections</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Deaths and hospitalizations</th>
<th>United States (per year)(^2)</th>
<th>Global (per year)(^3,4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>~900 deaths (mostly older adults)</td>
<td>~200K deaths (~50K among children)</td>
<td></td>
</tr>
<tr>
<td>~100K hospitalizations</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Societal costs</th>
<th>United States (per year)(^2)</th>
<th>Global (per year)(^3,4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>~$2B in healthcare costs and lost productivity</td>
<td>~$60B in healthcare costs and lost productivity</td>
<td></td>
</tr>
</tbody>
</table>

---

4. [https://www.who.int/teams/immunization-vaccines-and-biologicals/diseases/norovirus](https://www.who.int/teams/immunization-vaccines-and-biologicals/diseases/norovirus)
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
Modern a 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**
Latent + other vaccines
Commercial opportunity

Arpa Garay
Chief Commercial Officer
Common commercial characteristics for the latent + other vaccines franchise

<table>
<thead>
<tr>
<th>Latent + other vaccines</th>
</tr>
</thead>
<tbody>
<tr>
<td>• No seasonal pattern for sales, demand more constant throughout year</td>
</tr>
<tr>
<td>• Market increases by expanding eligible populations</td>
</tr>
<tr>
<td>• Similar vaccine procurement and contracting</td>
</tr>
</tbody>
</table>
Modernas current pipeline is targeting large addressable markets

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

~$10-25b+
Moderna’s latent vaccine development candidates have potential to address multi billion-dollar markets

<table>
<thead>
<tr>
<th>Latent and other vaccines</th>
<th>Moderna Program</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cytomegalovirus (CMV)</td>
<td>mRNA-1647</td>
</tr>
<tr>
<td>Epstein-Barr virus (EBV)</td>
<td>mRNA-1189</td>
</tr>
<tr>
<td></td>
<td>mRNA-1195</td>
</tr>
<tr>
<td>Herpes simplex virus (HSV)</td>
<td>mRNA-1608</td>
</tr>
<tr>
<td>Varicella zoster virus (VZV)</td>
<td>mRNA-1468</td>
</tr>
<tr>
<td>Human immunodeficiency virus (HIV)</td>
<td>mRNA-1644</td>
</tr>
<tr>
<td></td>
<td>mRNA-1574</td>
</tr>
</tbody>
</table>

**Worldwide Gardasil (HPV) Sales**

$540-$810 per course

**Worldwide Shingrix (VZV) Sales**

$370 per course

---

1. Gardasil is a registered trademark of Merck Sharp & 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

© 2023 Moderna, Inc. All rights reserved.
Norovirus disease burden in the US is similar in scale to other high value vaccine market diseases

Norovirus Disease

U.S. Disease Burden in Children <5

<table>
<thead>
<tr>
<th></th>
<th>Norovirus current day</th>
<th>Rotavirus pre-vaccine era</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>~4.2 M</td>
<td>~2.7 M</td>
</tr>
<tr>
<td>Outpatient visits</td>
<td>~815 K</td>
<td>~410 K</td>
</tr>
<tr>
<td>ED visits</td>
<td>~130 K</td>
<td>200 – 270 K</td>
</tr>
<tr>
<td>Hospitalizations</td>
<td>~25 K</td>
<td>55 – 70 K</td>
</tr>
<tr>
<td>Deaths</td>
<td>~40</td>
<td>20 – 60</td>
</tr>
</tbody>
</table>

U.S. Disease Burden in Adults 60+

<table>
<thead>
<tr>
<th></th>
<th>Norovirus current day</th>
<th>RSV pre-vaccine era</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>~3.5 M</td>
<td>2.5 – 3 M</td>
</tr>
<tr>
<td>Outpatient visits</td>
<td>~625 K</td>
<td>~1.4 M</td>
</tr>
<tr>
<td>ED visits</td>
<td>~95 K</td>
<td>~120 K</td>
</tr>
<tr>
<td>Hospitalizations</td>
<td>~50 K</td>
<td>100 – 150 K</td>
</tr>
<tr>
<td>Deaths</td>
<td>~1 K</td>
<td>8 – 12 K</td>
</tr>
</tbody>
</table>

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

Break
Rare disease therapeutics

Respiratory vaccines

Latent + other vaccines

RARE mRNA platform

Oncology therapeutics

Rare disease therapeutics
Rare disease therapeutics
Development

Kyle Holen, M.D.
SVP, Head of Development, Therapeutics and Oncology, Research & Development
Common characteristics for therapeutic development in rare diseases

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

<table>
<thead>
<tr>
<th>Rare Disease</th>
<th>PC</th>
<th>Ph. 1</th>
<th>Ph. 2</th>
<th>Ph. 3</th>
<th>Comm.</th>
</tr>
</thead>
<tbody>
<tr>
<td>PA (mRNA-3927)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CF (VX-522)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MMA (mRNA-3705)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OTC, PKU, CN-1 (mRNA-3139/-3210/-3351)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GSD1a (mRNA-3745)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
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
Clinical evidence with shared components over our rare disease portfolio are de-risking future programs

<table>
<thead>
<tr>
<th>Component</th>
<th>Indications</th>
<th>Data</th>
<th>Will inform</th>
</tr>
</thead>
</table>
| 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 |
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
Propionic Acidemia (PA)

Geoffrey Rezvani, M.D.
Program Leader, CV/Emerging Therapeutics and Oncology
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)**

- **Cohort 1** (0.3 mg/kg IV q3wk) N=3
- **Cohort 2** (0.3 mg/kg IV q2wk) N=3
- **Cohort 3** (0.45 mg/kg IV q2wk) N=3
- **Cohort 4** (0.6 mg/kg IV q2wk) N=3
- **Cohort 5** (0.9 mg/kg IV q2wk) N=3

**Dose confirmation** N=4

Identification of optimal dose triggers expansion
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
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
### 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)

![Metabolic Decompensation Events Profile](image-url)

- **DISCONTINUED**
- **ONGOING**
- MDE outside 2-week dosing interval
- MDE within retrospective period of 2-week dosing interval

Data cut 25 Aug 2023
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)
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
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
mRNA-3705-P101: summary of demographics and baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>Cohort 1 0.1 mg/kg Q3W (N=3)</th>
<th>Cohort 2 0.2 mg/kg Q2W (N=3)</th>
<th>Cohort 3 0.4 mg/kg Q2W (N=3)</th>
<th>Cohort 4 0.6 mg/kg Q2W (N=2)</th>
<th>Total (N=11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at enrollment, median (years)</td>
<td>12.17</td>
<td>2.67</td>
<td>7.83</td>
<td>11.54</td>
<td>7.83</td>
</tr>
<tr>
<td>Min, Max</td>
<td>4.5, 14.4</td>
<td>2.5, 39.5</td>
<td>5.8, 16.0</td>
<td>4.3, 18.8</td>
<td>2.5, 39.5</td>
</tr>
<tr>
<td>Age at disease onset, median (months)</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>58.5</td>
<td>0</td>
</tr>
<tr>
<td>Min, Max</td>
<td>0</td>
<td>0.1</td>
<td>0.10</td>
<td>0.117</td>
<td>0.117</td>
</tr>
<tr>
<td>Sex, n</td>
<td>Male</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>Weight</td>
<td>Weight at baseline, median (kg)</td>
<td>25.70</td>
<td>13.40</td>
<td>22.50</td>
<td>38.55</td>
</tr>
<tr>
<td></td>
<td>Min, Max</td>
<td>19.5, 41.4</td>
<td>12.3, 58.0</td>
<td>16.6, 54.9</td>
<td>16.5, 60.6</td>
</tr>
<tr>
<td>Phenotype</td>
<td>Mut0</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Mut-</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>
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
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

<table>
<thead>
<tr>
<th>Cohort 1</th>
<th>0.1mg/kg q3w</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMA Percentage Change from Baseline (%)</td>
<td></td>
</tr>
<tr>
<td>0.1 mg/kg Q3W</td>
<td>-2%*</td>
</tr>
<tr>
<td>0.2 mg/kg Q2W</td>
<td>-29%</td>
</tr>
<tr>
<td>0.4 mg/kg Q2W</td>
<td>-58%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cohort 1</th>
<th>0.1mg/kg q3w</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-Methylcitrate Percentage Change from Baseline (%)</td>
<td></td>
</tr>
<tr>
<td>0.1 mg/kg Q3W</td>
<td>14%</td>
</tr>
<tr>
<td>0.2 mg/kg Q2W</td>
<td>-4%</td>
</tr>
<tr>
<td>0.4 mg/kg Q2W</td>
<td>-36%</td>
</tr>
</tbody>
</table>

*Cohort 1 (0.1mg/kg q3w)
Cohort 2 (0.2mg/kg q2w)
Cohort 3 (0.4mg/kg q2w)

*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)
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
Phenylketonuria (PKU)
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\(^4\)

---

\(^1\) 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
Rare disease franchise
Commercial opportunity

Arpa Garay
Chief Commercial Officer
Common commercial characteristics for the rare disease therapeutics franchise

- High unmet medical need
- Increased awareness and prevalence after treatment
- High compliance with chronic, life-saving therapies
- Concentrated prescriber base
Moderna’s current pipeline is targeting large addressable markets

Rare disease therapeutics

~10b+
Moderna’s intracellular rare metabolic pipeline may address a multi-billion-dollar market

### Intracellular Rare Metabolic Total Addressable Market

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Estimated US Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Propionic acidemia (PA)</td>
<td>500 to 1,500</td>
</tr>
<tr>
<td>Methylmalonic acidemia (MMA)</td>
<td>800 to 1,000</td>
</tr>
<tr>
<td>Glycogen storage disorder type 1a (GSD1a)</td>
<td>2,000 to 4,000</td>
</tr>
<tr>
<td>Phenylketonuria (PKU)</td>
<td>10,000 to 20,000</td>
</tr>
<tr>
<td>Ornithine transcarbamylase deficiency (OTC)</td>
<td>1,000 to 2,000</td>
</tr>
</tbody>
</table>

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
## Attractive commercial opportunity in Rare Disease

<table>
<thead>
<tr>
<th>Feature</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High value medicines</strong></td>
<td>Chronic, life-saving therapies</td>
</tr>
<tr>
<td><strong>Increased patient identification and access drives diagnosis</strong></td>
<td>Epidemiology estimates often understated for rare diseases with no treatment options</td>
</tr>
<tr>
<td><strong>Efficient go-to-market model</strong></td>
<td>Concentrated base of patients through patient advocacy groups</td>
</tr>
<tr>
<td><strong>Unique regulatory benefits</strong></td>
<td>High unmet need allows for accelerated timelines and regulatory incentives</td>
</tr>
<tr>
<td><strong>IP and competition</strong></td>
<td></td>
</tr>
</tbody>
</table>
Oncology therapeutics

Respiratory vaccines

Latent + other vaccines

Rare disease therapeutics

Oncoology therapeutics
Oncology Development

Kyle Holen, M.D.
SVP, Head of Development, Therapeutics and Oncology, Research & Development
Common characteristics for therapeutic development in the oncology franchise

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

Programs

Individualized Neoantigen Therapy (INT) (mRNA-4157)
- Phase 3 adjuvant melanoma & NSCLC
- Additional indications

Triplet (mRNA-2752)
- Phase 1 ongoing

Checkpoint vaccine (mRNA-4359)
- Phase 1 ongoing

Partnerships

Expanding the reach of mRNA in oncology treatments
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
Investigator sponsored ductal carcinoma in situ (DCIS) study with Triplet (OX40L/IL-23/IL-36γ) (mRNA-2752)

Core Biopsy
DCIS

Pre-Tx MRI

Cohort Selection

No active treatment

Pembrolizumab IL + mRNA-2752
2-4 doses, 3 weeks apart

Pre-op MRI

Surgical resection
MD/Pt choice

Tissue sections prepared for immunologic assays

Tissue sections prepared for immunologic assays
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**
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

---

Arm 1a  Dose escalation
- DL 4
- DL 3
- DL 2
- DL 1

Arm 1b  Dose confirmation
- CDL 2
- CDL 1
- CDL 1 to CDL 3

Arm 2  Expansion
- Melanoma
- NSCLC

Estimated enrollment: 194 patients
Oncology therapeutics

Programs

**Individualized Neoantigen Therapy (INT)** (mRNA-4157)

- Phase 3 adjuvant melanoma & NSCLC
- Additional indications

**Triplet** (mRNA-2752)

- Phase 1 ongoing

**Checkpoint vaccine** (mRNA-4359)

- Phase 1 ongoing

Partnerships

Expanding the reach of mRNA in oncology treatments
Non-specific therapies like checkpoint inhibitors set the standard for immuno-oncology treatment
Despite success with checkpoint inhibitors, unmet medical need exists

Response rates to ICIs typically range from 10% to 30% depending on the tumor type

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

- Glioblastoma (11%)
- Melanoma (30%)
- Breast cancer (12%)
- Liver cancer (19%)
- Urothelial cancer (20%)
- Ovarian cancer (9%)
- Lymphoma (62%)
- Head and neck cancer (15%)
- Lung cancer (20%)
- Gastric cancer (11%)
- Sarcoma (8%)
- Renal cancer (23%)
- Colorectal cancer (3%)

References:
INT has the potential to transform the continuum of cancer treatment by specifically harnessing T-cells.
Oncology
Clinical update

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

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

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

**Key eligibility criteria**
- Stage IIIB, a IIIC, IIID, or IV cutaneous melanoma
- Complete surgical resection within 13 weeks prior to first pembrolizumab dose
- Disease-free at study entry
- ECOG PS 0-1
- Tissue available for NGS

**Combination treatment arm: mRNA-4157 (V940) + pembrolizumab**

- Up to 1 year of pembrolizumab treatment
- mRNA-4157 (V940) 1 mg IM Q3W for up to 9 doses + pembrolizumab 200 mg IV Q3W for up to 18 cycles (n = 107)

**Control treatment arm: Pembrolizumab only**

- Up to 1 year of pembrolizumab treatment
- Pembrolizumab 200 mg IV Q3W for up to 18 cycles (n = 50)

**Primary endpoint:**
- RFS<sup>c,d</sup>

**Secondary endpoints:**
- DMFS<sup>e</sup>, safety, tolerability

**Follow-up:**
- up to 5 years following the first dose of pembrolizumab

**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<sup>f</sup>

**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.

<sup>a</sup>Patients with stage IIIIB disease were eligible only if relapse occurred within 3 months of prior surgery of curative intent.

<sup>b</sup>According to the 8th edition of the American Joint Committee on Cancer staging manual.

<sup>c</sup>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.

<sup>d</sup>The primary analysis for RFS was specified to occur after all patients completed ≥12 months on study and ≥40 RFS events were observed. 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. The stratified log-rank test was used for comparison.

<sup>e</sup>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.


CI, confidence interval; mRNA, messenger RNA; RFS, recurrence-free survival.

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.

18-month DMFS


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

#### Table: Event, n (%) for mRNA-4157 (V940) + pembrolizumab (n = 104) vs. pembrolizumab alone (n = 50)

<table>
<thead>
<tr>
<th>Event, n (%)</th>
<th>mRNA-4157 (V940) + pembrolizumab (n = 104)</th>
<th>pembrolizumab alone (n = 50)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Any grade</td>
<td>Grade ≥3</td>
</tr>
<tr>
<td>Any AE</td>
<td>104 (100.0)</td>
<td>36 (34.6)</td>
</tr>
<tr>
<td>Any treatment-related AE</td>
<td>104 (100.0)</td>
<td>26 (25.0)</td>
</tr>
<tr>
<td>Serious AE\textsuperscript{a}</td>
<td>15 (14.4)</td>
<td>13 (12.5%)</td>
</tr>
</tbody>
</table>

#### Table: mRNA-4157 (V940) or combination-related AEs\textsuperscript{b} occurring in >20% of patients

<table>
<thead>
<tr>
<th>Event, n (%)</th>
<th>mRNA-4157 (V940) + pembrolizumab (n = 104)</th>
<th>pembrolizumab alone (n = 50)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any</td>
<td>98 (94.2)</td>
<td>12 (11.5)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>63 (60.6)</td>
<td>5 (4.8)</td>
</tr>
<tr>
<td>Injection site pain</td>
<td>58 (55.8)</td>
<td>0</td>
</tr>
<tr>
<td>Chills</td>
<td>52 (50.0)</td>
<td>0</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>50 (48.1)</td>
<td>1 (1.0)</td>
</tr>
<tr>
<td>Headache</td>
<td>33 (31.7)</td>
<td>0</td>
</tr>
<tr>
<td>Injection site erythema</td>
<td>33 (31.7)</td>
<td>0</td>
</tr>
<tr>
<td>Influenza-like illness</td>
<td>32 (30.8)</td>
<td>0</td>
</tr>
<tr>
<td>Nausea</td>
<td>26 (25.0)</td>
<td>0</td>
</tr>
<tr>
<td>Myalgia</td>
<td>22 (21.2)</td>
<td>1 (1.0)</td>
</tr>
</tbody>
</table>

#### Table: Pembro or combination related AEs\textsuperscript{c} occurring in >20% of patients

<table>
<thead>
<tr>
<th>Event, n (%)</th>
<th>mRNA-4157 (V940) + pembrolizumab (n = 104)</th>
<th>pembrolizumab alone (n = 50)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any</td>
<td>101 (97.1)</td>
<td>24 (23.1)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>72 (69.2)</td>
<td>6 (5.8)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>31 (29.8)</td>
<td>2 (1.9)</td>
</tr>
<tr>
<td>Pruritus</td>
<td>30 (28.8)</td>
<td>0</td>
</tr>
<tr>
<td>Nausea</td>
<td>23 (22.1)</td>
<td>0</td>
</tr>
<tr>
<td>Chills</td>
<td>22 (21.2)</td>
<td>0</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>22 (21.2)</td>
<td>0</td>
</tr>
</tbody>
</table>

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. \textsuperscript{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. \textsuperscript{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. \textsuperscript{c}AEs related to pembrolizumab include events attributed by the investigator to pembrolizumab alone and events attributed to both pembrolizumab and mRNA-4157 (V940).

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

<table>
<thead>
<tr>
<th>Event, n (%)</th>
<th>mRNA-4157 (V940) + pembro (n = 104)</th>
<th>pembro (n = 50)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Any grade</td>
<td>Grade ≥3&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Any</td>
<td>37 (35.6)</td>
<td>11 (10.6)</td>
</tr>
<tr>
<td>Adrenal insufficiency</td>
<td>5 (4.8)</td>
<td>4 (3.8)</td>
</tr>
<tr>
<td>Colitis</td>
<td>6 (5.8)</td>
<td>3 (2.9)</td>
</tr>
<tr>
<td>Hepatitis</td>
<td>1 (1.0)</td>
<td>0</td>
</tr>
<tr>
<td>Hyperthyroidism</td>
<td>6 (5.8)</td>
<td>0</td>
</tr>
<tr>
<td>Hypophysitis</td>
<td>1 (1.0)</td>
<td>0</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>21 (20.2)</td>
<td>0</td>
</tr>
<tr>
<td>Myositis</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Nephritis</td>
<td>3 (2.9)</td>
<td>3 (2.9)</td>
</tr>
<tr>
<td>Pancreatitis</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Pneumonitis</td>
<td>4 (3.8)</td>
<td>1 (1.0)</td>
</tr>
<tr>
<td>Sarcoidosis</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Severe skin reaction</td>
<td>3 (2.9)</td>
<td>0</td>
</tr>
<tr>
<td>Thyroiditis</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Type 1 diabetes mellitus</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Uveitis</td>
<td>1 (1.0)</td>
<td>0</td>
</tr>
</tbody>
</table>

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. <sup>a</sup>Includes grade 4 adrenal insufficiency and colitis (n = 1 each), attributed to pembrolizumab only and not mRNA-4157 (V940); no grade 5 events occurred. <sup>b</sup>No grade 4 or 5 events occurred.
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

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

NCT05933577
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


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

Immunogenicity profile of an adjuvant NSCLC patient

Greater than 3x increases in neoantigen specific CD8 T-cells were detected post 4\textsuperscript{th} 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

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 4\textsuperscript{th} vaccine dose to multiple neoantigens
* Is greater than 3x increased in neoantigen specific CD8 T-cells post treatment

Previously shared at ASCO 2019

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
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.
Potential INT indications

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

Signal Seeking (opening)
- Adjuvant Pancreatic
- Peri-Operative NSCLC
- Peri-Operative Gastric
Franchise financial opportunity

Jamey Mock
Chief Financial Officer
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
## Financial and operational benefits of our franchises

<table>
<thead>
<tr>
<th></th>
<th>Respiratory</th>
<th>Latent +</th>
<th>Oncology</th>
<th>Rare disease</th>
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</thead>
<tbody>
<tr>
<td><strong>Large sales opportunity</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>High value medicines</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
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<tr>
<td>Innovation driven value</td>
<td>✔</td>
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<tr>
<td>Annual recurring revenue stream</td>
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<tr>
<td><strong>Optimized manufacturing</strong></td>
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<tr>
<td>Low capital intensity beyond initial investment</td>
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<tr>
<td>Economies of scale</td>
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<td>Flexible manufacturing utilization</td>
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<tr>
<td><strong>More efficient R&amp;D investment</strong></td>
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<tr>
<td>Limited R&amp;D expense after initial Phase 3 investment</td>
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<td>Shared research expense</td>
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<tr>
<td>Small clinical studies</td>
<td></td>
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</tbody>
</table>
Modernas rate of success with our platform technology is higher than industry standard

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

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

<table>
<thead>
<tr>
<th>Spend Drivers</th>
<th>2024</th>
<th>2025</th>
<th>2026</th>
<th>2027</th>
<th>2028</th>
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<tr>
<td>#1 Respiratory</td>
<td>Respiratory</td>
<td>Latent &amp; other ID</td>
<td>Latent &amp; other ID</td>
<td>Latent &amp; other ID</td>
<td></td>
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<tr>
<td>#2 Latent &amp; other ID</td>
<td>Latent &amp; other ID</td>
<td>Respiratory</td>
<td>Oncology</td>
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<tr>
<td>#4 Rare Disease</td>
<td>Rare Disease</td>
<td>Rare Disease</td>
<td>Respiratory</td>
<td>Respiratory</td>
<td></td>
</tr>
<tr>
<td>#5 Platform investments</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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
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
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%
Conclusion

Stéphane Bancel
Chief Executive Officer
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

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

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

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Moderná’s four franchises provide foundation for future growth

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

- **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
The next few years look really exciting

### Respiratory vaccines

- **RSV** (older adults)
  - mRNA-1345
- **Flu/COVID**
  - mRNA-1083
- **Flu/COVID/RSV**
  - NextGen
- **RSV** 2-18Y
  - mRNA-1345
- **NextGen Flu**
  - mRNA-1011/-1020

### Latent/other vaccines

- **Seasonal Flu**
  - mRNA-1010
- **NextGen COVID**
  - mRNA-1283
- **Pandemic Flu**
  - mRNA-1018
- **Endemic hCOV**
  - mRNA-1287
- **VZV**
  - mRNA-1468

### Oncology

- **CMV**
  - mRNA-1647
- **Norovirus** (older adults)
  - mRNA-1403/-05
- **EBV (IM)**
  - mRNA-1189
- **Lyme**
  - mRNA-1975/-82
- **VZV**
  - mRNA-1468
- **HSV**
  - mRNA-1608

### Rare disease

- **INT** (adjuvant melanoma)
  - mRNA-4157
- **MMA**
  - mRNA-3705
- **PA**
  - mRNA-3927
- **INT** (undisclosed indication)
  - mRNA-4157
- **PKU**
  - mRNA-3210
- **GSD1a**
  - mRNA-3745
- **INT** (adjuvant NSCLC)
  - mRNA-4157

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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
Q&A

Thank you