Analyst Day 2025

November 20, 2025

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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: Moderna's anticipated commercial growth drivers, including geographic expansion and new product launches; Moderna's ability to achieve up to 10% revenue growth in 2026; Moderna's ability to expand its seasonal vaccine franchise to up to six approved products by 2028; anticipated growth and margin expansion levers; anticipated clinical readouts for Moderna's oncology pipeline; Moderna's expected GAAP operating expenses; Moderna's continued cost management and R&D prioritization and ability to reduce cash costs; Moderna's cash cost guidance; Moderna's balance sheet and targeted cash breakeven in 2028; Moderna's 2025 expected revenue and projected year-end cash balance; Moderna's investments in its oncology and rare disease programs; additional growth in 2027 and 2028; the expectation for early-stage pipeline investments to mature in 2029 and beyond; anticipated strong update of mNEXSPIKE in 2026; Moderna's global manufacturing network; the expectation that manufacturing improvements will improve gross margin by ten percentage points over the next three years; anticipated regulatory filings and potential approvals; total addressable markets; Moderna's ability to improve productivity through digital and AI tools; and Moderna's pipeline programs, including efficacy, safety, and anticipated milestones. In some cases, forward-looking statements can be identified by terminology such as "will," "may," "should," "could," "expects," "intends," "plans," "aims," "anticipates," "believes," "estimates," "predicts," "potential," "continue," or the negative of these terms or other comparable terminology, although not all forward-looking statements contain these words. 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, 2024, 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.

Financial figures in this presentation as of, and for the quarterly periods ended, September 30, 2025, and September 30, 2024, are unaudited.

Introduction

Stéphane Bancel
Chief Executive Officer

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Our mission

Deliver the greatest possible impact to **people** through mRNA **medicines**

Near-term strategy

Build a **large seasonal vaccine franchise** for high-risk populations

Marketed products

- spikevax™ COVID-19 Vaccine, mRNA
- mNEXSPIKE® COVID-19 Vaccine, mRNA
- mRESVIA® (Respiratory Syncytial Virus Vaccine)

Expected launches

- Flu
- Flu + COVID
- Norovirus

Invest cash generated into **oncology and rare disease therapeutics**

Oncology

Intismeran

- Adjuvant melanoma
- Adjuvant NSCLC
- Adjuvant NSCLC non-pCR post neoadjuvant
- Adjuvant renal cell carcinoma
- Adjuvant MIBC
- Adjuvant NMIBC
- Metastatic melanoma
- Metastatic NSCLC

- mRNA-4359
- mRNA-4106
- mRNA-2808
- mRNA-4203

Rare disease

- PA
- MMA

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Build a **large seasonal vaccine franchise** for at-risk populations

Growing population of older adults

Annual burden of seasonal infections

Established manufacturing and customer base

High barrier to entry

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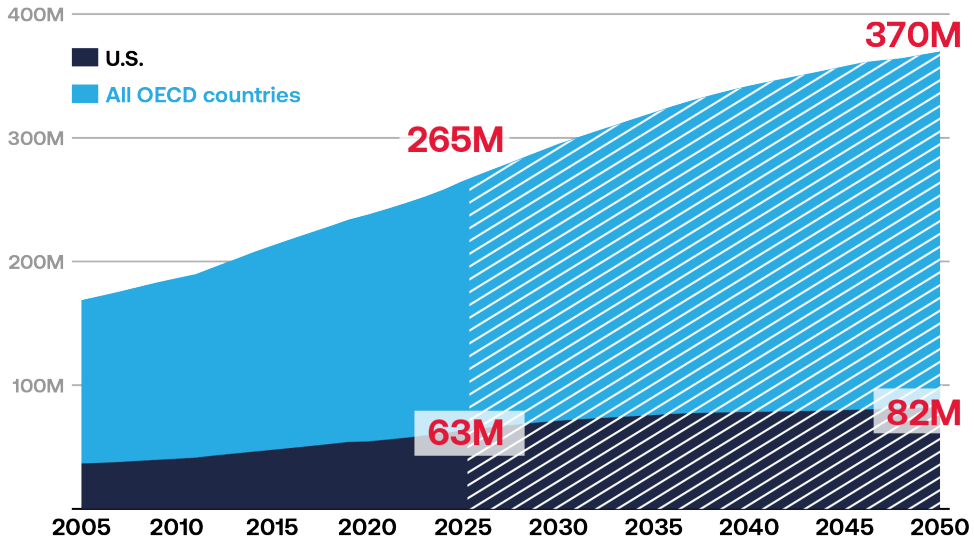
Growing population of older adults

OECD & U.S. population – 65 years of age or older

Across OECD countries, the older adult population (65+) is **projected to increase from 265M in 2025 to 370M by 2050**, a 40% increase



Data source: OECD

Over 100 countries recommend annual seasonal influenza vaccination for older adults and other high risk populations[1]

>90% of World Health Organization member states report having a COVID-19 vaccination policy for older adults[2]

1. https://pubmed.ncbi.nlm.nih.gov/39299001/
2. https://www.mdpi.com/2076-393X/13/4/401?utm

Annual burden of seasonal infections in the U.S.

Flu burden in the U.S. during the 24/25 season

47M – 82M
estimated flu illnesses

21M – 37M
estimated flu-related medical visits

610K – 1.3M
estimated flu-related hospitalizations

27K – 130K
estimated flu-related deaths

Source: https://www.cdc.gov/flu-burden/php/data-vis/2024-2025.html

COVID burden in the U.S. during the 24/25 season

14M – 20M
estimated COVID illnesses

3M – 5M
estimated COVID-related outpatient visits

380K – 540K
estimated COVID-related hospitalizations

44K – 63K
estimated COVID-related deaths

Source: https://www.cdc.gov/covid/php/surveillance/burden-estimates.html

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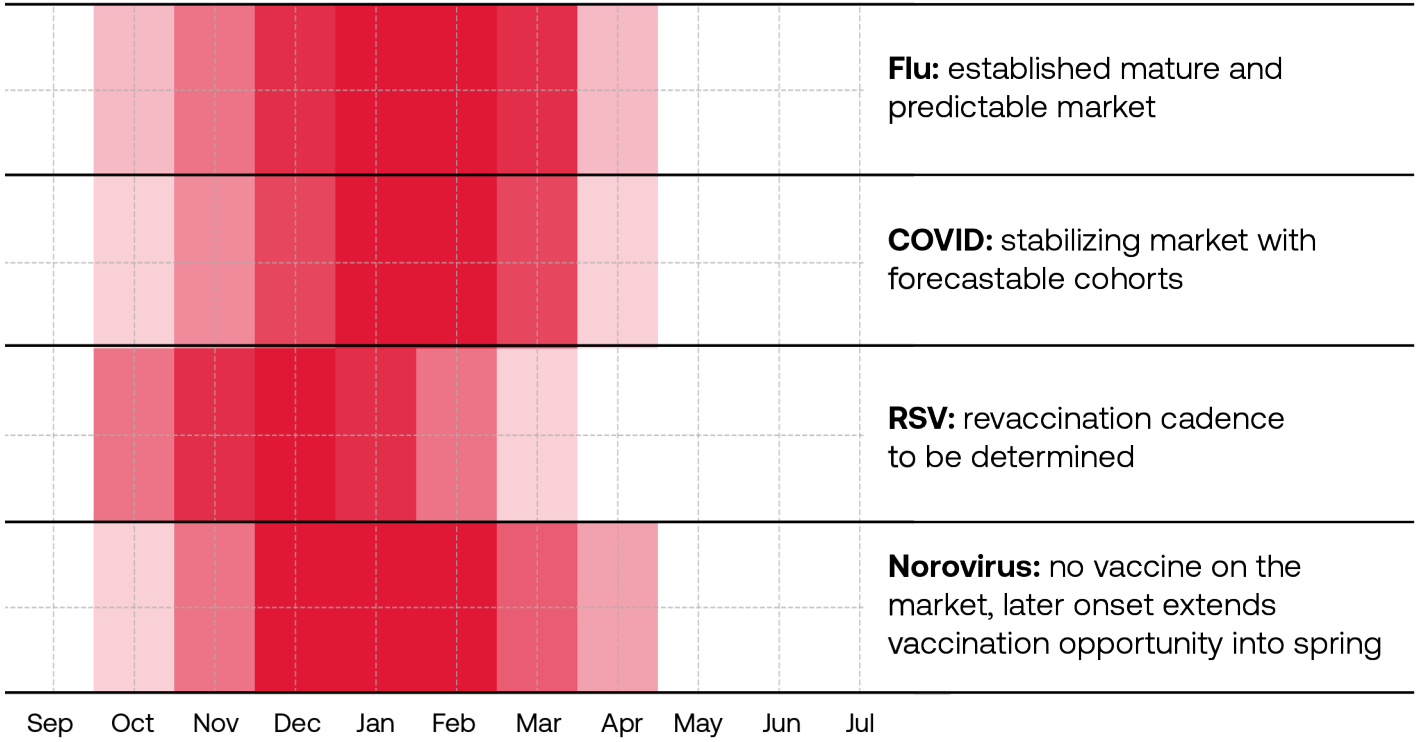
Annual burden of seasonal infections in the U.S.

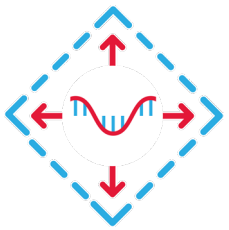
- Predictable seasonal cadence
- Flu and COVID align for combination strategy
- Established strain/variant updates for flu and COVID
- Potential advantage for late strain selection

Seasonal virus activity in the U.S.



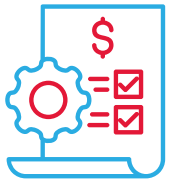
Qualitative data source: CDC

Established manufacturing and customer base



Fully built and scalable mRNA manufacturing

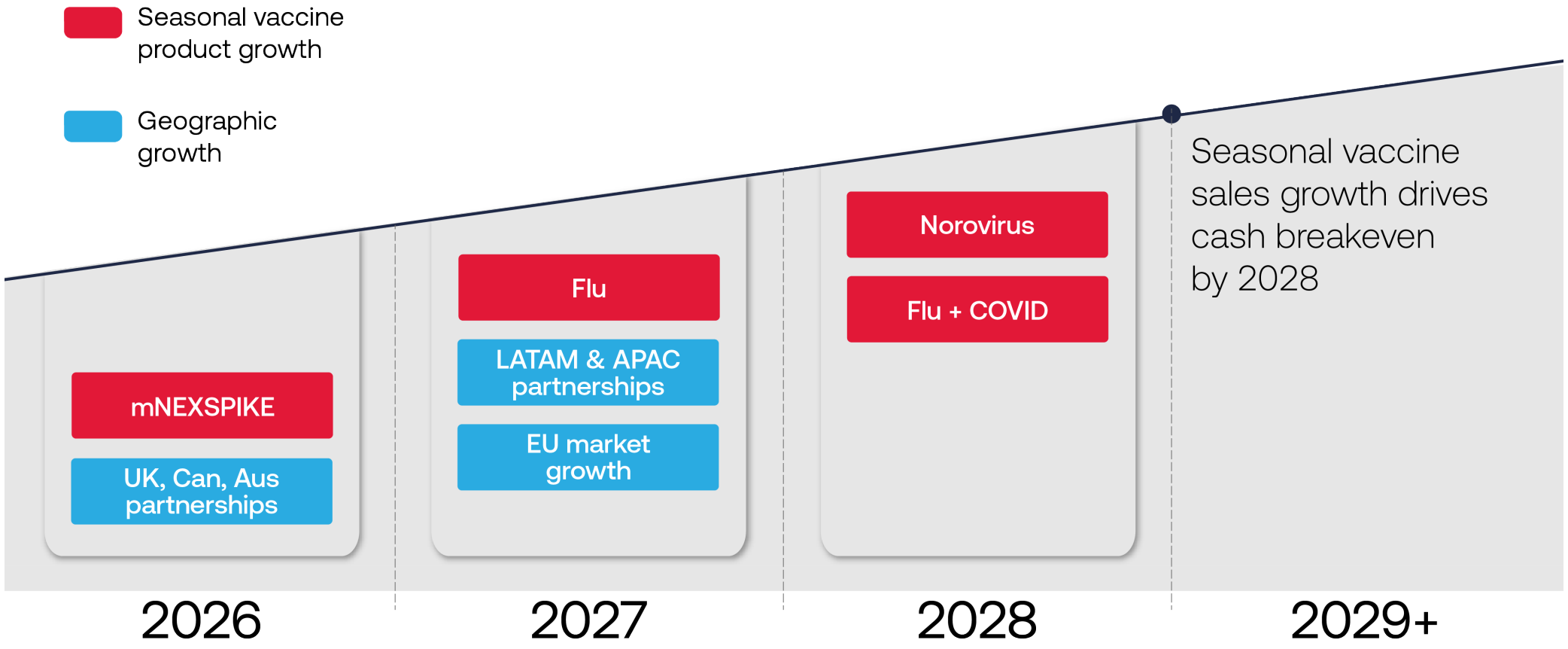
Market access and reimbursement via approval + routine recommendation



Manageable lifecycle investments

Motivated vaccination channel and established prescriber behavior

Over the next three years, we expect our seasonal vaccines to be the backbone of our revenue growth



Improving operating margin for vaccines business

Growth & margin expansion levers

- **Grow revenue** from new products and geographic expansion
- **Improve gross margin** with volume increase and productivity
- **Lower R&D costs** as Phase 3 respiratory studies conclude
- **Leverage existing commercial infrastructure** as we introduce new products

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Near-term strategy

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Rare disease

- PA
- MMA

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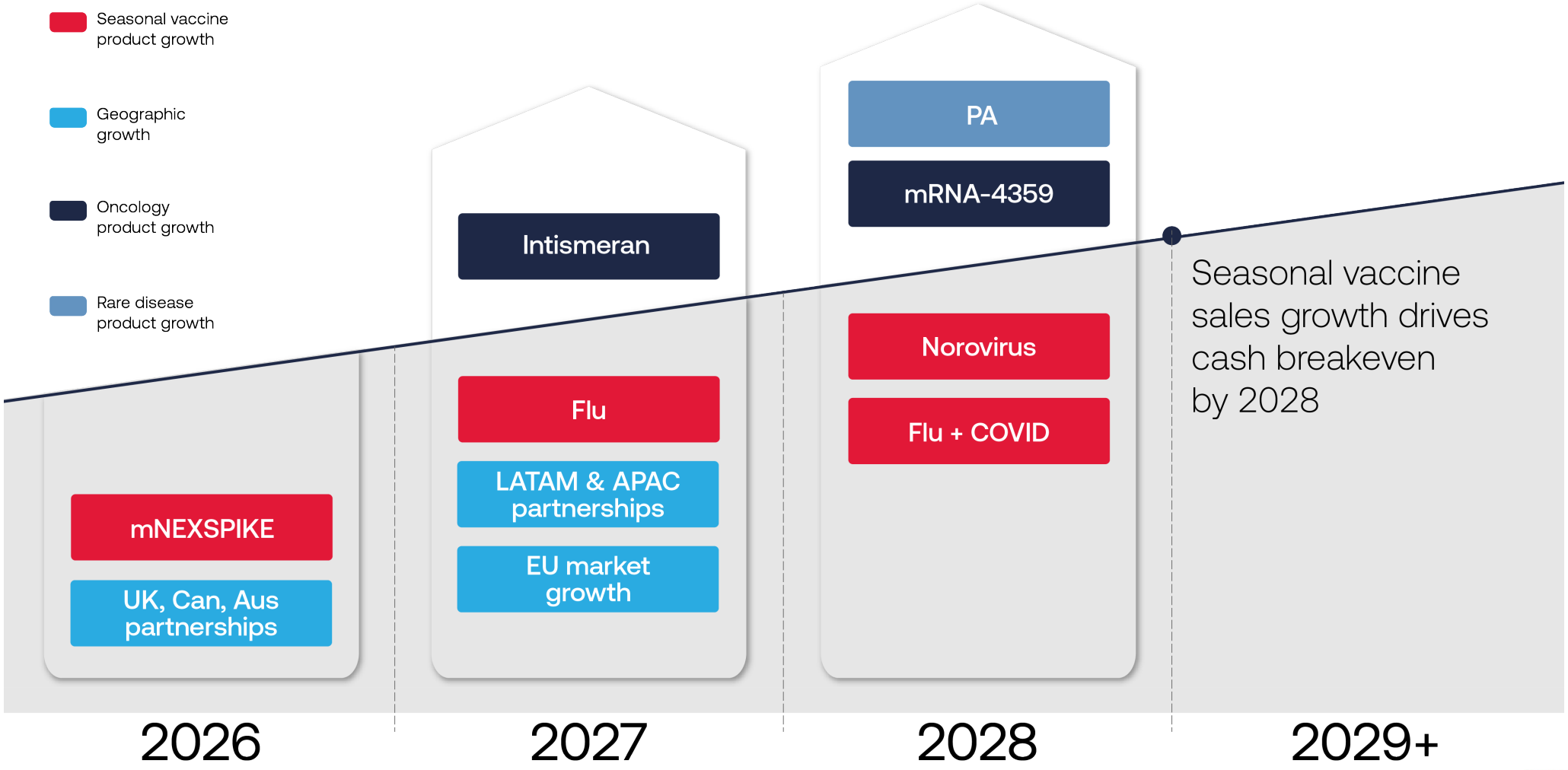
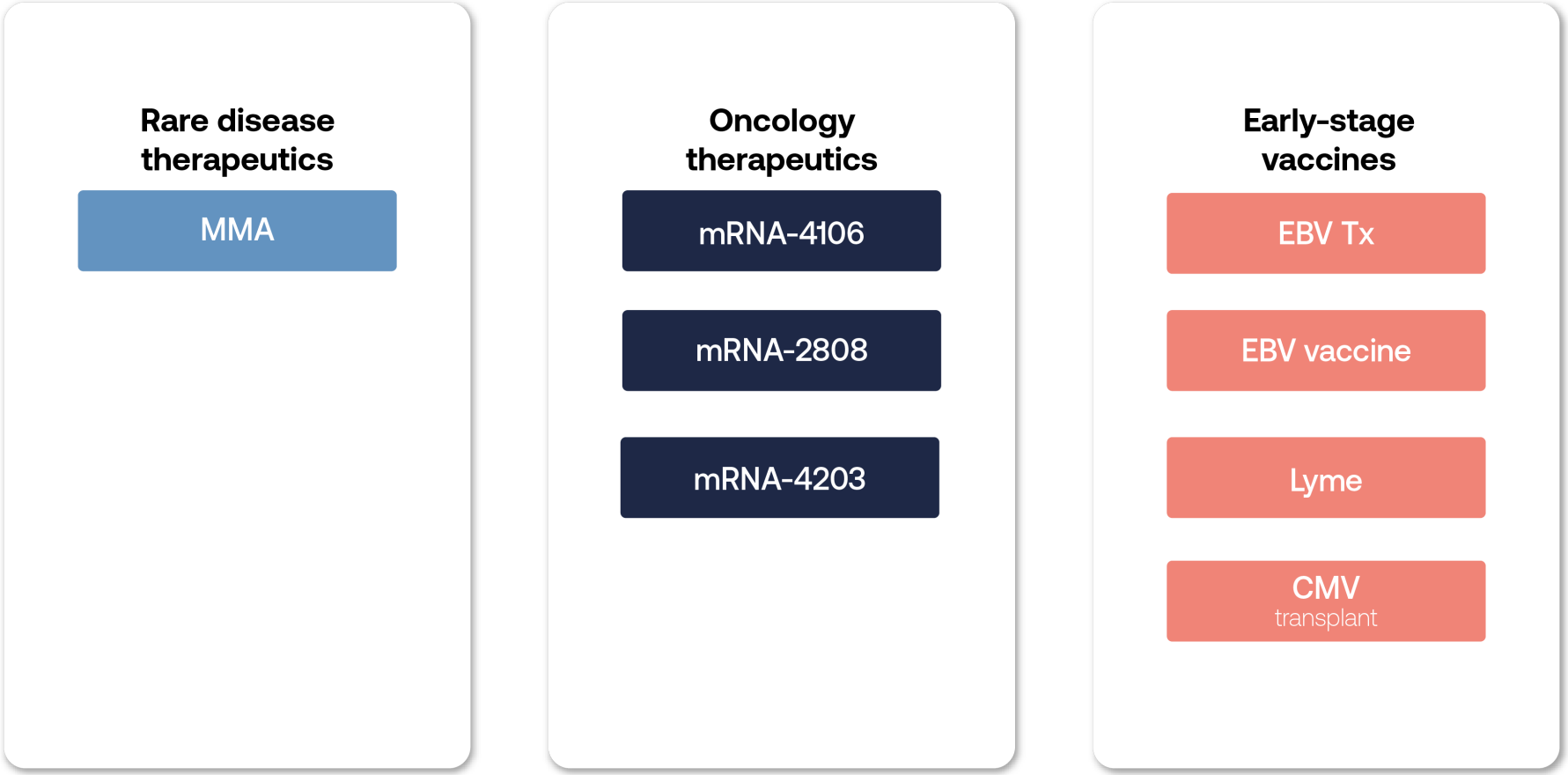
Investments in late-stage oncology and rare disease programs set the stage for additional growth in 2027-2028



Our early-stage pipeline investments are expected to mature in 2029 and beyond



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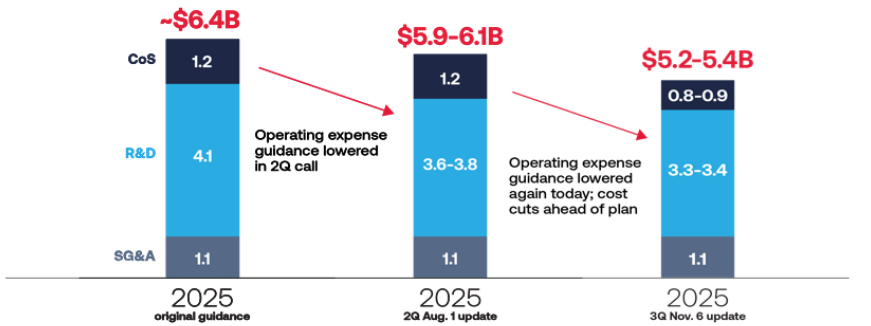
Strong progress on cost reduction initiatives

2025 GAAP operating expense ahead of plan by $1.1B

GAAP costs

in billions



Non-cash items in chart above include:			
Stock-based compensation	$0.6B estimate	$0.6B estimate	$0.5B estimate
Depreciation & amortization	$0.3B estimate	$0.3B estimate	$0.2B estimate
Cash costs at midpoint[1]	**~$5.5B** estimate	**~$5.1B** estimate	**~$4.6B** estimate

[1]Cash costs = GAAP costs - (stock-based compensation & depreciation & amortization)

Will update improvements to 2026 and 2027 cost framework at Analyst Day

Continue to target cash breakeven in 2028

9

Numbers may not add due to rounding

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Beyond our cost reduction plan, **our focus is on improving productivity through digital and AI tools**

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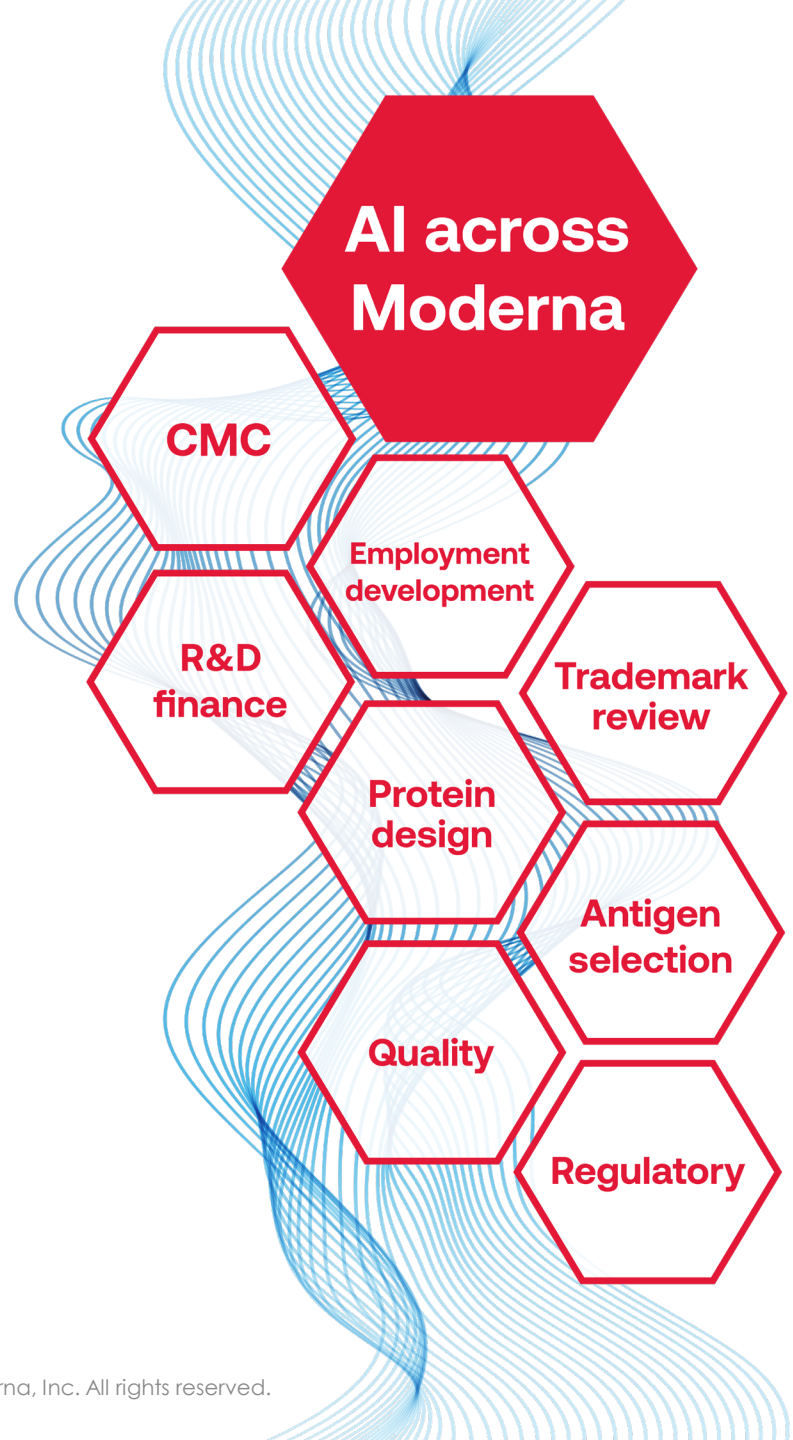

Join us for
AI in Action presentations and demos
after lunch today

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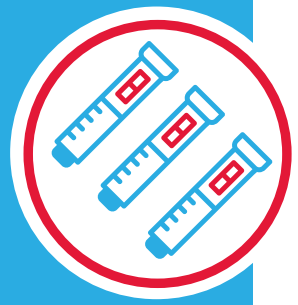
Analyst Day Agenda

Introduction	**Stéphane Bancel**, *Chief Executive Officer*
Building sustainable growth with our seasonal vaccines portfolio	**Stephen Hoge, M.D.**, *President*
Global manufacturing network as a driver of growth and cost savings	**Jerh Collins**, *Chief Technical Operations and Quality Officer*
Financial review and outlook	**Jamey Mock**, *Chief Financial Officer*
Seasonal Vaccines • COVID • Flu • Combination vaccines • RSV • Norovirus	**Jacqueline Miller, M.D.**, *Chief Medical Officer* **Darin Edwards, Ph.D.**, *ED, Program Leader, Infectious Disease* **Raffael Nachbagauer, M.D., Ph.D.**, *VP, Platform and Technology Integration, Development* **Christine Shaw, Ph.D.**, *VP, Portfolio Head, Infectious Disease and Rare* **Jacqueline Miller, M.D.**, *Chief Medical Officer*
Vaccines in early development • CMV (bone marrow transplant) • EBV & EBV Tx • Lyme	**Jacqueline Miller, M.D.**, *Chief Medical Officer*
Coffee Break	
Oncology • Oncology pipeline overview • Intismeran autogene • mRNA-4359 • Early-stage emerging oncology	**Kyle Holen, M.D.**, *SVP, Head of Development, Oncology* **Michelle Brown, M.D., Ph.D.**, *VP, Portfolio Head, Oncology* **Kyle Holen, M.D.**, *SVP, Head of Development, Oncology* ***Rose Loughlin, Ph.D.*** *EVP, Research*
Rare Disease Therapeutics	**Rituparna Das, M.D., Ph.D.**, *VP, Clinical Development Head, Respiratory and Rare*
Conclusion – Looking Forward	**Stéphane Bancel**, *Chief Executive Officer*
General Q&A	**Stéphane Bancel, Jamey Mock, Stephen Hoge, Jacqueline Miller, Kyle Holen, Rose Loughlin**



Commercial vaccine strategy

Stephen Hoge, M.D.
President

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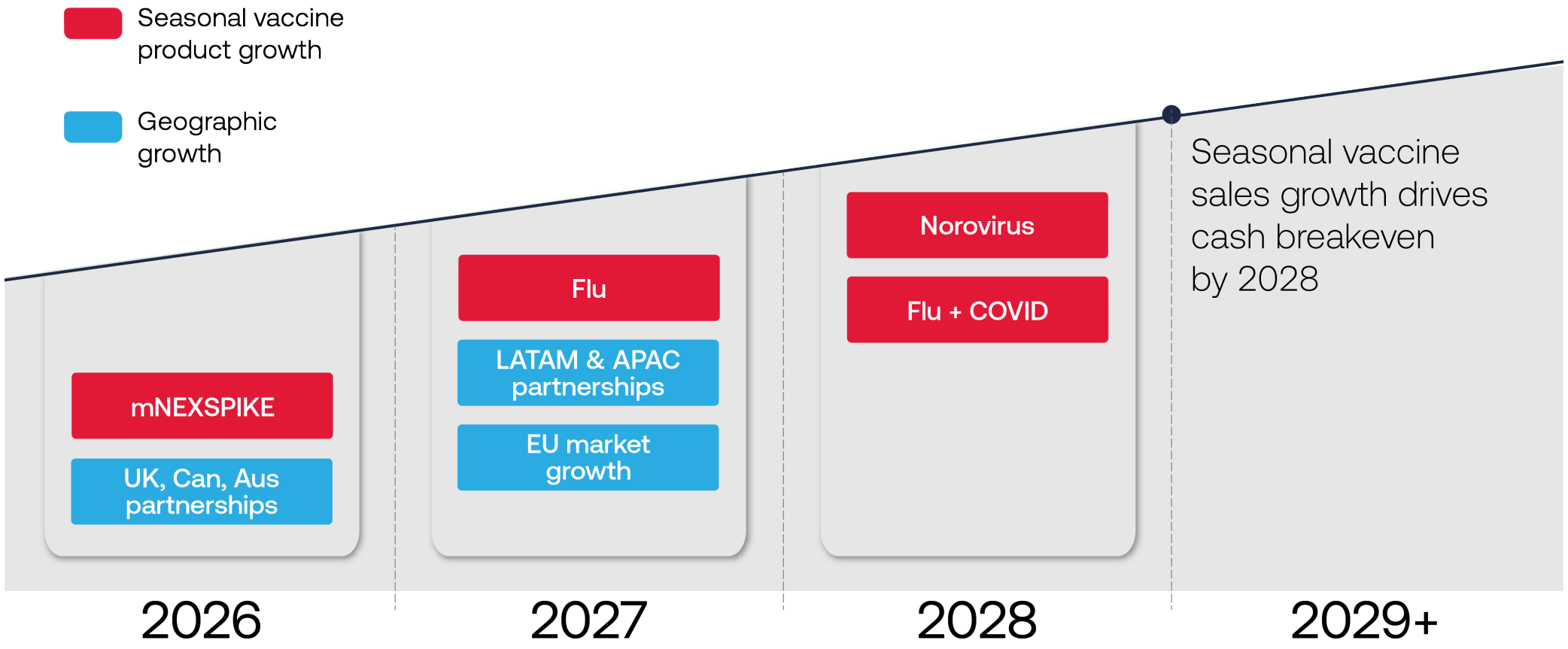
Seasonal vaccines: growth from geographic expansion and new launches drive cash breakeven in 2028



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2028

Norovirus

Flu + COVID

2027

Flu

LATAM & APAC partnerships

EU market entry

2026

mNEXSPIKE

UK, Can, Aus partnerships

2026 growth driver: Annualized impact from UK, Canada, Australia partnerships

Multi-year partnerships providing recurring revenue

UK

- 69M population
- ~$0.2B in revenue 1Q26 for spring booster
- Expect order for fall 2026 season

Canada

- 41M population
- Expect annualized impact from strategic partnership to start in 2026

Australia

- 27M population
- Expect annualized impact from strategic partnership to start in 2026

Partnership features

- Long-term agreements
- R&D investment
- Supports national security & defense
- Onshore manufacturing

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2028

- Norovirus
- Flu + COVID

2027

- Flu
- LATAM & APAC partnerships
- EU market entry

2026

- **mNEXSPIKE**
- UK, Can, Aus partnerships

2026 growth driver: mNEXSPIKE

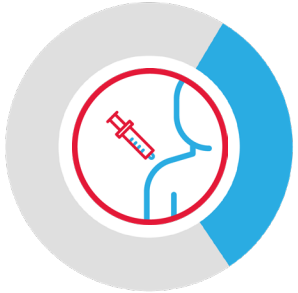
Expect strong uptake to continue in the U.S. and geographic expansion into new markets

Solid launch-year performance

U.S. mNEXSPIKE 25/26 season-to-date share of total retail market[1]

23% of total retail market

U.S. mNEXSPIKE 25/26 season-to-date share of total 65+ retail market[1]



32% of 65+ retail market

1. Based on information licensed from IQVIA: IQVIA NPA Extended Insights for the periods 08/29/2025-11/07/2025, reflecting estimates of real-world activity. All rights reserved.

What's next in 2026

Continue to drive uptake

- U.S.

Targeting launches in:

- Europe
- Canada
- Australia
- Japan
- Taiwan

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2028

- Norovirus
- Flu + COVID

2027

- Flu
- LATAM & APAC partnerships
- EU market entry

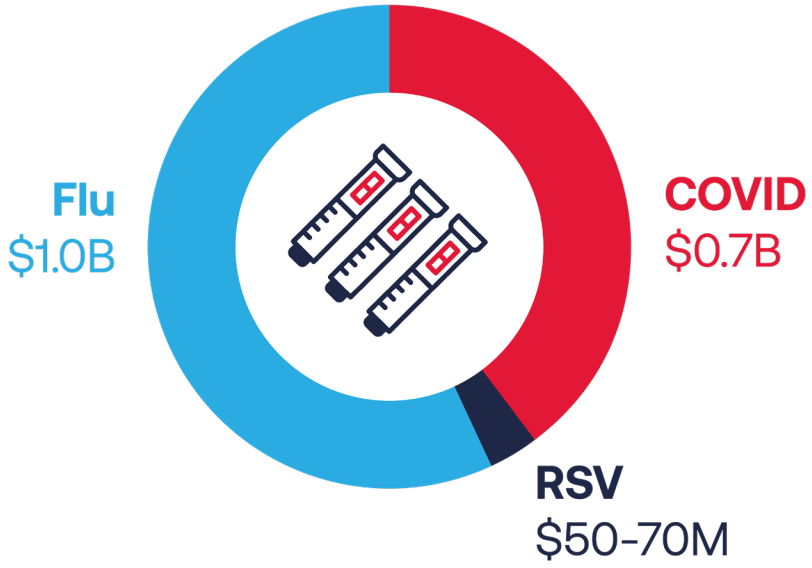
2026

- mNEXSPIKE
- UK, Can, Aus partnerships

2027 growth driver: EU opportunity

Europe represents a significant market for respiratory virus vaccines, in which we will potentially have 5 approved products by 2027/28

2024 total sales for respiratory vaccines in the EU



Total EU respiratory vaccine sales in 2024 were $1.75B; Moderna 2024 EU sales were <$0.1B

Source: Flu – reported company sales and internal estimates; COVID – publicly reported vaccination rates and internal estimates; RSV – reported company sales; IQVIA MIDAS 2024 data (reflecting estimates of real-world activity; all rights reserved); and internal estimates.

Share gain opportunities

- Competitor COVID contract lapses year-end 2026
- RSV approved, expect reimbursement to be established
- mNEXSPIKE, combo flu + COVID, and flu approvals expected

2028

Norovirus

Flu + COVID

2027

Flu

LATAM & APAC partnerships

EU market entry

2026

mNEXSPIKE

UK, Can, Aus partnerships

2027 growth driver: Targeting long-term partnerships in Latin America and Asia-Pacific

First mRNA PDP in Brazil

Productive Development Partnership (PDP) approved by the government of Brazil on September 5, 2025

2025/2026 COVID strain update submitted to Brazilian regulator

Exploring similar partnerships in Latin America and Asia-Pacific

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2028

Norovirus

Flu + COVID

2027

Flu

LATAM & APAC partnerships

EU market entry

2026

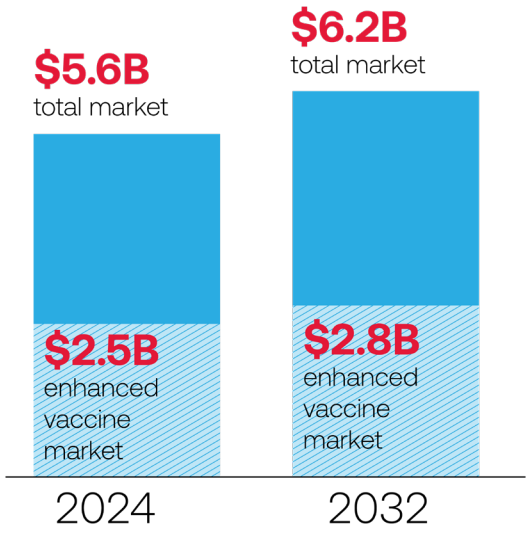
mNEXSPIKE

UK, Can, Aus partnerships

2027 growth driver: Flu (mRNA-1010)

Expect to enter global flu vaccine market in the 2027/28 season

Total estimated global flu vaccine market growth[1]



Global flu market expected to grow +11% from 2024 to 2032
Opportunity for mRNA-1010 to enter large established flu market

Expect to file with regulators by January 2026

- U.S.
- EU
- Canada
- Australia

1. Evaluate Pharma, Sanofi market analysis, and internal estimates

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2028

- Norovirus
- Flu + COVID

2027

- Flu
- LATAM & APAC partnerships
- EU market entry

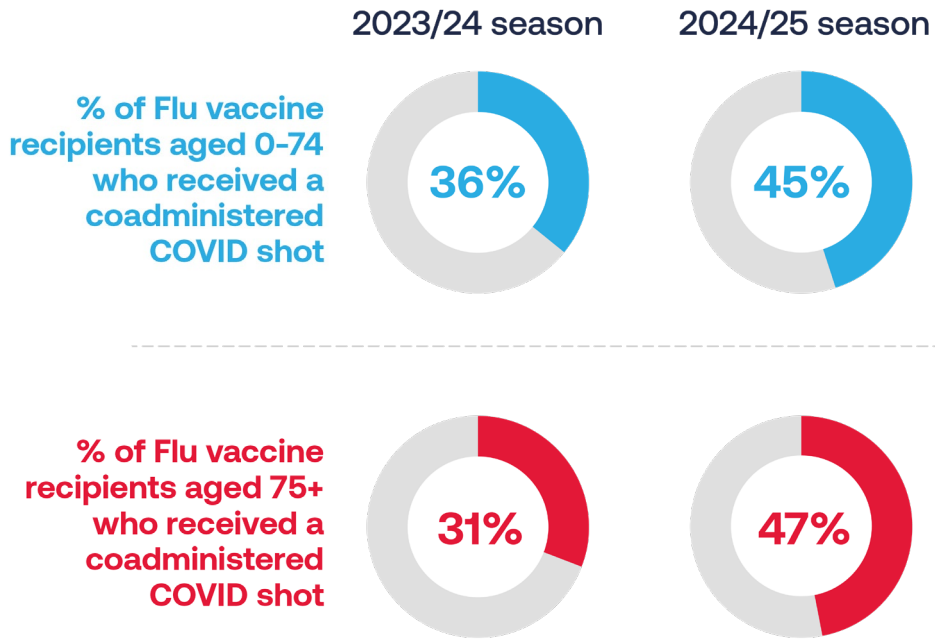
2026

- mNEXSPIKE
- UK, Can, Aus partnerships

2028 growth driver: Flu + COVID combo (mRNA-1083)

First-to-market combination flu + COVID vaccine could benefit from coadministration trends in seasonal vaccination behavior

Coadministration of flu and COVID vaccines increased in the 2024/2025 season over the 2023/2024 season in the U.S. retail channel[1]



Filing status of mRNA-1083

- Filing under review with the European Medicines Agency (EMA)
- Submitted for approval to Health Canada
- Awaiting further guidance from FDA on refiling in the U.S.

1. Based on information licensed from IQVIA: Anonymized U.S. Retail Patient-Level Data for the periods 07/01/2023-12/31/2023 and 07/01/2024-12/31/2024, reflecting estimates of real-world activity.

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2028

Norovirus

Flu + COVID

2027

Flu

LATAM & APAC partnerships

EU market entry

2026

mNEXSPIKE

UK, Can, Aus partnerships

2028 growth driver: Norovirus (mRNA-1403)

First-to-market opportunity with a novel seasonal vaccine

Target population

155 million people

Market segments

- Older adults
- Occupational risks
- Health risks

Norovirus opportunity in the U.S.

Channels

Delivered mainly through retail pharmacies using existing infrastructure

Seasonality

Peak Norovirus season is typically Nov. – Apr., overlapping with respiratory viruses

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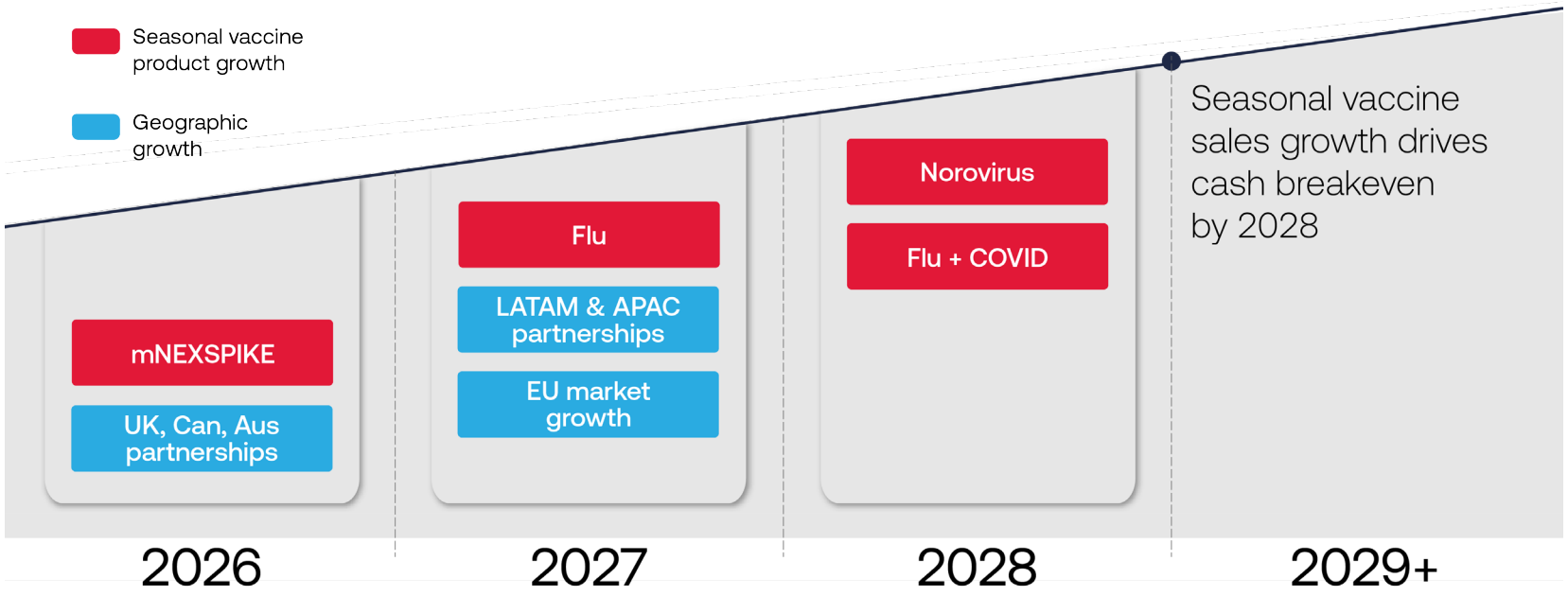
Our existing commercial infrastructure supports seasonal vaccine growth drivers



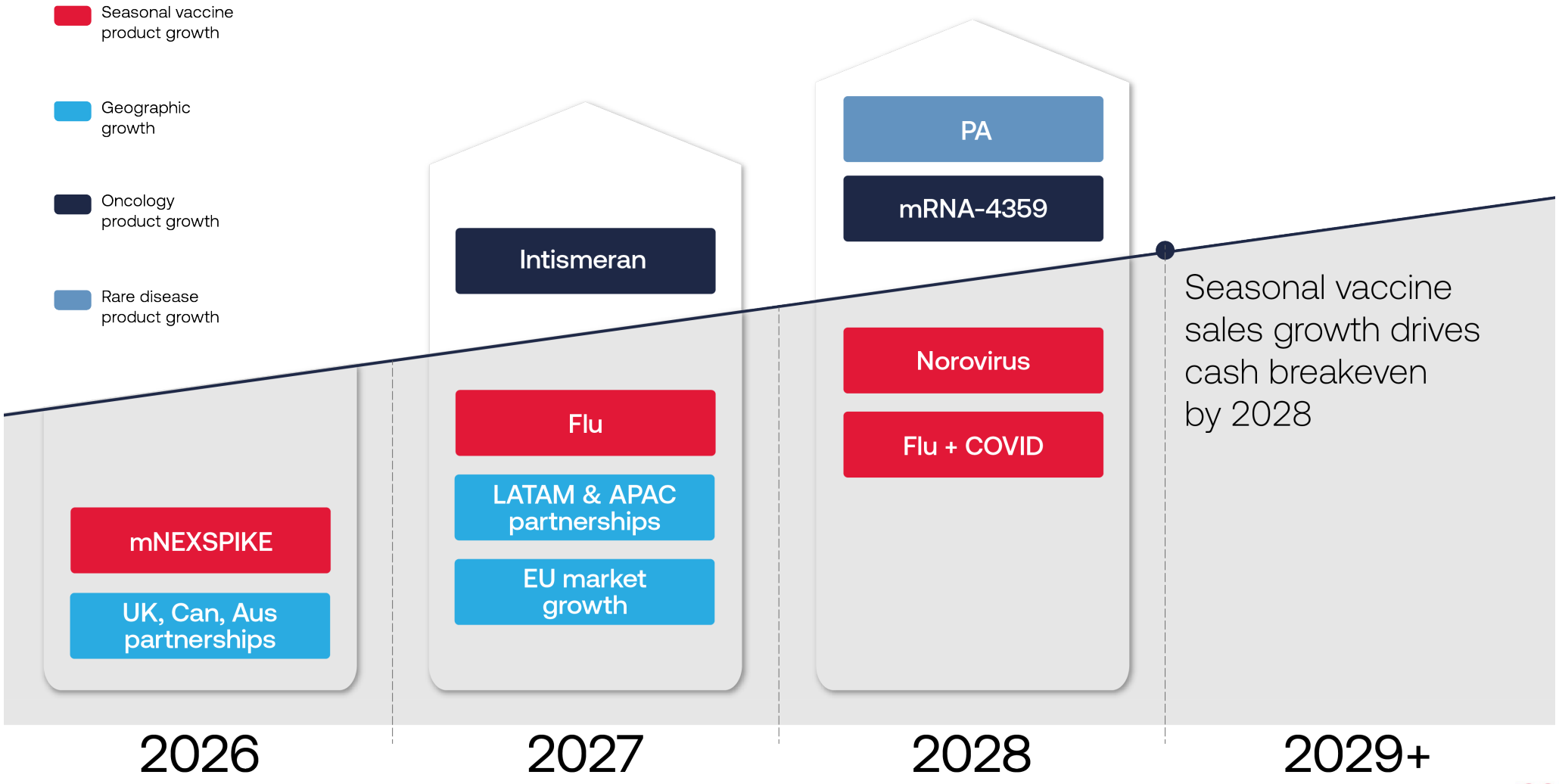
A focused Moderna U.S. commercial team engages the same customers across our seasonal portfolio

- Retail
- Government
- IDNs

Commercial teams supporting UK, Canada, and Australia partnerships are built out; partnerships provide revenue visibility

EU commercial infrastructure is in place and targeted investments will be made as needed

Investments in late-stage oncology and rare disease programs set the stage for additional growth in 2027-2028



Early-stage investments begin to mature in 2029 and beyond

Rare disease therapeutics

- MMA

Oncology therapeutics

- mRNA-4106
- mRNA-2808
- mRNA-4203

Early-stage vaccines

- EBV Tx
- EBV vaccine
- Lyme
- CMV transplant

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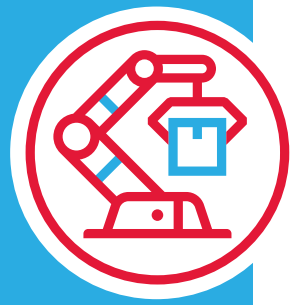

Global production network

Jerh Collins
Chief Technical Operations
and Quality Officer

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Our global manufacturing network: delivering products for multi-year strategic partnerships and ready for new launches

Optimization of global manufacturing network

- Added 3 Moderna-built and managed facilities in the UK, Canada and Australia
- Exited 8 contract manufacturers since 2023
- Announced new drug product facility in the U.S.

Shows Moderna sites and partner CMO; excludes contract manufacturing partners dedicated to in country manufacturing for strategic partnerships

Norwood: Enabling scalable, end-to-end, cost-efficient production

Norwood
UNITED STATES

Continuously improving manufacturing efficiency

Incorporates **automation, robotics, and AI** to increase cost efficiency and reduce waste

New fill/finish capability gives us end-to-end control and flexibility with greater speed

- Adding 2 filling lines + 1 high-speed packaging line
- 100M pre-filled syringe units/year
- Uses existing space → **low incremental capital investment** and high workforce synergies
- Supports **lower cost per dose** and stronger U.S. supply reliability
- Site is expected to be operational and **supplying product to the U.S. in 2027**

Three new global sites enable local access to mRNA medicines and drive revenue diversification

Laval
CANADA

Harwell
UNITED KINGDOM

Clayton
AUSTRALIA

Strategic Partnerships

- Moderna-built and managed facilities dedicated to domestic supply under **long-term agreements**
- Reinforce Moderna's mRNA manufacturing leadership
- Position company for geographically diverse, cost-optimized growth

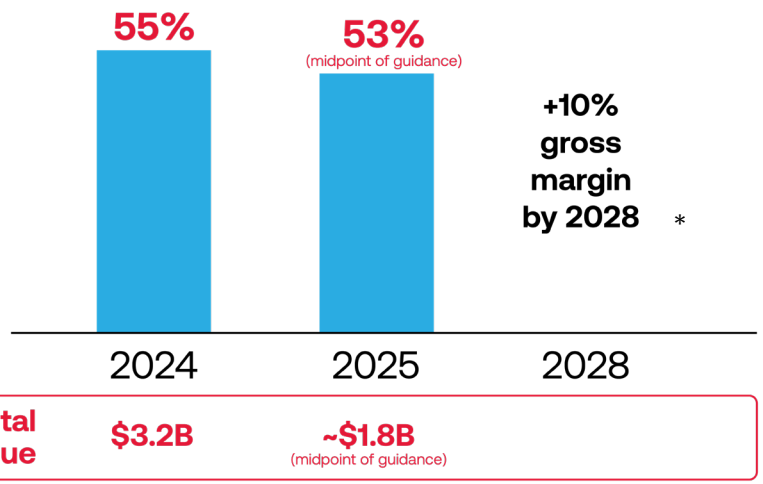
Operational Excellence

- **Margins consistent with U.S.** operations; added capacity supports **long-term cost optimization**
- Focused on **optimizing utilization** and **enhancing productivity** through digital tools and lean operations

Shows Moderna sites only; excludes contract manufacturing partners

Expect manufacturing efficiency to improve gross margin by 10 percentage points over the next three years

10 percentage point gross margin improvement*



*Gross margin = (Total revenue-cost of sales)/Total revenue

Margin Expansion Drivers

Volume

- Leverage volume from geographic and product growth drivers through facilities

Procurement & productivity

- Internal fill finish capacity
- Supplier pricing negotiations
- Automation and robotics

Waste reduction

- Expected inventory write-offs down ~30% from 2024 to 2025
- Expected CMO winddown/unutilized down ~75% from 2024 to 2025

We will continue to leverage digital tools and AI to enhance these drivers

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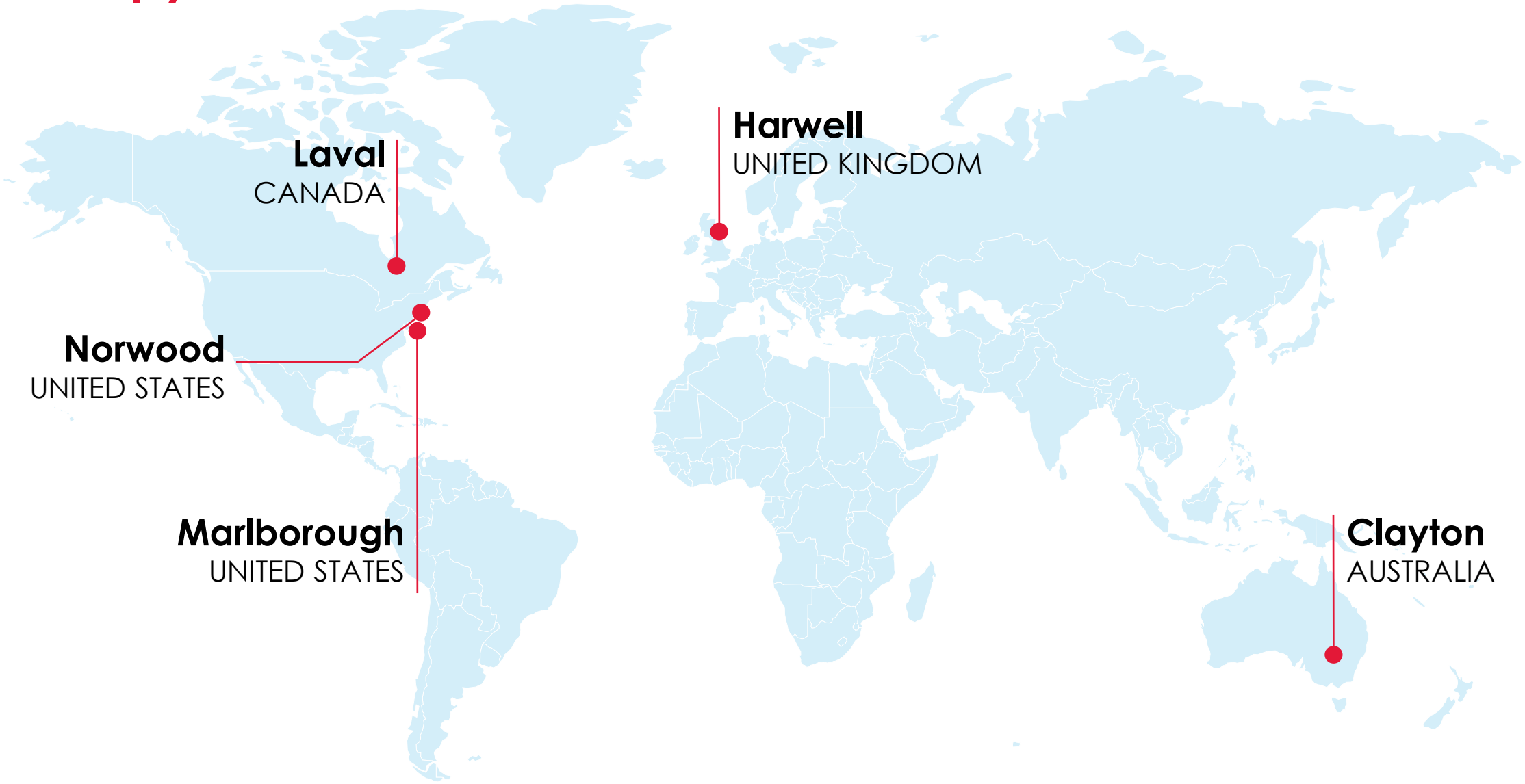
Marlborough: Purpose-built for individualized neoantigen therapy, intismeran



Marlborough: Enabling intismeran and the next wave of product innovation

Marlborough
UNITED STATES

Facility Design

- Built for **end-to-end operations** with **speed, scalability, and flexibility**
- Designed with **expandable capacity**

Innovation & Efficiency

- Incorporates **digital automation, robotics, and smart skid design**
- Enables **lower production costs** and greater operational efficiency

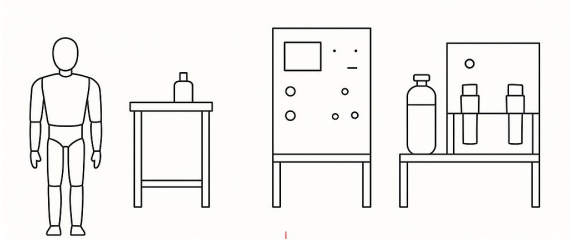
Readiness & Timeline

- Began **clinical batch supply in Sept 2025**
- On track for **commercial launch**

Shows Moderna sites only; excludes contract manufacturing partners

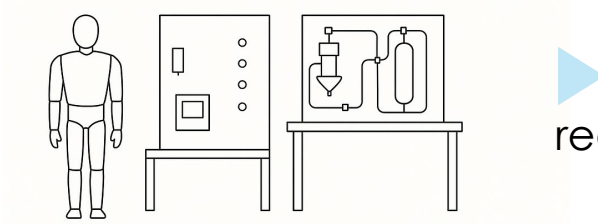
We are methodically right-sizing the intismeran manufacturing process to improve turnaround time and reduce costs

Initial configuration	Current configuration	Future configuration



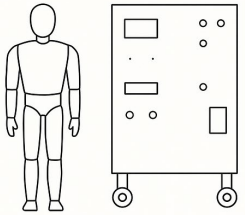
Equipment footprint
~120 sq ft

3X reduction



Equipment footprint
~40 sq ft

3X reduction



Equipment footprint
~13 sq ft

These intentional design changes **minimize material waste and labor requirements**, further improving turnaround time and costs

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Placeholder for video featuring
Moderna's Marlborough facility

Financial review

Jamey Mock
Chief Financial Officer

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Financial framework

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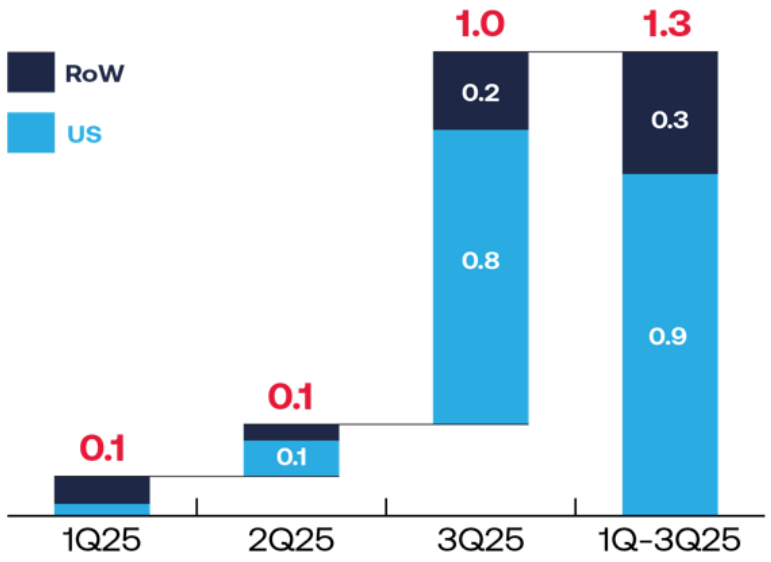
3Q25 review

3Q25 revenue of ~$1.0B, 1Q-3Q total of ~$1.3B

Numbers may not add due to rounding

Revenue through 3Q25

in billions



4Q and FY 2025 outlook

	Expected 4Q revenue	Total expected FY 2025 revenue
U.S.	$0.1 – 0.4B	$1.0 – 1.3B
RoW	$0.3 – 0.4B	$0.6 – 0.7B
Total	**$0.3 – 0.7B**	**$1.6 – 2.0B**

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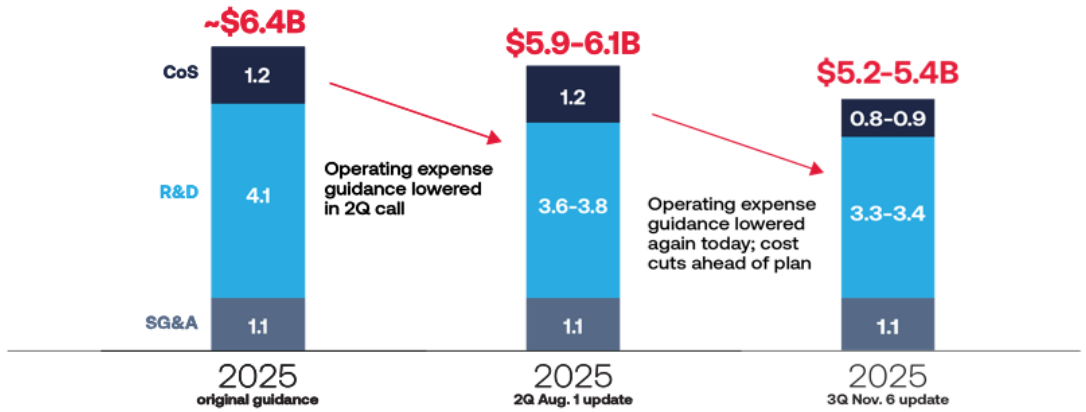
3Q25 review

2025 GAAP operating expense ahead of plan by $1.1B

GAAP costs

in billions



Non-cash items in chart above include:			
Stock-based compensation	$0.6B estimate	$0.6B estimate	$0.5B estimate
Depreciation & amortization	$0.3B estimate	$0.3B estimate	$0.2B estimate
Cash costs at midpoint[1]	**~$5.5B** estimate	**~$5.1B** estimate	**~$4.6B** estimate

[1]Cash costs = GAAP costs - (stock-based compensation & depreciation & amortization)

Will update improvements to 2026 and 2027 cost framework at Analyst Day

Continue to target cash breakeven in 2028

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Numbers may not add due to rounding

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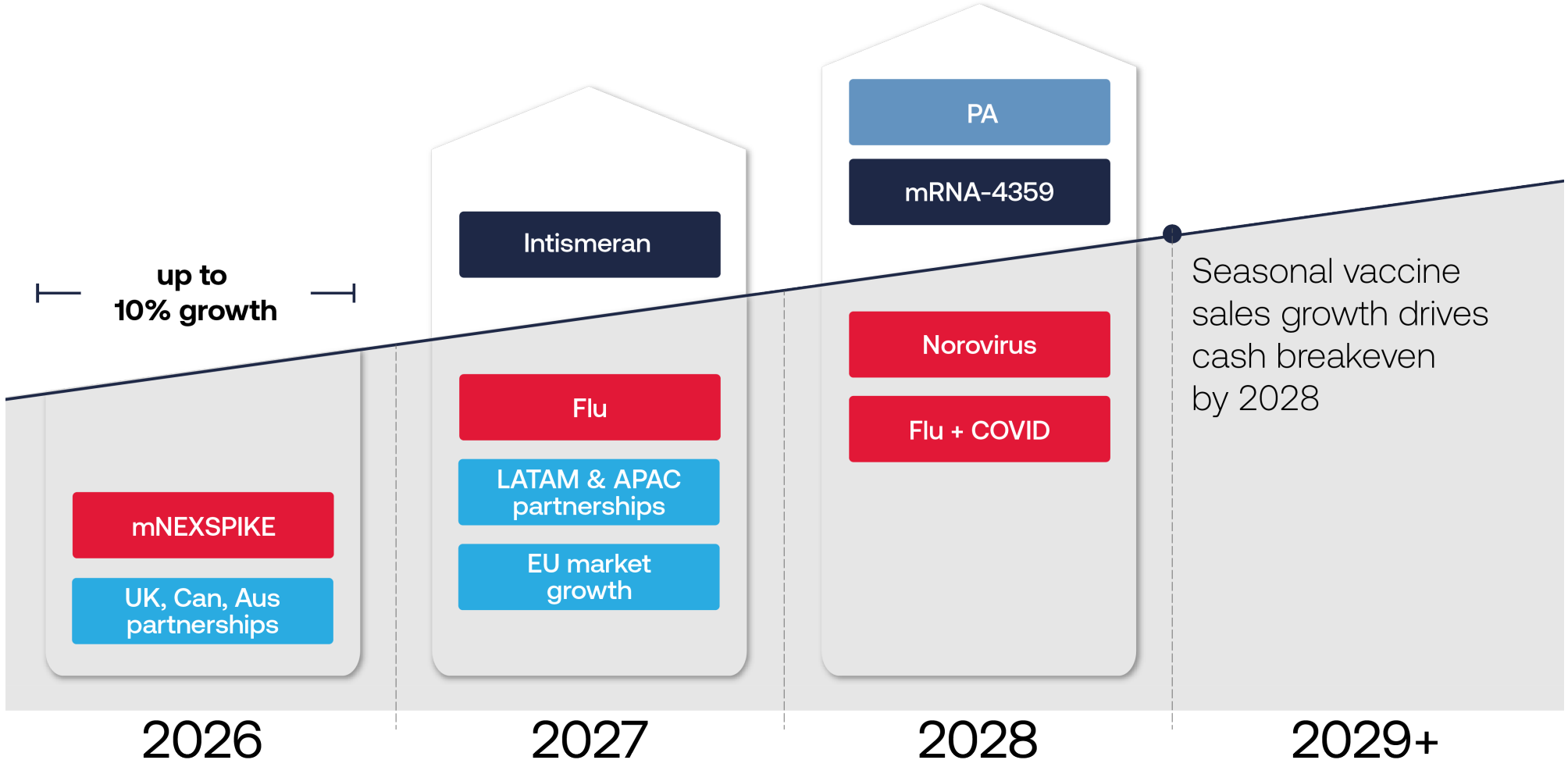
Numerous opportunities to drive sustainable growth; expecting up to 10% growth in 2026



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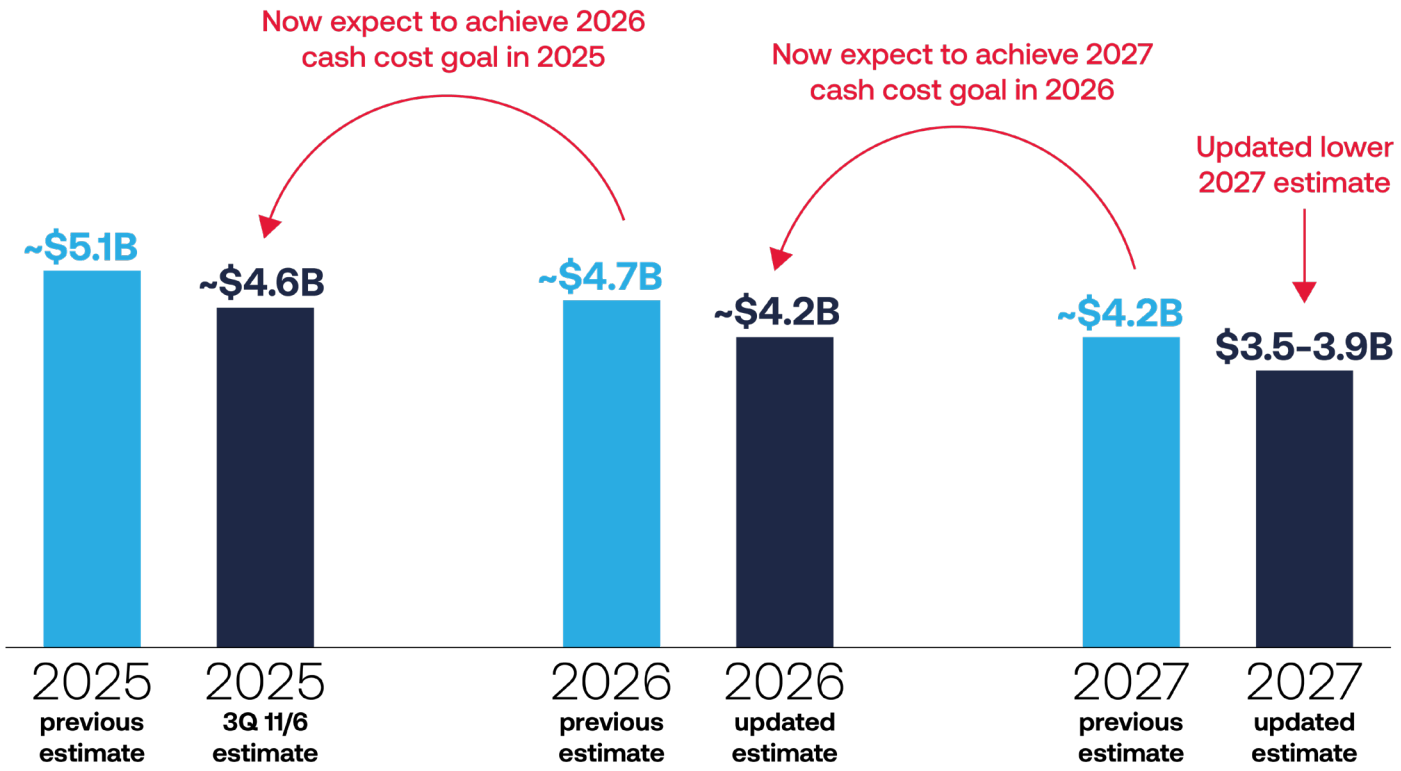
Improving previous cash cost guidance

Cash costs[1,2]



GAAP cost estimates	~$6.0B	~$5.3B	$5.5B	~$4.9B	~$4.9B	$4.2-4.6B

[1]Cash costs = GAAP costs - (stock-based compensation & depreciation & amortization); [2]Prior guidance ranges were listed as 2025: GAAP $5.9-6.1B, cash costs at midpoint ($5.1B); 2026: GAAP $5.4-5.7B, cash costs at midpoint ($4.7B); 2027: GAAP $4.7-$5.0B, cash costs at midpoint (~$4.2B)

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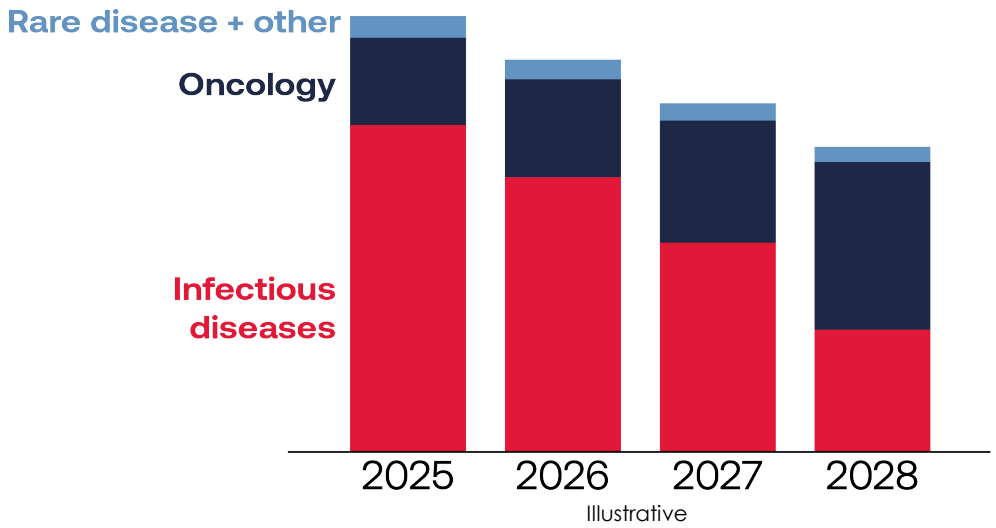
Evolution of our R&D investments

Large infectious disease investments concluding by 2028; increasing investment allocation into oncology



Infectious diseases

- Phase 3 Norovirus trial ongoing; starting additional season
- Post-marketing commitments for COVID vaccines in 2026/2027
- Phase 3 respiratory studies concluding by 2028

Oncology

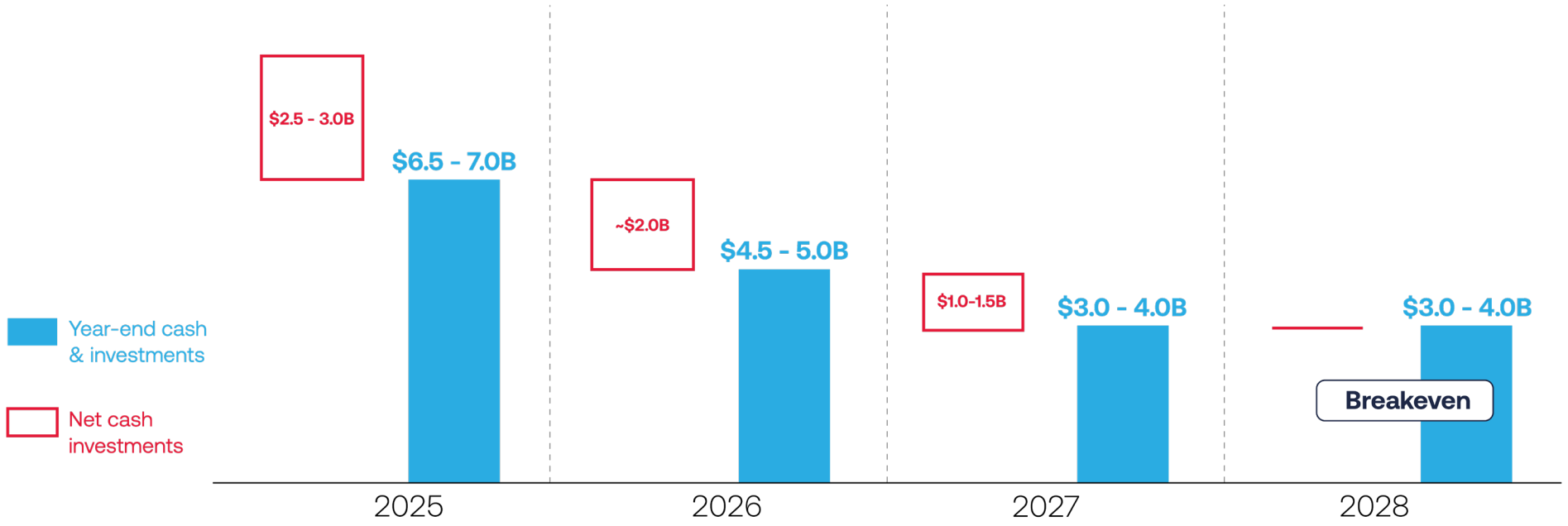
- Deliver on 7 late-stage intismeran studies
- Execute mRNA-4359 development plan
- Invest in early-stage oncology programs

Rare disease + other

- Execute registrational studies in rare diseases
- Invest in early-stage autoimmune therapeutics

Our balance sheet sufficiently funds our investments through cash breakeven in 2028

Annual year-end cash and investments through breakeven



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Enhancing strong balance sheet with opportunistic, attractive credit facility ($1.5B in non-dilutive financing)

Rationale

- Flexibility to manage uncertainties and future opportunities
- Strong capital markets present an opportunity to raise capital at favorable rates
- Attractive and flexible loan terms
  - Low-cost capital
  - Non-dilutive on a share basis
  - Optional drawdown of DDTL[1] until 2028
  - Minimal prepayment penalty
  - Strong health care lender in Ares team

Key loan terms

- **Amount:** $1.5B facility ($0.6B at close, $0.9B as DDTL)
- **Maturity:** 5 years from close
- **Interest rate:** SOFR + 550bps
- **Amortization:** None (Interest only)

Permitted transactions[2]

- Licensing & collaboration agreements
- Royalty monetization
- Share repurchase

Financial covenants

- Over $5B market cap: no financial covenants
- Under $5B market cap:
  - Minimum liquidity with ≤$1B drawn: $500M
  - Minimum liquidity with>$1B drawn: $750M

1. Delayed draw term loan
2. Subject to terms of loan agreement

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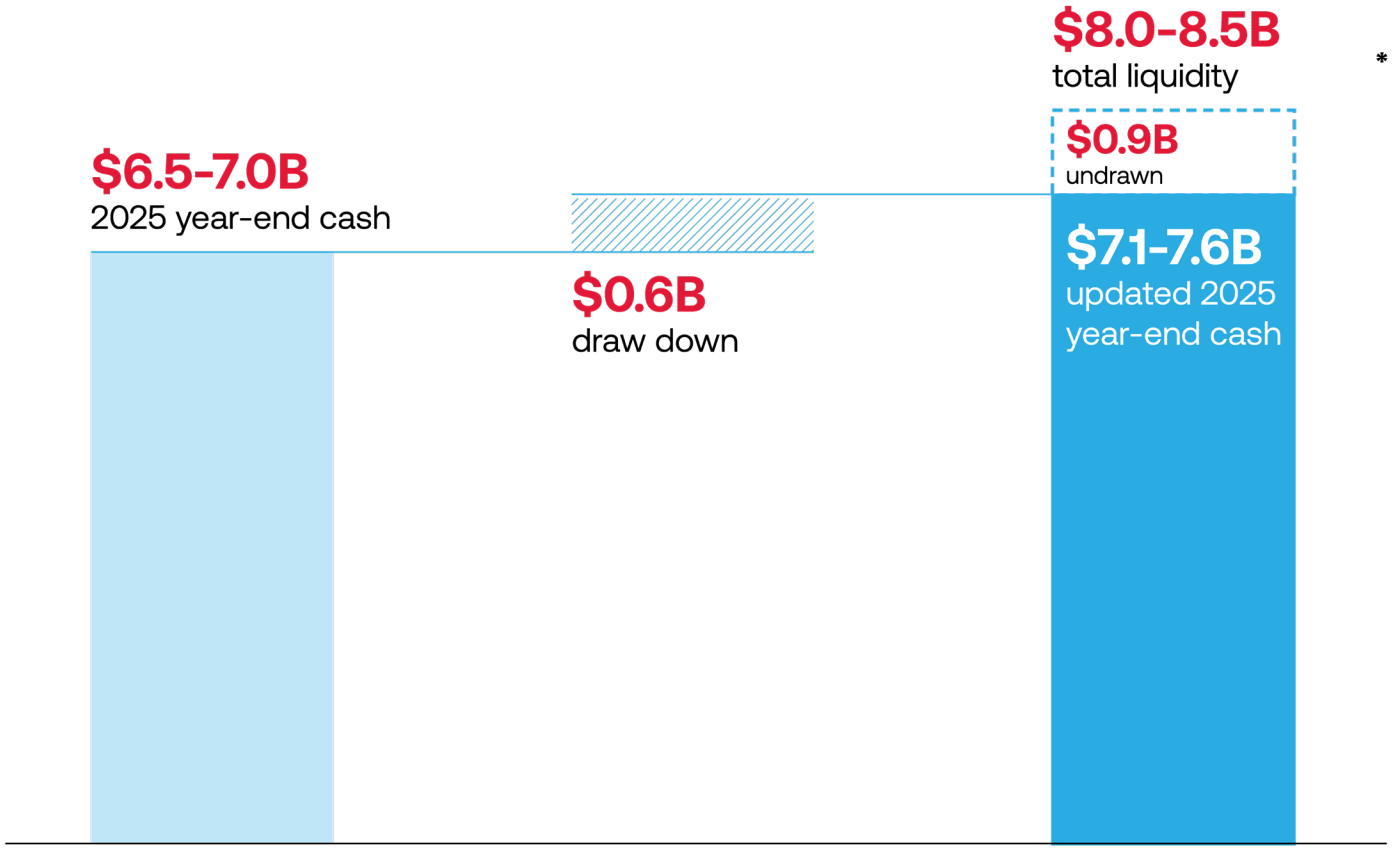
Confident in strong financial framework with enhanced liquidity

2025 year-end cash and investment balance increased by initial draw from credit facility



*Total liquidity = cash + investments + undrawn amount from credit facility

Current plan provides $4.4-5.4B liquidity at year-end 2027 heading into breakeven year in 2028

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Key takeaways

Poised to deliver up to 10% revenue growth in 2026
with multiple growth opportunities in 2027 and beyond

Driving gross margin expansion over coming years
(10%+ over 3 years)

Evolving R&D investments to diversify further
into oncology

Reducing 2027 projected cash costs
to $3.5-3.9 billion and targeting 2028 cash breakeven

Confident in strong financial framework
with enhanced liquidity

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Seasonal vaccines portfolio

Jacqueline Miller, M.D.
Chief Medical Officer

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Seasonal vaccines pipeline

Seasonal virus vaccines

			Preclinical	Ph 1	Ph 2	Ph 3	Commercial
Respiratory viruses Adults	**COVID-19 vaccine**	Spikevax®					
	COVID-19 vaccine	mNEXSPIKE®					
	Flu vaccine	mRNA-1010					
	RSV vaccine	mRESVIA®					
	Flu + COVID vaccine	mRNA-1083					
	Pandemic Flu	mRNA-1018					
	RSV + hMPV vaccine	mRNA-1365					
Respiratory viruses Adolescents & Pediatrics	**COVID-19 vaccine**	Spikevax®					
	RSV vaccine	mRNA-1345					
Enteric viruses	**Norovirus vaccines**	mRNA-1403					
		mRNA-1405					

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COVID-19

Darin Edwards, Ph.D.
Executive Director, Program Leader, Infectious Disease

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mRNA-1283 pivotal Phase 3 trial design

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

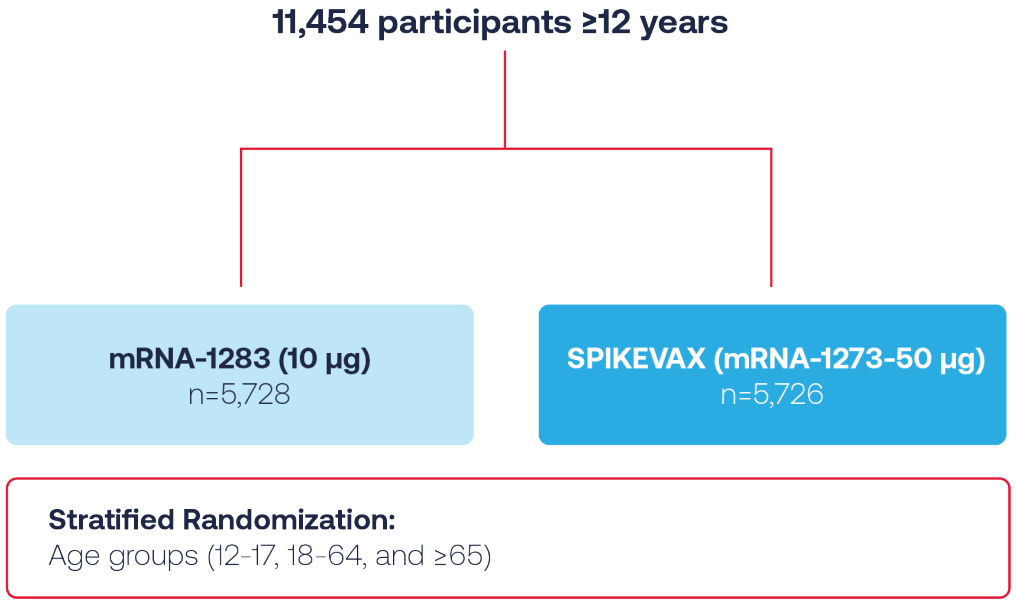
Number of participants dosed
11,454 medically stable adults ≥ 12 years old

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

Bivalent vaccine encoding the ancestral and BA.4/5

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

Site location
US, UK and Canada



Demographics and Baseline Characteristics Balanced Between Groups

Study 301 - Safety Set

	mRNA-1283 (10 µg) N = 5706	SPIKEVAX (50 µg) N = 5711
Mean age, years (range)	**51.1 (12, 96)**	**51.2 (12, 90)**
Median age, years	**56**	**55**
Age subgroup, % (n)		
12-17 years	**8.7%** (497)	**8.7%** (495)
18-64 years	**62.7%** (3575)	**62.6%** (3576)
≥65 years	**28.6%** (1634)	**28.7%** (1640)
Race/Ethnicity, % (n)		
White	**81.8%** (4670)	**82.5%** (4711)
Black or African American	**11.2%** (640)	**11.1%** (635)
Asian	**3.9%** (225)	**3.2%** (183)
Hispanic or Latino	**13.5%** (769)	**13.0%** (741)
≥1 pre-existing COVID-19 comorbidity (CDC definition)	**46.0%** (2626)	**46.6%** (2664)

Race/ethnicity generally representative of US population

https://www.cdc.gov/covid/risk-factors/index.html;; https://www.census.gov/quickfacts/fact/table/US/RHI225223

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Prior SARS-CoV-2 Infection and Time Since Last COVID-19 Vaccination Balanced Between Groups

Study 301 - Safety Set

Eligibility criteria

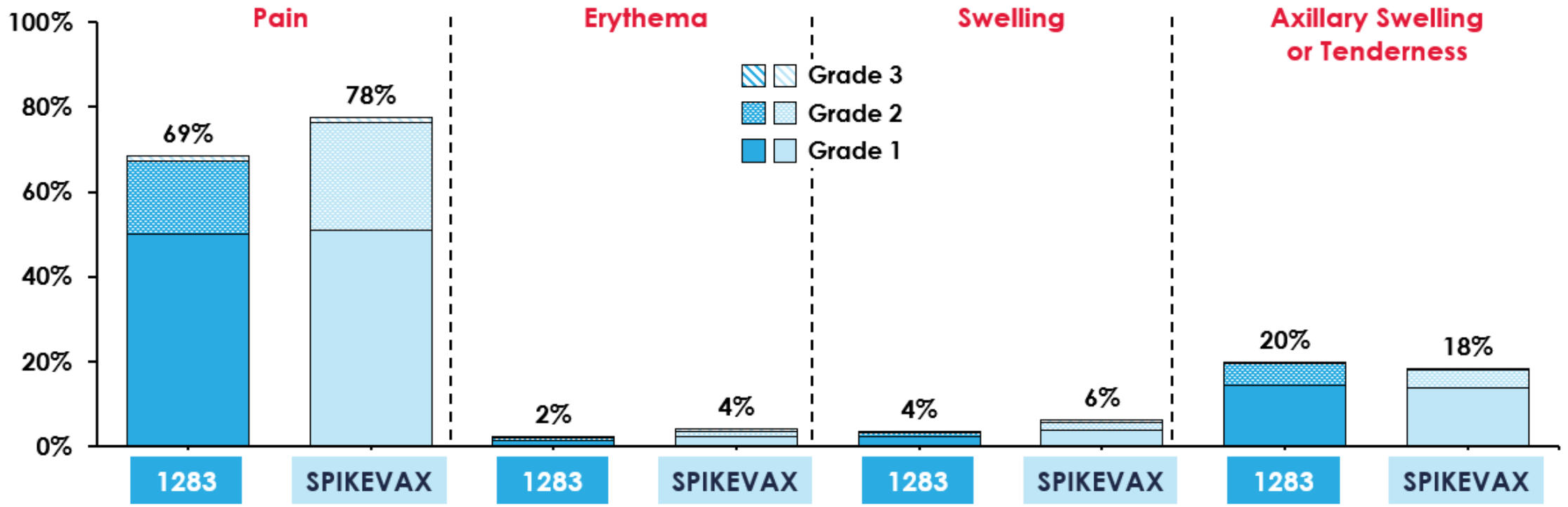
- All study participants previously received primary series of COVID-19 vaccine
- Adults ≥18 years received ≥1 dose beyond primary series

	mRNA-1283 (10 µg) N = 5706	SPIKEVAX (50 µg) N = 5711
Prior SARS-CoV-2 Infection[1]	**73.8%**	**74.8%**
Months since last COVID-19 vaccination, median (Q1, Q3)	**9.8** (7.6, 16.9)	**9.8** (7.7, 16.7)

1. Evidence of SARS-CoV-2 infection pre-study vaccination (defined by a positive RT-PCR test, and/or a positive serology test based on binding antibody specific to SARS-CoV-2 nucleocapsid)
2. Q - quartile

Solicited Local Adverse Reactions within 7 Days of Vaccination with mRNA-1283 and SPIKEVAX

Study 301 – Solicited Safety Set

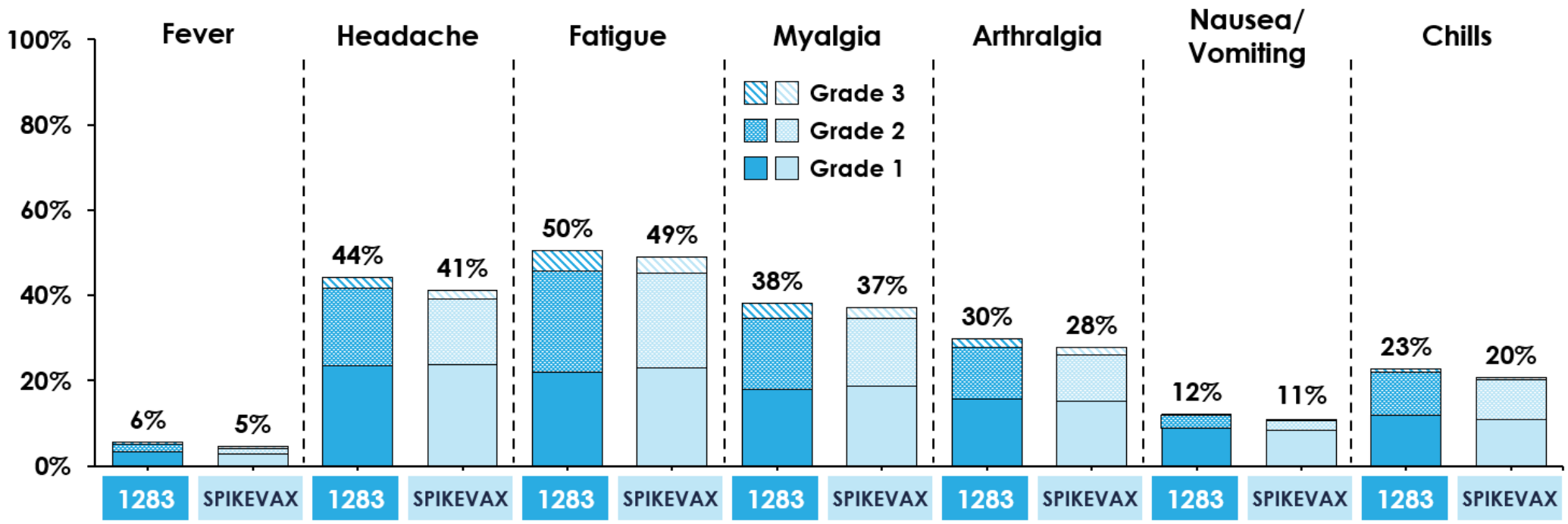


- Pain at the injection site was most frequently observed solicited local adverse reaction for both groups
- 1 – 2 days median duration for local adverse reactions

Feb 23, 2024 data cutoff; mRNA-1283, N = 5702; mRNA-1273, N = 5706; no grade 4 reactions

Solicited Systemic Adverse Reactions within 7 Days of Vaccination with mRNA-1283 and SPIKEVAX

Study 301 – Solicited Safety Set



- Fatigue, headache, and myalgia most frequently observed solicited systemic adverse reactions for both groups
- 1-2 days median duration for systemic adverse reactions

Feb 23, 2024 data cutoff; mRNA-1283, N = 5702; mRNA-1273, N = 5706. One participant in the mRNA-1273 group had a grade 4 fever. No grade 4 reactions.

COVID-19 Case Definition and Surveillance

CDC COVID-19 Definition[1]

- Virologic confirmation of SARS-CoV-2 infection via PCR
- Presence of ≥1 symptom consistent with COVID-19 within 14 days of positive PCR
  - Fever or chills
  - Cough
  - Shortness of breath or difficulty breathing
  - Fatigue
  - Muscle or body ache
  - Headache
  - Nausea or vomiting
  - Loss of taste or smell
  - Sore throat
  - Congestion or runny nose
  - Diarrhea

COVID-19 Surveillance

- Biweekly symptom surveillance conducted using an electronic diary prompt
  - Participants with symptoms seen for clinical evaluation and collection of respiratory samples for SARS-CoV-2 PCR

1. https://ndc.services.cdc.gov/case-definitions/coronavirus-disease-2019-covid-19/

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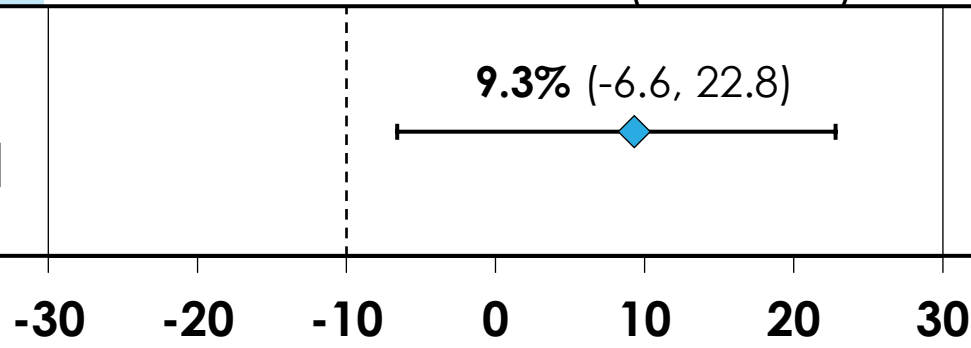
Prespecified Success Criteria Met for Relative Vaccine Efficacy of mRNA-1283 vs SPIKEVAX

Per-Protocol Set for Efficacy (Median 8 Months)

Participants with COVID-19, % [n/N]	mRNA-1283 (10 µg)	SPIKEVAX (50 µg)	Relative Vaccine Efficacy Based on Hazard Ratio (99.4% CI)[1,2]	P-value[3]
Primary rVE Objective (≥12 year)	**9.9%** [560/5679]	**10.8%** [617/5687]	**9.3%** (-6.6, 22.8)	**0.0005**



Noninferiority success criteria met

- Lower bound of two-sided 99.4% (alpha-adjusted) CI of rVE > -10% (1-sided alpha spending: 0.0028)

Based on CDC COVID-19 definition

1 rVE =1-hazard ratio, hazard ratio estimated using a stratified Cox proportional hazard model (stratified by age group at randomization) and with treatment group as a fixed effect.

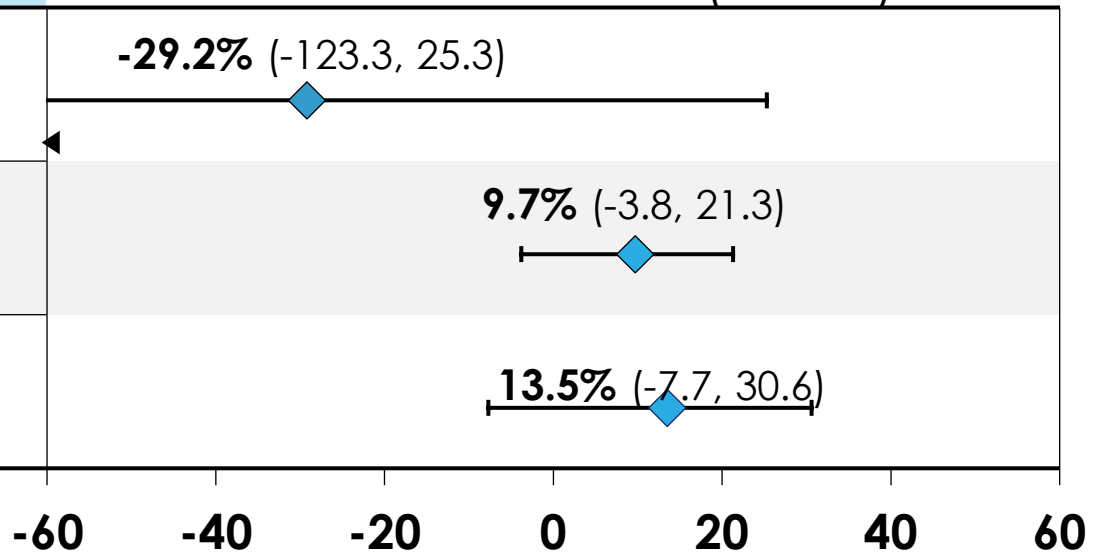
2 Alpha-adjusted 2-sided (99.4%) CI was calculated using the Lan-DeMets O'Brien-Fleming Spending function (nominal one-sided alpha of 0.0028)

3 P-value based on the stratified Cox proportional hazard model to test the null hypothesis log (hazard ratio)>=log(1.1)

Relative Vaccine Efficacy of mRNA-1283 vs SPIKEVAX in Participants by Age

COVID-19 Events[1] through 31 Jan 2024 – Per-Protocol Set for Efficacy

Participants with COVID-19, % [n/N]	mRNA-1283 (10 µg)	SPIKEVAX (50 µg)	Relative Vaccine Efficacy Based on Hazard Ratio (95% CI)[1,2]
12-17 Years	**5.9%** [29/491]	**4.7%** [23/490]	**-29.2%** (-123.3, 25.3)
18-64 Years	**10.7%** [382/3558]	**11.8%** [422/3562]	**9.7%** (-3.8, 21.3)
≥ 65 Years	**9.1%** [149/1630]	**10.5%** [172/1635]	**13.5%** (-7.7, 30.6)



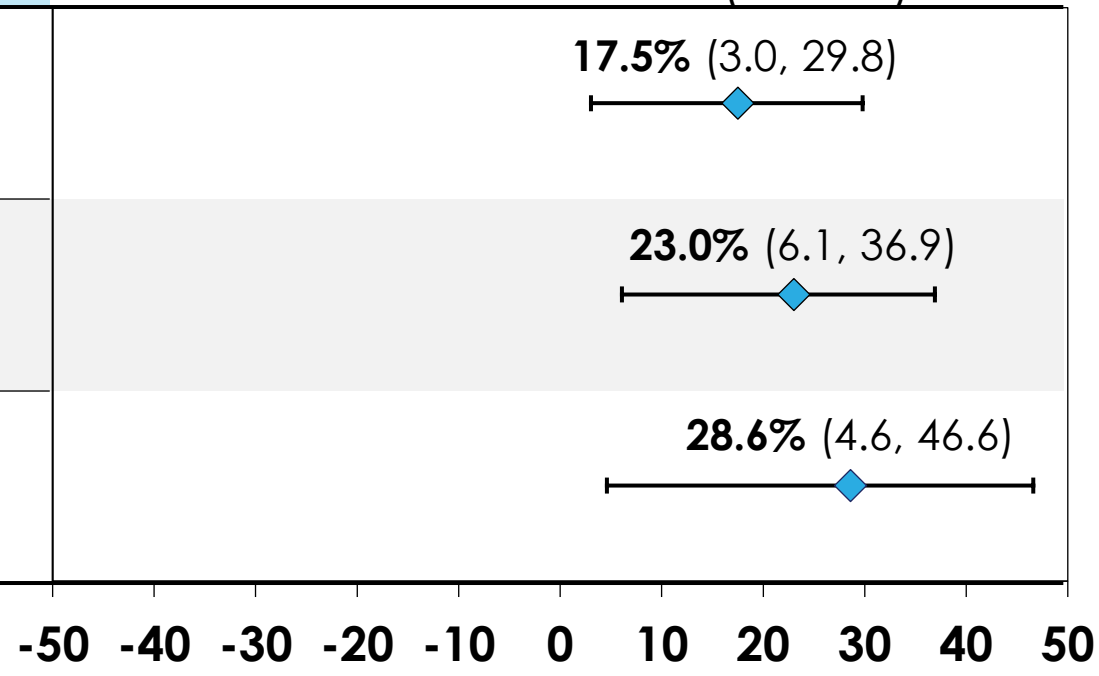
- Highest relative vaccine efficacy in adults ≥65 years
- Limited number of COVID-19 cases in 12-17-year-olds results in imprecise relative vaccine efficacy estimate

1.Based on CDC COVID-19 definition; 2. Posthoc analysis of RVE in ≥50-year-olds (3399 received mRNA-1283, 3431 received mRNA-1273);
rVE – relative vaccine efficacy = 1-hazard ratio, hazard ratio was estimated using a Cox proportional hazard model and with treatment group as a fixed effect.

Relative vaccine efficacy favorable for mRNA-1283 for individuals with comorbidities and older adults

***Post Hoc* Analysis – Based on CDC Definition for COVID-19 Risk[1]**

Participants with COVID-19, % [n/N]	mRNA-1283 (10 µg)	SPIKEVAX (50 µg)	Relative Vaccine Efficacy Based on Hazard Ratio (95% CI)[1]
≥ 1 comorbidities	**10.2%** [267/2617]	**12.4%** [329/2658]	**17.5%** (3.0, 29.8)
And ≥ 50 Years	**9.6%** [169/1755]	**12.4%** [228/1833]	**23.0%** (6.1, 36.9)
And ≥ 65 years	**8.5%** [78/913]	**11.8%** [110/929]	**28.6%** (4.6, 46.6)



1. https://www.cdc.gov/covid/risk-factors/index.html

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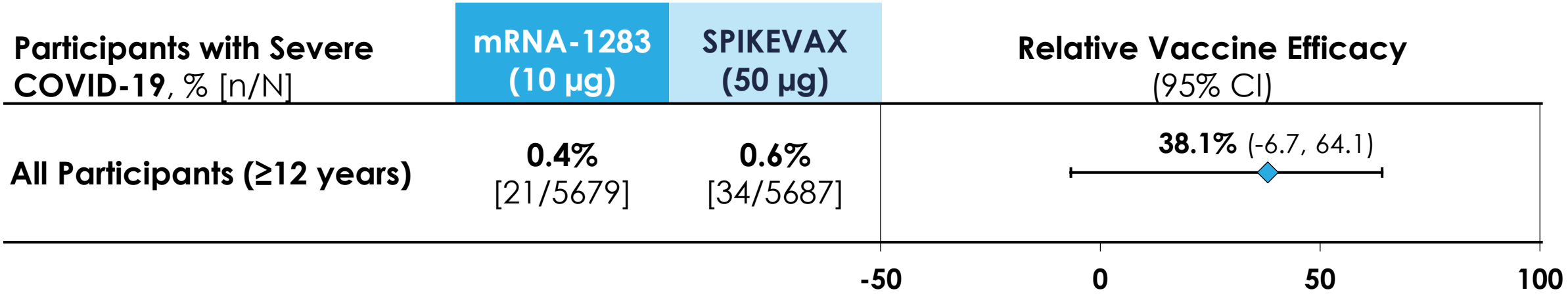
Relative Vaccine Efficacy of mRNA-1283 vs SPIKEVAX Demonstrated in Prevention of Severe COVID-19

Post Hoc Analysis – Protocol Set for Efficacy, through 31 Jan 2024

- **SPIKEVAX effective in prevention of severe COVID-19 in pivotal efficacy trial and real-world effectiveness studies[1-3]**
- **55 cases of severe COVID-19 identified in this trial**

Severe criteria per FDA guidance (originally used in mRNA-1273 efficacy trial)[1]

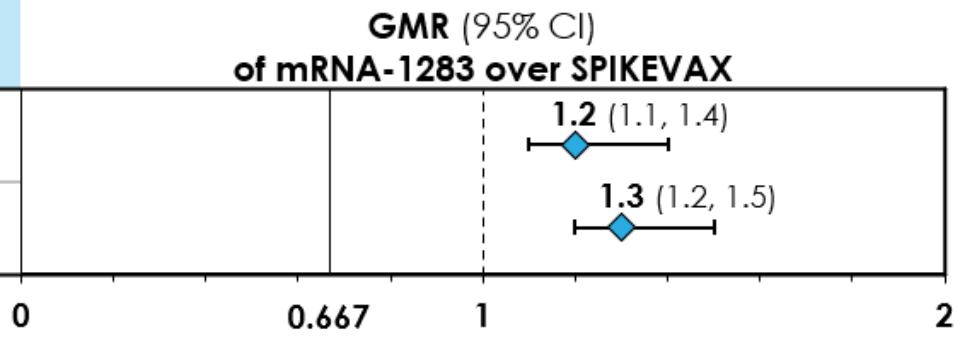


1. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/development-and-licensure-vaccines-prevent-covid-19; 2. Zheng et al *Intl J Inf Dis* 2022; 3. Link-Gelles ACIP 2024.
Severe defined as respiratory failure/ARDS, renal/hepatic/neurologic dysfunction, admission to ICU/death, or vital sign abnormalities indicative of severe systemic illness or BP abnormalities indicative of shock (respiratory rate ≥30 per minute, heart rate ≥125 beats per minute, or SpO2 ≤93% on room air at sea level or PaO2/FiO2 <300 mmHg, systolic BP <90 mmHg, diastolic BP <60 mmHg, or requiring vasopressors)

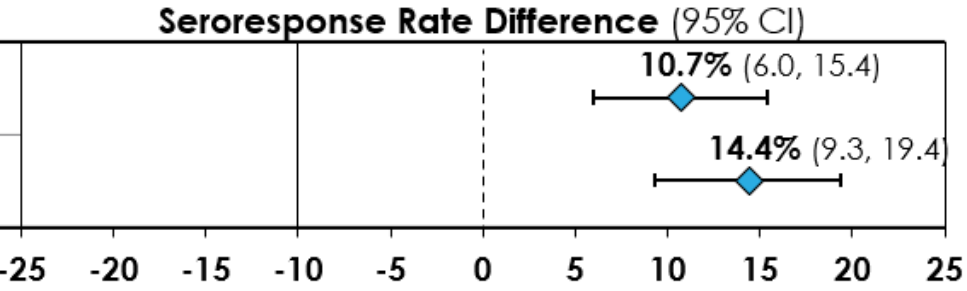
mRNA-1283 Elicited Higher Antibody Response at Day 29 Compared to SPIKEVAX

Study 301 – Per-Protocol Immunogenicity Set (Randomly Selected Subset)

GMC (95% CI)[1]	mRNA-1283 (10 µg) N = 621	SPIKEVAX (50 µg) N = 568
Original SARS-CoV-2	**10632** (9960, 11349)	**8577** (8013, 9180)
BA.4/BA.5	**2341** (2167, 2529)	**1754** (1618, 1901)



Seroresponse Rate, % (95% CI)		
Original SARS-CoV-2	**83.6%** (80.4, 86.4)	**72.9%** (69.0, 76.5)
BA.4/BA.5	**79.9%** (76.5, 83.0)	**65.5%** (61.4, 69.4)



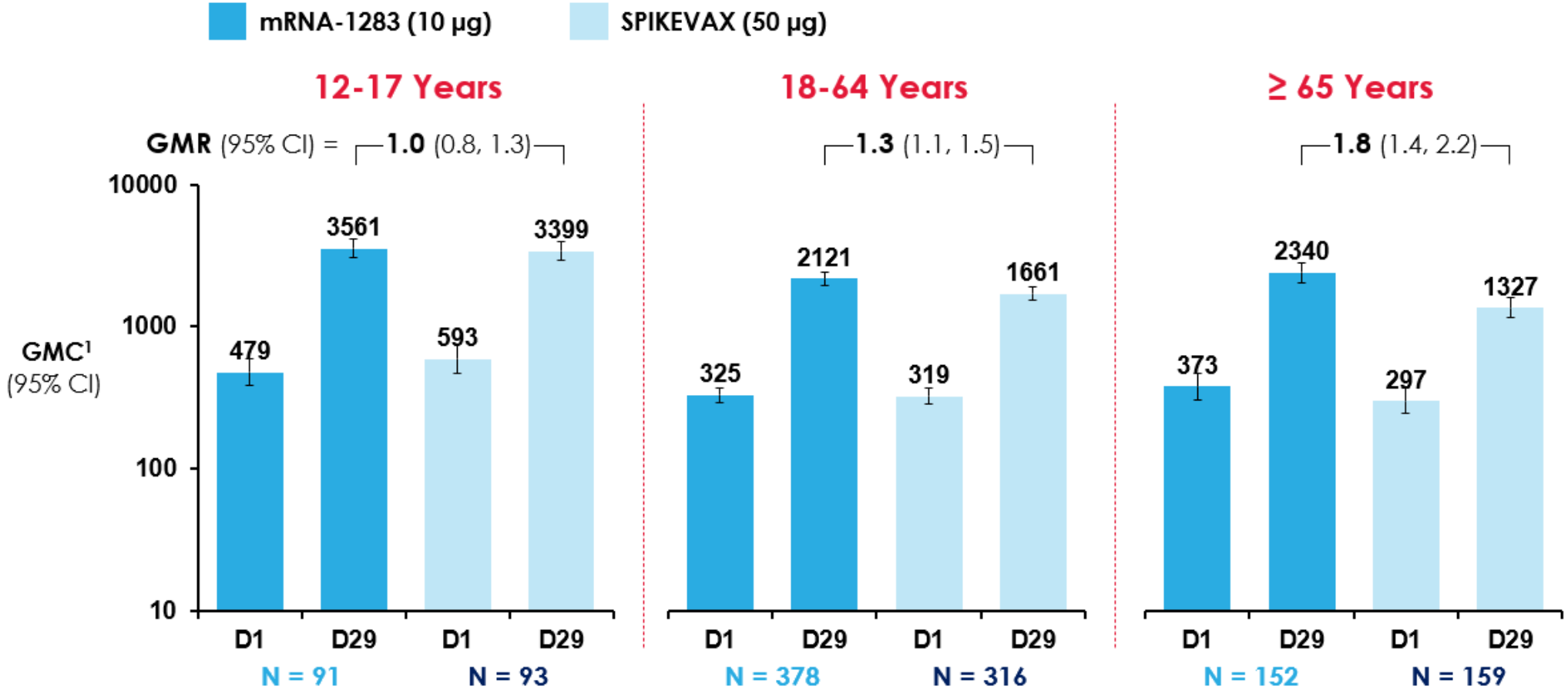
Noninferiority success criteria met

- **GMR:** Lower 95% CI of GMR was >0.667
- **Seroresponse rate difference:** Lower 95% CI of difference >–10%

Seroresponse rate defined as antibody value change from baseline below lower limit of quantification (LLOQ) to ≥4 × LLOQ, or ≥4-fold rise if baseline ≥ LLOQ and <4 × LLOQ, or ≥2-fold rise if baseline is ≥4 × LLOQ; GMC – geometric mean concentration; GMR – geometric mean ratio 1. GMC estimated based on ANCOVA model

Highest BA.4/BA.5 Neutralizing Antibody Geometric Mean Ratio (GMR) at Day 29 in Adults ≥65 Years Old

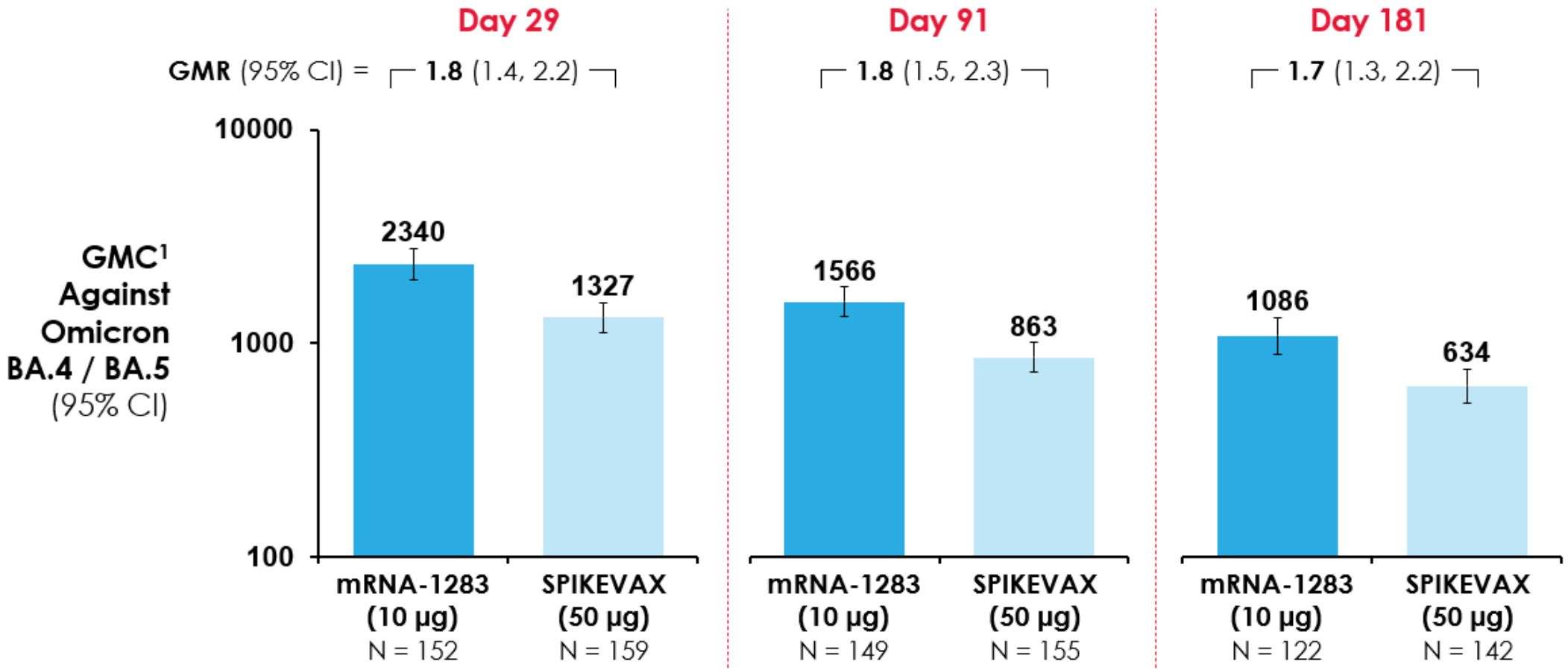
Study 301 – Per Protocol Immunogenicity (Randomly Selected Subset)



1. GMC estimated based on ANCOVA model

mRNA-1283 Elicited Consistently Higher Antibody Responses Compared to SPIKEVAX Over Time - Adults ≥65 Years of Age

Study 301 – Per-Protocol Immunogenicity Set (Randomly Selected Subset)



1. GMC estimated based on ANCOVA model

COVID (mRNA-1283) summary

Safety

- mRNA-1283 generally well tolerated with an acceptable safety profile

Relative Vaccine Efficacy (rVE) & Immunogenicity

- Prespecified rVE non-inferiority objective met
  - mRNA-1283 vs mRNA-1273 rVE of **9.3%** ; 99.4% CI: -6.6, 22.8
- Trend for higher rVE point estimates with advancing age and comorbidity
  - ≥65 years old: **13.5%** mRNA-1283 vs mRNA-1273; 95% CI: -7.7, 30.6
  - ≥65 years old and ≥1 comorbidity (*Post hoc*): **28.6%** mRNA-1283 vs mRNA-1273; 95% CI: 4.6, 46.6
- Pre-specified non-inferiority objectives met
  - mRNA-1283 elicited higher immune responses than SPIKEVAX
  - GMR highest in participants ≥65 years old (GMR 1.8; 95% CI: 1.4, 2.2)

Next steps

- Approved in US; continue drive uptake
- Approved in Canada, targeting strain update in 2026
- Filed and targeting 2026 approvals and strain updates in Australia, Europe, Japan and Taiwan

Huang G, Wilson E, Kohli A, et al. mRNA-1010, an mRNA-based influenza vaccine, is safe and efficacious in adults aged ≥50 years, including individuals at high risk for severe disease. Presented at: 10th ESWI Influenza Conference; October 20-23, 2025; Valencia, Spain.

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Influenza

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

Vice President, Platform and Technology Integration, Development

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Influenza Morbidity and Mortality

Globally, **~1 billion cases of influenza occur annually**[1]

Flu burden in the U.S. during the 24/25 season

47M – 82M
estimated flu-related illnesses

27K – 130K
estimated flu-related deaths

Source: https://www.cdc.gov/flu-burden/php/data-vis/2024-2025.html

Age[2] **and Chronic conditions**[3] **increase the risk of influenza complications**

- Age ≥65 years increases the risk of influenza-related hospitalization and death
- Comorbidities (e.g., chronic lung disease, asthma, heart disease), High BMI, and Immunocompromise

Influenza infection heightens risk of heart attack[4], stroke[5], and COPD exacerbation[6]

Some countries recommend enhanced influenza vaccines for adults ≥65 years

- 24.2% relative vaccine efficacy for Fluzone HD vs seasonal SD vaccine[7]

BMI, body mass index; Centers for Disease Control and Prevention; WHO, World Health Organization.

1. World Health Organization. Weekly Epidemiological Record. 2022;97: 185-208; 2. Langer J, et al. Adv Ther. 2023; 40 (4):1601-1627 3. CDC. People at Increased Risk for Flu Complications. https://www.cdc.gov/flu/highrisk/index.htm 4. Kwong JC et al. N Engl J Med. 2018; 378 (4): 345-353. 5. Boehme AK et al. Ann Clin Transl Neurol. 2018; 5(4):456-463 6. Seemungal TAR et al. Am J Respir Crit Care Med. 2001; 164(9):1618-1623 7. CDC. Flu and People over 65 Years and Older. https://www.cdc.gov/flu/highrisk/65over.htm

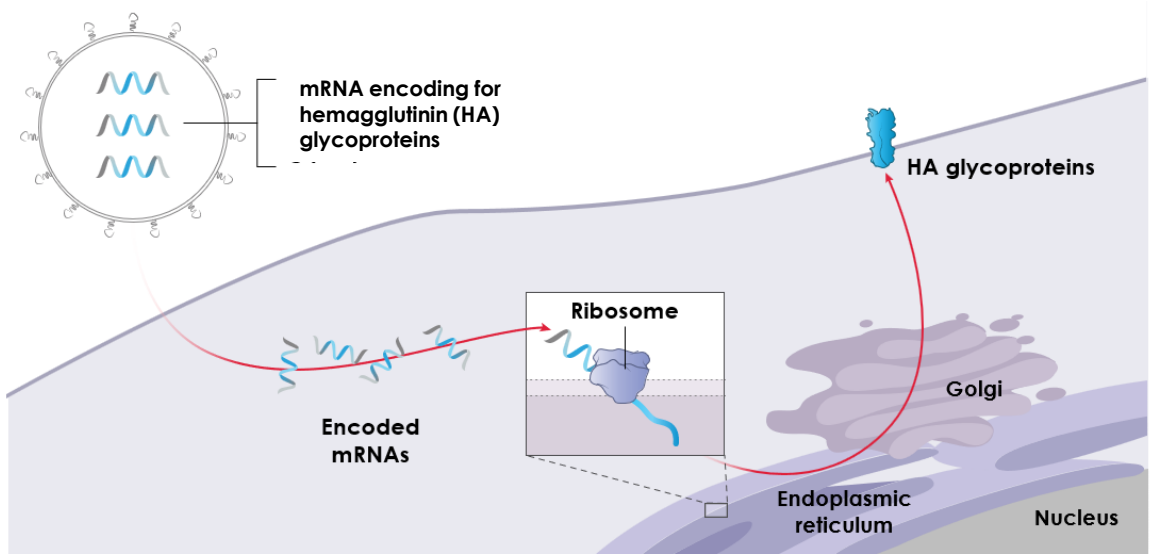
mRNA-1010: an mRNA-based seasonal influenza vaccine candidate

Potential to address several limitations associated with currently licensed influenza vaccines[1-4]

- Encodes exact protein (precise match)
- No requirement for egg-based or other complex culture systems
- Reduced production time allowing for strain selection closer to start of influenza season and decreasing risk for mismatch

Elicits superior immunogenicity compared to licensed standard dose (in adults aged 18-64 years) and high dose (in adults aged ≥65 years) licensed influenza vaccine comparators[5]

mRNA-1010 encodes membrane-bound HAs of WHO-recommended seasonal influenza strains



HA, hemagglutinin; WHO, World Health Organization.

1. World Health Organization. *Wkly Epidemiol Rec*. 2022;19:185–208. 2. Barr IG, et al. *NPJ Vaccines*. 2018; 3:44. 3. Dolgin E. *Nat Rev Drug Discov*. 2021; 20:801-803. 4.Okoli GN, et al. *Vaccine*. 2021; 39:1225-1240. 5. Soens M, et al. *Vaccine*. 2025; 50:126874.

mRNA-1010 P304 Phase 3 trial design

The Phase 3 was designed to test safety and vaccine efficacy of mRNA-1010 (NCT06602024)

Design
Randomized, double-blind, active-controlled Phase 3 trial

Participants
40,703 Adults ≥50 Years randomized and received study vaccination (Safety Set)

Vaccination schedule
Single dose of mRNA-1010 or licensed SD influenza vaccine

Duration
Follow up through 6 months (Day 181) or end of influenza season, whichever occurred later

Site locations
11 countries

40,703 adults ≥50 years randomized and received study vaccination (safety set)

mRNA-1010 (37.5 µg TIV)	Licensed SD Influenza Vaccine (45 µg TIV or 60 µg QIV)
n=20,350	n=20,353

Stratified Randomization:
Age groups - 50-64 years, ≥65 years[a]

Influenza vaccine status in previous influenza season (received/not received)

QIV, quadrivalent; SD, standard dose; TIV, trivalent.
[a]47.8% of participants were ≥65 years; 11.6% of participants were ≥75 years old.
Active comparators include Fluarix (TIV), Fluarix Tetra, Influsplit® Tetra, Alpharix® Tetra.

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mRNA-1010 P304: Study objectives

Randomized, Double-Blind, Active-Controlled Phase 3 Trial

Primary objectives

- **Noninferiority and superiority of rVE mRNA-1010 vs licensed SD influenza vaccines** against protocol-defined Influenza-Like Illness (ILI) by **any influenza A or B strains**
- **Safety and reactogenicity** of mRNA-1010

Secondary objectives

- rVE of mRNA-1010 vs licensed SD influenza vaccine against protocol-defined ILI by **vaccine matched Influenza A and B strains**
- **Immunogenicity in a subset of participants**

Exploratory objectives

- rVE of mRNA-1010 vs licensed SD influenza vaccine against **medically attended ILI**

Influenza-like Illness (ILI) Case Definition

Respiratory Illness
Sneezing, nasal congestion, rhinorrhea, sore throat, cough, sputum production, wheezing, or difficulty breathing

Protocol-Defined ILI

≥ 1 systemic symptom: Oral temperature >37.2°C (>99.0°F), chills, feverish, tiredness, headaches, or myalgia

AND

≥ 1 respiratory symptom: Sore throat, cough, sputum production, wheezing, or difficulty breathing

All cases required **RT-PCR confirmation** within 7 days of illness onset

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mRNA-1010 P304: Demographics and baseline characteristics were balanced between groups

Safety Set

Characteristic		≥50 Years mRNA-1010 (n = 20,350)	≥50 Years Licensed SD Influenza Vaccines (n = 20,353)
Median age, years		**64**	**64**
Female, n (%)		11,516 (**56.6**)	11,633 (**57.2**)
Age group, n (%)	50-64 Years	10,624 (**52.2**)	10,615 (**52.2**)
	≥65 Years	9726 (**47.8**)	9738 (**47.8**)
	≥75 Years	2354 (**11.6**)	2363 (**11.6**)
Vaccinated previous influenza season n (%)		9569 (**47.0**)	9547 (**46.9**)
Race/Ethnicity, n (%)	White	16,814 (**82.6**)	16,811 (**82.6**)
	Black or African American	2687 (**13.2**)	2698 (**13.3**)
	Asian	496 (**2.4**)	483 (**2.4**)
	Hispanic/Latino ethnicity	2147 (**10.6**)	2067 (**10.2**)
Frailty in adults aged ≥65 yrs , n (%) (≥4 on Edmonton scale)		2575 (**12.7**)	2583 (**12.7**)
Baseline high-risk conditions, n (%)		11,591 (**57.0**)	11,614 (**57.1**)

Most common high-risk conditions:

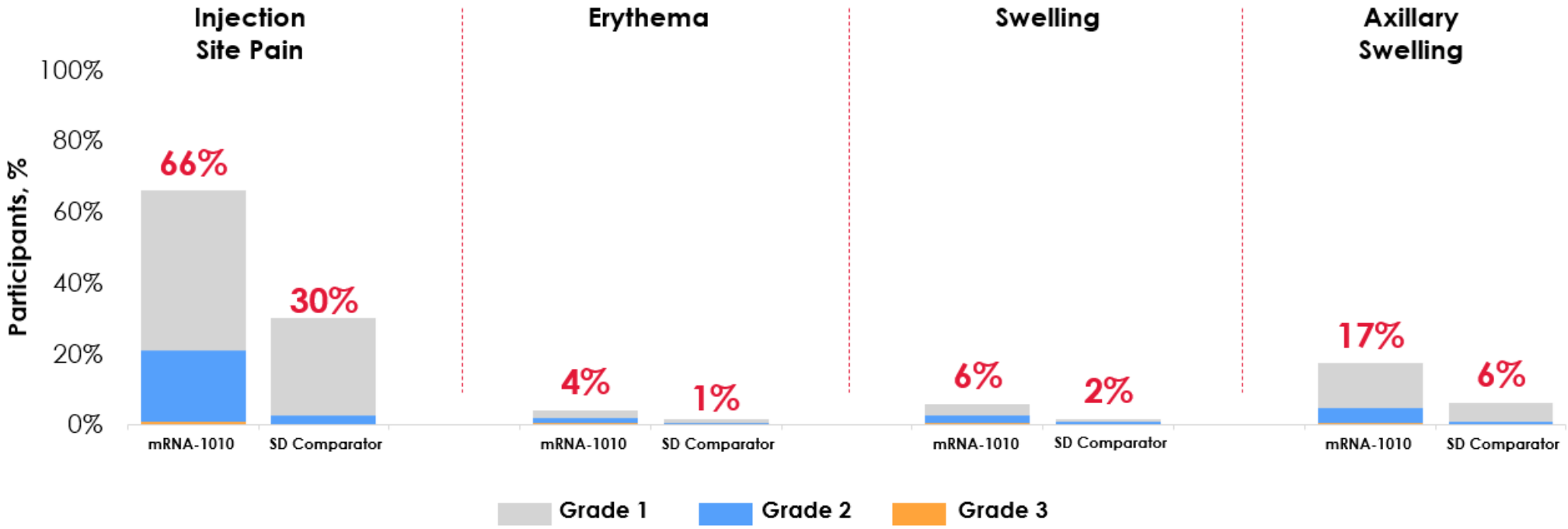
- Diabetes
- Asthma
- Obesity (BMI ≥30 kg/m²)
- Chronic obstructive pulmonary disease
- Atrial fibrillation

BMI, body mass index; SD, standard dose.

Malkin E, Kohli A, Clark R, et al. mRNA-1010, an mRNA-Based Influenza Vaccine, Is Safe and Efficacious in Adults Aged ≥50 Years. Presented at: IDWeek 2025; October 19-22, 2025; Atlanta, GA..

Solicited local adverse reactions for adults ≥50 Years within 7 days of injection were mostly mild to moderate and of short duration

Solicited Safety Set



- Local reactions were higher with mRNA-1010 vs licensed SD comparator
- Low frequency of grade 3 reactions were observed; most reactions grade 1 or 2 and of short duration (median, 2 days)
- Most frequently reported local reaction was injection site pain in both groups
- Fewer, and milder, reactions were reported by participants >75 in both groups, but the pattern remained similar

SD, standard dose.
mRNA-1010, n = 3015; licensed SD influenza vaccines, n = 2997. No grade 4 reactions.
Licensed SD influenza vaccines are composed of Fluarix (TIV), Fluarix Tetra, Influsplit® Tetra, and Alpharix® Tetra.

Huang G, Wilson E, Kohli A, et al. mRNA-1010, an mRNA-based influenza vaccine, is safe and efficacious in adults aged ≥50 years, including individuals at high risk for severe disease. Presented at: 10th ESWI Influenza Conference; October 20-23, 2025; Valencia, Spain.

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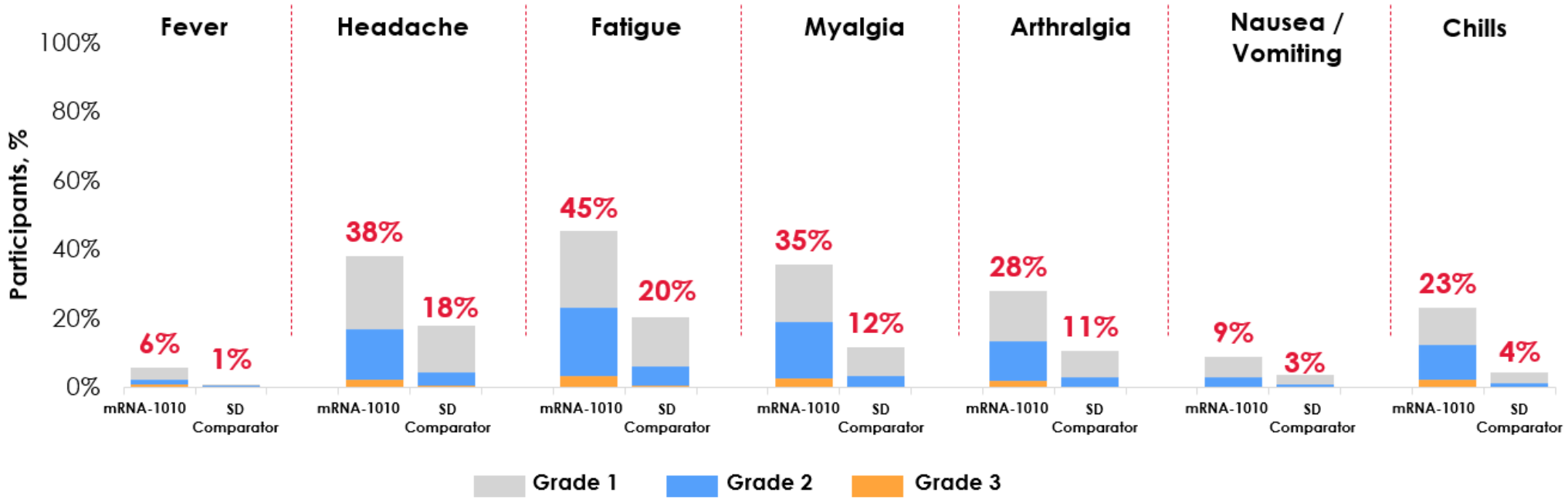
Solicited Systemic Adverse Reactions for Adults ≥50 Years Within 7 Days of Injection Were Mostly Mild to Moderate and of Short Duration

Solicited Safety Set



- Systemic reactions were higher with mRNA-1010 than licensed SD comparator
- Low frequency of grade 3 reactions were observed; most reactions were grade 1 or 2 and of short duration (median, 2 days)
- Most frequently reported systemic reactions were fatigue and headache across both groups
- Fewer, and milder, reactions were reported by participants >75 in both groups, but the pattern remained similar

SD, standard dose.
mRNA-1010, n = 3015; licensed SD influenza vaccines, n = 2997. No grade 4 reactions.
Licensed SD influenza vaccines are composed of Fluarix (TIV), Fluarix Tetra, Influsplit® Tetra, and Alpharix® Tetra.

Huang G, Wilson E, Kohli A, et al. mRNA-1010, an mRNA-based influenza vaccine, is safe and efficacious in adults aged ≥50 years, including individuals at high risk for severe disease. Presented at: 10th ESWI Influenza Conference; October 20-23, 2025; Valencia, Spain.

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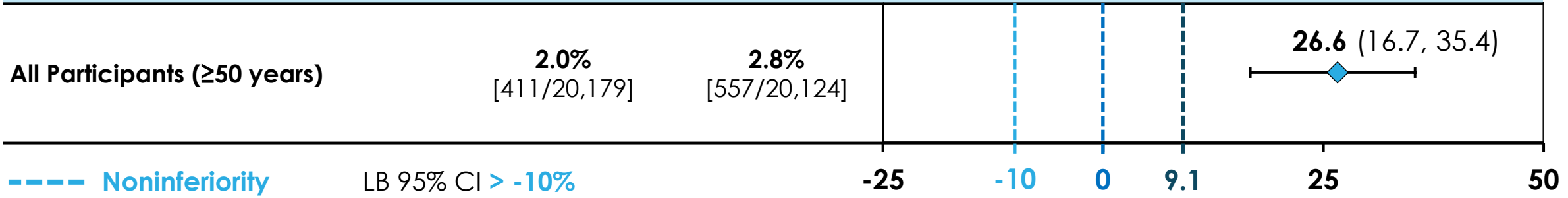
mRNA-1010 P304: Prespecified Success Criteria Met for rVE of mRNA-1010 vs Licensed SD Influenza Vaccines

Primary Endpoint - Per-Protocol Set (Median 6 months of follow up)

Participants With RT-PCR Confirmed Protocol-Defined ILI Regardless of Influenza Strain, % [n/N]	mRNA-1010	Licensed SD Influenza Vaccines	Relative Vaccine Efficacy, (%)[a] (95% CI)
All Participants (≥50 years)	**2.0%** [411/20,179]	**2.8%** [557/20,124]	**26.6** (16.7, 35.4)



Highest Superiority Success Criterion Met

LB of 95% CI >9.1%; 1-sided *P* = 0.0005

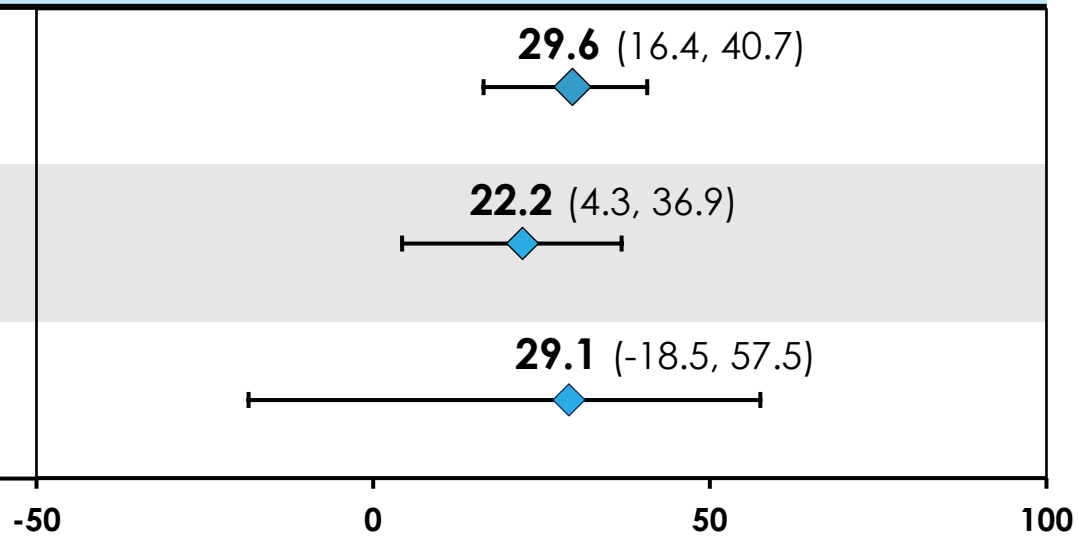
CI, confidence interval; ILI, influenza-like illness; LB, lower bound; RT-PCR, reverse transcription polymerase chain reaction; rVE, relative vaccine efficacy; SD, standard dose.
[a]rVE =100 × (1-hazard ratio [mRNA-1010 vs. active comparator]), hazard ratio estimated using a stratified Cox proportional hazard model (stratified by age group at randomization and previous influenza vaccination status) and with treatment group as a fixed effect.

Malkin E, Kohli A, Clark R, et al. mRNA-1010, an mRNA-Based Influenza Vaccine, Is Safe and Efficacious in Adults Aged ≥50 Years. Presented at: IDWeek 2025; October 19-22, 2025; Atlanta, GA..

Relative Vaccine Efficacy Favorable for mRNA-1010 vs Licensed SD Influenza Vaccines Across Influenza Strains

Per-Protocol Set

Participants With ILI[a] by Influenza Strain,% [n/N]	mRNA-1010	Licensed SD Influenza Vaccines	Relative Vaccine Efficacy, (%)[b] (95% CI)
Influenza A H1N1	**1.1%** [223/20,179]	**1.6%** [315/20,124]	**29.6** (16.4, 40.7)
Influenza A H3N2	**0.8%** [158/20,179]	**1.0%** [202/20,124]	**22.2** (4.3, 36.9)
Influenza B Victoria	**0.1%** [25/20,179]	**0.2%** [35/20,124]	**29.1** (-18.5, 57.5)



CI, confidence interval; ILI, influenza-like illness; RT-PCR, reverse transcription polymerase chain reaction; rVE, relative vaccine efficacy, SD, standard dose
[a]Based on RT-PCR-confirmed protocol-defined ILI
[b]rVE =100 × [1-hazard ratio [mRNA-1010 vs. active comparator]), hazard ratio estimated using a stratified Cox proportional hazard model (stratified by age group at randomization and previous influenza vaccination status) and with treatment group as a fixed effect.

Malkin E, Kohli A, Clark R, et al. mRNA-1010, an mRNA-Based Influenza Vaccine, Is Safe and Efficacious in Adults Aged ≥50 Years. Presented at: IDWeek 2025; October 19-22, 2025; Atlanta, GA..

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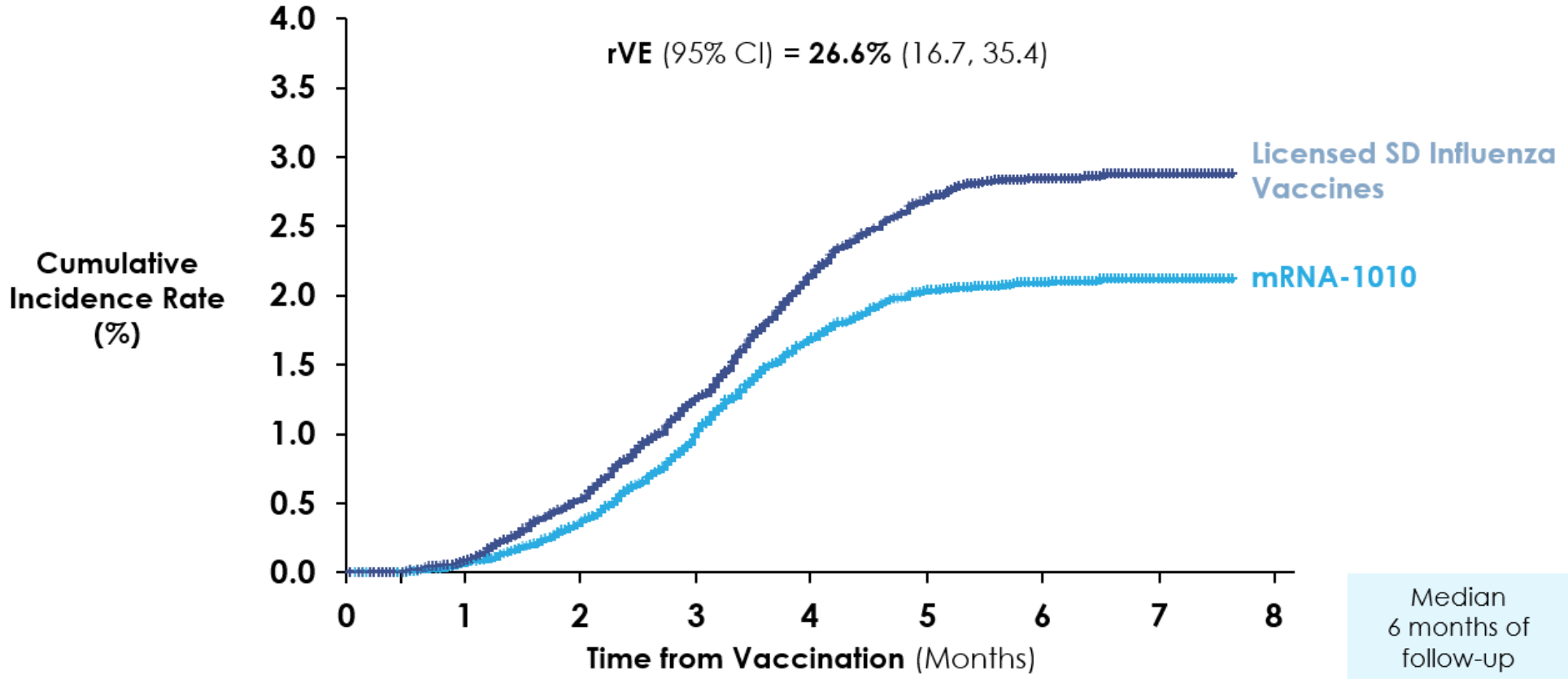
mRNA-1010 P304: Cumulative Incidence Rates of Influenza-Like Illness Over the 2024-2025 Influenza Season Favored mRNA-1010

Per-Protocol Set



Licensed SD Influenza Vaccines	At Risk	20124	19871	19663	19383	19027	18774	10098	1932	0
	Events	0	16	104	250	428	532	555	557	557
mRNA-1010	At Risk	20179	19930	19765	19506	19151	18925	10180	1962	0
	Events	0	14	74	205	333	400	409	411	411

Median 6 months of follow-up

Malkin E, Kohli A, Clark R, et al. mRNA-1010, an mRNA-Based Influenza Vaccine, Is Safe and Efficacious in Adults Aged ≥50 Years. Presented at: IDWeek 2025; October 19-22, 2025; Atlanta, GA..

Relative Vaccine Efficacy Favorable for mRNA-1010 vs Licensed SD Influenza Vaccines Regardless of Age

Per-Protocol Set

Participants With ILI[a] by Age, % [n/N]	mRNA-1010	Licensed SD Influenza Vaccines	Relative Vaccine Efficacy, (%)[b] (95% CI)
50-64 Years	**2.2%** [229/10,542]	**2.9%** [307/10,501]	**26.1** (12.3, 37.7)
≥65 Years	**1.9%** [182/9637]	**2.6%** [250/9623]	**27.4** (12.1, 40.0)
65-74 Years	**1.9%** [138/7307]	**2.6%** [191/7289]	**28.0** (10.4, 42.2)
≥75 Years	**1.9%** [44/2330]	**2.5%** [59/2334]	**25.3** (-10.4, 49.5)

CI, confidence interval; ILI, influenza-like illness; RT-PCR, reverse transcription polymerase chain reaction; rVE, relative vaccine efficacy; SD, standard dose.
[a]Based on RT-PCR-confirmed protocol-defined ILI regardless of influenza strain.
[b]rVE =100 × (1-hazard ratio [mRNA-1010 vs active comparator]), hazard ratio estimated using a stratified Cox proportional hazard model (stratified by previous influenza vaccination status) and with treatment group as a fixed effect.

Huang G, Wilson E, Kohli A, et al. mRNA-1010, an mRNA-based influenza vaccine, is safe and efficacious in adults aged ≥50 years, including individuals at high risk for severe disease. Presented at: 10th ESWI Influenza Conference; October 20-23, 2025; Valencia, Spain.

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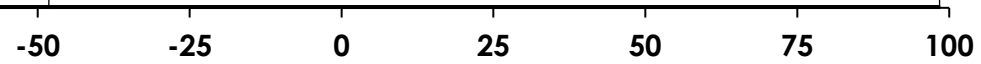
Relative Vaccine Efficacy Favorable for mRNA-1010 in Individuals with High-Risk Conditions and Frailty

Per-Protocol Set

Participants With ILI[a] by Category, % [n/N]		mRNA-1010	Licensed SD Influenza Vaccines	Relative Vaccine Efficacy, (%)[b] (95% CI)
High Risk Conditions	**≥50 years with ≥1 high-risk condition[c]**	**2.1%** [241/11,465]	**2.7%** [309/11,457]	**22.3%** (8.0, 34.3)
Frailty status[d] ≥65 years	**Fit (0-3)**	**2.0%** [140/7079]	**2.7%** [190/7059]	**26.8%** (8.9, 41.1)
	Vulnerable (4-5)	**1.6%** [28/1737]	**2.3%** [39/1708]	**28.9%** (-15.5, 56.3)
	Frail (6 or more)	**1.7%** [14/806]	**2.5%** [21/837]	**30.3%** (-37.1, 64.6)
BMI	**≥30 kg/m²**	**1.9%** [153/8032]	**2.6%** [211/8001]	**27.5%** (10.6,41.1)



BMI, body mass index; CI, confidence interval; ILI, influenza-like illness; RT-PCR, reverse transcription polymerase chain reaction; rVE, relative vaccine efficacy; SD, standard dose.
[a]Based on RT-PCR-confirmed protocol-defined ILI regardless of influenza strain.
[b]rVE =100×(1-hazard ratio [mRNA-1010 vs active comparator]), hazard ratio estimated using a stratified Cox proportional hazard model (stratified by age group and previous influenza vaccination status) and with treatment group as a fixed effect.
[c]High-risk conditions: BMI ≥30 kg/m², diabetes, pulmonary disorders, cardiac disorders, nervous systems disorders, etc.
[d]Frailty status based on Edmonton Frail Scale; Edmonton Frail Scale total score is only applicable to participants ≥65 years old.

Huang G, Wilson E, Kohli A, et al. mRNA-1010, an mRNA-based influenza vaccine, is safe and efficacious in adults aged ≥50 years, including individuals at high risk for severe disease. Presented at: 10th ESWI Influenza Conference; October 20-23, 2025; Valencia, Spain.

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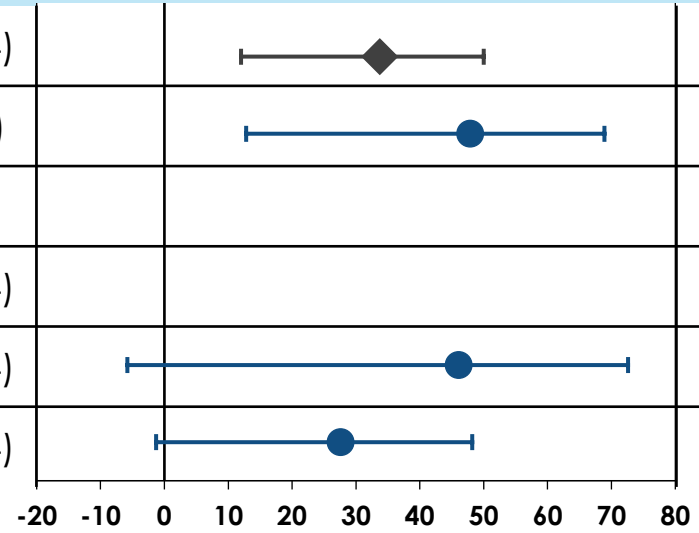
mRNA-1010 P304: Exploratory analysis of medically attended RT-PCR confirmed protocol-defined ILI in participants ≥50 years

Per-Protocol Set

Healthcare Encounters Associated With RT-PCR Confirmed Protocol-Defined ILI, % (n/N)[a]		mRNA-1010	Licensed SD Influenza Vaccines	Relative Vaccine Efficacy, (%) (95% CI)
Any healthcare encounter		**0.4%** (80/20,179)	**0.6%** (120/20,214)	**33.7 (12.0, 50.0)**
Seeking a Higher level of Care	Any	**0.11%** (22/20,179)	**0.21%**(42/20,214)	**47.9 (12.8, 68.9)**
	Hospitalization	**0.02%** (4/20,179)	**0.04%** (8/20,214)	-
	ER visit[b]	**0.03%**(6/20,179)	**0.06%** (12/20,214)	-
	Urgent care visit[b]	**0.06%**(13/20,179)	**0.12%** (24/20,214)	**46.1 (-5.8, 72.6)**
Routine clinic	**Outpatient clinic visit**	**0.29%** (59/20,179)	**0.40%** (81/20,214)	**27.6 (-1.3, 48.2)**



CI, confidence interval; ED, emergency department; ILI, influenza-like illness; PP, per-protocol; RT-PCR, reverse transcription polymerase chain reaction; rVE, relative vaccine efficacy; SD, standard dose.
[a]rVE is calculated based on the healthcare encounters associated with the first RT-PCR-confirmed protocol-defined ILI beginning at least 14 days after study intervention through the end of the influenza season caused by any influenza A or B strains, regardless of vaccine match.
Percentage was based on the total number of participants in the study vaccination PP set. If a case was associated with multiple healthcare encounter types, the participant was counted only once. rVE (95% CI) is not calculated if the total number of cases across both vaccine groups is <20.
[b]ER visits include severe conditions that require immediate medical attention; urgent care visits include less severe conditions that are not an emergency but may require medical attention.[1]
1. Kaiser Permanente. What's the difference between urgent care and emergency care. https://healthy.kaiserpermanente.org/health-wellness/healtharticle.difference-between-urgent-and-emergency-care.

Malkin E, Kohli A, Clark R, et al. mRNA-1010, an mRNA-Based Influenza Vaccine, Is Safe and Efficacious in Adults Aged ≥50 Years. Presented at: IDWeek 2025; October 19-22, 2025; Atlanta, GA..

Flu (mRNA-1010) summary

Safety	• Reactogenicity was higher with mRNA-1010; however, most solicited adverse reactions were grade 1 or 2 and transient • Acceptable safety profile
Efficacy	• mRNA-1010 showed higher efficacy across age groups, influenza strains, including participants at high risk of severe influenza, compared to SD vaccines • Efficacy was maintained over the duration of the influenza season • mRNA-1010 also prevented more severe, medically-attended influenza
Next steps	• Expect to file with regulators in the US, EU, Canada and Australia by January 2026

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Combination vaccines

Christine Shaw, Ph.D.
Vice President, Portfolio Head, Infectious Disease and Rare

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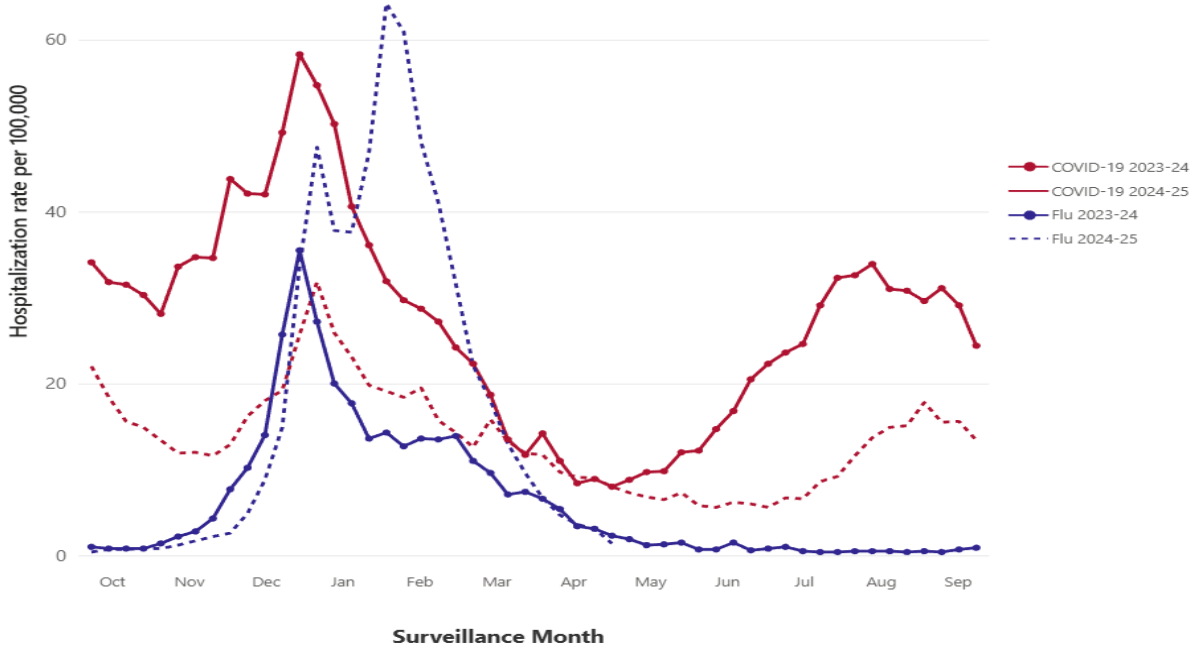
The burden of flu and COVID underscores the importance of a combination vaccine to potentially increase vaccine uptake in the U.S.

Offering a combo vaccine could elevate the COVID vaccine rate closer to that of flu, with the potential to substantially lower the combined burden of disease

Adults ≥ 75 years of age

COVID still causes significant hospitalizations each week in the U.S.

Hospitalization rate per 100K population in the 2023/2024 and 2024/2025 seasons



SOURCE: https://www.cdc.gov/resp-net/dashboard/index.html

Vaccine coverage rate (VCR) is lower for COVID than flu

	2023/2024	2024/2025
COVID VCR[1]	38%	46%
Flu VCR[2]	75%	76%
Flu vaccine recipient receiving COVID vaccine the same day[3]	31%	47%

1. https://www.cdc.gov/covidvaxview/weekly-dashboard/adult-vaccination-coverage.html
2. https://www.cdc.gov/fluvaxview/dashboard/adult-coverage.html
3. Based on information licensed from IQVIA: Anonymized U.S. Retail Patient-Level Data for the periods 07/01/2023-12/31/2023 and 07/01/2024-12/31/2024, reflecting estimates of real-world activity. All rights reserved.

mRNA-1083-P301 Phase 3 study

Study was designed to test the immunogenicity and safety of mRNA-1083

Design
Randomized, observer-blind, active control study

Participants
~8,000 adults ≥ 50 years of age

Vaccination schedule
2 injections on Day 1 (mRNA-1083 + placebo or licensed influenza vaccine + COVID-19 vaccine)

Duration: 6 months
Participants followed up for 6 months

Site locations
Northern hemisphere (United States)

Phase 3 clinical study

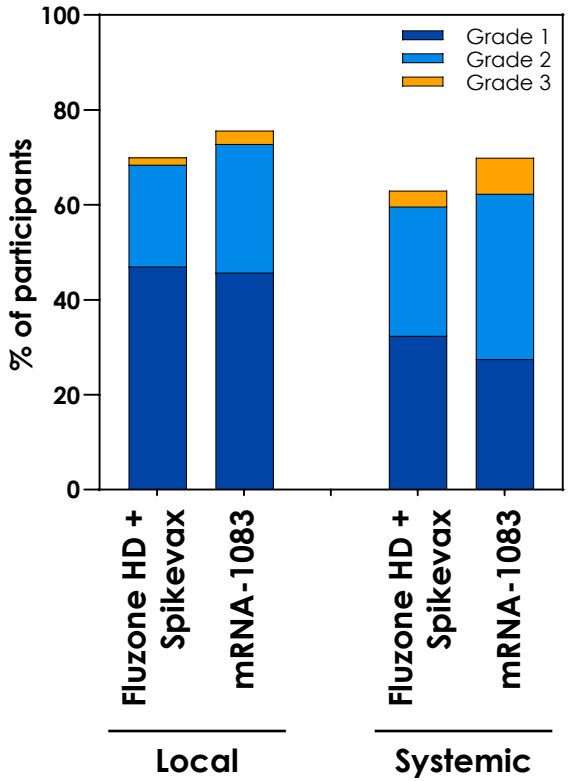
Cohort A: Ages ≥ 65 years	Cohort B: Ages ≥ 50 to 64 years
mRNA-1083 + placebo N~2000	mRNA-1083 + placebo N~2000
Fluzone HD + Spikevax N~2000	Fluarix + Spikevax N~2000

Publication: https://jamanetwork.com/journals/jama/fullarticle/2833668

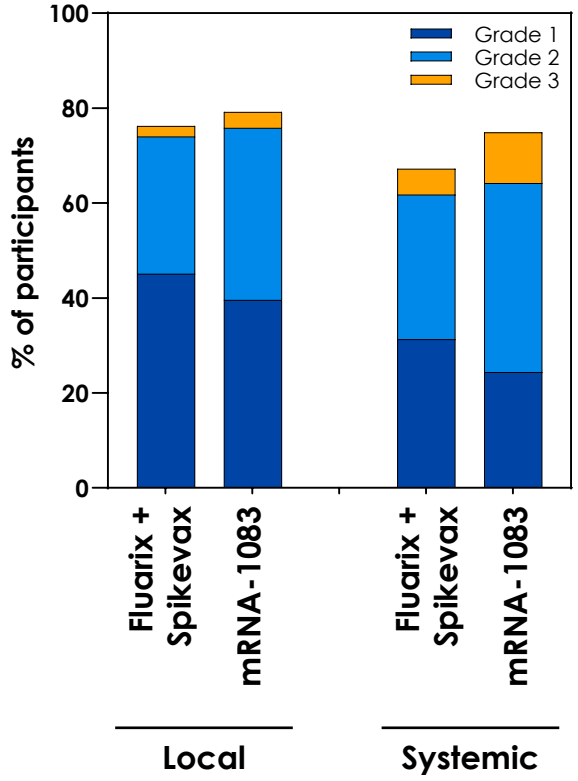
mRNA-1083 showed an acceptable reactogenicity profile compared to co-administered influenza and COVID-19 vaccines

- Majority of solicited adverse reactions reported as grade 1 or 2 in severity and of short duration
- Reactogenicity was lower in 65+ cohort than in the ≥50 to 64 years of age cohort

Cohort A: ≥65 years



Cohort B: ≥50 to 64 years



Grade 4 systemic SARs were ≤ 0.1% and were balanced between mRNA-1083 and comparator groups
Data from D91 primary analysis

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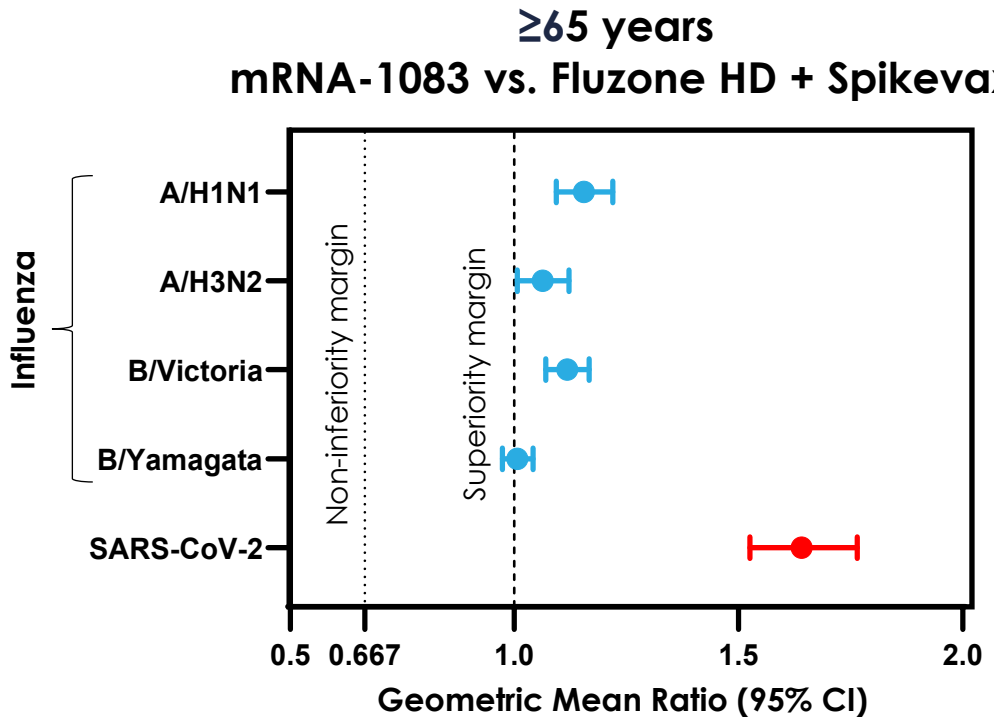
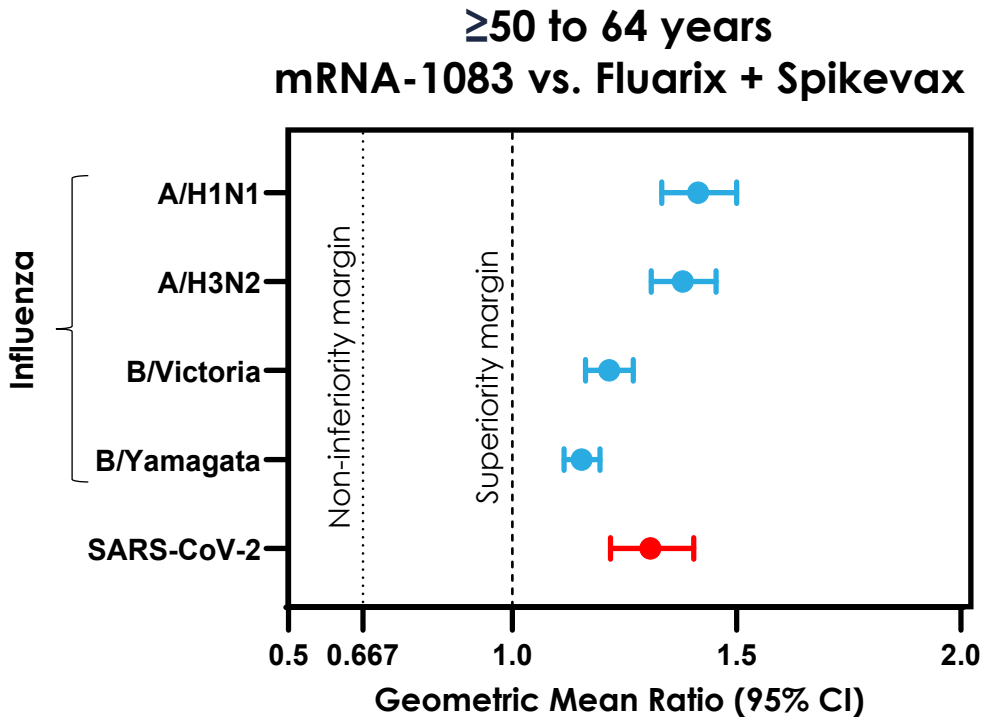
mRNA-1083 met all primary immunogenicity endpoints in Phase 3

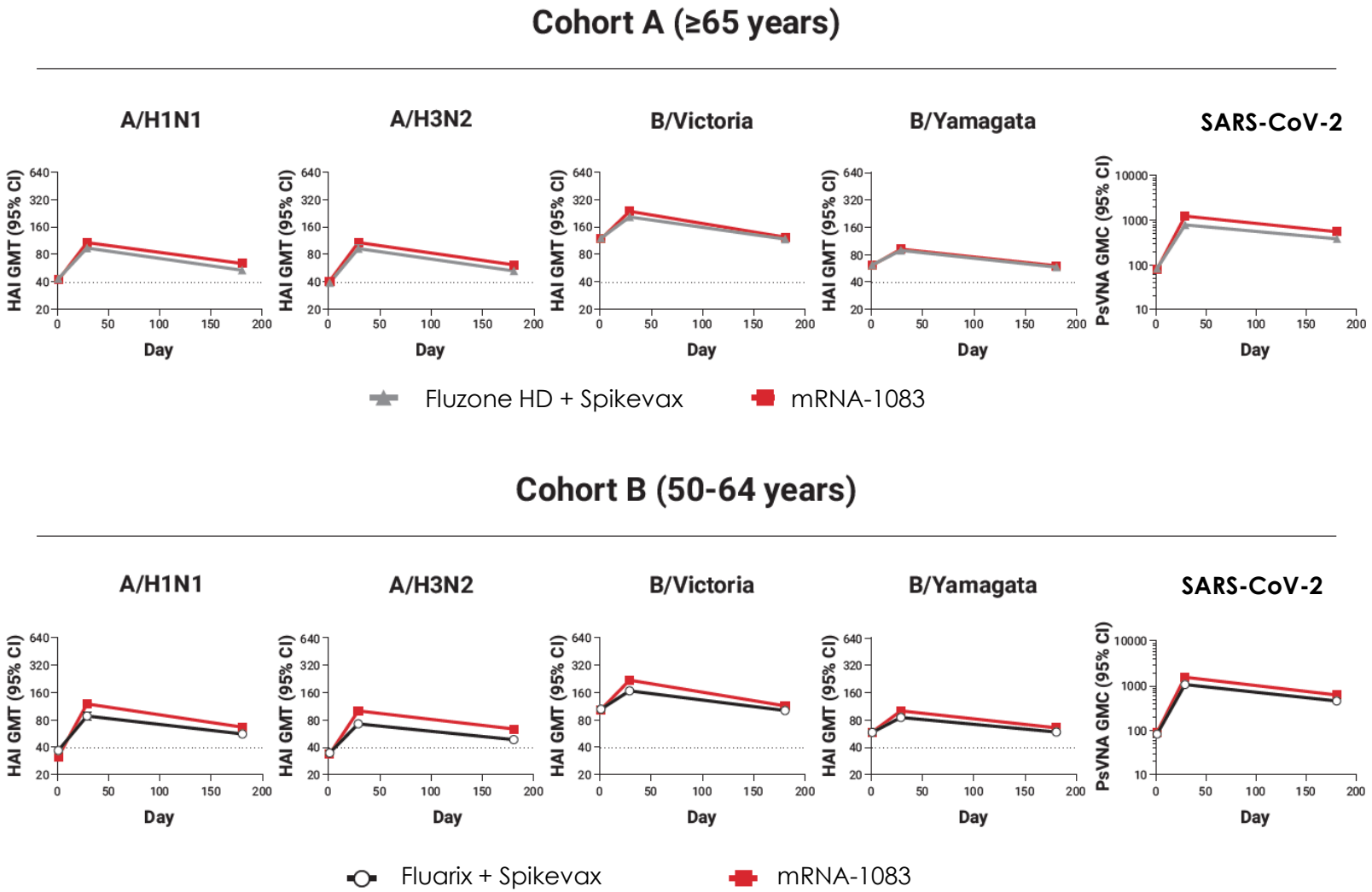




- Noninferiority criteria were met for all immunogenicity endpoints (GMT ratios; seroconversion and seroresponse rates)
- mRNA-1083 induced a higher antibody response compared to licensed influenza/COVID-19 vaccines, including Fluzone HD, for 3 clinically relevant influenza strains (A/H1N1, A/H3N2, B/Victoria) and SARS-CoV-2

mRNA-1083 elicited robust humoral immune responses against vaccine-matched strains that persisted through 6 months post-vaccination

Influenza and SARS-Cov-2 antibody through 6 months in mRNA-1083 Study



Antibody titers for all components of mRNA-1083 remain above or at similar levels relative to active comparators through 6 months post vaccination

Flu + COVID combo (mRNA-1083) summary and next steps

Reactogenicity / Safety	• mRNA-1083 showed an acceptable safety and reactogenicity profile compared to co-administered influenza and COVID-19 vaccines
Immunogenicity	• mRNA-1083 met all 10 co-primary immunogenicity endpoints in Phase 3 study • mRNA-1083 elicited a higher immune response against SARS-CoV-2 and clinically relevant influenza strains in both 50–64-year-old and 65 + year old cohorts • Antibodies are established surrogates of protection against influenza and COVID-19 • Both components (mRNA-1283 and mRNA-1010) of the mRNA-1083 vaccine have demonstrated efficacy in pivotal Phase 3 trials. mRNA-1283 is licensed in the U.S.
Next steps	• Phase 3 filing under review with the European Medicines Agency (EMA) • Submitted for approval to Health Canada • Awaiting further guidance from FDA on refiling in the U.S.

RSV

Christine Shaw, Ph.D.
Vice President, Portfolio Head, Infectious Disease and Rare

RSV hospitalization rate is markedly higher in the older adult population

RSV burden in the U.S. during the 24/25 season

3.6M – 6.5M
estimated RSV-related outpatient visits

190K – 350K
estimated RSV-related hospitalizations

10K – 23K
estimated RSV-related deaths

SOURCE: https://www.cdc.gov/rsv/php/surveillance/burden-estimates.html

Study shows that RSV vaccine uptake at 66% in older adults would reduce outpatient care by up to 53.6%, hospitalizations by up to 60.5%, and RSV-related deaths up to 60.4%.[1]

1. Moghadas, S. M., et al. (2023). Cost-effectiveness of Prefusion F Protein-based Vaccines Against Respiratory Syncytial Virus Disease for Older Adults in the United States. Clinical Infectious Diseases. doi.org/10.1093/cid/ciad658

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mRESVIA (mRNA-1345) is approved in 40 countries for adults 60+, and in 31 of those it's also approved for high-risk adults 18–59

United States	**Austria (EU)**	**Germany (EU)**	**Poland (EU)**
Canada	**Belgium (EU)**	**Greece (EU)**	**Portugal (EU)**
United Kingdom	**Bulgaria (EU)**	**Hungary (EU)**	**Romania (EU)**
Australia	**Croatia (EU)**	**Ireland (EU)**	**Slovakia (EU)**
Switzerland	**Cyprus (EU)**	**Italy (EU)**	**Slovenia (EU)**
Japan	**Czech Republic (EU)**	**Latvia (EU)**	**Spain (EU)**
Taiwan	**Denmark (EU)**	**Lithuania (EU)**	**Sweden (EU)**
United Arab Emirates	**Estonia (EU)**	**Luxembourg (EU)**	**Iceland (EEA)**
Qatar	**Finland (EU)**	**Malta (EU)**	**Liechtenstein (EEA)**
Saudi Arabia	**France (EU)**	**Netherlands (EU)**	**Norway (EEA)**

Bold countries have licensure in adults over 60 years of age and adults 18-59 years of age with high-risk conditions

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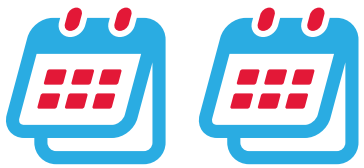
Broad RSV vaccine (mRNA-1345) development program includes two revaccination studies

12 Month Revaccination

Adults ≥50 years
Study 302 – Part C



24 Month Revaccination

Adults ≥60 years
Study 301 – Part B

NCT05127434, NCT05330975

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Broad RSV vaccine (mRNA-1345) development program includes two revaccination studies

12 Month Revaccination

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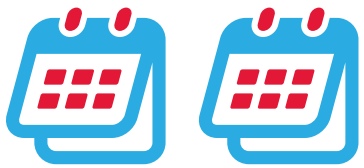
Study 302 – Part C



24 Month Revaccination

Adults ≥60 years
Study 301 – Part B

NCT05127434, NCT05330975

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RSV vaccine (mRNA-1345) 12-month revaccination study 302 – Part C

Primary Objectives

Safety

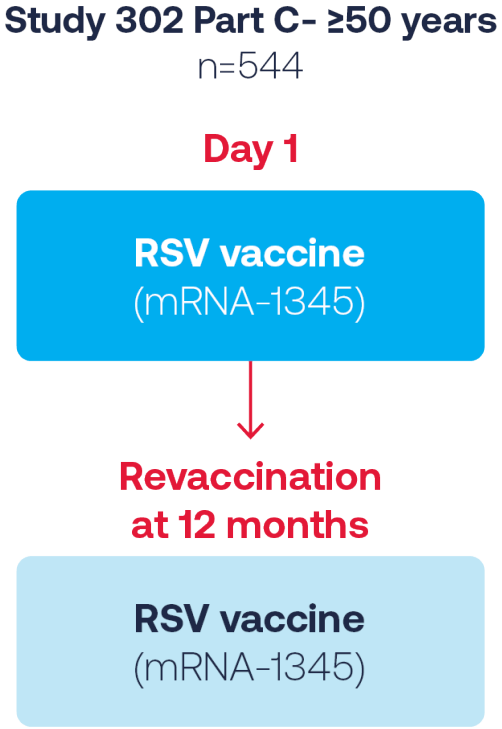
To evaluate the safety and tolerability of revaccination with mRNA-1345 administered 1 year following a primary dose

Immunogenicity

To demonstrate noninferiority of nAb response against RSV-A and RSV-B based on GMRs of nAbs following revaccination compared with the primary dose

Success Criteria for Noninferiority of Immune Response at Day 29

Noninferiority for immunogenicity co-primary endpoints (RSV-A and RSV-B) was demonstrated if the lower bound of 95% CI of the GMT ratio exceeded 0.667 using a non-inferiority margin of 1.5



Demographics and Baseline Characteristics for 12-month revaccination study 302 – Part C

Safety set

		mRNA-1345 (50 µg) N = 543
Age (Years)	**Median (range)**	**62.0** (50, 91)
Age group 1, n (%)	**50-59 years**	**210** (38.7)
	60-74 years	**295** (54.3)
	≥75 years	**38** (7.0)
Age group 2, n (%)	**50-59 years**	**210 (38.7)**
	≥60 years	**333 (61.3)**
Sex, n (%)	**Female**	**313** (57.6
Race/Ethnicity, n (%)	**White**	**412** (75.9)
	Black or African American	**107** (19.7)
	Asian	**7** (1.3)
	Hispanic / Latino Ethnicity	**234** (23%)

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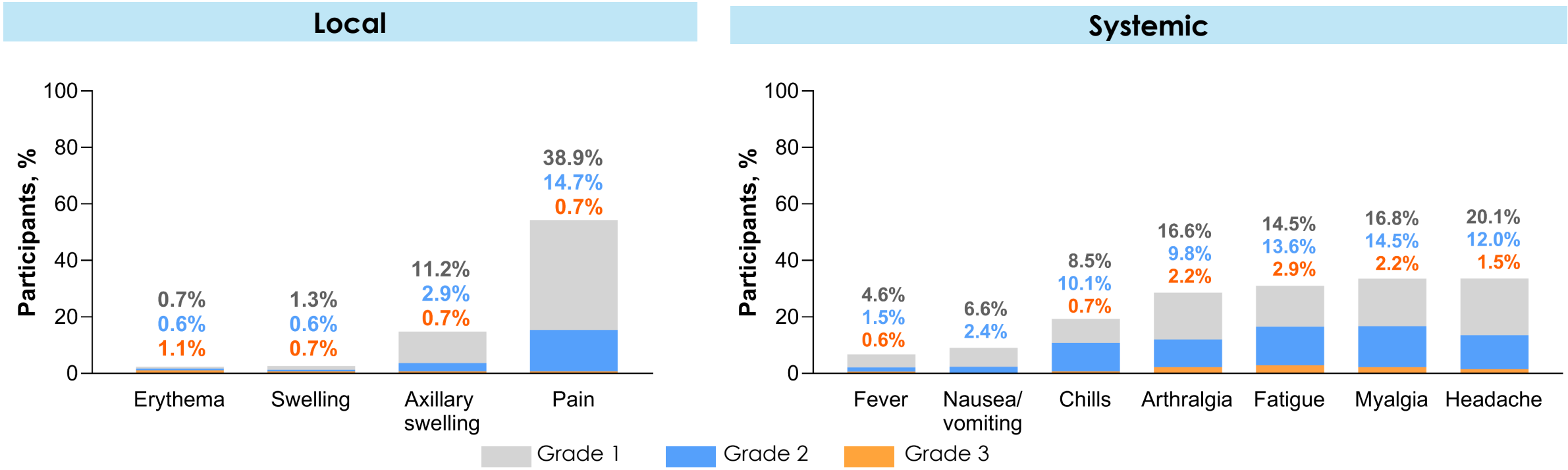
Solicited Adverse Reactions Within 7 Days After 12-month Revaccination

Solicited Safety Set



- Solicited local and systemic ARs were primarily grade 1 or 2 in severity, with a median time to onset within 1-2 days and a median duration of 2 days
- Pain at the injection site (mostly grade 1) was the most frequently reported local AR
- Arthralgia, fatigue, myalgia, and headache were the most frequently reported systemic ARs

AR, adverse reaction.
There were no local grade 4 events. Three grade 4 fevers were reported; all were e-diary entry errors.

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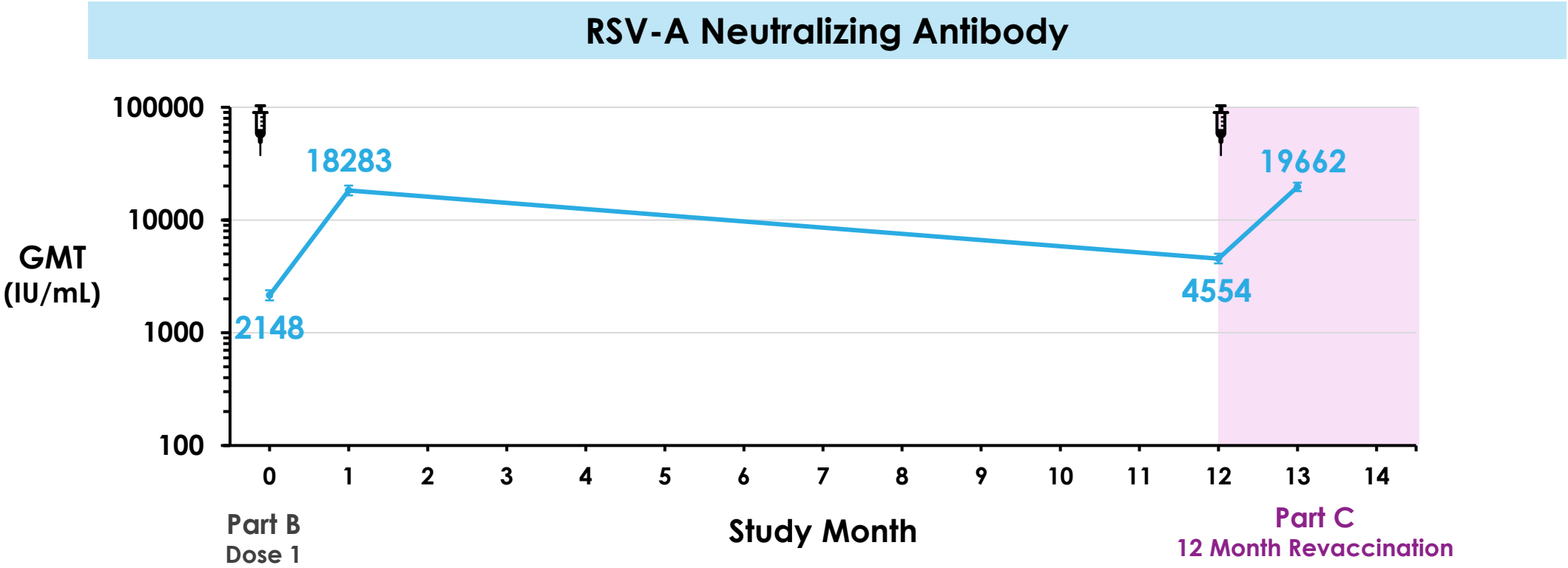
Revaccination at 12 Months with mRNA-1345 Meets Pre-Specified Noninferiority Criteria

Study 302C – Adults ≥50 Years – Per Protocol Set (N=524)



- RSV-A neutralizing antibodies detectable at 12 months post-vaccination
- Revaccination 1 year after primary vaccination elicits responses similar to those following primary dose
- Revaccination met non-inferiority success criteria for RSV-A & RSV-B (LB of 95% CI of GMR > 0.667)

Broad RSV vaccine (mRNA-1345) development program includes two revaccination studies

12 Month Revaccination

Adults ≥50 years
Study 302 – Part C

24 Month Revaccination

Adults ≥60 years
Study 301 – Part B

NCT05127434, NCT05330975

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RSV vaccine (mRNA-1345) 24-month revaccination study 301 – Part B

Design
Adults≥ 60 years old

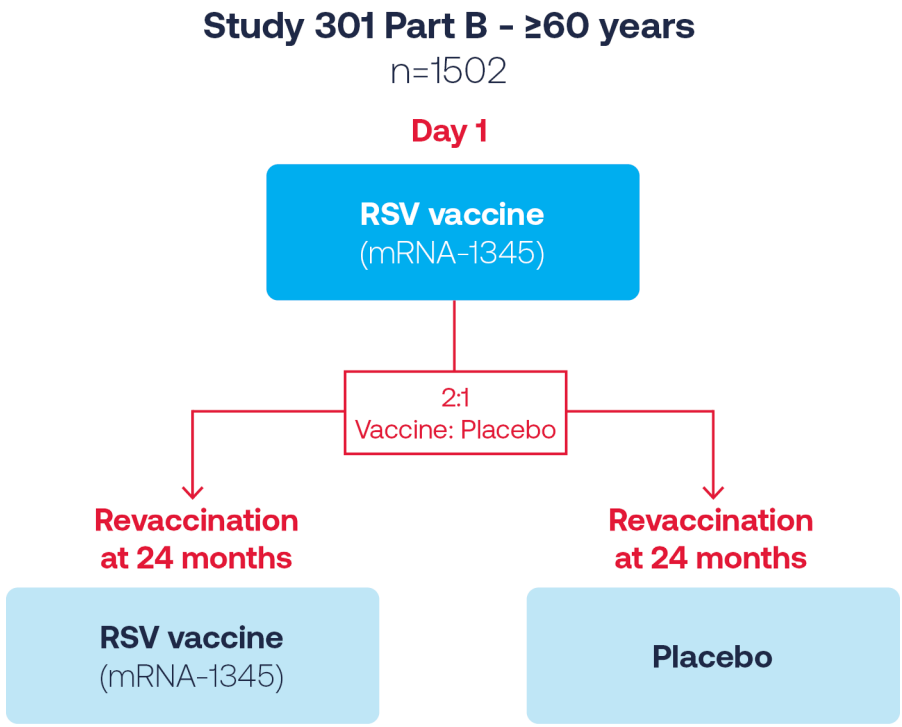
Participants
1502 adults ≥ 60 years old; 504 received placebo and 998 received mRNA-1345

Vaccination schedule
All participants received a primary dose in part A of the study;

Part B participants were randomly assigned 2:1 to receive revaccination with mRNA or placebo 24 months after the primary dose

Duration
Participants followed for additional 6 months after 24 month dose

Primary objectives
Safety, tolerability and immunogenicity



Demographics and Baseline Characteristics for 24-month revaccination study 301 – Part B

Safety Set

		mRNA-1345 (50 µg) N = 998
Age (Years)	**Median (range)**	**68.0** (60-91)
Sex, n (%)	**Female**	**508** (51%)
Race/Ethnicity, n (%)	**White**	**798** (80%)
	Black or African American	**161** (16%)
	Asian	**14** (1%)
	Hispanic / Latino Ethnicity	**234** (23%)
Comorbidities, n (%)	**≥1 Comorbidity**	**321** (32%)
	Diabetes (Type 1 or 2)	**194** (19%)
	Asthma	**85** (9%)
	Chronic Obstructive Pulmonary Disease (COPD)	**54** (5%)
	Advanced Liver or Renal Disease	**11** (1%)
	Chronic Heart Failure (CHF)	**13** (1%)
	Chronic Respiratory Disease	**2** (0.2%)
Body Mass Index, n (%)	**≥30 kg/m^2**	**317** (32%)

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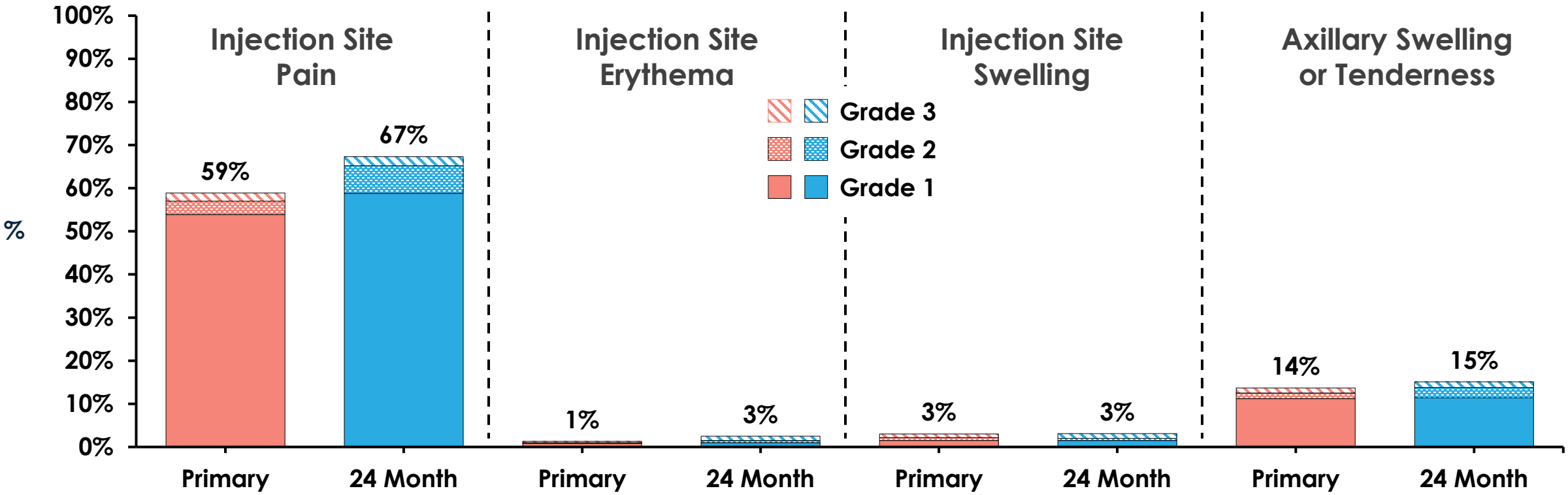
Solicited Local Adverse Reactions Within 7 Days of Revaccination with RSV Vaccine (mRNA-1345) at 24 Months

Study 301 Part B – Adults ≥60 Years (N=995); Solicited safety set

Mostly grade 1, median onset day 2, median duration of 2 days



Revaccination 24 months after primary dose well tolerated

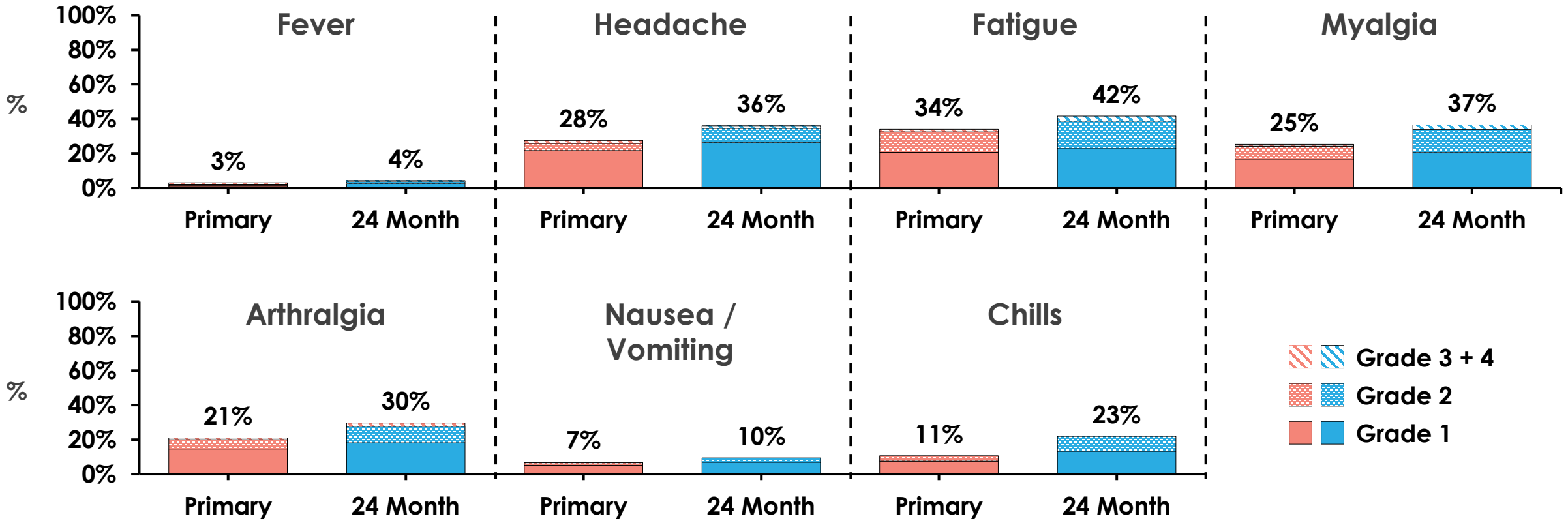
Study 301B primary N=1498; P301B 24 month N=995; No grade 4 local adverse reactions

End of study analysis (last subject last visit Oct 23, 2024)

Solicited Systemic Adverse Reactions within 7 Days of Revaccination with RSV Vaccine (mRNA-1345) at 24 Months

Study 301 Part B – Adults ≥60 Years (N=995); Solicited safety set

Mostly grade 1-2, median onset day 2, median duration of 2 days



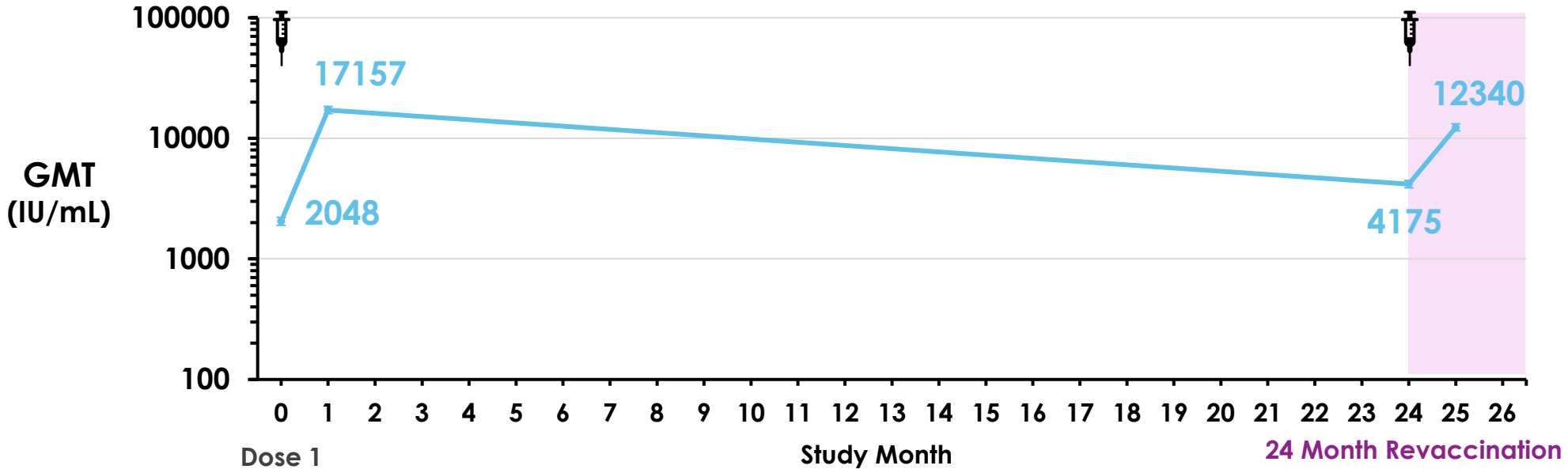
Revaccination 24 months after primary dose was well tolerated

Study 301B primary N=1498; Study 301B 24 month N=995; 1 grade 4 fever after revaccination
End of study analysis (last subject last visit Oct 23, 2024)

Revaccination at 24 Months with mRNA-1345 Meets Pre-Specified Noninferiority Criteria

Study 301B – Adults ≥60 Years – Per Protocol Set (N=956)

RSV-A Neutralizing Antibody



- RSV-A neutralizing antibodies detectable at 24 months post-vaccination
- Revaccination at 24 months after primary vaccination elicits responses similar to those following primary dose
- Revaccination met non-inferiority success criteria for RSV-A & RSV-B (LB of 95% CI of GMR > 0.667)

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Summary – RSV Vaccine (mRNA-1345) Revaccination at 12 and 24 months

Immunogenicity & safety

- Revaccination generally well tolerated; acceptable safety profile
- No reports of GBS, ADEM, acute myocarditis and/or pericarditis
- Durability of immune response demonstrated out to 24 months
- Revaccination at 12 or 24 months:
- Restores immune response; met noninferiority criteria
- Expected to provide comparable vaccine efficacy to that after primary dose

Public health impact of revaccination

- Revaccination has the potential to provide sustained protection against RSV

Next steps

- Monitoring guidance from recommending bodies on RSV revaccination approach and timing

Norovirus

Jacqueline Miller, M.D.
Chief Medical Officer

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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)[2,3]
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/burden.html
3. https://www.who.int/teams/immunization-vaccines-and-biologicals/diseases/norovirus

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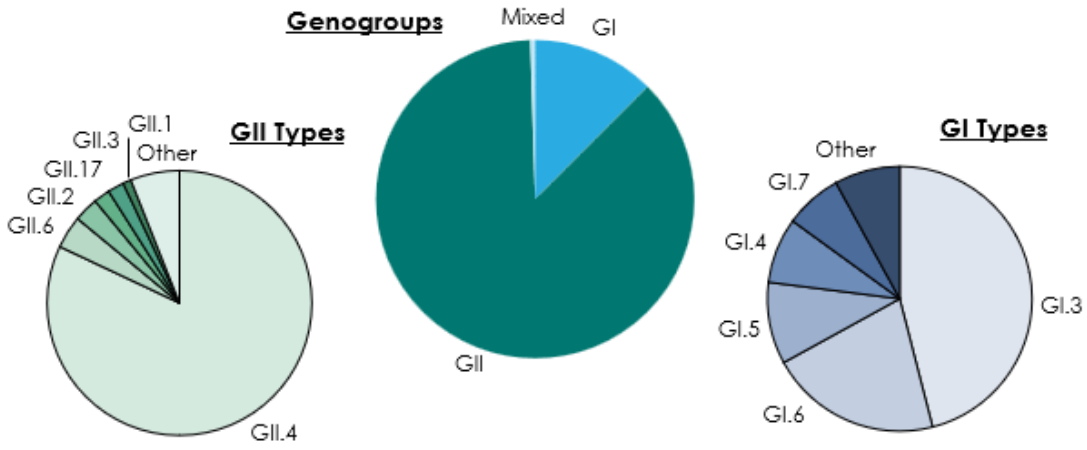
Noroviruses are a diverse group with limited cross-genotype protection, allowing for repeated infections throughout life

Norovirus has broad variant variability; The virus is classified into 10 genogroups and 49 genotypes

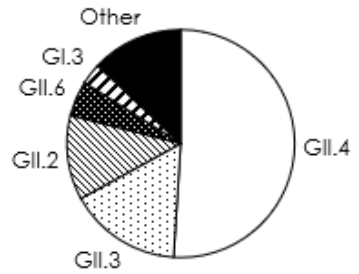
Vaccine development has been challenging to date due to the broad and shifting diversity of genotypes which requires frequent vaccine updates

To protect against >70-80% of noro-AGE in young children and older adults, a multivalent vaccine design is required

Norovirus genogroups and genotypes in long term care facility outbreaks in the US
2009-2018
Adapted from Calderwood et al, 2022



Global distribution of norovirus genotypes among hospitalized children <5, NoroSurv
2016-2020



NoV, norovirus; VP1, major capsid protein; Cannon et al Emerging Infect. Dis. 2021; Calderwood et al. Clin Infect Dis 2022; Carlson KB et al npj Vaccines 2024

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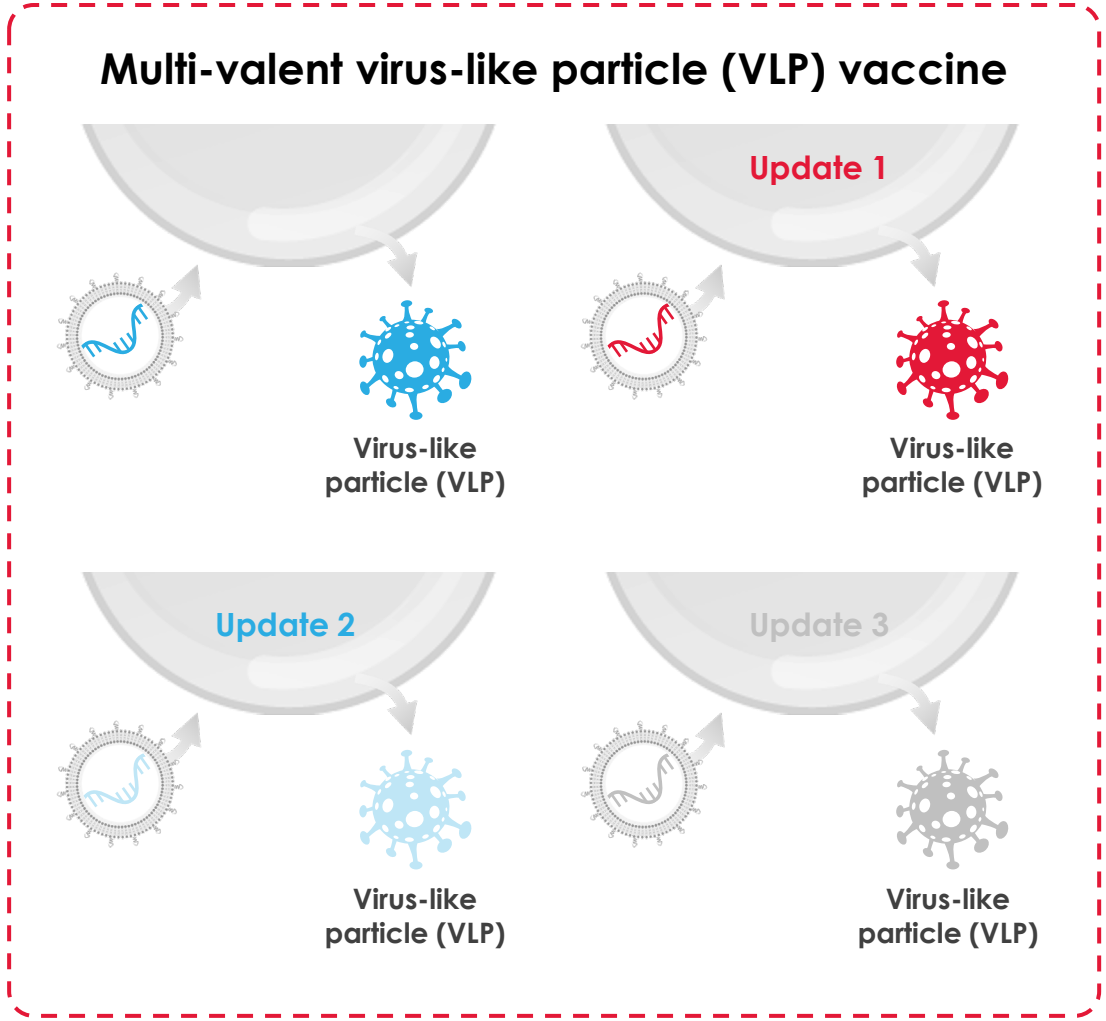
mRNA technology provides ability to make multivalent VLPs that can be quickly updated

mRNA vaccines allow for intracellular production of multi-valent 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



mRNA-1403/1405 Phase 1 trial design

The Phase 1 was designed to evaluate the safety, reactogenicity and immunogenicity of mRNA-1403 and mRNA-1405 in participants 18-49 and 60-80 years of age

Design
Randomized, observer-blind, placebo-controlled study

Number of participants
664 healthy volunteers 18-49 or 60-80 years old*

Vaccination schedule
1-2 doses of mRNA-1403, mRNA-1405 or placebo in 0,1 month schedule

Duration:
Participants will be followed up for 12 months after last study injection

Site location
US

Total N = 664
11 arms, n~60 per arm

2 x mRNA-1403 Dose Level 1	**2 x mRNA-1405** Dose Level 1
2 x mRNA-1403 Dose Level 2	**2 x mRNA-1405** Dose Level 2
2 x mRNA-1403 Dose Level 3	**2 x mRNA-1405** Dose Level 3
2 x mRNA-1403 Dose Level 4	**2 x mRNA-1405** Dose Level 4
1 x Placebo, 1 x mRNA-1403 Dose Level 4	**1 x Placebo, 1 x mRNA-1405** Dose Level 4
2 x Placebo	

*>40% of participants enrolled were 60-80 years old

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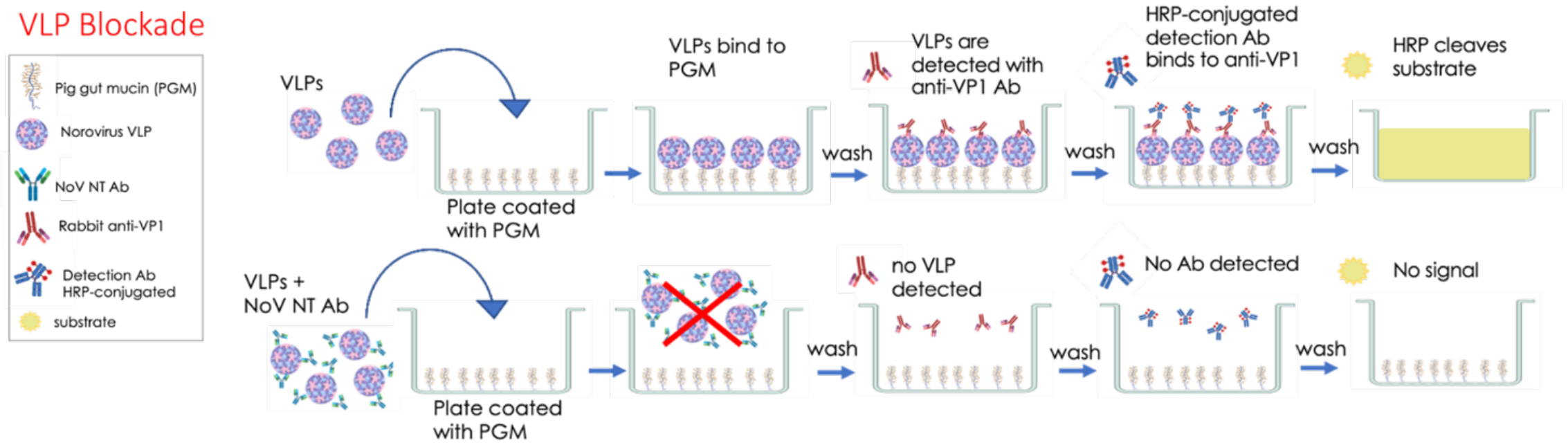
Norovirus HBGA-blocking antibody assay

Surrogate nAb assay

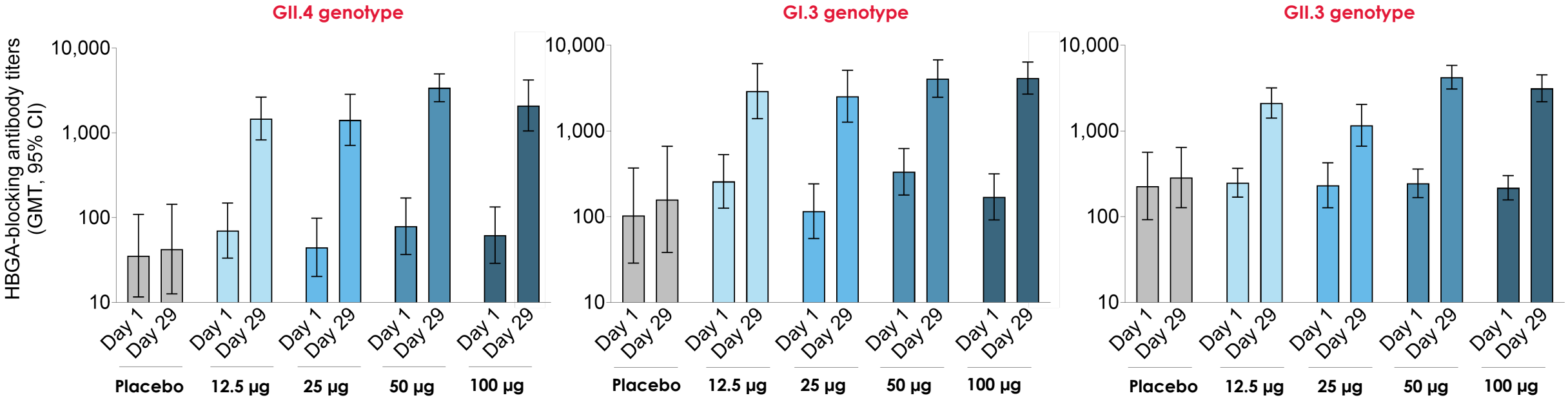


- HBGAs - complex terminal carbohydrates present on cells and secretions - serve as receptor(s)/attachment factor(s) for many NoVs
- Serum HBGA-blocking titers shown to with serum nAb titers
- ↑HBGA-blocking titers associate with ↓clicorrelatenical gastroenteritis rate in human challenge studies

HBGA, histo-blood group antigen; nAb, neutralizing antibody; VLP, virus like particle; NoV, norovirus; Atmar et al. J Infect Dis 2020;221:739; Reeck et al. J Infect Dis 2010;202:1212

A single dose of mRNA-1403 also elicited robust HBGA-blocking antibody titers against vaccine-matched NoV genogroup I and II genotypes in older adults

Older adults (60-80 years old)



HBGA, Histo-blood group antigen; NoV, norovirus

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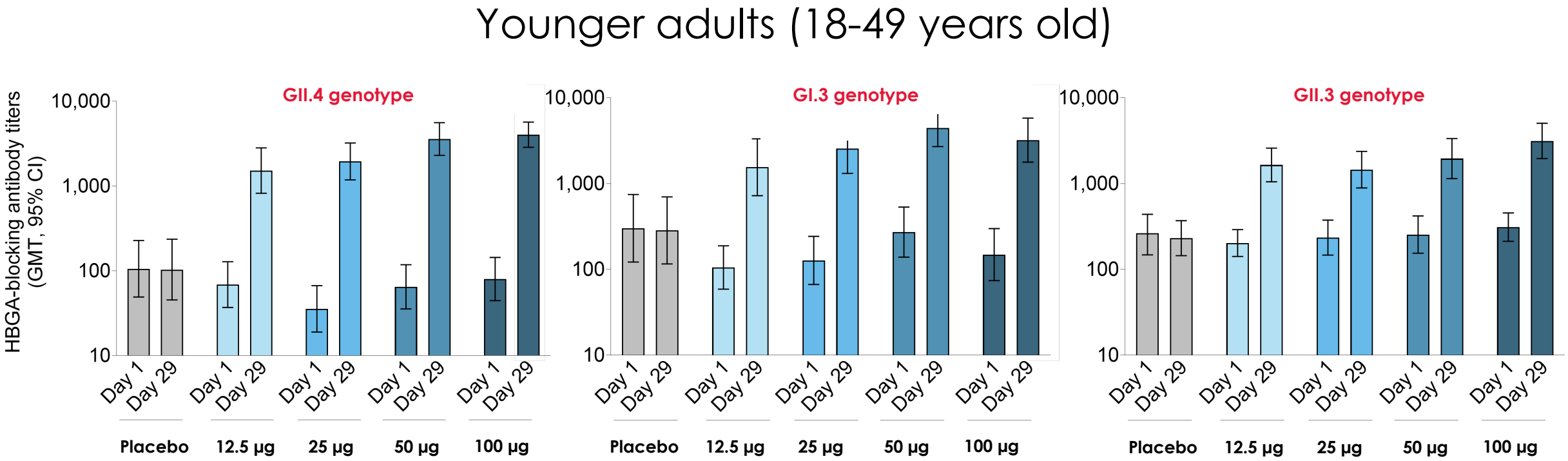
A single dose of mRNA-1403 elicited robust HBGA-blocking antibody titers against vaccine-matched NoV genogroup I and II genotypes in younger adults



HBGA, Histo-blood group antigen; NoV, norovirus

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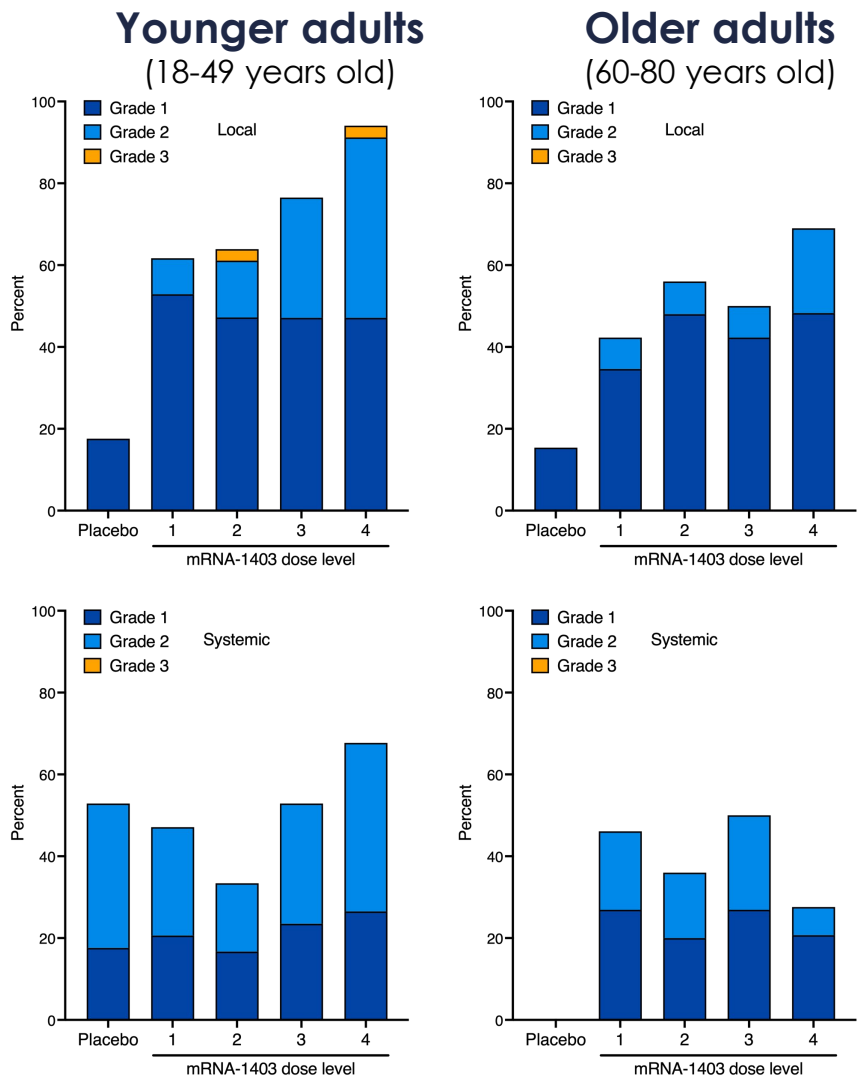
Single dose of mRNA-1403 was well-tolerated across all dose levels evaluated

Data from interim analysis on mRNA-1403 candidate through completion of Day 29 visits

Single dose of mRNA-1403 showed a favorable reactogenicity profile across dose levels evaluated with most solicited adverse reactions reported as grade 1 or 2 and few grade 3 reactions

Generally well-tolerated with an acceptable safety profile



mRNA-1403 Phase 3 study design

Phase 3 was designed to test the efficacy, safety and immunogenicity of a trivalent norovirus vaccine

Design
Randomized, observer-blind, placebo-controlled study

Number of participants
~35,000 adults ≥ 18 years old

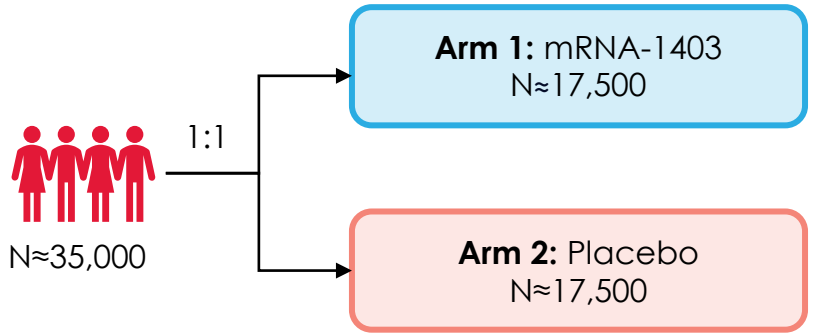
Vaccination schedule
Single dose of mRNA-1403 or Placebo

Duration
~25 months including screening period

Site location
Season 1 2024/25:
- Northern Hemisphere (United States, Canada, UK, Japan)
- Southern Hemisphere and Equatorial Region (Panama, Australia)

NEW COHORT → Season 2 2025/26:
- Northern Hemisphere (United States, UK)

Phase 3 Study Design



NOVA 301 TRIAL

Norovirus summary

Safety

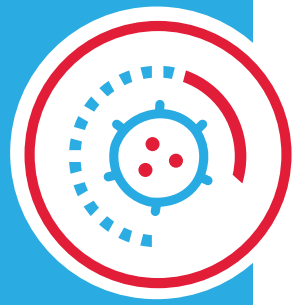
- Single dose of mRNA-1403 was well-tolerated and showed a favorable reactogenicity profile across dose levels
- Acceptable safety profile

Immunogenicity

- Robust HBGA-blocking antibody titers observed against vaccine-matched norovirus genogroup I and II selected strains across all dose levels evaluated
- Similar mRNA-1403 induced HBGA-blocking antibody titers observed in younger adult and older adult age groups

Next steps

- Advancing into additional 2025-2026 northern hemisphere cohort in Phase 3 vaccine efficacy study
- Phase 3 readout will be subject to case accruals; expect interim analysis in 2026



Vaccines in early development

Jacqueline Miller, M.D.
Chief Medical Officer

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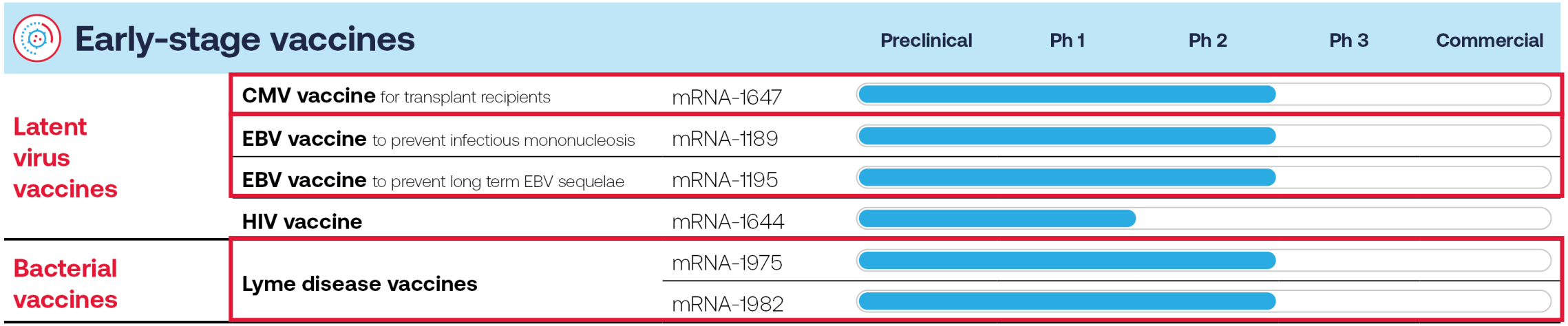
Early-stage vaccines pipeline



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CMV in transplant population

mRNA-1647

CMV is a major health risk in the transplant population

Significant risks associated with CMV infection post SOT/HCT[1]

- Graft rejection
- End-organ CMV disease (EOD)

Unmet need

- No approved vaccines against CMV for transplant setting
- High cost and toxicity of antiviral prophylaxis
- Antiviral prophylaxis is the standard of care and has been associated with decreased CMV-specific T-cell reconstitution and late-onset CMV infections[4,5]

47K
Solid Organ Transplantation (SOT)[2]

23K
Hematopoietic Stem Cell Transplant (HCT)[3]

~70K transplants in the US annually

(1) https://pubmed.ncbi.nlm.nih.gov/32603496/ (2) https://insights.unos.org/OPTN-metrics/. Data for year 2023. (3) https://bloodstemcell.hrsa.gov/data/donation-and-transplantation-statistics Data for year 2021 (4) Lin, Blood Adv, 2023. (5) Zamora D. et al. Blood.2021;138(1):34-43.

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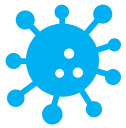
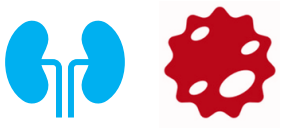
Why might mRNA-1647 be effective in a transplant population?



Sterilizing immunity is a challenging endpoint in vaccine development

- Many effective vaccines do not prevent infection but are highly effective preventing severe disease
- Examples: influenza, rotavirus, tetanus, varicella



Established and validated clinical endpoints exist in the transplant setting

- Immunosuppression of CMV positive patients increases risk of latent CMV reactivation due to T-cell suppression
- CMV infection and reactivation lead to syndromes such as viremia or disease which can be utilized as clinical endpoints

mRNA-1647 has the potential to prevent CMV viral replication and/or disease in transplant populations

- CMV cell-mediated immunity has an essential role in controlling CMV replication and preventing progression to CMV end-organ disease[1]
- 1647 generates early T-cell responses in HCT patients

The development of a safe and effective CMV vaccine is an unmet need and may benefit patients at risk including immunocompromised hosts

1 Kumar D et al. Am J Transplant. 2019;19:P2505-2516.

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Background: CMV in transplant recipients

Cytomegalovirus (CMV) is associated with substantial morbidity and mortality in immunocompromised patients, including allogeneic hematopoietic cell transplantation (HCT) recipients

Letermovir is approved and currently being used as standard prophylaxis against CMV in Recipient+ HCT recipients (until day +100) in most transplant centers

Despite its efficacy in preventing CMV reactivation, letermovir has been associated with decreased CMV-specific T cell reconstitution and late-onset CMV infections[1]

The development of a safe and effective CMV vaccine is an unmet need and may benefit patients at risk including immunocompromised hosts

1. Zamora D. et al. Blood.2021;138(1):34-43

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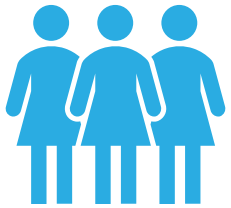
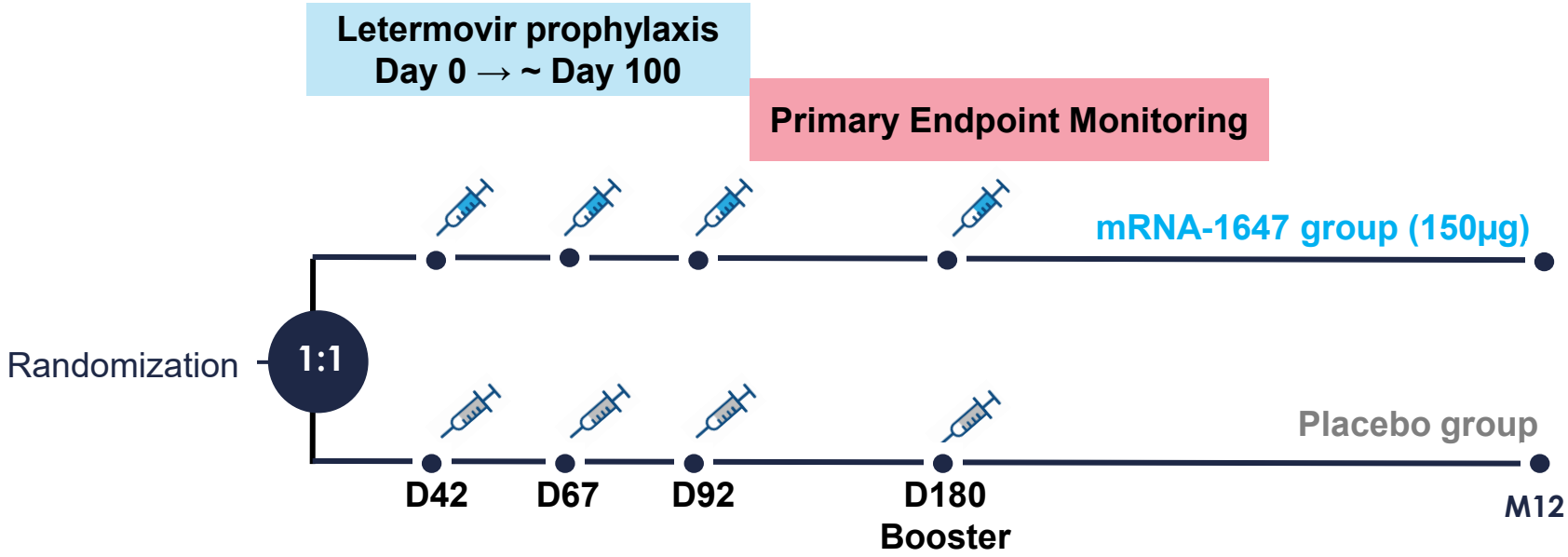
CMV transplant (mRNA-1647) Phase 2 trial design



CMV-seropositive adults ≥18 years with prior allogeneic HCT N=224

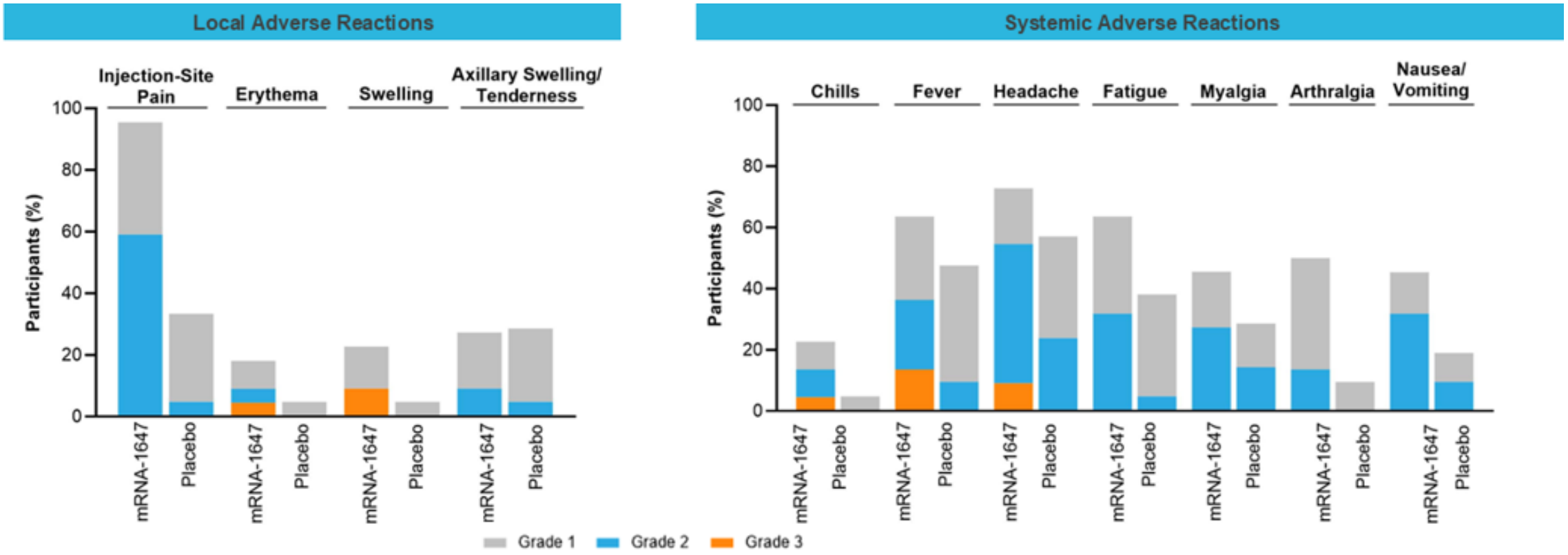


Primary efficacy endpoint: Time to clinically significant CMV infection (as measured by time to initiation of anti-CMV antiviral therapy) in the period following cessation of anti-CMV antiviral therapy and Month 9 post-HCT

Secondary efficacy endpoints:
Safety and Tolerability: Solicited local and systemic ARs 7d post-injection; Unsolicited AEs 25d post-injection; Grade 3–4 AEs and SAEs through end of study; Grade 3–4 acute GVHD through end of study

Immunogenicity: CMV-specific T-cell mediated immune responses, CMV-specific humoral immune responses

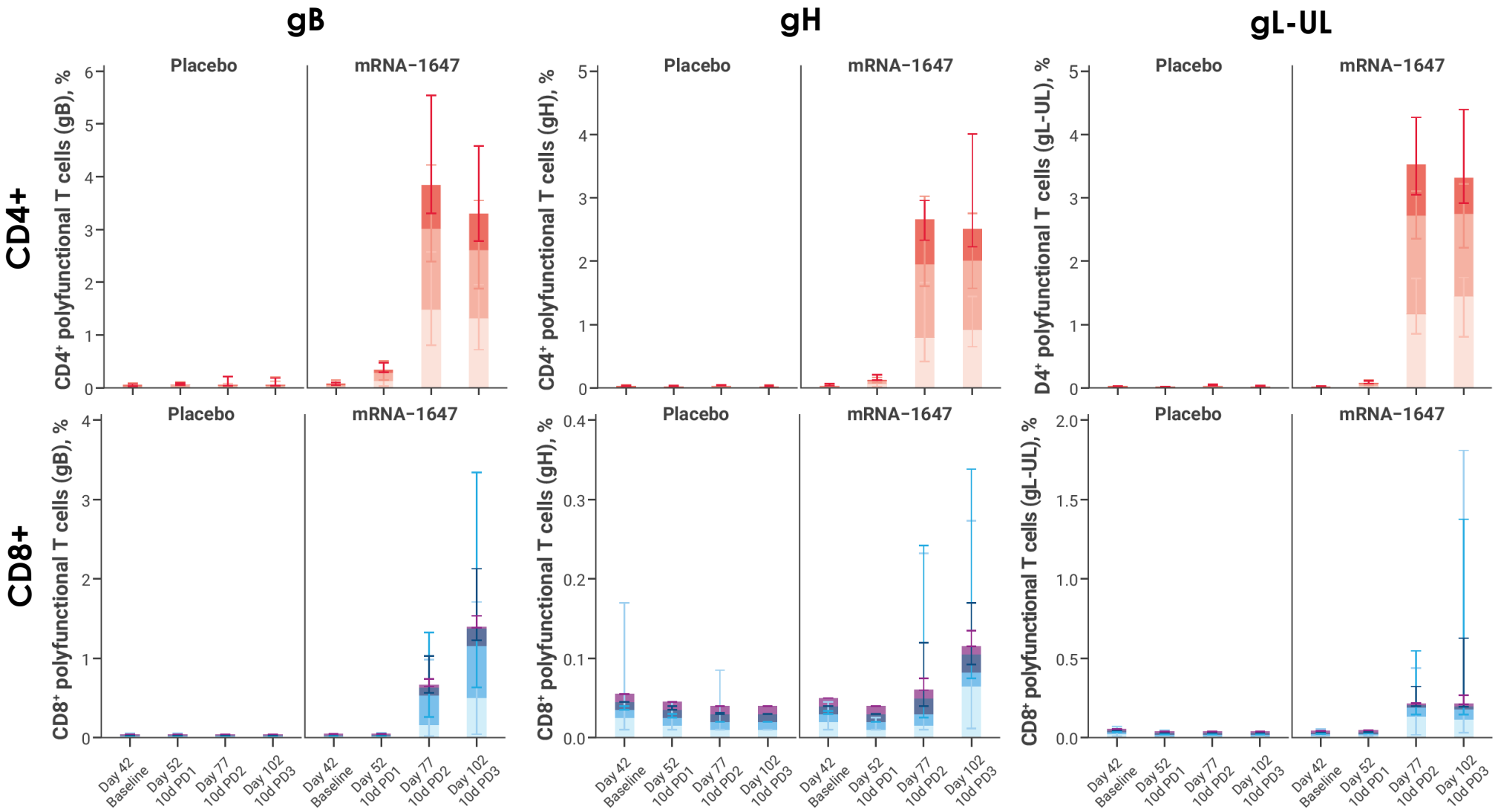
Solicited adverse reactions with 7 days after any injection



- Solicited local and systemic ARs were mostly grade 1–2 and no grade 4 ARs were reported
- For mRNA-1647, the most common solicited local ARs were injection-site pain; the most common solicited systemic ARs were headache, fever, and fatigue

AR, adverse reaction.
Summary of participants with solicited local adverse reactions within 7 days after vaccination by grade; placebo (n = 21); mRNA-1647 (n = 22).

P205 Interim Analysis: mRNA-1647 Generated CMV-Specific CD4+ and CD8+ T-Cell Responses in CMV-Seropositive HCT Recipients



T-cell responses are robust and polyfunctional

gL-UL comprises peptide pools of CMV gL UL128, UL130, and UL131A. Stacked bar plots represent the frequency of antigen-specific CD4+ or CD8+ non-naïve T cells exhibiting 2, 3, 4, or 5 functional markers. Each cell is counted once within its respective functional group (i.e., subsets are mutually exclusive). Functions assessed for CD4+ T cells were IFN-γ, IL-2, TNF-α, and CD40L; for CD8+ T cells were IFN-γ, IL-2, TNF-α, CD107a, and granzyme B.

CMV in transplant population summary

Safety

- Solicited local and systemic ARs were mostly grade 1–2 and no grade 4 ARs were reported
- For mRNA-1647, the most common solicited local ARs were injection-site pain; the most common solicited systemic ARs were headache, fever, and fatigue

Immunogenicity

- P205 interim analysis demonstrated that mRNA-1647 induced antigen-specific, polyfunctional CD4+ and CD8+ T-cell responses in high-risk CMV-seropositive HCT recipients
- Of note, robust cell-mediated immune responses were observed as early as 77 days after transplant, despite the suppressed immune status of HCT recipients

Next steps

- Phase 2 data readout

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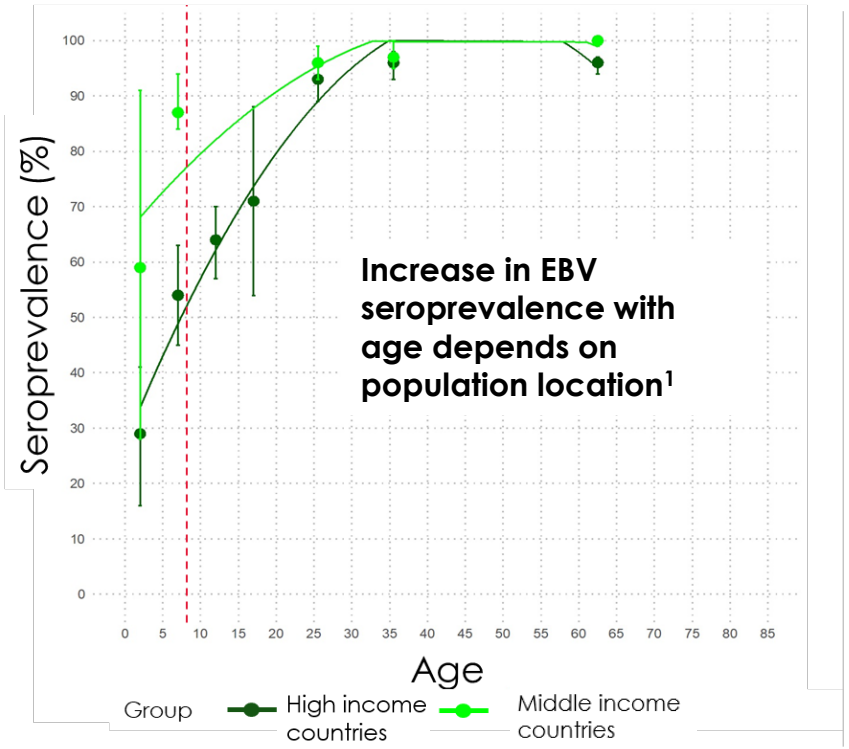
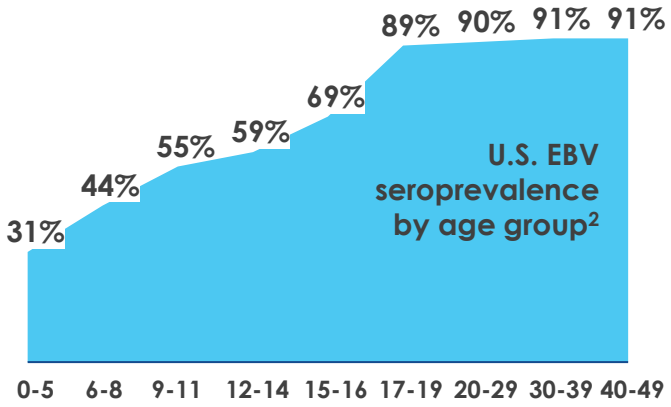
EBV

mRNA-1189 and mRNA-1195

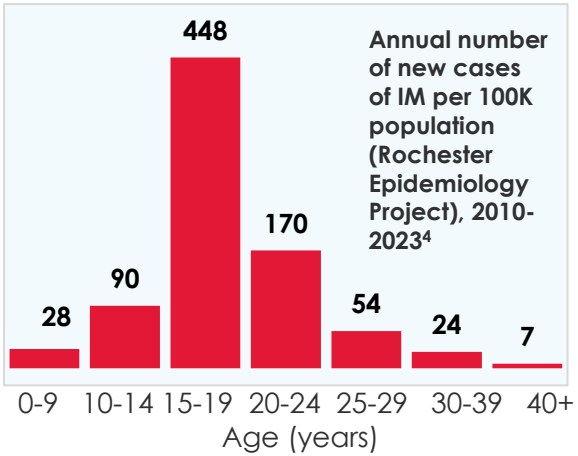
Epidemiology of EBV and infectious mononucleosis (IM)

EBV infects the vast majority of the world population by adulthood (~95% seropositivity)





Studies in Europe and North America show a more gradual increase in seroprevalence which did not exceed 90% until age 22[3]

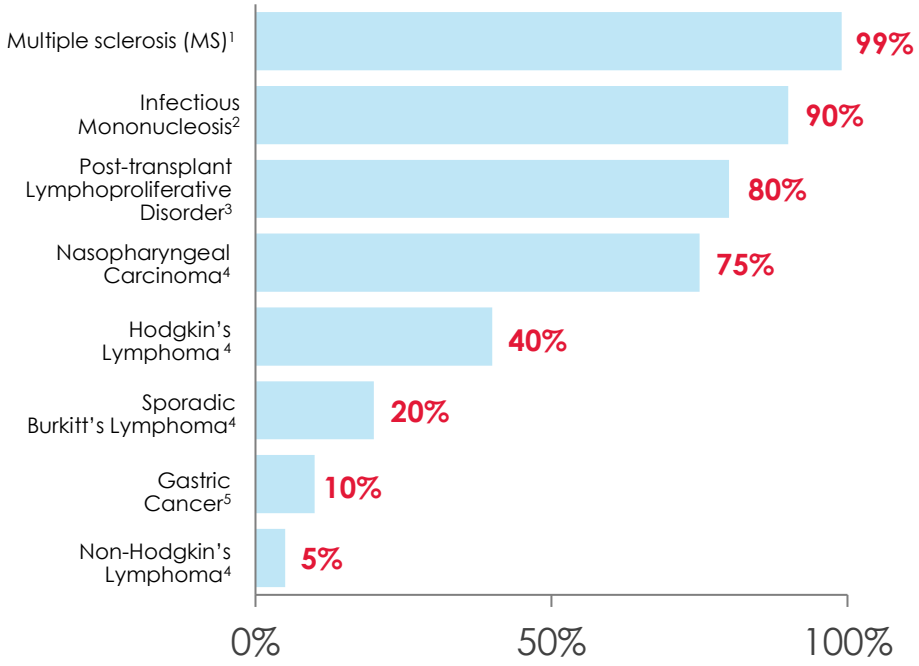


EBV accounts for over 90% of cases of IM[5]. Annual incidence of IM in the general U.S. population is estimated to be at least 45 cases per 100,000[6], with **peak incidence occurring at ages 15-19y[7]**

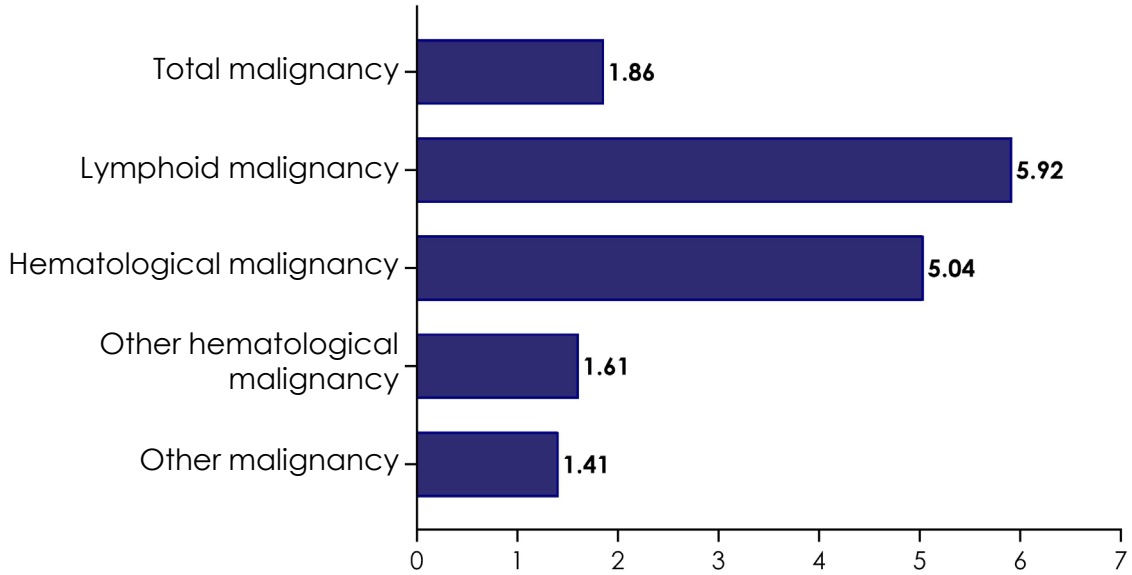
Sources: 1. Muckian et al., BMJ Glob Health. 2025 Aug 14;10(8):e015534. doi: 10.1136/bmjgh-2024-015534 . 2. Balfour et al., J Infect Dis. 2013 Oct 15;208(8):1286-93. doi: 10.1093/infdis/jit321, Moderna data on file. 3. Winter et al J Glob Health. 2020 Jun;10(1):010404. doi: 10.7189/jogh.10.010404. 4. Moderna data on file, Rochester Epidemiology Project 5 Fugl et al., BMC Fam Pract 20, 62 (2019). https://doi.org/10.1186/s12875-019-0954-3. 6. Tyring S, Moore AY, Lupi O (2016). *Mucocutaneous Manifestations of Viral Diseases: An Illustrated Guide to Diagnosis and Management* (2 ed.). CRC Press. p. 123. 7. Kuri et al 2020 BMC Public Health 20, 912 (2020). https://doi.org/10.1186/s12889-020-09049-x

EBV infection is associated with cancer incidence, with increased risk following symptomatic IM

Association of EBV by Indication in the United States



Increased risk of malignancies following EBV related IM (adjusted risk)[6]



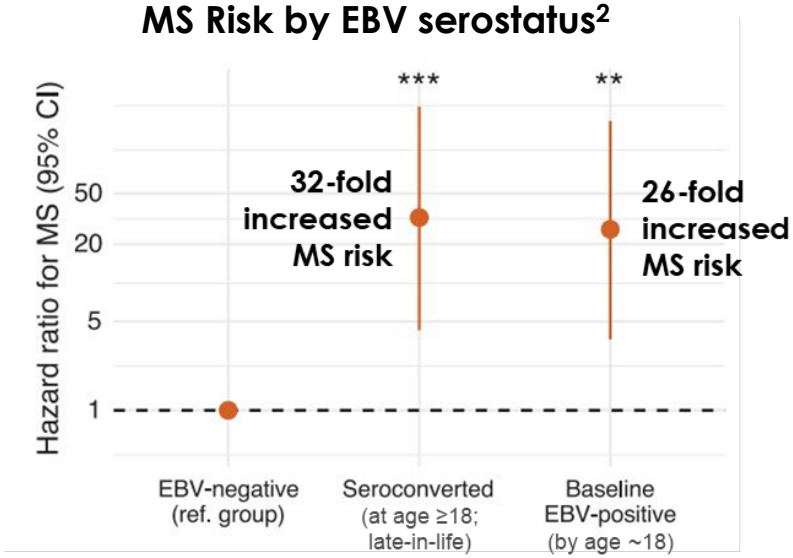
Globally, EBV-associated cancers account for over **200,000** new cases of cancer annually and **150,000** cancer deaths, representing about **1% and 2% of total global cancer incidence and cancer deaths**, respectively[6]

1. Ascherio and Munger, Semin Neurol. 2016 Apr;36(2):103-14 doi: 10.1055/s-0036-1579693; 2. Dunmire et al., J Clin Virol. 2018 May;102:84-92. doi: 10.1016/j.jcv.2018.03.001; https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6518816/; 3. Nijland et al., Transplant Direct. 2015 Dec 15;2(1):e48. doi: 10.1097/TXD.0000000000000557; 4. Gequelin et al., Rev Bras Hematol Hemoter. 2011;33(5):383-8. doi: 10.5581/1516-8484.2011010 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3415781/; 5. https://dceg.cancer.gov/research/cancer-types/stomach-gastric/ebv-associated-gastric-cancer; 6. Cai et al., Front Oncol. 2022 Dec 14;12:991069. doi: 10.3389/fonc.2022.991069

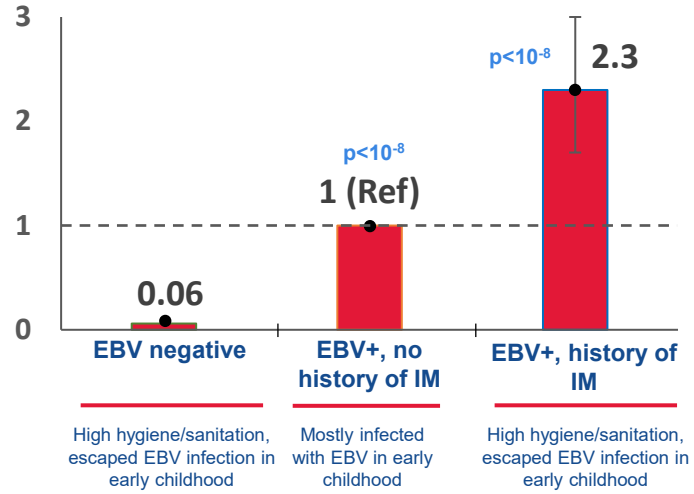
Etiologic link between EBV and multiple sclerosis (MS)

- **Nearly 1M people in the U.S. have MS** [1]
- EBV seropositivity is nearly universal in MS and seronegative individuals have a negligible risk of MS
- Recent landmark study established a **~32 fold increased risk of developing MS following EBV seroconversion**[2]
- It was previously established that **infectious mononucleosis** is an MS risk factor, beyond the contribution of EBV alone; in addition, the epidemiology of IM and MS are similar

MS Risk by EBV serostatus[2]



MS Risk by history of IM and EBV serostatus[3]



Sources: 1. https://www.nationalmssociety.org/About-the-Society/MS-Prevalence; 2 Bjornevik et al., Science. 2022 Jan 21;375(6578):296-301. doi: 10.1126/science.abj8222; 3. Ascherio and Munger, Semin Neurol. 2016 Apr;36(2):103-14. doi: 10.1055/s-0036-1579693.

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EBV is associated with several serious medical conditions that could be addressed through mRNA

Infectious Mononucleosis

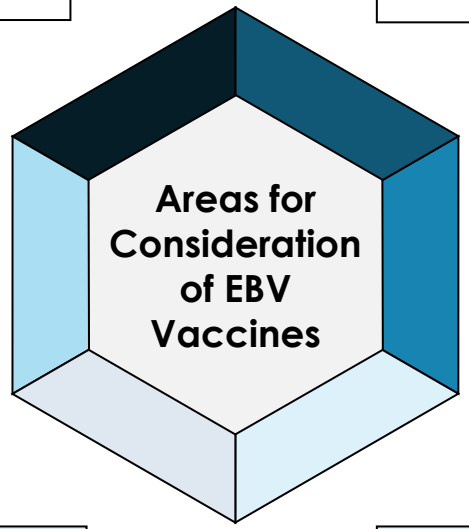
Established causative link to primary EBV infection predominantly in young adolescents

Multiple Sclerosis

Supported by large volume of scientific data and mechanistic link, including recent high-profile publications

Chronic Active EBV (CAEBV)

Direct application of an EBV Tx vaccine, though CAEBV is quite rare with largely unknown epidemiology



Post-transplant Lymphoproliferative Disorder (PTLD)

PTLD has a fully validated causal link to EBV and thus strongly supported by biology

Autoimmune Disease (excl. MS)

Large body of data supporting correlative link between EBV infection and various autoimmune diseases (SLE, Crohn's etc.)

Prophylactic Oncology Applications
Hodgkin's, Burkitt, and Nasopharyngeal Carcinoma

Solid scientific link to EBV, albeit lengthy time to onset

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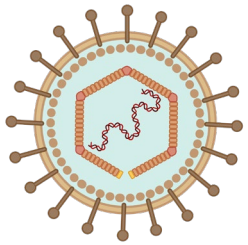
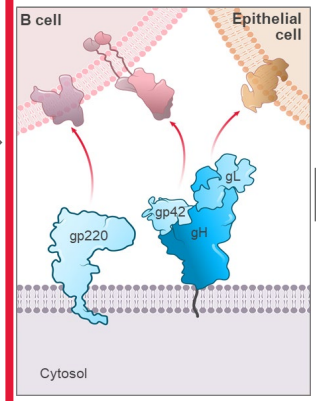
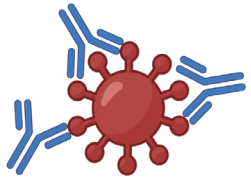
Moderna's vaccines aim to tackle multiple EBV-associated conditions

mRNA-1189

EBV



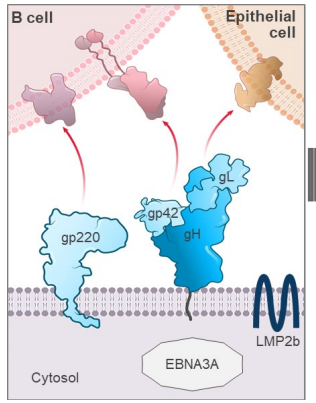


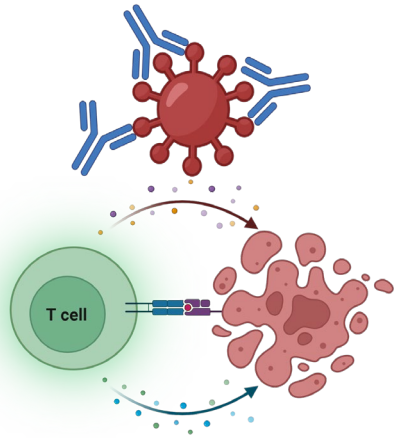


Humoral response to target **lytic** replication and primary infection

- Vaccine composed of **lytic antigens** to build robust **antibody response** against EBV
- **Primary indication: Infectious Mononucleosis (IM)**
  - Prevention of IM; prevention of EBV infection as potential upside
- Prevention of long-term sequelae

mRNA-1195





Humoral and **CMI** response to target **lytic** replication and **latent** infection

- Vaccine composed of **lytic** and **latent antigens**
- **Primary indication(s):**
  - **Treatment of Multiple Sclerosis**
    - Immune dysregulation of/by EBV may be one of the underlying mechanisms of action
    - Vaccine MOA: restoring robust immune control of lytic and latent infection
  - **Post-transplant Lymphoproliferative Disorder (PTLD)**

EBV (mRNA-1189) Phase 1 trial design

Data previously shared*

Design
Randomized observer-blind, placebo-controlled dose-ranging study

Number of participants
Part A: 272 EBV seronegative and EBV seropositive adults (18-30 years old)
Part B: 150 healthy EBV seronegative adolescents (12-17 years old)

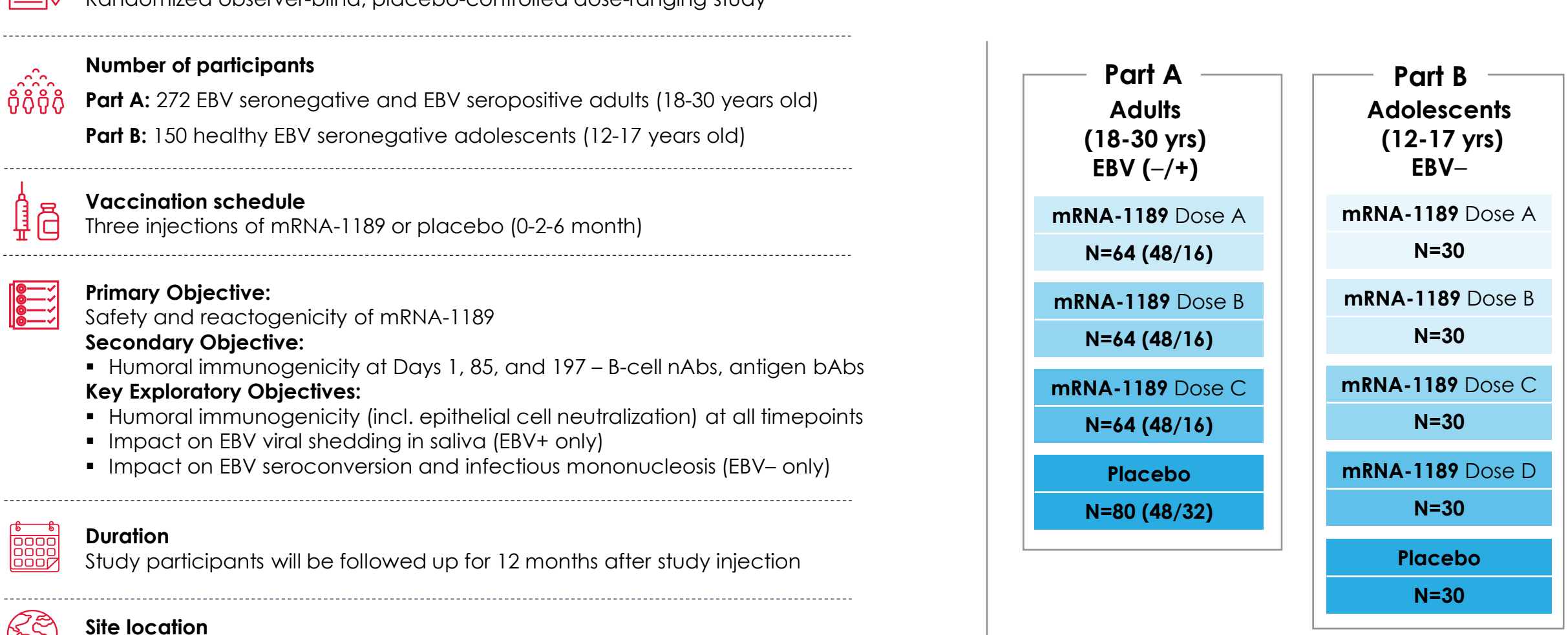
Vaccination schedule
Three injections of mRNA-1189 or placebo (0-2-6 month)

Primary Objective:
Safety and reactogenicity of mRNA-1189
Secondary Objective:
- Humoral immunogenicity at Days 1, 85, and 197 – B-cell nAbs, antigen bAbs

Key Exploratory Objectives:
- Humoral immunogenicity (incl. epithelial cell neutralization) at all timepoints
- Impact on EBV viral shedding in saliva (EBV+ only)
- Impact on EBV seroconversion and infectious mononucleosis (EBV– only)

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

Site location
US



nAbs, neutralizing antibodies; bAbs, binding antibodies

*shared at Vaccines Day 2024, Gordon Research Conference Jun'24, RNA bench to bedside IV Dec'24, National Academy of Sciences Meeting May'25

EBV (mRNA-1189) Phase 2 trial design

Fully enrolled

Design
Randomized, observer-blind, placebo-controlled, dose-ranging

Number of participants
420 EBV+ and EBV– healthy adolescents and adults 10 to 21 yrs of age

Vaccination schedule
Three injections of mRNA-1189 or placebo (0-2-6 month)

Primary Objective:
Safety and reactogenicity of mRNA-1189

Secondary Objective:
- Humoral immunogenicity at Days 1, 85, and 197 – B-cell nAbs, antigen bAbs

Key Exploratory Objectives:
- Humoral immunogenicity (incl. epithelial cell neutralization) at all timepoints
- Impact on EBV viral shedding in saliva (EBV+ only)
- Impact on EBV seroconversion and infectious mononucleosis (EBV– only)

Duration
Study participants followed up for 12 months after last study injection; planning long-term extension for additional 18-24 months

Part C

Adolescents and Adults (10-21 yrs) EBV(-/+)

mRNA-1189 Dose A
N=105 (75/30)
mRNA-1189 Dose B
N=105 (75/30)
mRNA-1189 Dose C
N=105 (75/30)
Placebo
N=105 (75/30)

nAbs, neutralizing antibodies; bAbs, binding antibodies

EBV (mRNA-1189) vaccine summary and next steps

Safety

- mRNA-1189 was generally well tolerated in adults and adolescents in Phase 1 (Part A and B)

Immunogenicity

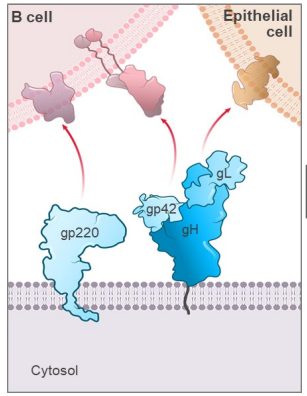
- Participants across mRNA-1189 dose groups showed increases in functional and binding antibodies from baseline following mRNA administration regardless of serostatus
- Following 3 injections, titers in mRNA-1189 recipients crossed baseline EBV-seropositive threshold
- mRNA-1189 reduced measurable viral DNA and frequency of shedding in saliva of EBV-seropositive recipients

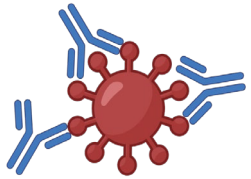
Next steps

- Phase 1 final data from part A and B expected Q1 2026
- Phase 2 data expected H1 2026

Moderna's vaccines aim to tackle multiple EBV-associated conditions

mRNA-1189





Humoral response to target **lytic** replication and primary infection

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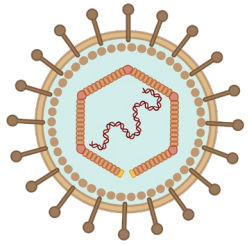
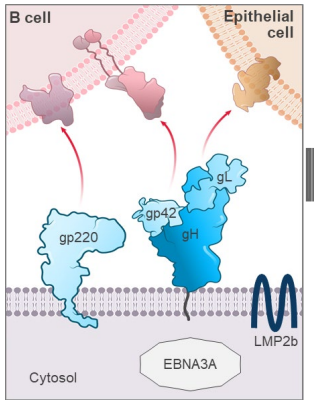
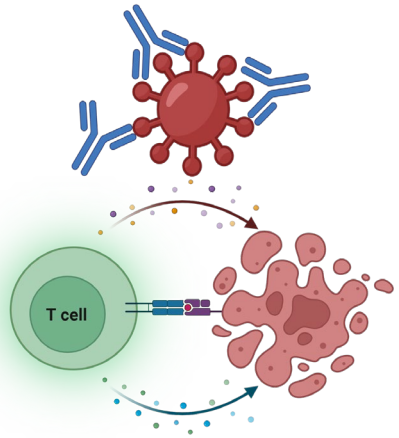
- **Primary indication: Infectious Mononucleosis (IM)**
  - Prevention of IM; prevention of EBV infection as potential upside
- Prevention of long-term sequelae

EBV



mRNA-1195





Humoral and **CMI** response to target **lytic** replication and **latent** infection

- Vaccine composed of **lytic** and **latent antigens**
- **Primary indication(s):**
  - **Treatment of Multiple Sclerosis**
    - Immune dysregulation of/by EBV may be one of the underlying mechanisms of action
    - Vaccine MOA: restoring robust immune control of lytic and latent infection
  - **Post-transplant Lymphoproliferative Disorder (PTLD)**

mRNA-1195 Phase 1 Part A trial design (mRNA-1195-P101)

Sharing new data today

Design
Randomized, observer-blind, placebo-controlled, dose-ranging

Number of participants
350 healthy EBV-seropositive adults (18-55 years old)

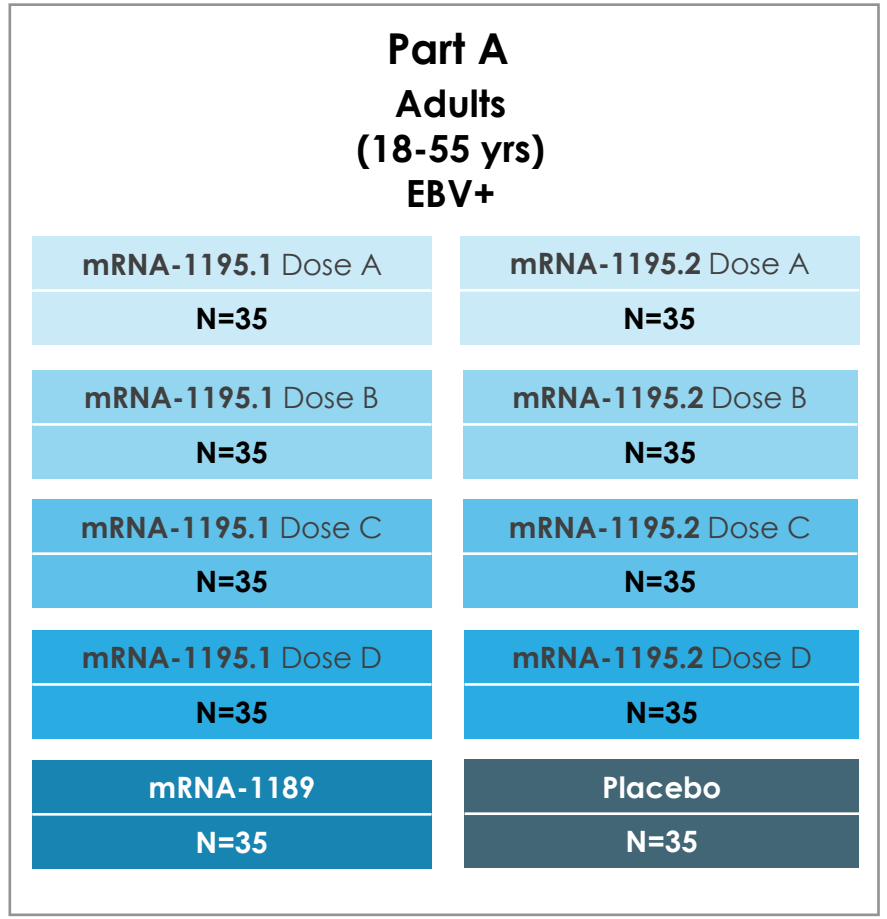
Vaccination schedule
Three injections mRNA-1195 (two different compositions), mRNA-1189 or placebo (0-2-6 month)

Primary Objective:
Safety and reactogenicity of mRNA-1195

Secondary Objective:
- Humoral immunogenicity at Days 1, 85, and 197 – B-cell nAbs, antigen bAbs

Key Exploratory Objectives:
- Humoral immunogenicity (incl. epithelial cell neutralization) at all timepoints
- Impact on EBV viral shedding in saliva
- Cellular immunogenicity (T-cell responses)

Duration
Study participants followed up for 6 months after last study injection



nAbs, neutralizing antibodies; bAbs, binding antibodies

mRNA-1195 was well tolerated with an acceptable safety profile: Local and systemic reactogenicity

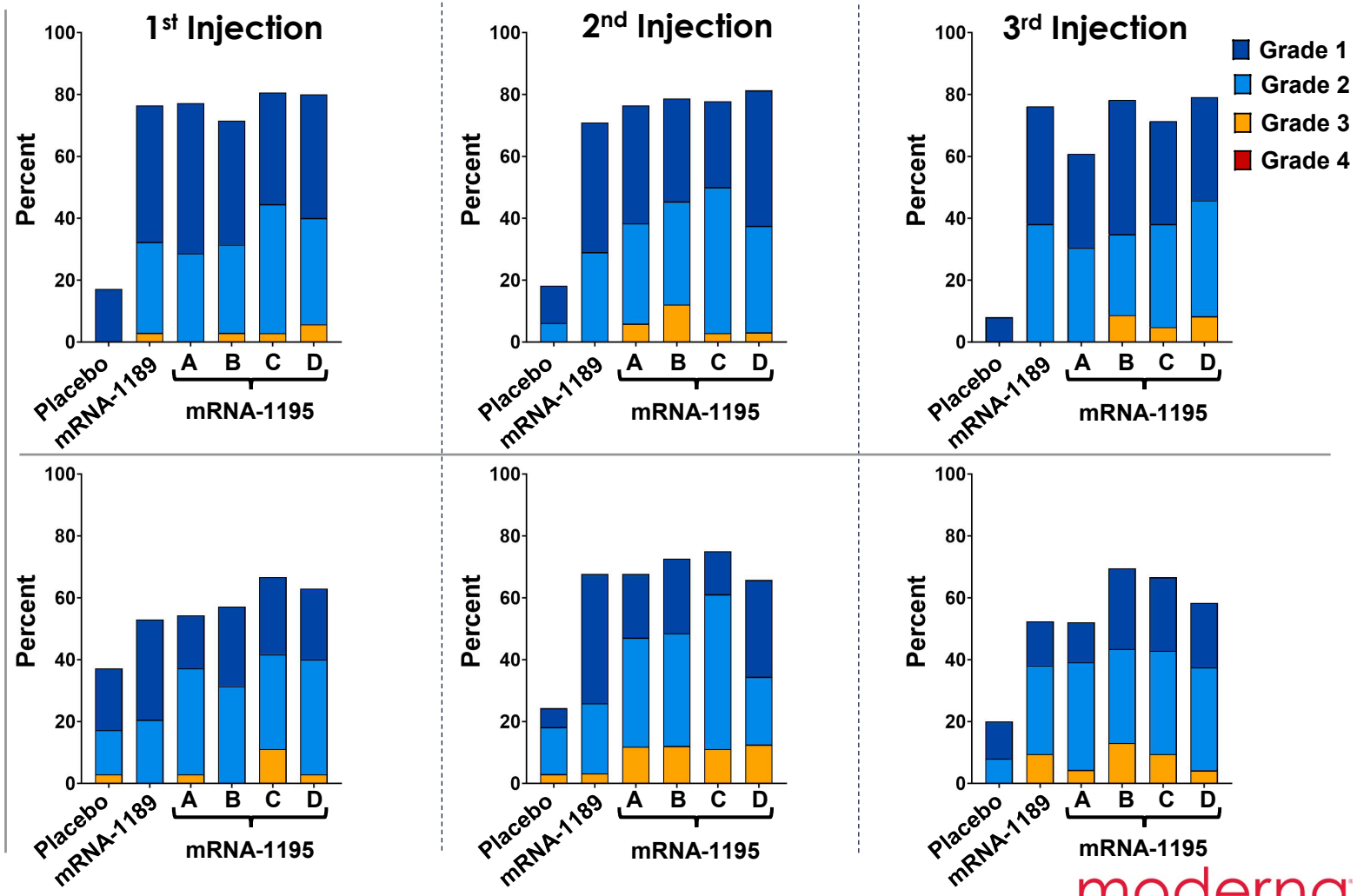
P101 Part A Data | = D1, D57, D169

Local reactogenicity

- Pain was the most common local solicited adverse reaction following any injection

Systemic reactogenicity

- Headache, fatigue, myalgia, and arthralgia were most common following any injection

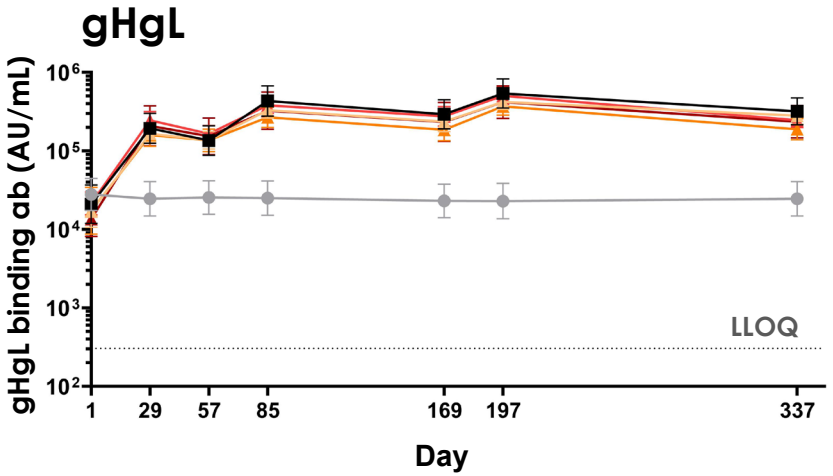


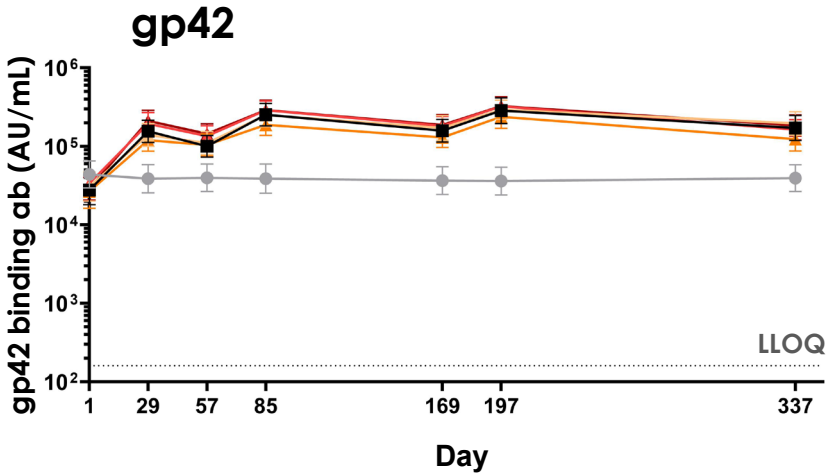
- Displayed is percentage of participants reporting any solicited adverse reaction within 7 days post injection; solicited local reactions include pain, swelling, erythema and axillary swelling; solicited systemic reactions include headache, fatigue, myalgia, arthralgia, nausea/vomiting, chills and fever

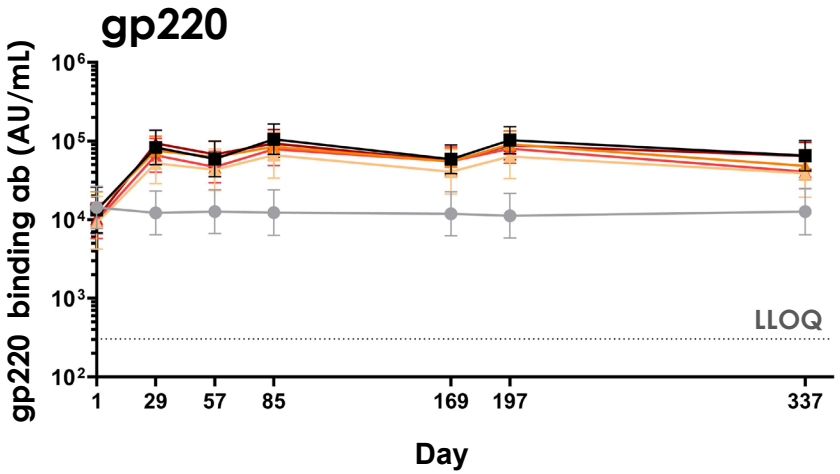
Humoral Immunogenicity: Binding antibodies to glycoproteins are boosted across mRNA-1195 dose levels

P101 Part A Data | = D1, D57, D169

- All mRNA groups had detectable boost in **gHgL**, **gp42** and **gp220** binding antibodies following mRNA injection
- Responses persisted above baseline through Day 337, 6 months post dose 3
- No pronounced dose response across dose levels tested







= Placebo
= mRNA-1189

mRNA-1195
= Dose A
= Dose B
= Dose C
= Dose D

Day 1 = Baseline
Day 29 = 1 month post dose 1
Day 85 = 1 month post dose 2
Day 197 = 1 month post dose 3
Day 337 = 6 months post dose 3

ab, antibodies

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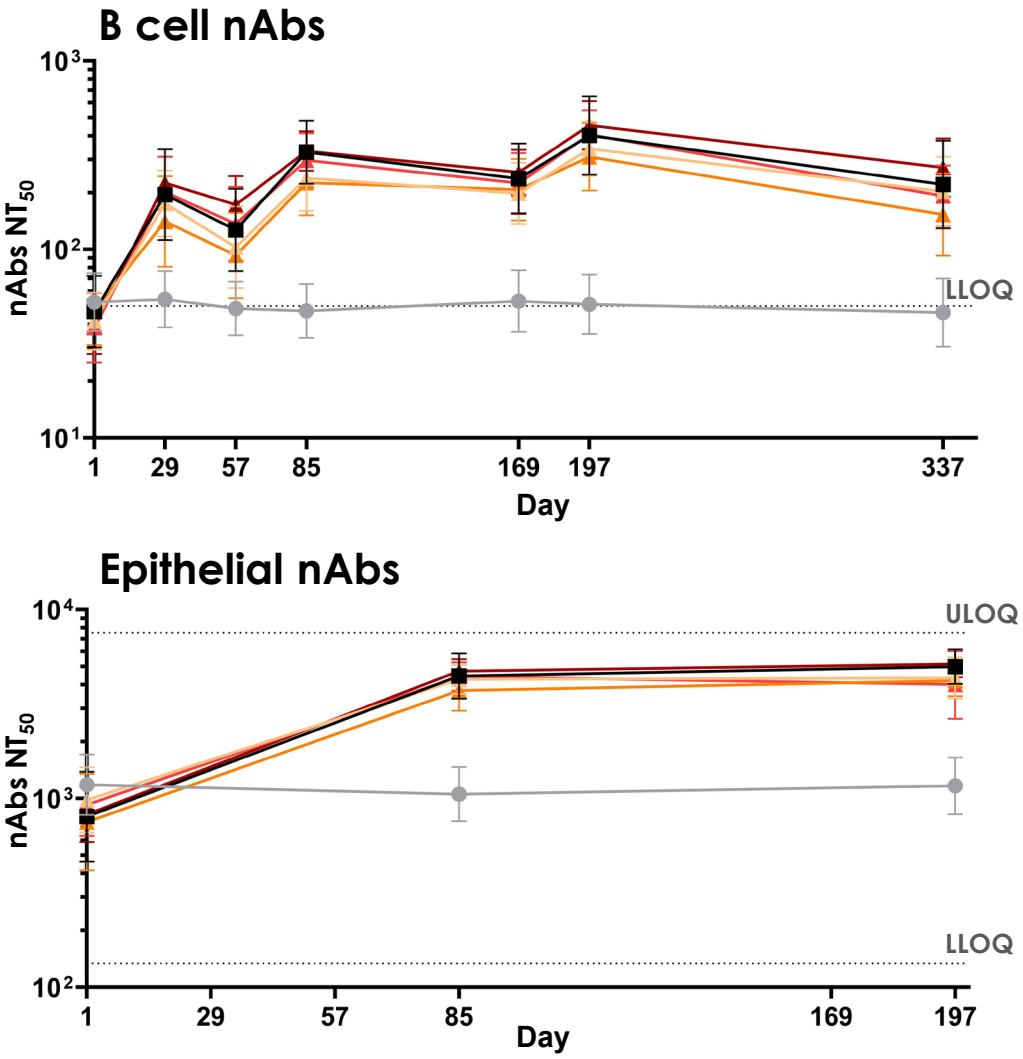
Humoral Immunogenicity: Serum B-cell and epithelial nAbs are boosted across mRNA-1195 dose levels

P101 Part A Data | = D1, D57, D169

- All mRNA-1189 and mRNA-1195 groups had detectable boost in **B-cell and Epithelial nAbs** following mRNA injection
- Similar responses across dose levels tested with overlapping confidence intervals
- B cell nAb responses persisted above baseline through Day 337, 6 months post dose 3



= Placebo
= mRNA-1189

mRNA-1195
= Dose A
= Dose B
= Dose C
= Dose D

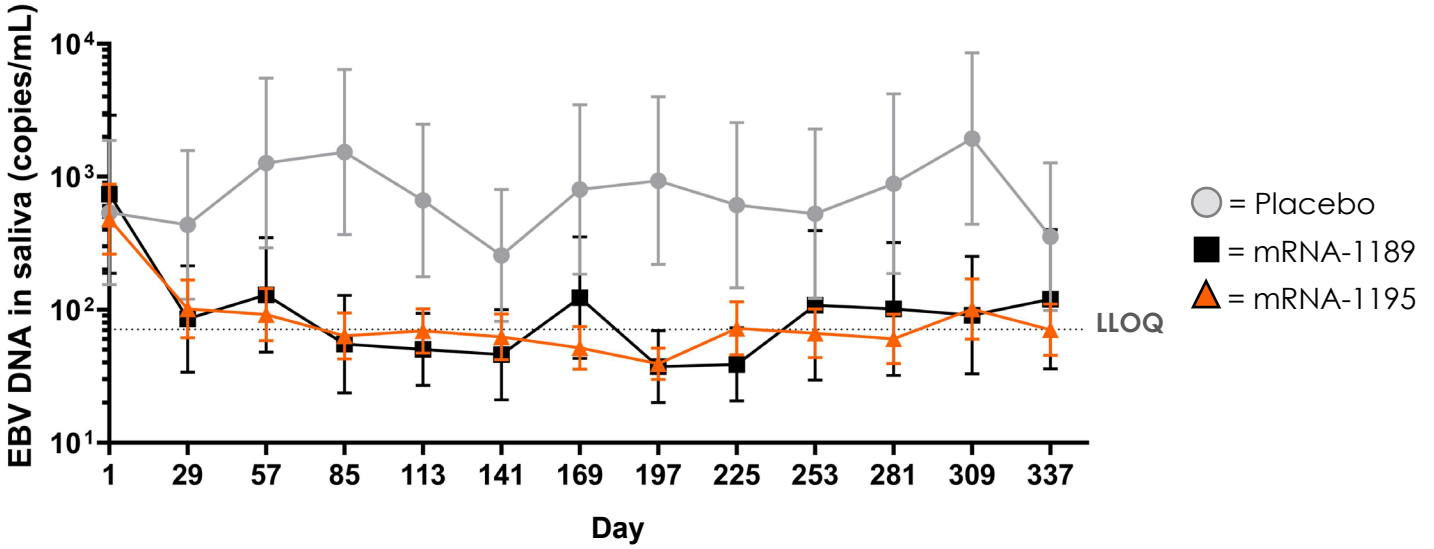
Day 1 = Baseline
Day 29 = 1 month post dose 1
Day 85 = 1 month post dose 2
Day 197 = 1 month post dose 3
Day 337 = 6 months post dose 3

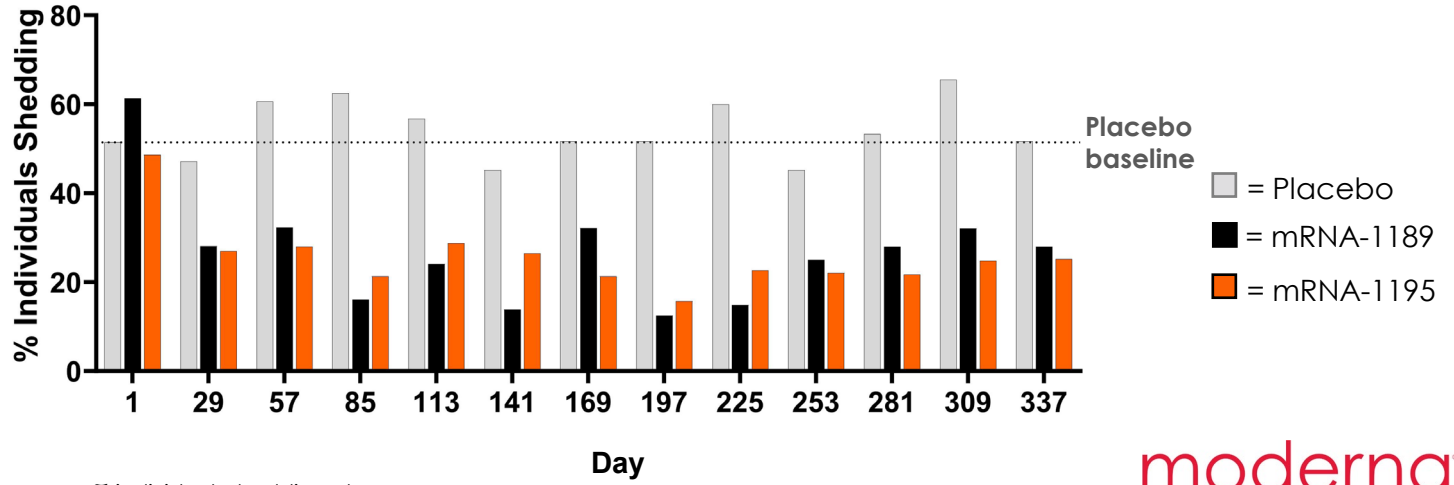
Epithelial nAbs tested only at select timepoints shown

mRNA-1195 impacts EBV shedding in saliva

P101 Part A Data | = D1, D57, D169

- mRNA-1195 dose levels were consolidated and analyzed together to provide better qualitative description of the viral shedding data
- All mRNA groups had detectable **decrease in EBV DNA** shed in saliva compared to placebo group starting 1 month after the 1st injection and persisting through 6 months after the 3rd injection
- Compared to placebo, the **frequency of individuals shedding was reduced** in the mRNA-1195 and mRNA-1189 groups, confirming findings in mRNA-1189 Phase 1

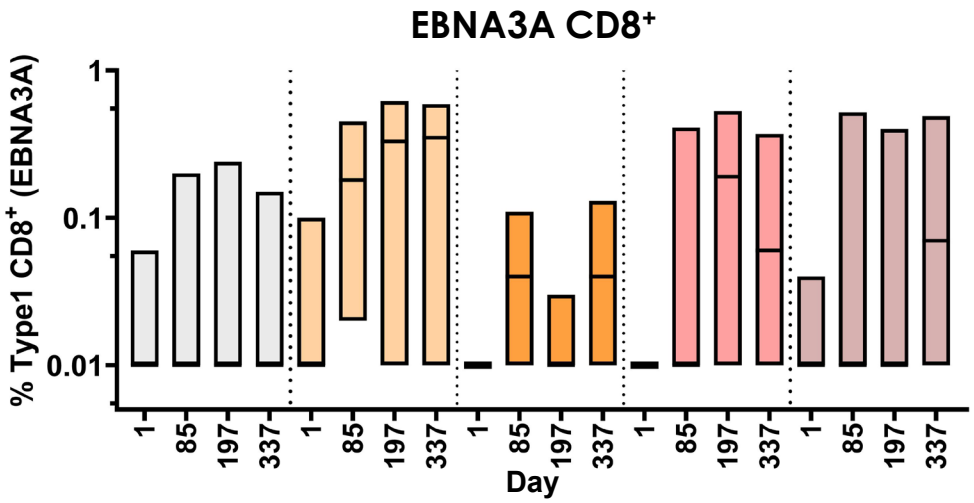


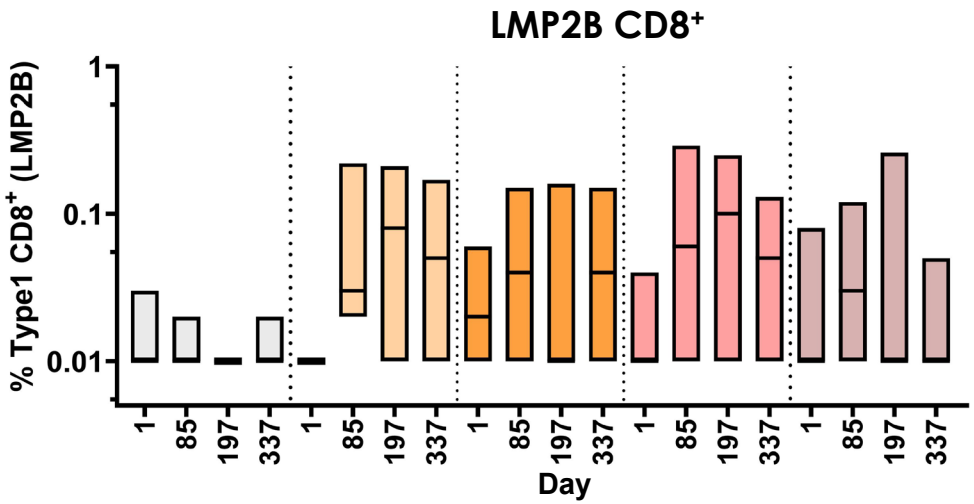


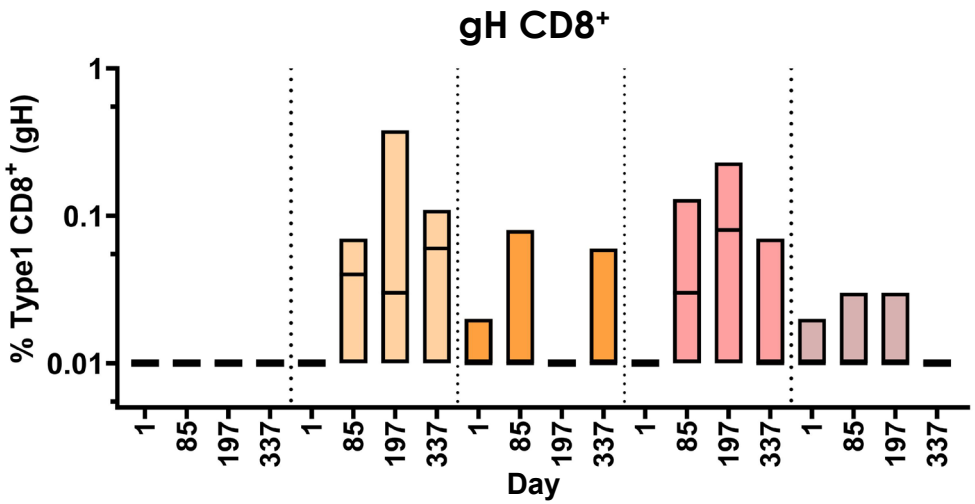
% individuals shedding above LLOQ of 71 copies/mL

Cell-mediated Immunogenicity – CD8+ responses to latent and lytic antigens are boosted across mRNA-1195 dose levels

P101 Part A Data | = D1, D57, D169







= Placebo

mRNA-1195
= Dose A
= Dose B
= Dose C
= Dose D

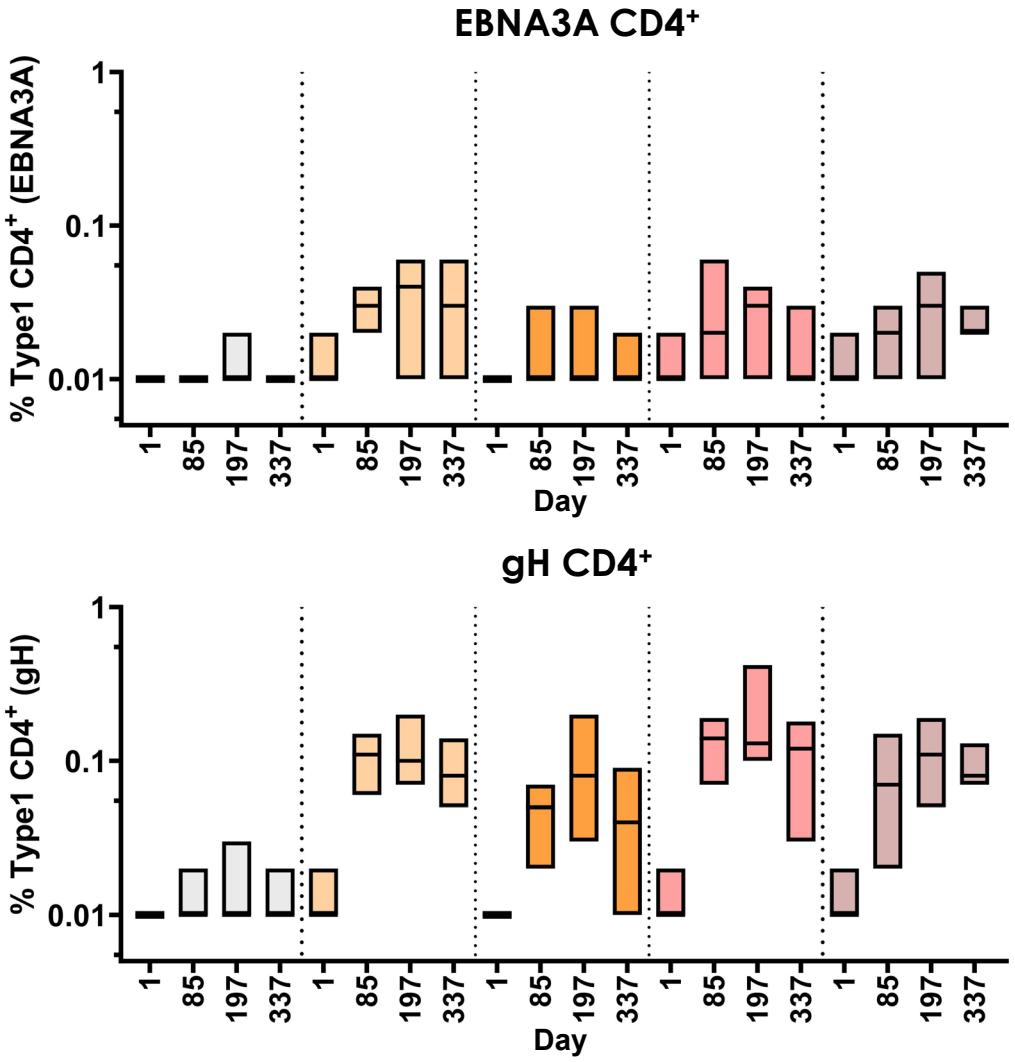
Day 1 = Baseline
Day 85 = 1 month post dose 2
Day 197 = 1 month post dose 3
Day 337 = 6 months post dose 3

- Range of CD8+ responses detected at baseline in EBV+ participants across treatment arms, suggesting heterogeneity in general population
- Overall trend towards increased CD8+ responses to EBNA3A, LMP2B and gH following 2 or 3 injections
- Responses persisted through Day 337, 6 months post dose 3, in most mRNA groups

Cell-mediated Immunogenicity – CD4+ responses to latent and lytic antigens are boosted across mRNA-1195 dose levels

P101 Part A Data | = D1, D57, D169

- Baseline CD4+ T cell responses detected at low levels across EBV+ participants in all groups
- Overall trend towards increased CD4+ responses to EBNA3A and gH following 2 or 3 injections
- Responses persisted through Day 337, 6 months post dose 3, in mRNA groups



= Placebo

mRNA-1195
= Dose A
= Dose B
= Dose C
= Dose D

Day 1 = Baseline
Day 85 = 1 month post dose 2
Day 197 = 1 month post dose 3
Day 337 = 6 months post dose 3

Note: Box plots show interquartile range (Q1-Q3) with lines indicating median

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EBV (mRNA-1195) phase 1 part B trial design

Fully enrolled

Design
Randomized, observer-blind, placebo-controlled, dose-ranging

Number of participants
120 healthy EBV-seronegative and EBV-seropositive adults (18-30 years old)

Vaccination schedule
Three injections of selected mRNA-1195 composition or placebo (0-2-6 month)

Primary Objective:
Safety and reactogenicity of mRNA-1195

Secondary Objective:
- Humoral immunogenicity at Days 1, 85, and 197 – B-cell nAbs, antigen bAbs

Key Exploratory Objectives:
- Humoral immunogenicity (incl. epithelial cell neutralization) at all timepoints
- Impact on EBV viral shedding in saliva (EBV+ only)
- Cellular immunogenicity (T-cell responses)

Duration: 18-months
Study participants followed up for 12 months after last study injection

Part B
Adults (18-30 yrs) EBV(-/+)

mRNA-1195 Dose A
N=30 (15/15)
mRNA-1195 Dose B
N=30 (15/15)
mRNA-1195 Dose C
N=30 (15/15)
Placebo
N=30 (15/15)

nAbs, neutralizing antibodies; bAbs, binding antibodies

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mRNA-1195-P201 Phase 2 proof of concept in MS Design

Ongoing

Design
Randomized 1:1:1, observer-blind, placebo-controlled, dose-ranging

Number of participants
180 EBV+ adults 18 to <55 yrs of age diagnosed with RRMS, CIS, RIS in the last 24 months (i.e. early in their MS disease course)

Vaccination schedule
3 injections at 0, 2, 6 month schedule of selected composition of mRNA-1195 at Dose A or Dose B, or Placebo

Primary Objective:
Safety and reactogenicity of mRNA-1195

Secondary Objective:
- Impact of mRNA-1195 on formation of new Gd-enhancing T1 lesions
- Impact of mRNA-1195 on formation of new and/or newly enlarging T2 lesions
- impact of mRNA-1195 on time to first new MS disease activity
- Humoral immunogenicity of mRNA-1195

Key Exploratory Objectives:
- Impact of mRNA-1195 on other markers of MS disease activity
- Impact of mRNA-1195 on EBV viral activity
- Additional assessments of mRNA-1195 immunogenicity including cellular immunogenicity

EBV+ pwMS (18-55 years of age) n=180

mRNA-1195 Dose A
N=60
mRNA-1195 Dose B
N=60
Placebo
N=60

nAbs, neutralizing antibodies; bAbs, binding antibodies; pwMS, people with MS

EBV Tx mRNA-1195 summary and next steps

Safety

- Phase 1 interim analysis data demonstrate that mRNA-1195 is generally well tolerated in EBV-seropositive adults 18-55 yrs

Immunogenicity

- EBV-seropositive participants across mRNA-1195 dose groups showed increases in B-cell nAbs and epithelial nAbs, and binding antibodies to glycoproteins from baseline following 3 injections
- mRNA-1195 boosted $CD8^+$ and $CD4^+$ T cell responses to latent and glycoprotein antigens in EBV-seropositive participants across tested dose levels
- Humoral and cell-mediated immunity responses persisted above baseline through 6 months after the last injection
- mRNA-1195 reduced measurable viral shedding in saliva of EBV-seropositive recipients through 6 months after the last injection

Next steps

- Phase 1 part B data expected in 2H2026
- Phase 2 MS study DSMB decision based on sentinel cohort data targeted for 1H2026

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Lyme Disease

mRNA-1982/mRNA-1975

Lyme disease is the most common vector borne disease in the Northern Hemisphere

Lyme follows a bimodal age distribution, affecting mainly children under 15 and older adults

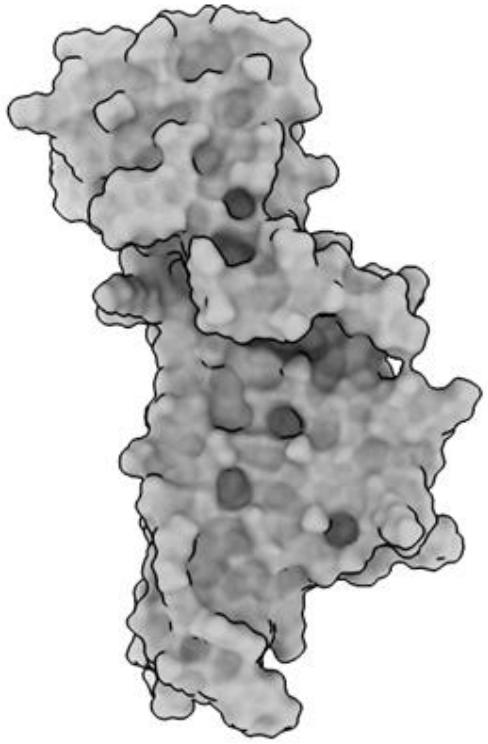
Cases per year in major geographies:
US: 475K[1]
EU: 200k[2]

Patients may develop rash, fever, fatigue, headache, and joint pain or swelling. If untreated, symptoms can persist and lead to arthritis, or neurological and cardiac complications.

No approved human vaccine currently on the market

[1]PMID: 33496229
[2]PMID: 26966194

Moderna's investigational Lyme vaccine strategy targets a proven protective antigen, OspA



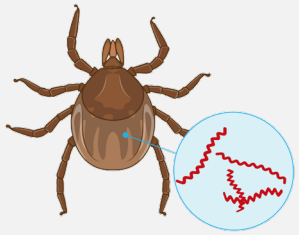
Outer Surface Protein A (OspA) Expression

On in the tick gut

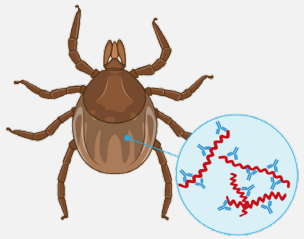
Off during human infection

<u>Product concept</u>: The OspA lipoprotein is a transmission blocking vaccine antigen

Vaccine, when injected, elicits high levels of anti-OspA antibodies



Borrelia infected tick attaches to vaccinated human and begins blood meal



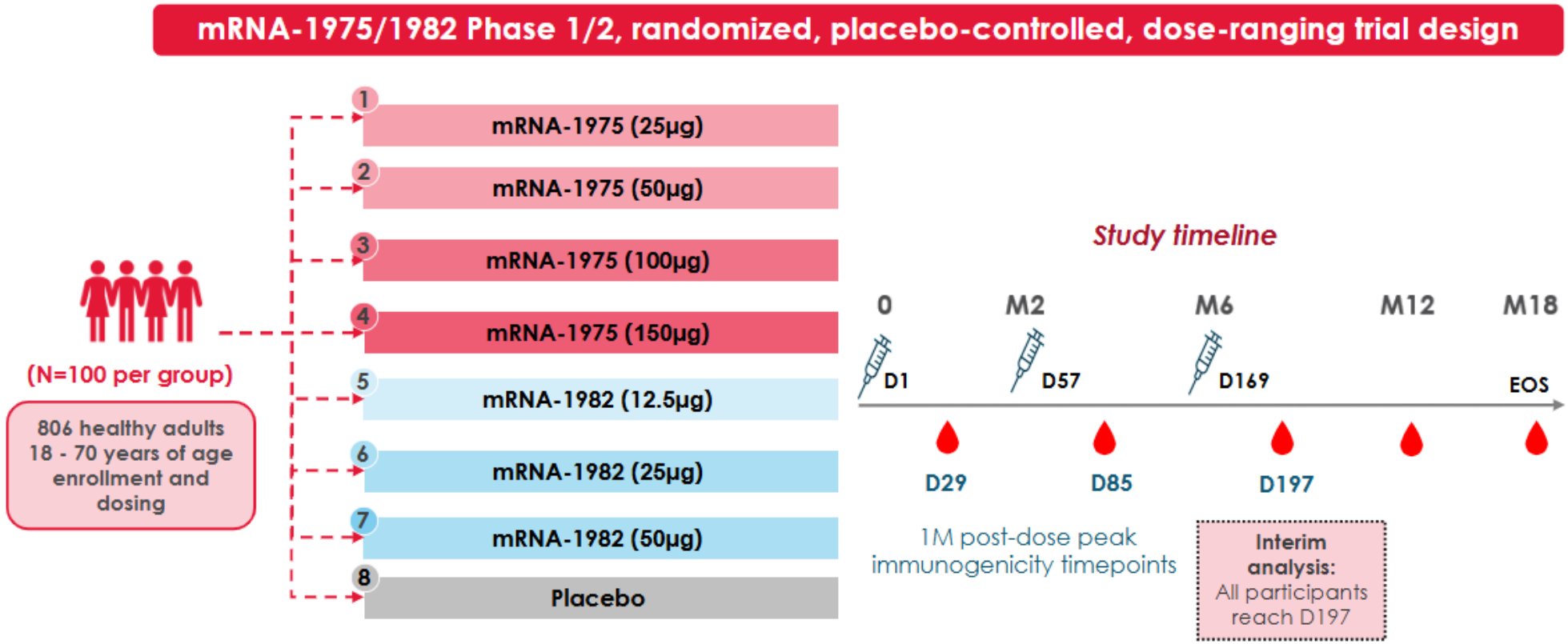
Antibodies kill *Borrelia* in midgut, preventing transmission to human host

mRNA-1982 = **OspA ST1** targets *Borrelia burgdorferi*, which causes almost all the Lyme disease in North America

mRNA-1975 = **OspA ST1-7** targets the four major *Borrelia* species causing disease in US and Europe

Illustrations created with BioRender.com

Lyme (mRNA-1975/1982) Phase 1/2 trial design



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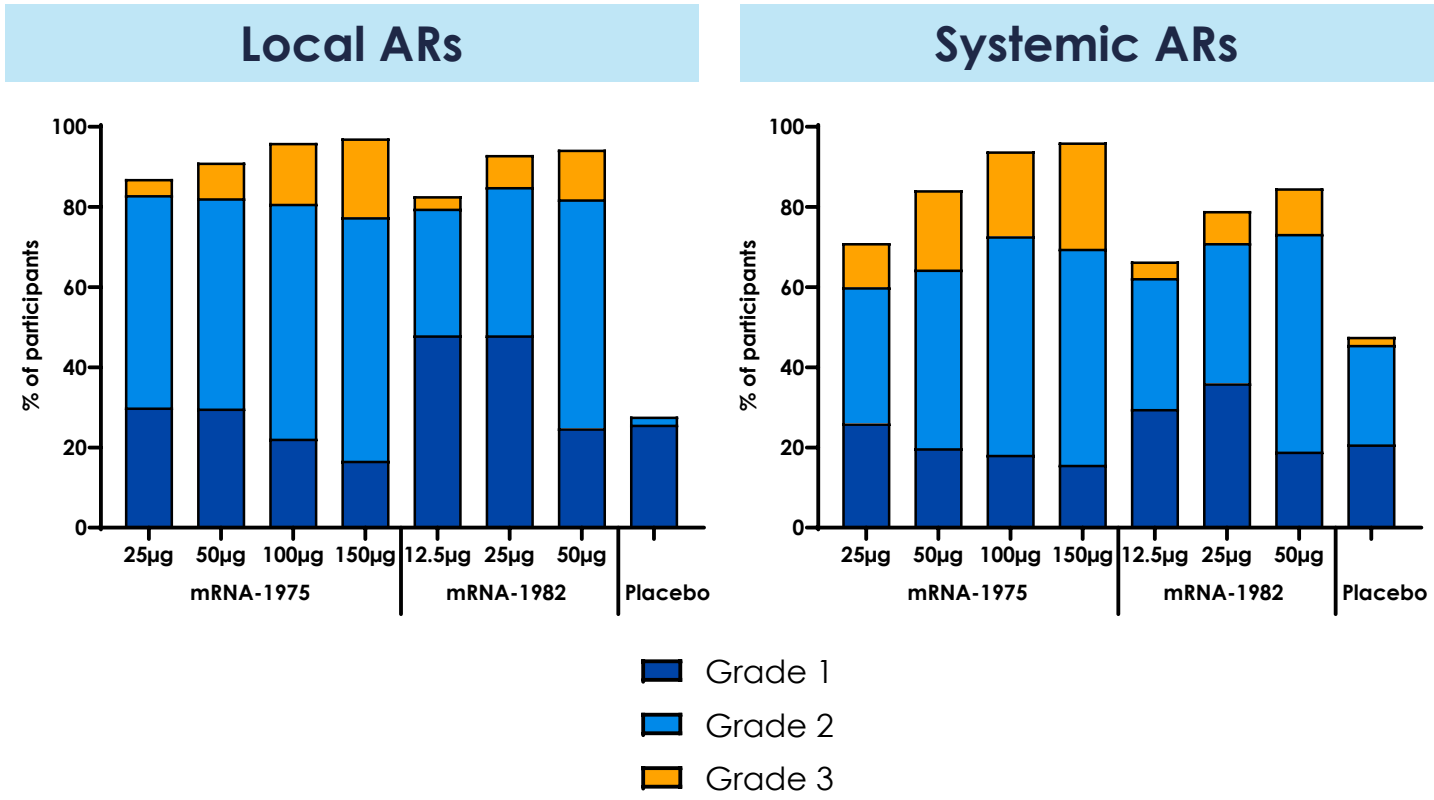
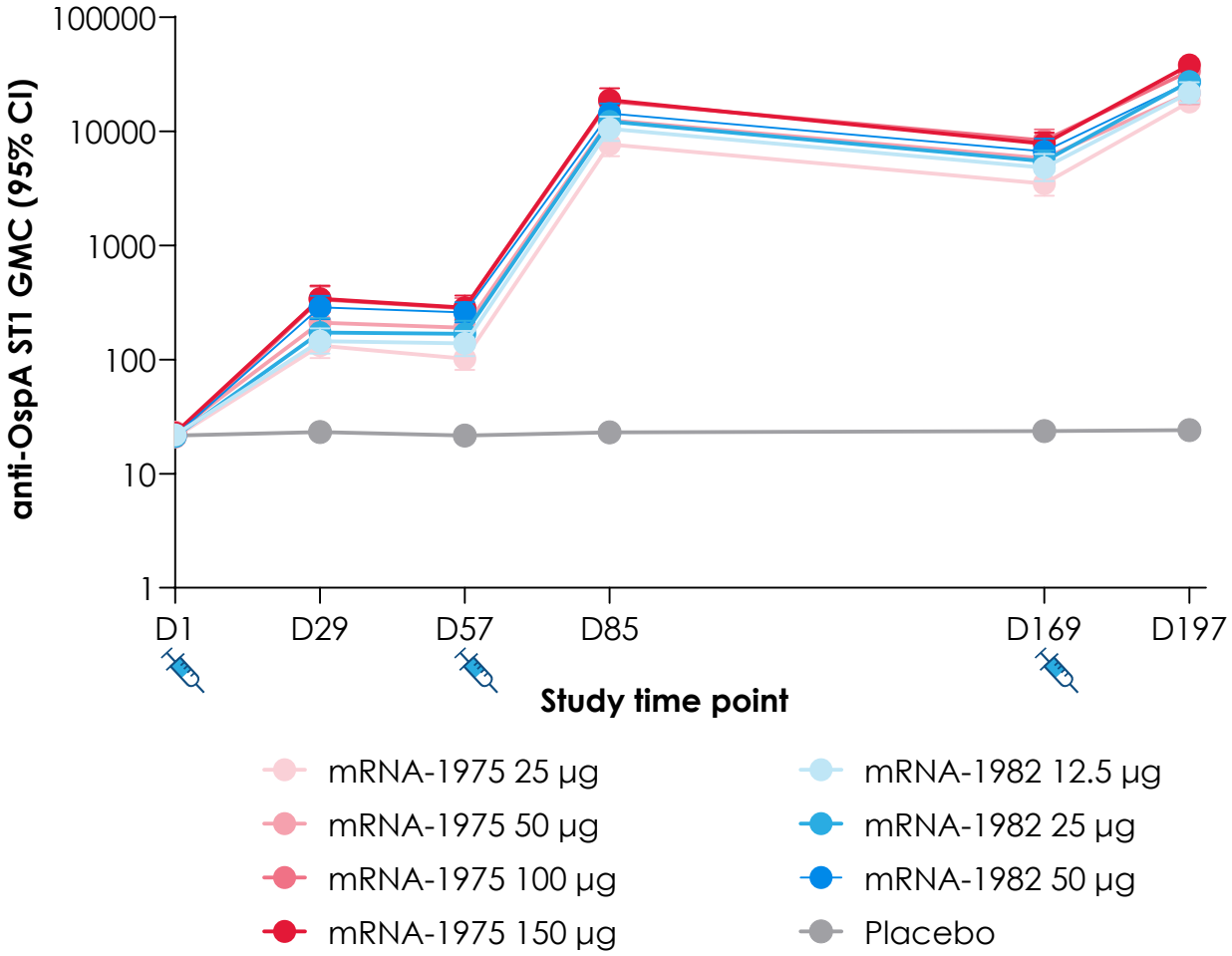
Reactogenicity is associated with total mRNA dose rather than OspA valency



- Generally well-tolerated, with an acceptable safety profile
- The proportions of participants reporting any solicited local and systemic ARs increased in a dose dependent manner.
- The majority of the ARs were grade 1-2 in severity.
- No grade 4 ARs were reported.

Both vaccines elicited robust anti-OspA IgG antibody responses



- Anti-ST1 IgG titers shown
- mRNA-1975 induced robust anti–ST2-7 IgG titers with comparable kinetics.
- Both vaccines elicited dose-dependent anti-OspA–binding IgG, with larger fold increases after each injection.

High levels of circulating IgG correlated with protection in the LYMErix™ Phase 3 trial[1]

[1]PMID: 9673298

Lyme (mRNA-1975/1982) vaccine summary and next steps

Safety	• mRNA-1975 and mRNA-1982 were generally well tolerated a with an acceptable safety profile
Immunogenicity	• Both vaccines elicited robust, dose-dependent anti-OspA binding IgG antibody responses that increased with each successive injection
Next steps	• Phase 2 portion of Phase 1/2 will be a dose ranging study evaluating new formulation

Agenda resumes with Oncology after short coffee break

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Oncology portfolio

Kyle Holen, M.D.
Senior Vice President, Head of Development, Oncology

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Placeholder for video featuring
an oncology patient story

Encouraging safety profile presented from intismeran Phase 2 trial and mRNA-4359 Phase 1 trial at major medical meetings

LBA9512

3-year safety follow-up on safety demonstrates a manageable profile consistent with the primary analysis

	mRNA-4157 (V940) + pembrolizumab (n = 104)		Pembrolizumab (n = 50)	
Event, n (%)	Any grade	Grade ≥ 3	Any grade	Grade ≥ 3
Any AE	104 (100%)	36 (34.6%)	46 (92.0%)	18 (36.0%)
Any treatment-related AE	104 (100%)	26 (25.0%)	41 (82.0%)	10 (20.0%)
Serious AE[a]	15 (14.4%)		5 (10.0%)	
Immune-related AE[b]	39 (37.5%)	11 (10.6%)		

mRNA-4157 (V940) + pembrolizumab (n = 104), n (%)	Grade 1	Grade 2	Grade 3
Patients with mRNA-4157 (V940)–related AE[c]	35 (33.7%)	51 (49.0%)	12 (11.5%)
Fatigue	40 (38.5%)	18 (17.3%)	5 (4.8%)
Injection site pain	37 (35.6%)	22 (21.2%)	0
Chills	48 (46.2%)	3 (2.9%)	0
Pyrexia	34 (32.7%)	15 (14.4%)	1 (1.0%)
Headache	20 (19.2%)	13 (12.5%)	0
Injection site erythema	29 (27.9%)	4 (3.8%)	0
Influenza-like illness	21 (20.2%)	10 (9.6%)	0
Nausea	23 (22.1%)	3 (2.9%)	0
Myalgia	16 (15.4%)	5 (4.8%)	1 (1.0%)

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 Te grade; [a]Based on established list of pembrolizumab immune-related AEs (CMQ Pembrolizumab AEOSI); [b]mRNA-4157 (V940)–related AEs included events attributed by the investigator to mRNA-41 AE, adverse event; AEOSI, adverse event of special interest; CMQ, customized MedDRA queries.

2024 ASCO ANNUAL MEETING #ASCO24

PRESENTED BY: Jeffrey S. Weber, MD, PhD

mRNA-4359 + Pembrolizumab Demonstrated a Manageable Safety Profile

- mRNA-4359-related AEs were mostly grade 1/2 injection site reactions and self-limited systemic AEs (eg, fatigue, pyrexia, chills)
- Pembrolizumab AEs were consistent with its known safety profile
  - Pembrolizumab-related AEs occurred in 66% of patients (grade 3, 10%)
  - Pembrolizumab-related AEs with >10% incidence were fatigue (28%), diarrhea, (10%), pruritus (10%), and vomiting (10%)
- 13.8% of patients experienced immune-related AEs (eg, colitis, pancreatitis, gastritis, nephritis, and secondary adrenocortical insufficiency)
- No DLTs occurred for either dose level
- No grade 4 or 5 treatment-related AEs occurred

	mRNA-4359 400 µg Q3W + pembro 400 mg Q6W (n = 14)	mRNA-4359 1000 µg Q3W + pembro 400 mg Q6W (n = 15)
Duration of mRNA-4359 therapy, median (range), wk	12.5 (0.1–81.1)	6.1 (0.1–29.6)
Duration of pembro therapy, median (range), wk	10.1 (0.1–80.6)	5.9 (0.1–60.4)
mRNA-4359–related AEs, n (%)	14 (100)	12 (80)
Grade 3[a]	1 (7)[b]	1 (7)[c]
mRNA-4359–related AEs with incidence ≥20% in either cohort, n (%)		
Injection site pain	10 (71)	8 (53)
Fatigue	7 (50)	7 (47)
Pyrexia	7 (50)	4 (27)
Injection site erythema	4 (29)	1 (7)
Chills	3 (21)	2 (13)
Influenza-like illness	3 (21)	5 (33)
Vomiting	2 (14)	5 (33)
Decreased appetite	2 (14)	3 (20)
Nausea	2 (14)	3 (20)

[a]There were no grade 4 or 5 treatment-related AEs. [b]1 patient experienced grade 3 pulmonary embolism. [c]1 patient experienced grade 3 fatigue and increased blood lactic acid. Data cutoff: February 28, 2025.

Presented by: David J. Pinato

BERLIN 2025 ESMO congress

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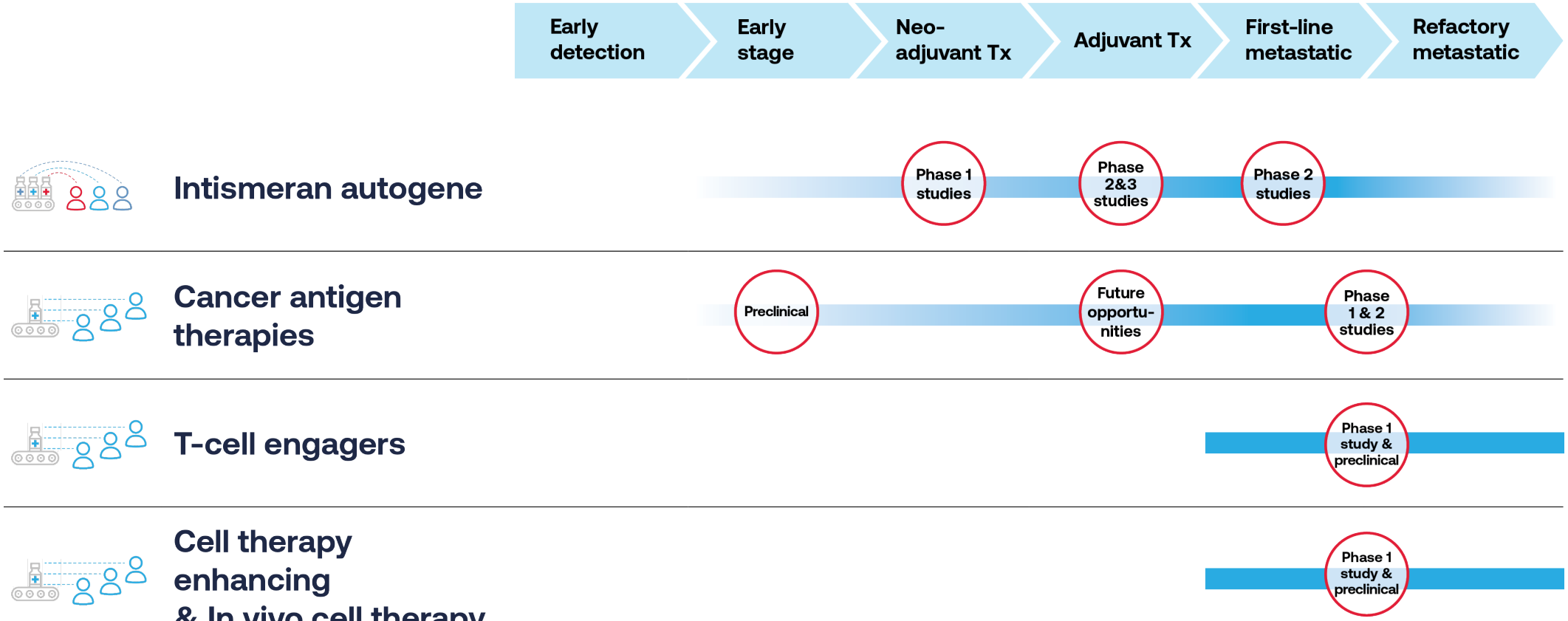
Moderna oncology research and development programs across cancer disease stages



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Moderna oncology pipeline

Oncology therapeutics

			Preclinical	Ph 1	Ph 2	Ph 3	Commercial
Intismeran autogene (Partnered with Merck)	**Adjuvant melanoma**	mRNA-4157					
	Adjuvant NSCLC	mRNA-4157					
	Adjuvant NSCLC non-pCR post neoadjuvant	mRNA-4157					
	Renal cell carcinoma (RCC)	mRNA-4157					
	Bladder cancer (MIBC)	mRNA-4157					
	Bladder cancer (NMIBC)	mRNA-4157					
	First-line metastatic melanoma	mRNA-4157					
	First-line metastatic squamous NSCLC	mRNA-4157					
	Early and advanced solid tumors	mRNA-4157					
Cancer antigen therapies	**Advanced solid tumors**	mRNA-4359					
	Solid tumors	mRNA-4106					
	Lynch Syndrome						
T-cell engagers	**Multiple myeloma**	mRNA-2808					
	Intracellular antigen T cell engagers (Partnered with Immatics)						
Cell therapy enhancers and *in vivo* cell therapy	**Solid tumors** (Partnered with Immatics)	mRNA-4203 + anzu-cel (IMA203)					
	CAR-T						
	CAR-M						

Abbreviations: NSCLC, non-small cell lung cancer; pCR, non-pathological complete response; RCC, renal cell carcinoma; MIBC, muscle-invasive bladder carcinoma; NMIBC, non-muscle invasive bladder cancer

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Intismeran autogene
mRNA-4157 (V940)

Michelle Brown, MD, Ph.D.
Vice President, Portfolio Head, Oncology

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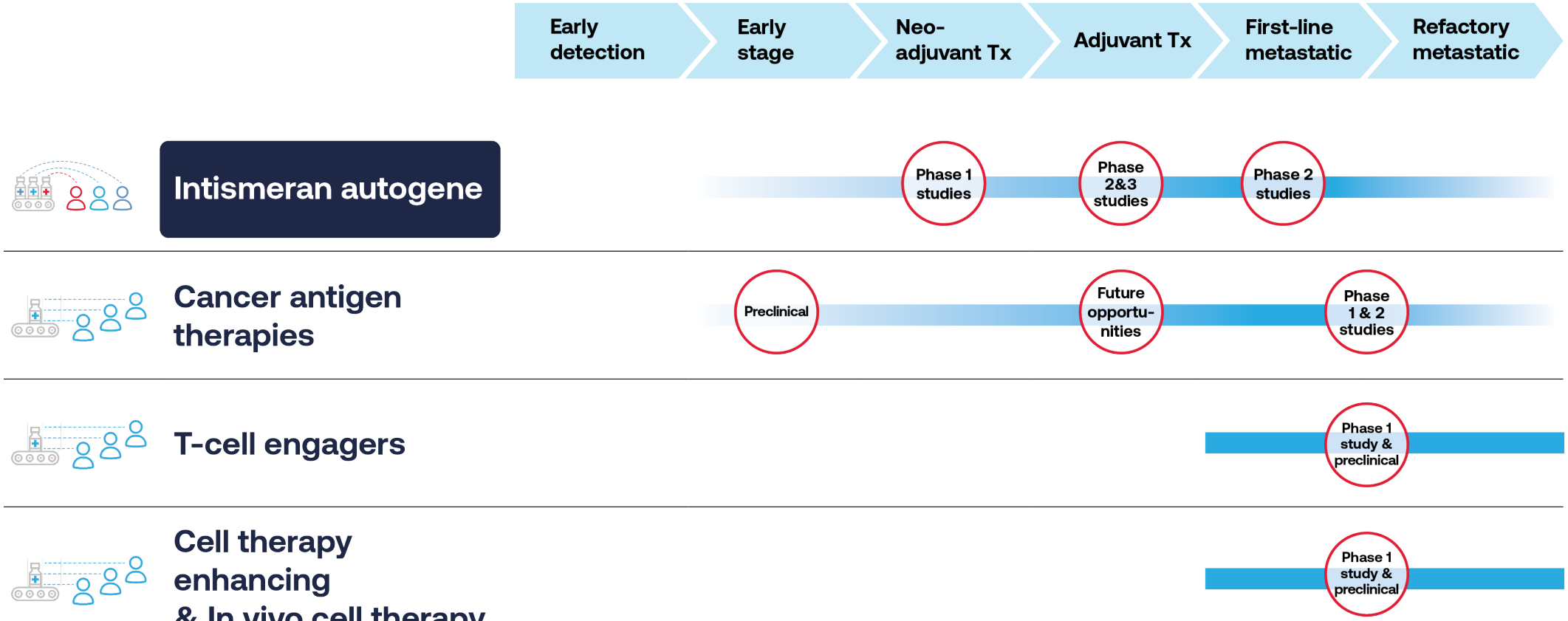
Moderna oncology research and development programs across cancer disease stages



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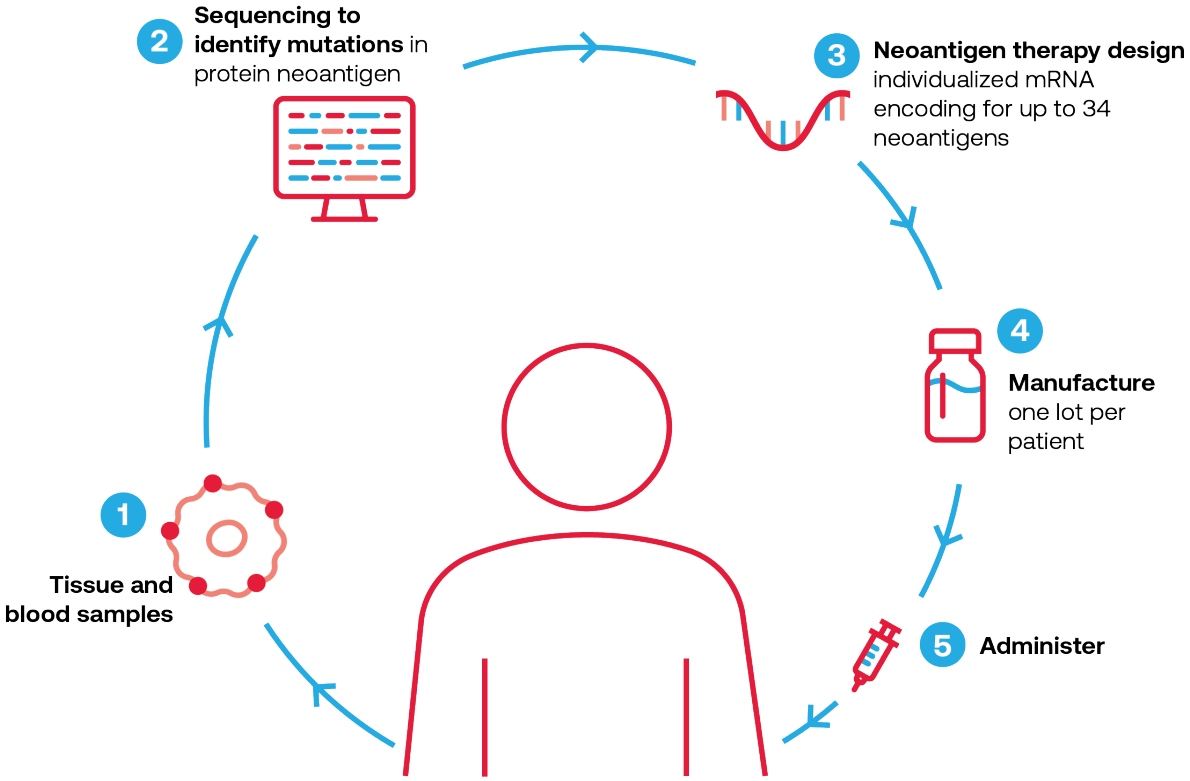
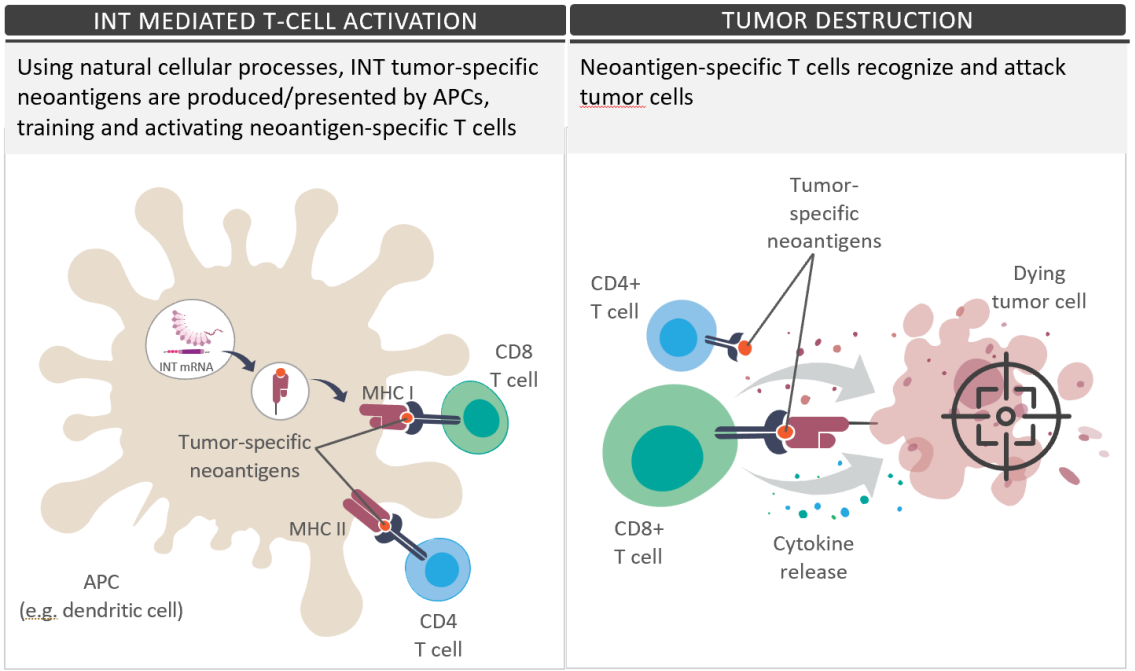
Intismeran autogene proposed mechanism of action

Intismeran is an investigational lipid encapsulated messenger ribonucleic acid (mRNA)-based individualized neoantigen therapy (INT) that consists of an mRNA that encodes neoantigens designed specifically to each individual patient's tumor mutanome and human leukocyte antigen (HLA) type





Combination of intismeran with checkpoint inhibitor pembrolizumab may further enhance tumor destruction by neoantigen specific T cells

APC = antigen-presenting cell; CD = cluster of differentiation; INT = individualized neoantigen therapy; MHC = major histocompatibility complex; mRNA = messenger ribonucleic acid

1. Khattak A, et al. AACR 2023 (Abstract CT001).

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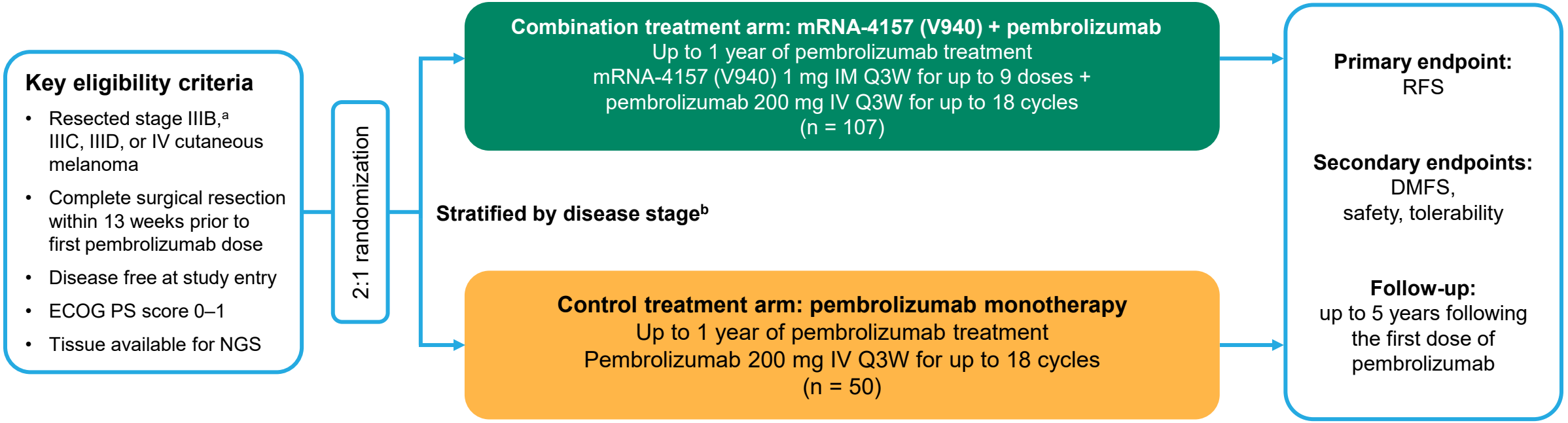
Randomized Phase 2 trial design comparing mRNA-4157/V940 in combination with pembro to pembro alone in adjuvant melanoma

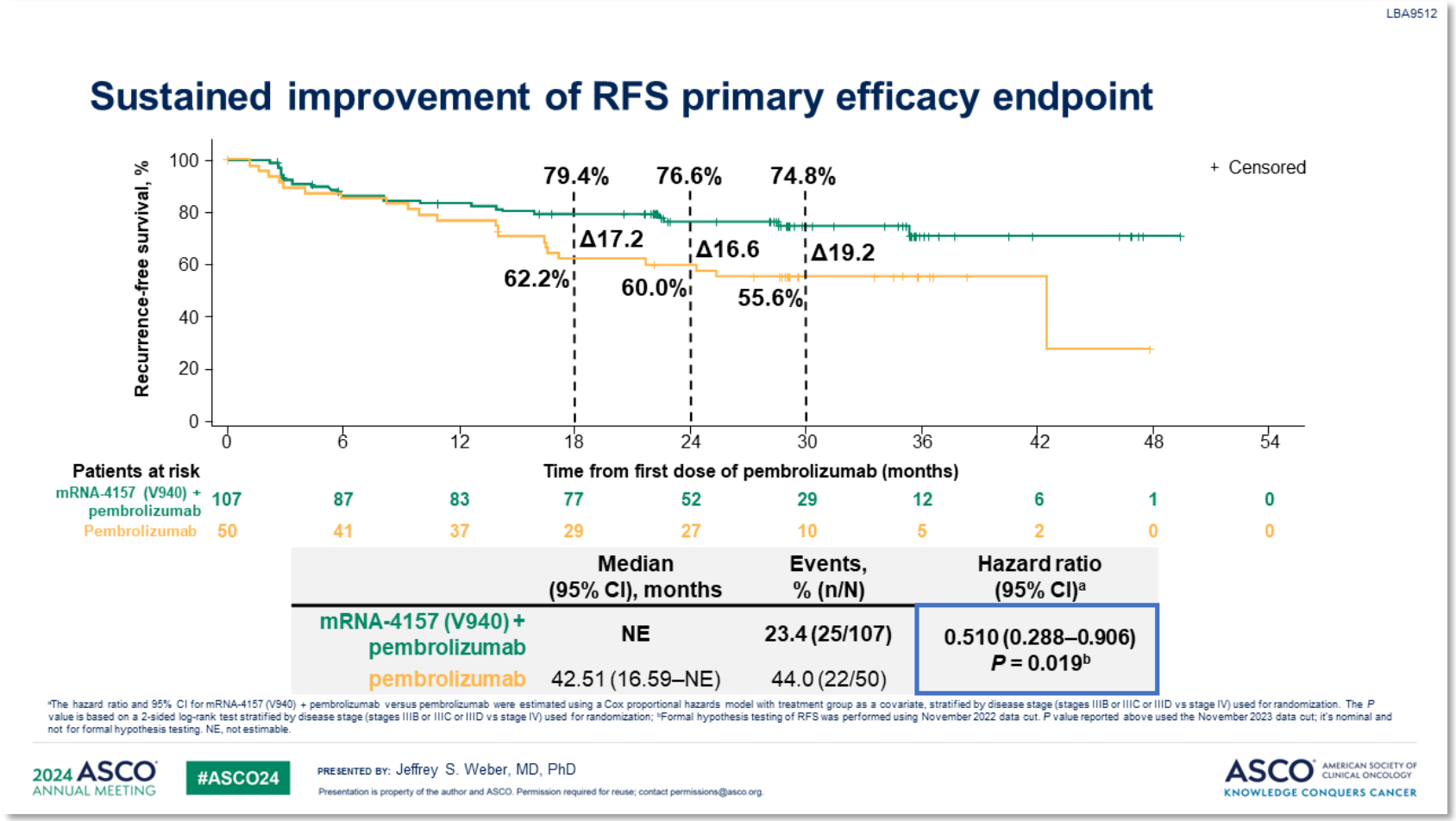


Designed with 80% power to detect a hazard ratio of 0.5 with 40 RFS events (with a 1-sided alpha of 0.1 per protocol)
Primary analysis **triggered after a minimum of 1-year planned follow-up[c]** (November 14, 2022 data cut) and at least 40 RFS events have been observed. DMFS analysis was prespecified for testing following positive RFS in the ITT population

Supportive analysis was **triggered after a minimum of 2 years of planned follow-up[c]** (November 3, 2023 data cut)
Median planned follow-up[c]: ~3yrs

[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]Defined as the time from the first dose date (or date of randomization if not treated) to date of clinical cut-off.
ECOG PS, Eastern Cooperative Oncology Group performance status; IM, intramuscular; ITT, intent-to-treat; IV, intravenous; NGS, next-generation sequencing; Q3W, every 3 weeks.

Recurrence free survival rate of mRNA-4157/V940 in combination with pembro was 74.8% as compared to 55.6% for pembro alone from 30 months from the first pembro dose



In the Phase 2 study, at a median planned follow-up of ~ 3 years, **mRNA-4157 (V940) in combination with pembro reduced the risk of recurrence or death by 49%**

(n=157)

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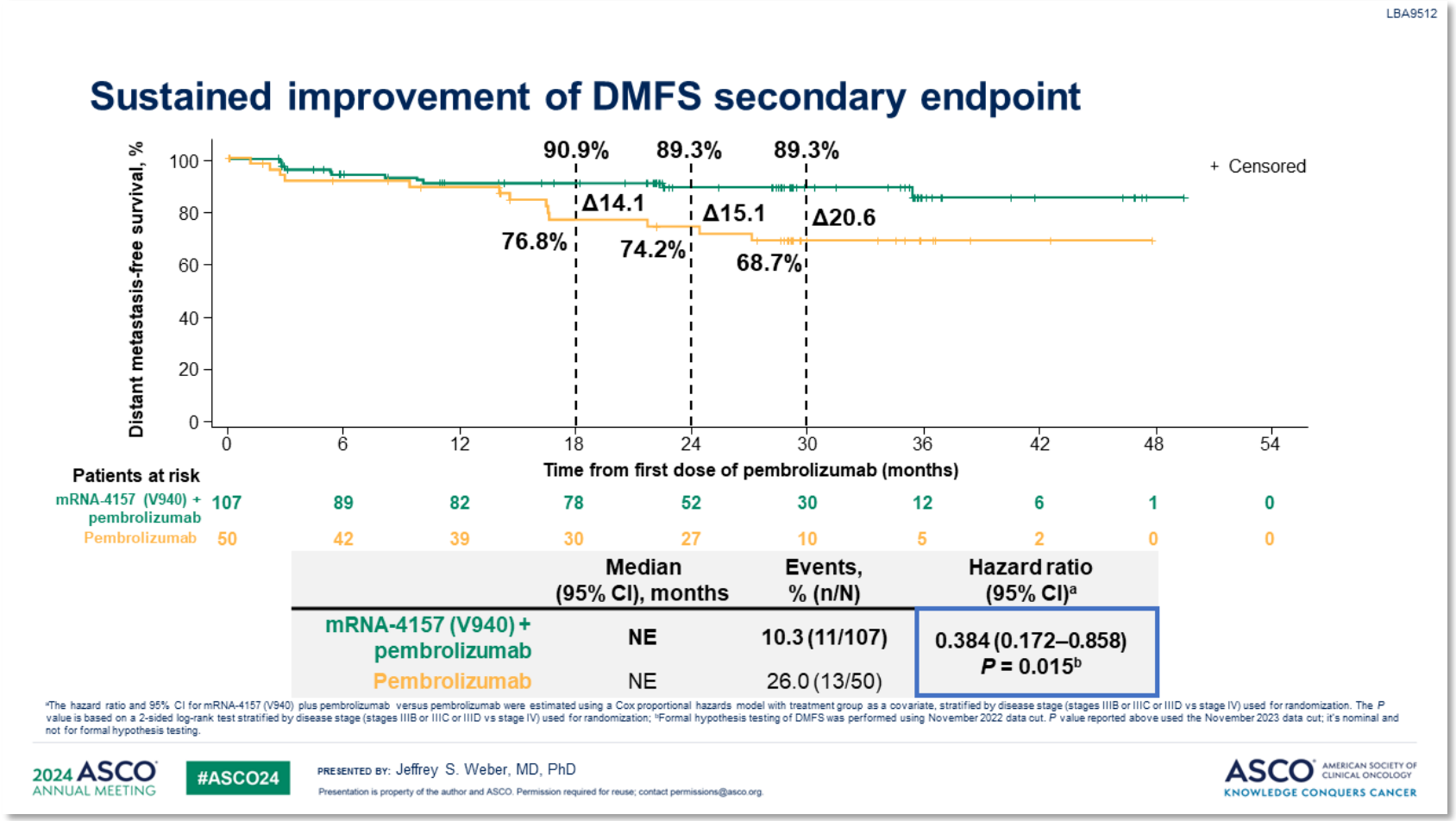
Distant metastasis-free survival is a key secondary endpoint of the Phase 2 study



At the ~ 3 years of follow-up analysis, mRNA-4157 (V940) in combination with pembro also continued to demonstrate a meaningful improvement in distant metastasis-free survival (DMFS) compared with pembro alone, reducing the risk of developing distant metastasis or death by 62%.

(n=157)

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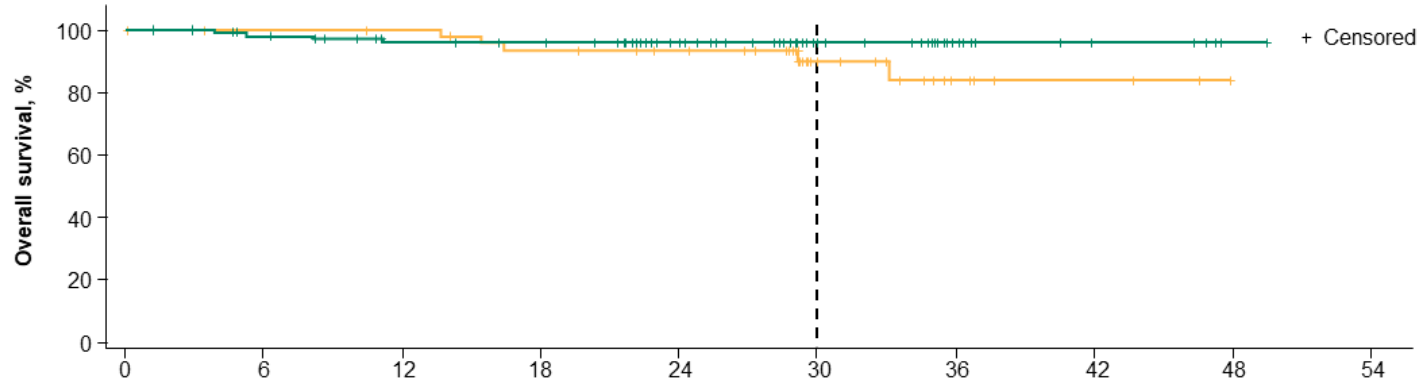
At ~3 years of follow-up mRNA-4157 (V940) in combination with pembro shows an encouraging trend in overall survival

LBA9512

Overall survival shows encouraging trend with mRNA-4157 (V940) + pembrolizumab



Patients at risk										
mRNA-4157 (V940) + pembrolizumab	107	100	92	90	65	35	14	6	1	0
Pembrolizumab	50	48	47	43	40	18	7	3	0	0

	Median (95% CI), Months	Events, % (n/N)	Hazard ratio (95% CI)[a]
mRNA-4157 (V940) + pembrolizumab	NE	3.7 (4/107)	0.425 (0.114–1.584)
Pembrolizumab	NE	10.0 (5/50)	

[a]The hazard ratio and 95% CI for mRNA-4157 (V940) plus pembrolizumab versus pembrolizumab were 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.

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PRESENTED BY: Jeffrey S. Weber, MD, PhD

ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY
KNOWLEDGE CONQUERS CANCER

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3-year follow-up: Safety continues to demonstrate a manageable profile consistent with the primary analysis

	mRNA-4157 (V940) + pembrolizumab (n = 104)		Pembrolizumab (n = 50)	
Event, n (%)	**Any grade**	**Grade ≥ 3**	**Any grade**	**Grade ≥ 3**
Any AE	104 (**100%**)	36 (**34.6%**)	46 (**92.0%**)	18 (**36.0%**)
Any treatment-related AE	104 (**100%**)	26 (**25.0%**)	41 (**82.0%**)	10 (**20.0%**)
Serious AE[a]	15 (**14.4%**)		5 (**10.0%**)	
Immune-related AE[b]	39 (**37.5%**)	11 (**10.6%**)	18 (**36%**)	7 (**14.0%**)

mRNA-4157 (V940) + pembrolizumab (n = 104), n (%)	Grade 1	Grade 2	Grade 3	Grade 4/5	Total (n = 104)
Patients with mRNA-4157 (V940)–related AE[c]	**35 (33.7%)**	**51 (49.0%)**	**12 (11.5%)**	**0**	**98 (94.2%)**
Fatigue	40 (38.5%)	18 (17.3%)	5 (4.8%)	0	63 (60.6%)
Injection site pain	37 (35.6%)	22 (21.2%)	0	0	59 (56.7%)
Chills	48 (46.2%)	3 (2.9%)	0	0	51 (49.0%)
Pyrexia	34 (32.7%)	15 (14.4%)	1 (1.0%)	0	50 (48.1%)
Headache	20 (19.2%)	13 (12.5%)	0	0	33 (31.7%)
Injection site erythema	29 (27.9%)	4 (3.8%)	0	0	33 (31.7%)
Influenza-like illness	21 (20.2%)	10 (9.6%)	0	0	31 (29.8%)
Nausea	23 (22.1%)	3 (2.9%)	0	0	26 (25.0%)
Myalgia	16 (15.4%)	5 (4.8%)	1 (1.0%)	0	22 (21.2%)

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 were not evaluated by toxicity grade; [b]Based on established list of pembrolizumab immune-related AEs (CMQ Pembrolizumab AEOSI); [c]mRNA-4157 (V940)–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. AE, adverse event; AEOSI, adverse event of special interest; CMQ, customized MedDRA queries.

Weber ASCO 2024

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Intismeran autogene is in multiple clinical studies across tumor types and disease stages

Intismeran autogene

		Preclinical	Ph 1	Ph 2	Ph 3	Commercial	
Adjuvant melanoma	mRNA-4157						Fully enrolled
Adjuvant NSCLC	mRNA-4157						
Adjuvant NSCLC non-pCR post neoadjuvant	mRNA-4157						
Renal cell carcinoma (RCC)	mRNA-4157						Fully enrolled
Bladder cancer (MIUC)	mRNA-4157						
Bladder cancer (NMIBC)	mRNA-4157						
First-line metastatic melanoma	mRNA-4157						
First-line metastatic squamous NSCLC	mRNA-4157						
Early and advanced solid tumors	mRNA-4157						

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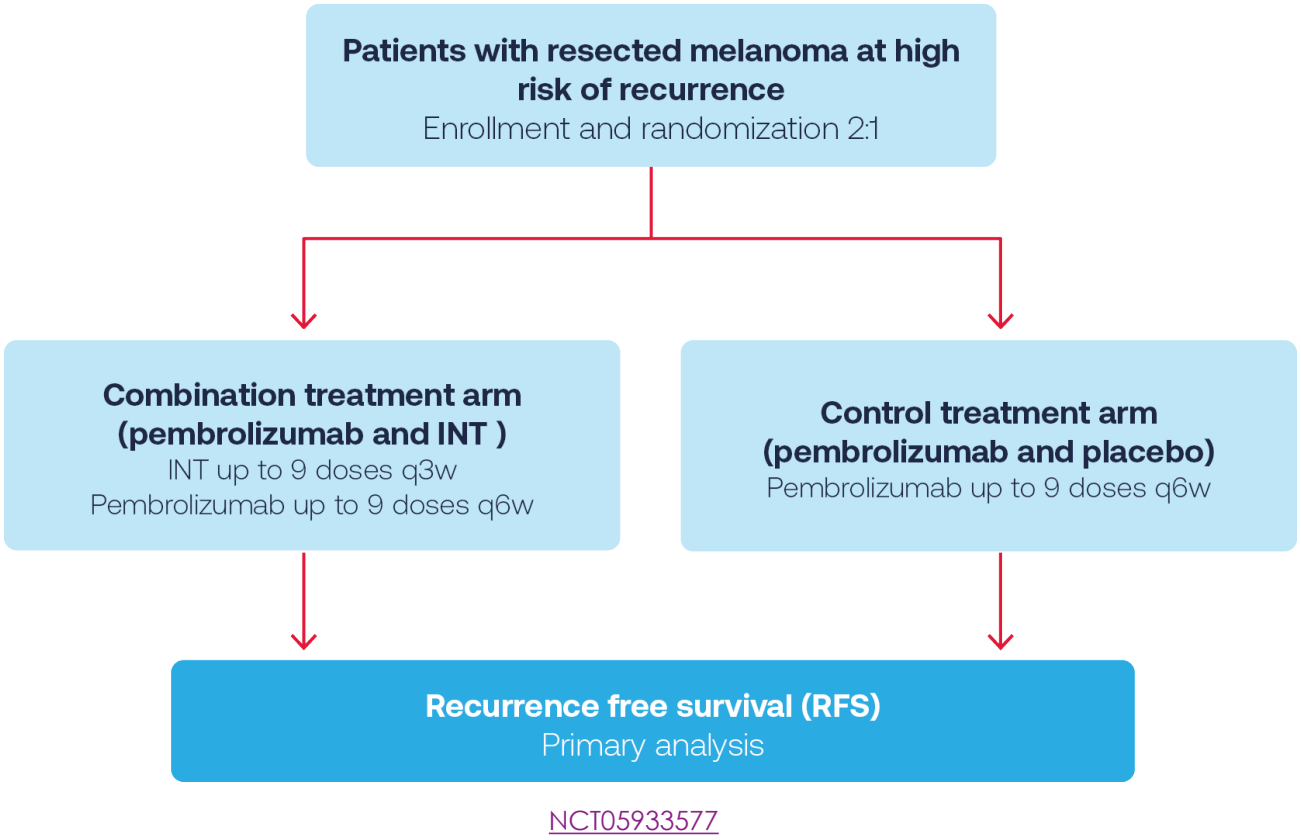
Adjuvant melanoma Phase 3 (mRNA-4157 / V940) trial design

Primary endpoint is recurrence free survival compared to pembro



NCT05933577

Randomized, double-blind placebo controlled, mRNA-4157 + pembrolizumab (KEYTRUDA®) vs. placebo + pembrolizumab (2:1) (INTerpath-001)

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

Phase 3 trial is fully enrolled

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Intismeran summary

Safety

- Showed a manageable safety profile without potentiation of immune-related AEs compared with pembrolizumab monotherapy

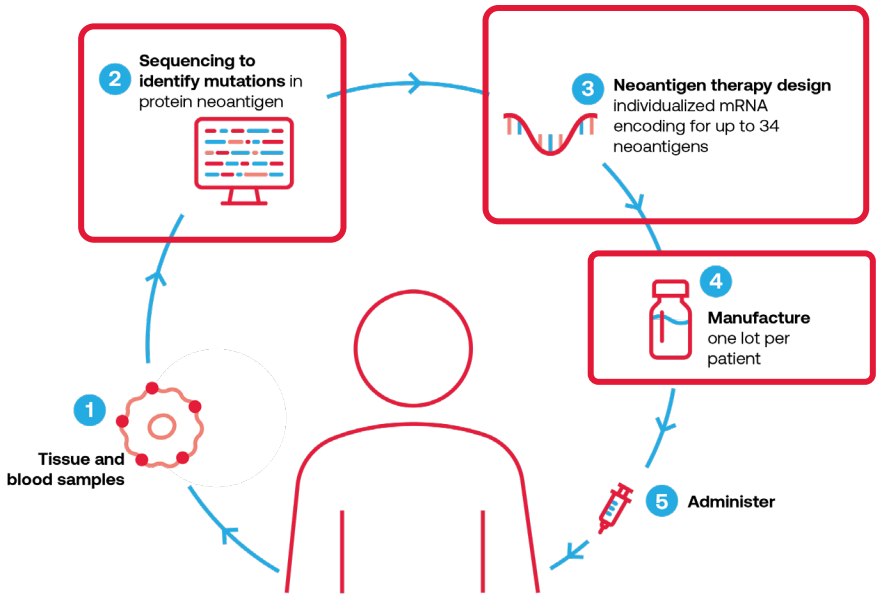
Efficacy

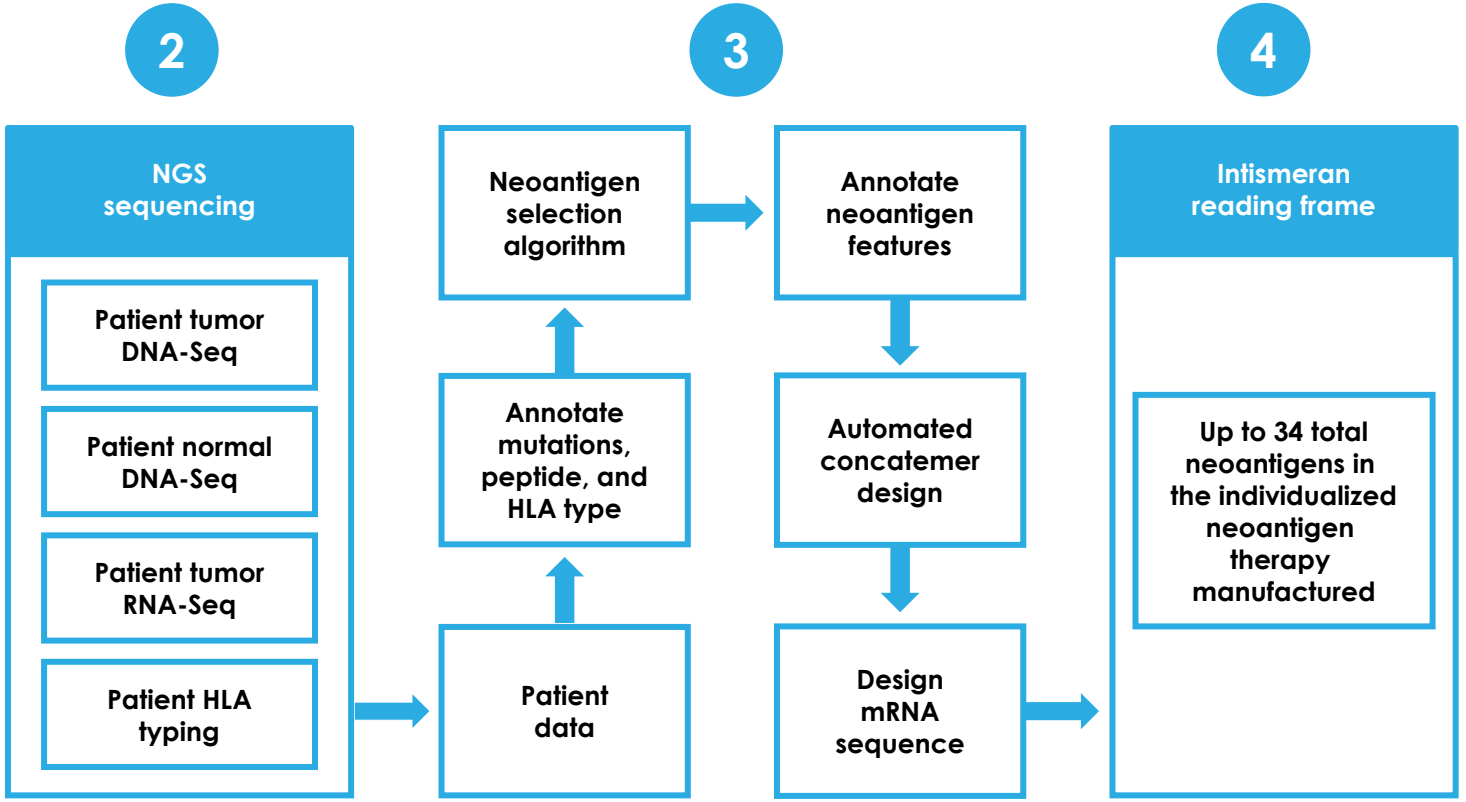
- In Phase 2, mRNA-4157 (V940) + pembrolizumab demonstrated a durable **clinically significant improvement in RFS & DMFS** at 3 years follow-up compared to standard of care pembrolizumab in high-risk resected melanoma:
  - 49% reduction (HR 0.51) in the risk of recurrence or death (RFS)
  - 62% reduction (HR 0.38) of distant recurrence or death (DMFS)
- 3-year exploratory endpoint showed **encouraging trend in overall survival (OS)**

Next steps

- Phase 2 five–year median follow-up adjuvant melanoma data readout
- Phase 3 adjuvant melanoma data readout
- Phase 2 randomized renal cell carcinoma data readout
- Execute multiple late-stage studies across indications

Deterministic Machine Learning Algorithm for Neoantigen Selection





APC = antigen-presenting cell; CD = cluster of differentiation; INT = individualized neoantigen therapy; MHC = major histocompatibility complex; mRNA = messenger ribonucleic acid

1. Khattak A, et al. AACR 2023 (Abstract CT001).

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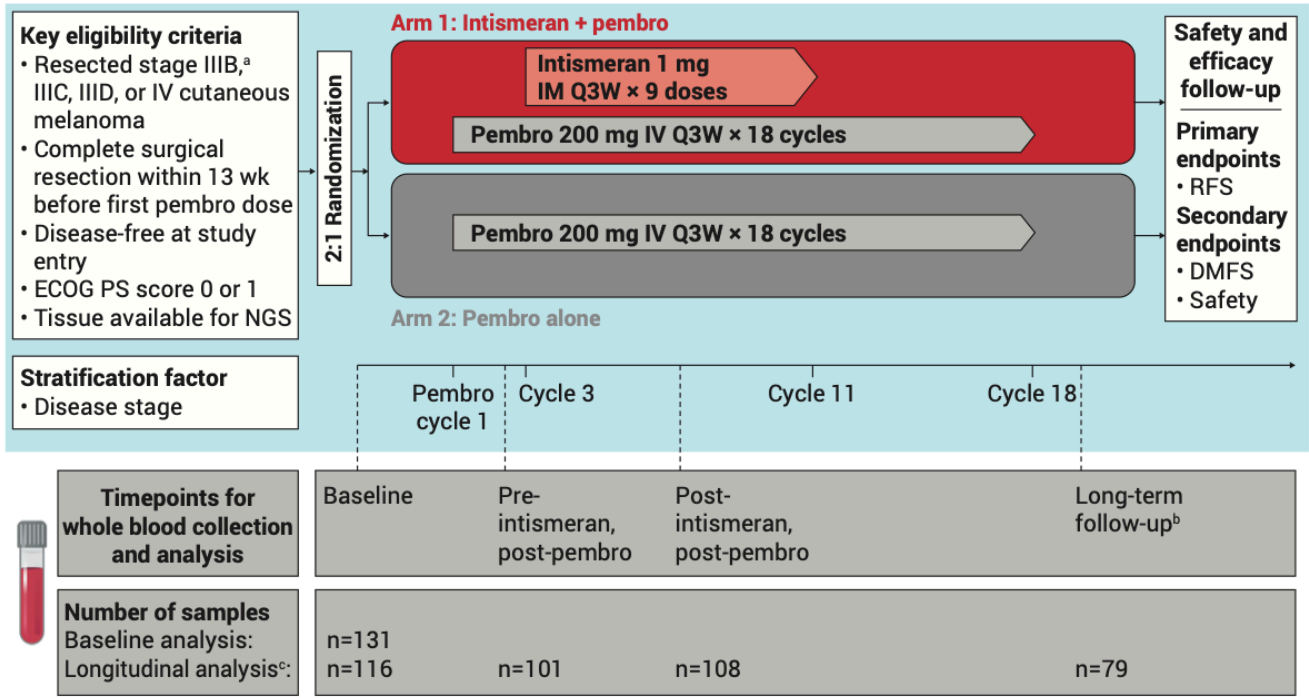
Analysis of individualized neoantigens in intismeran from the adjuvant melanoma Phase 2 trial

Objective

- To characterize the overlap of neoantigens in intismeran design in the mRNA-4157-P201 study
- To characterize the dynamics of TCR repertoire responses in peripheral blood following intismeran plus pembro or pembro alone

Methods

- Tumor and blood samples underwent Nextgen sequencing (NGS); neoantigens were analyzed for all patients treated with intismeran + pembrolizumab.
- Serial blood bulk TCR-seq with β-chain clonotypes downsampled and normalized to the top 10k by unique molecular identifier (UMI) rank-sum



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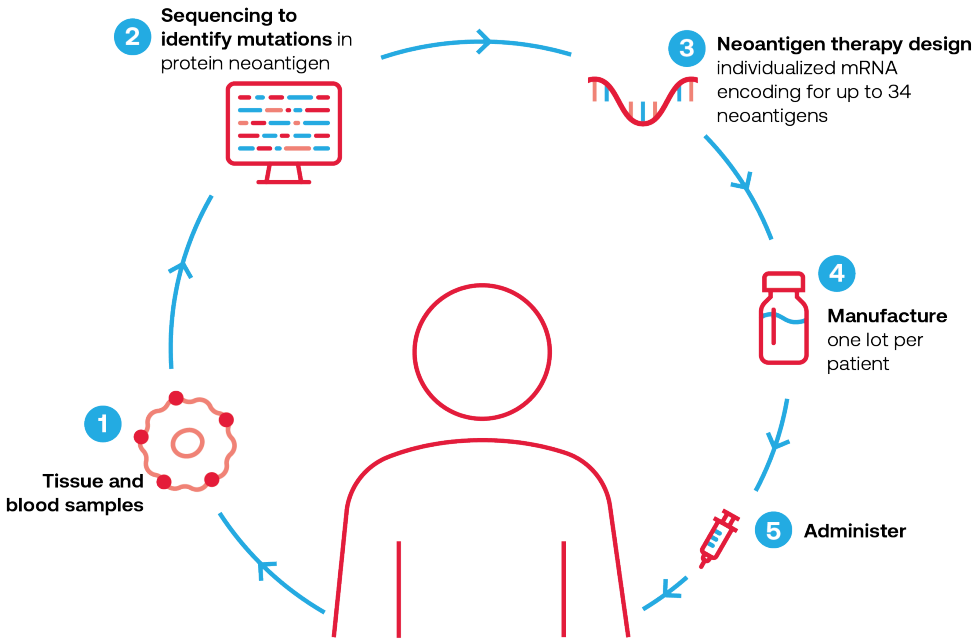
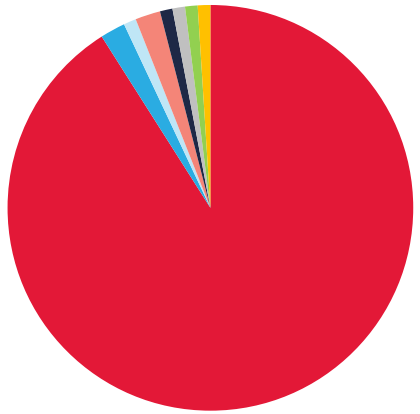
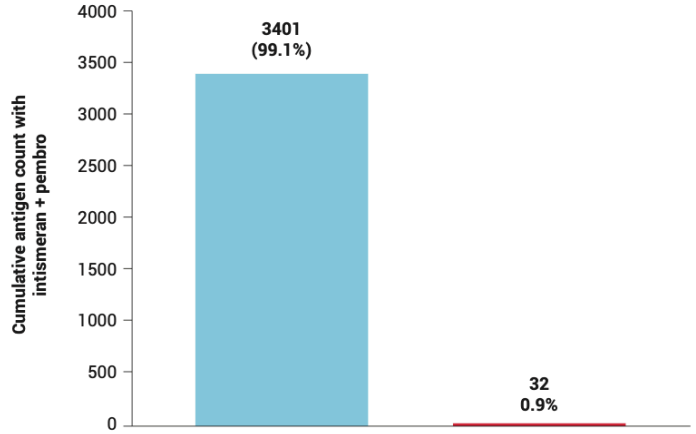
Most patients in the phase 2 adjuvant melanoma trial received intismeran with the full 34 neoantigens with little to no overlap across neoantigens





91% of patients in the combination arm had an intismeran with 34 neoantigens

Khattak A, et al. AACR 2023 (Abstract CT001), published as table Lancet Article Appendix https://doi.org/10.1016/ S0140-6736(23)02268-7



In total, 3,433 neoantigens were selected across 107 patients in the intismeran plus pembro arm

99.1% of neoantigens were unique

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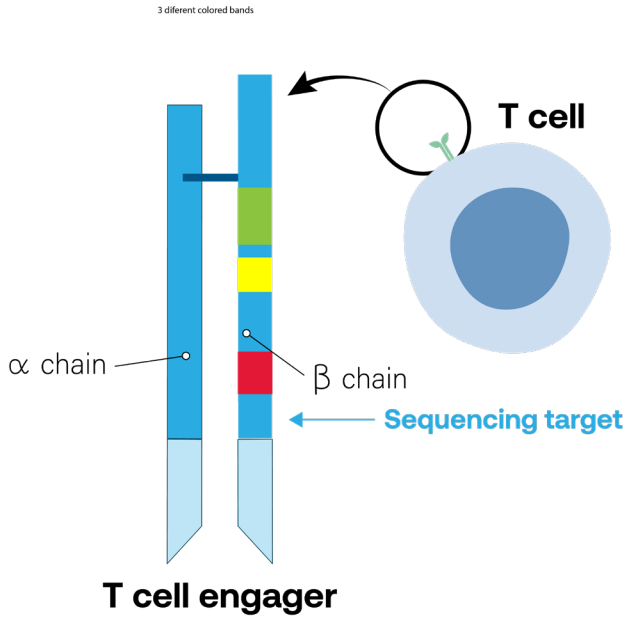
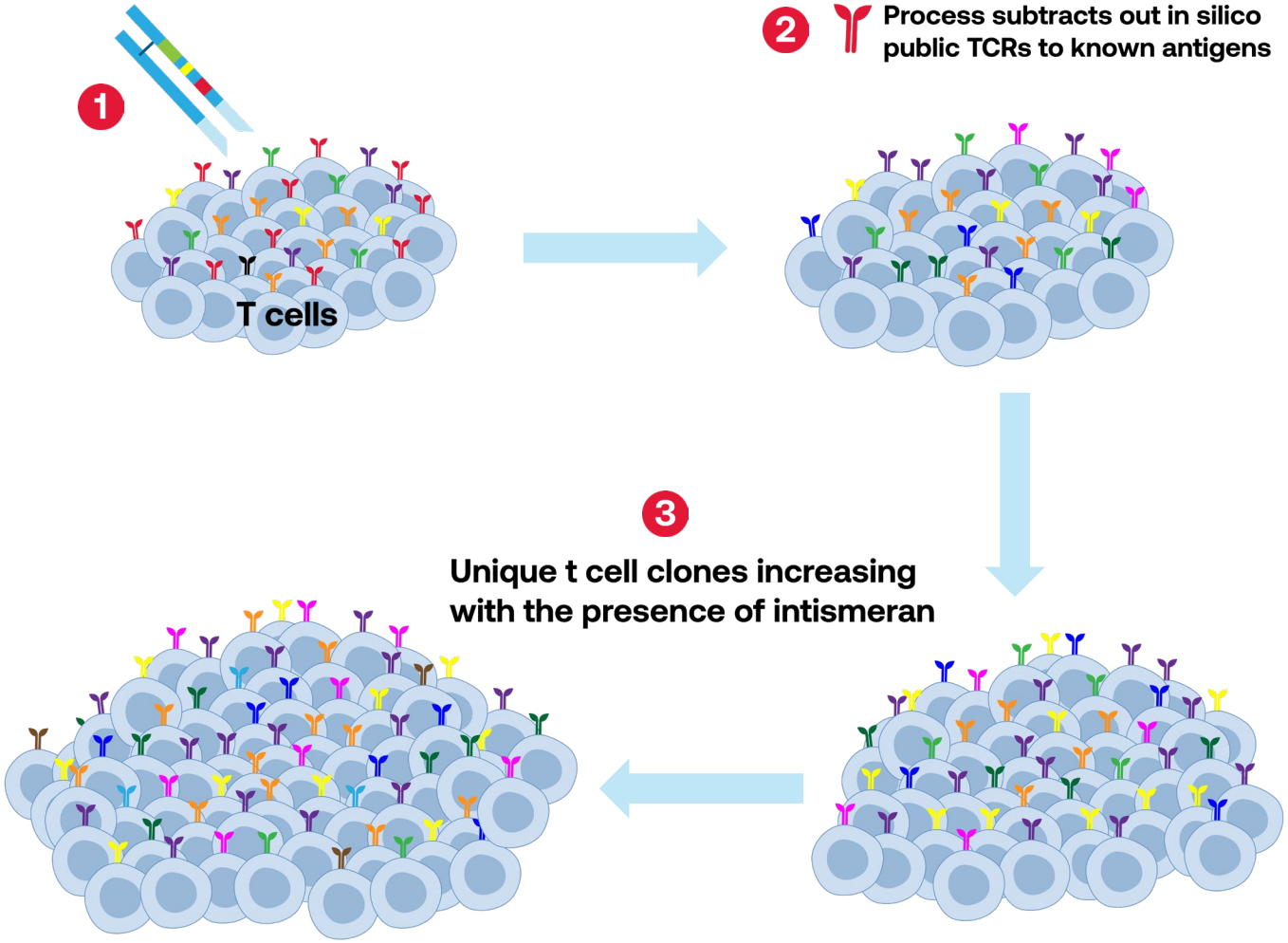
TCR beta chain specificity and variability allows it to be used to assess the dynamics of T-cell repertoire responses to immunotherapy[1]



The unique nucleotide sequence of the T-cell receptor (TCR) beta chain can be used to follow T-cell repertoire responses to immunotherapy



1. Valpione S, et al. Nat Commun. 2021;12(1):4098.

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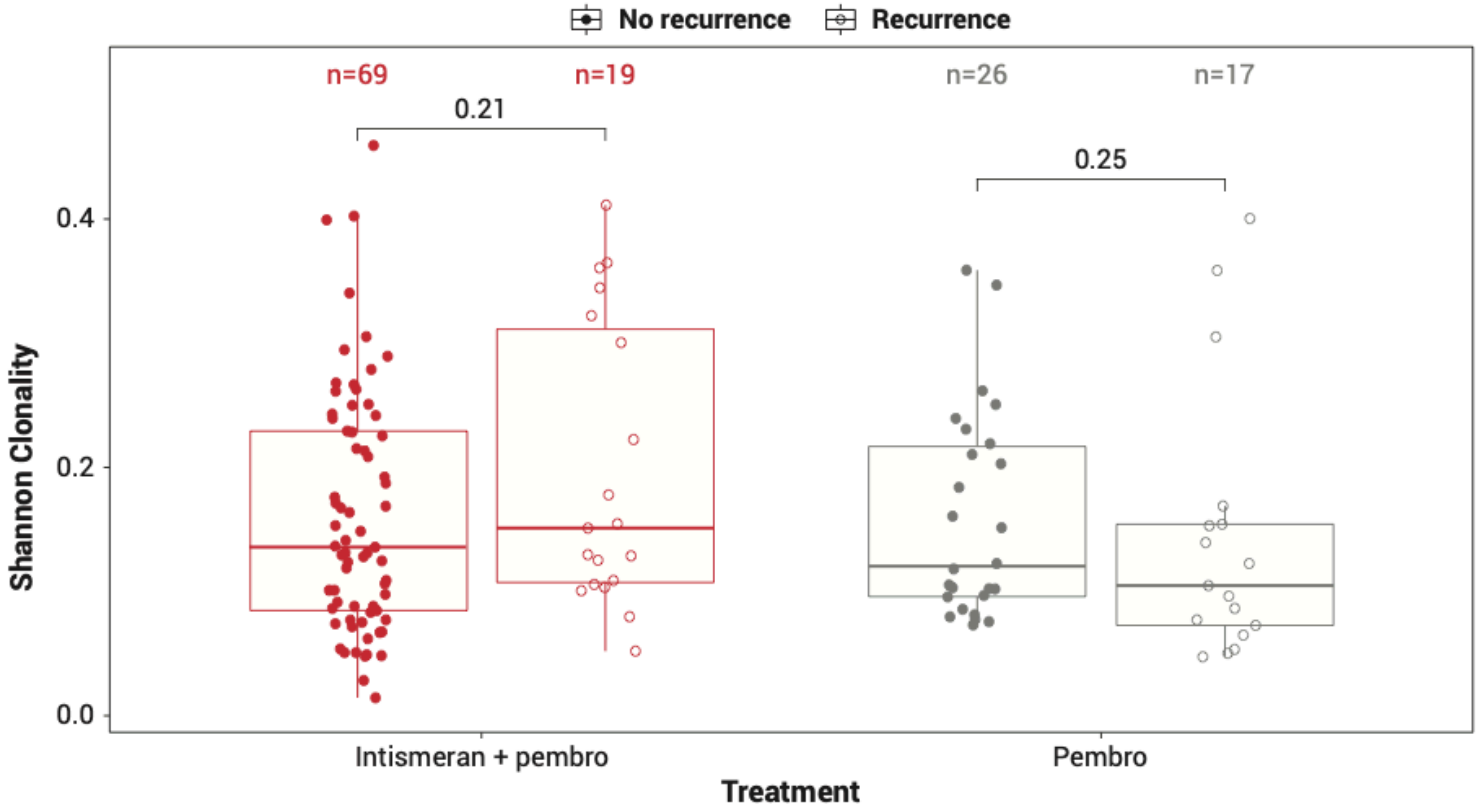
Baseline TCR clonality was not associated with RFS with intismeran + pembro or pembro alone



Intismeran, Intismeran autogene; Pembro, pembrolizumab; RFS, recurrence-free survival; TCR, T-cell receptor.

From the baseline analysis population, no statistically significant difference was observed in baseline TCR clonality between the intismeran + pembro arm and the pembro alone arm (P=0.338).

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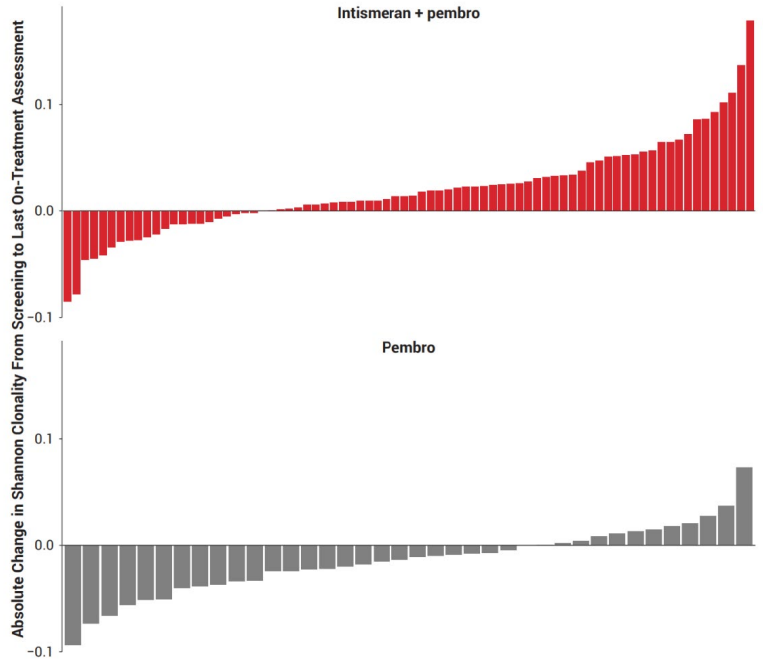
Treatment with intismeran plus pembro induced largely patient-specific novel T-cell clonal expansion, with the majority of expanded TCR clones identified as unique

Figure 3. Longitudinal analysis showed intismeran + pembro induced T-cell clonal expansion in 71% of patients versus 32% for pembro alone

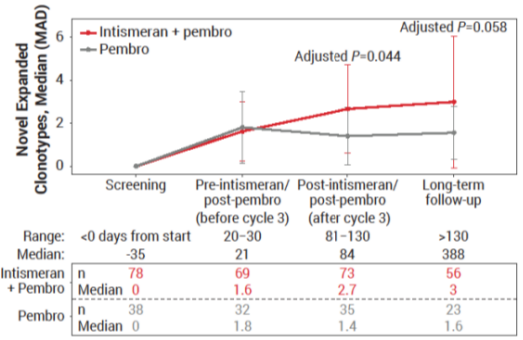
A. Waterfall plots of changes in Shannon clonality between the screening and last on-treatment timepoints (each bar represents a patient)



B. Median number and sum frequency of novel expanded clonotypes at screening vs last on-treatment timepoint

	Intismeran + Pembro	Pembro	Adjusted *P* value, Intismeran + Pembro vs Pembro
Patients, n	78	38	
Median number of novel expanded clones	38.5	22	0.058
Median sum of novel expanded clones, % of all blood T-cells	2.9%	1.6%	**0.007**[b]

C. Cumulative frequency of expanded novel clonotypes at screening and after treatment[c]



		<0 days from start	20–30	81–130	>130
Range:					
Median:		-35	21	84	388
Intismeran + Pembro	n	78	69	73	56
	Median	0	1.6	2.7	3
Pembro	n	38	32	35	23
	Median	0	1.8	1.4	1.6

Figure 6. Frequency of novel TCR clones at landmark timepoints

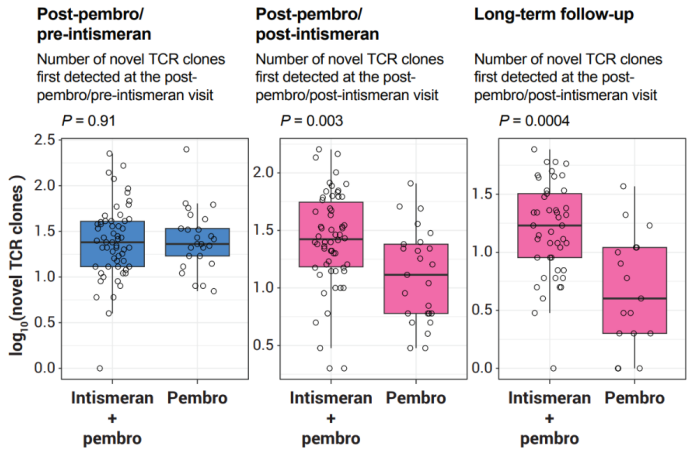
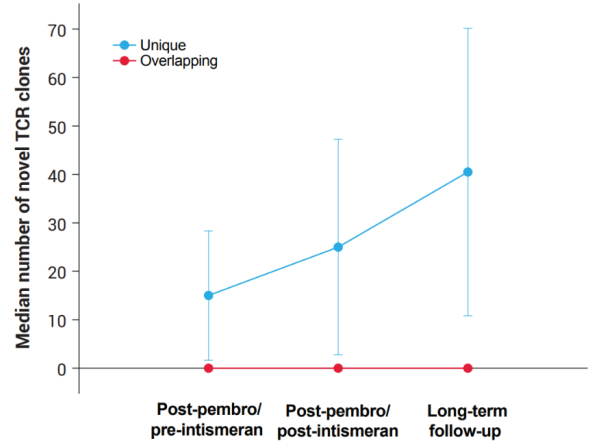


Figure 5. Median number of TCR clones at landmark timepoints (post-pembro/ pre-intismeran, post-pembro/post-intismeran, and long-term follow-up)



		Post-pembro/ pre-intismeran	Post-pembro/ post-intismeran	Long-term follow-up
Unique	Median (min–max)	15 (1–208)	25 (2–187)	40.5 (0–185)
Overlapping	Median (min–max)	0 (0–3)	0 (0–4)	0 (0–2)

Errors bars show the median absolute deviation.

Figures 3 and B: Lu et al 2025 AACR Poster Presentation,
Figures 5 and 6: Sullivan et al 2025 SMR Poster Presentation

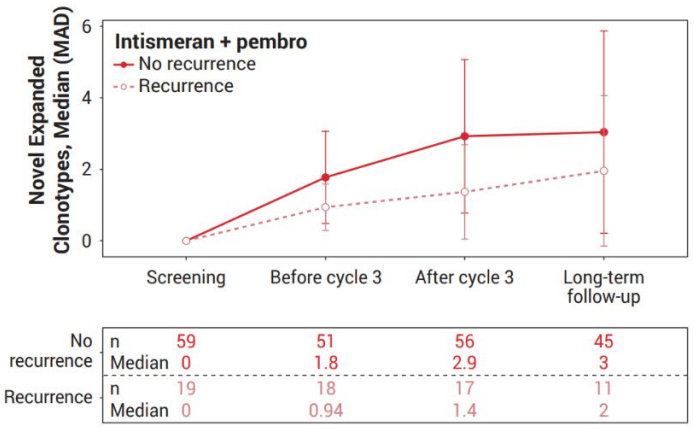
Expansion of novel clonotypes was positively associated with clinical benefit in combination arm, but not in monotherapy arm

Figure 5. Expansion of novel clonotypes was positively associated with RFS for intismeran + pembro but not for pembro alone

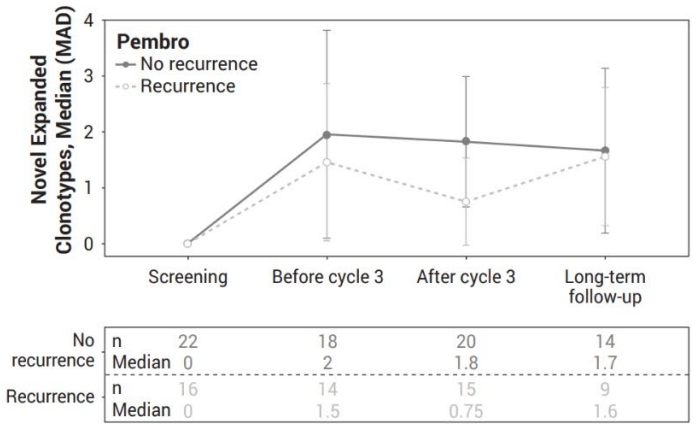
A. Median number and sum frequency of novel expanded clonotypes for screening vs last on-treatment timepoint by recurrence status

	Intismeran + Pembro Response			Pembro Response		
	No Recurrence	Recurrence	Adjusted *P* value, Recurrence vs No Recurrence	No Recurrence	Recurrence	Adjusted *P* value, Recurrence vs No Recurrence
Patients, n	59	19		22	16	
Median number of novel expanded clones	40	16	**0.014**[a]	25	19	0.85
Median sum of novel expanded clones, % of all blood T-cells	3%	1.4%	**0.029**[a]	1.7%	1.6%	0.87

B. Cumulative frequency of expanded novel clonotypes at screening and after treatment with intismeran + pembro by recurrence status[b]



C. Cumulative frequency of expanded novel clonotypes at screening and after treatment with pembro by recurrence status[b]



Lu et al 2025 AACR Poster Presentation

Summary from analysis of individualized neoantigens in intismeran from the adjuvant melanoma Phase 2 trial intismeran summary slide

Conclusions

- Baseline TCR clonality was not associated with RFS with intismeran + pembro or pembro alone
- Expansion of novel T-cell clonotypes in peripheral blood was observed to a greater extent after intismeran + pembro compared with pembro alone
- Expansion of novel clonotypes was positively associated with RFS with intismeran + pembro but not with pembro alone
- These data suggest TCR repertoire dynamics may serve as a pharmacodynamic biomarker for individualized neoantigen therapies

Next steps

- Evaluation of neoantigen specificity of the novel expanded clonotypes is ongoing

mRNA-4359

Kyle Holen, MD
Senior Vice President, Head of Development, Oncology

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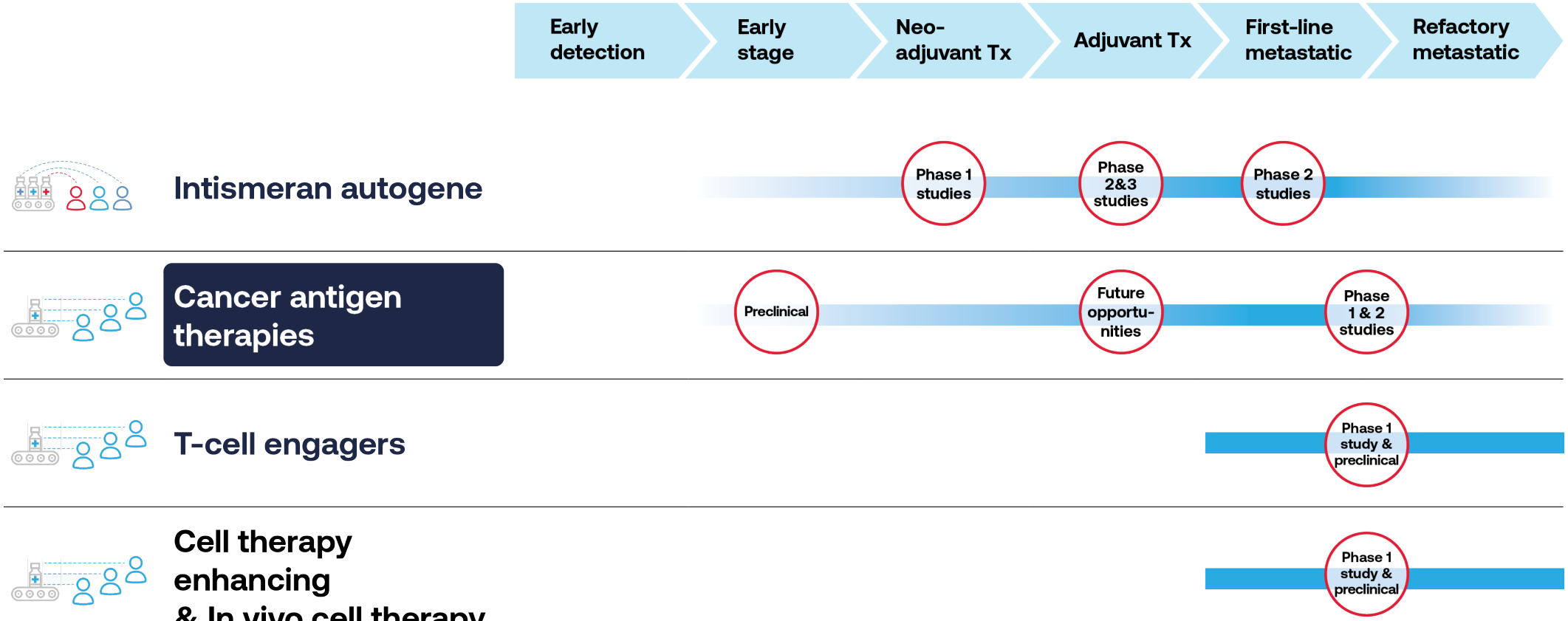
Moderna oncology research and development programs across cancer disease stages



Three investigational off-the-shelf cancer antigen therapy candidates in development

Cancer antigen therapies

		Preclinical	Ph 1	Ph 2	Ph 3	Commercial
Advanced solid tumors	mRNA-4359					
Solid tumors	mRNA-4106					
Lynch Syndrome						

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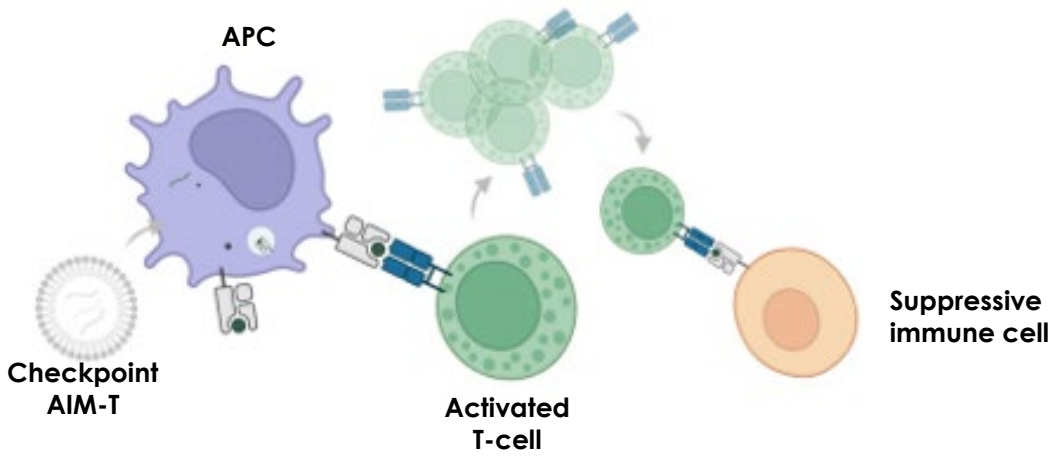
mRNA-4359 targets both immunosuppressive and cancer cells that overexpress PD-L1 and IDO

mRNA-4359



Harnessing T-cells with off-the-shelf cancer antigen therapies

- Encodes for PD-L1 and IDO
- Targets both immunosuppressive cells and cancer cells
- Applicable to many different cancer types

Study design and key objectives

Arm 1a presented at ESMO 2024

Arm 1a (Dose escalation)
Monotherapy
Advanced or metastatic solid tumors
COMPLETED

Arm 1b presented at ESMO 2025

Arm 1b (Dose confirmation)
Combination therapy
Advanced or metastatic Checkpoint Inhibitor refractory melanoma/NSCLC
ONGOING

- **Safety and tolerability** of mRNA-4359 alone and in combination with pembrolizumab
- **Antitumor activity** of mRNA-4359 alone and in combination with pembrolizumab (ORR, DCR, DOR, PFS)
- **T-cell profile changes** (peripheral and tumor) after treatment of mRNA-4359 alone or in combination with pembrolizumab

Note: for more information about mRNA-4359, see the Checkpoint AIM-T Program Pack
1. Link to 2024 ESMO presentation

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Clinical Outcomes and PD-L1 Expression Analyses from a Trial of mRNA-4359 Plus Pembrolizumab in Checkpoint Inhibitor–Resistant/Refractory Melanoma

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[1]Imperial College London, Hammersmith Hospital, London, UK; [2]University of Piemonte Orientale, Novara, Italy; [3]Massachusetts General Hospital, Boston, MA, USA; [4]One Clinical research, Hollywood Private Hospital and Edith Cowan University, Perth, WA, Australia; [5]Guy's Hospital, King's College London, London, UK; [6]University of Colorado, Aurora, CO, USA; [7]University Hospital Southampton NHS Trust and University of Southampton, Southampton, UK; [8]University of Birmingham, Birmingham, UK; [9]University of Glasgow, Glasgow, UK; [10]Washington University in St Louis, St Louis, MO, USA; [11]John Theurer Cancer Center - Hackensack Meridian Health, Hackensack, NJ, USA; [12]UCSF, San Francisco, CA, USA; [13]NEXT Madrid, University Hospital Quiron Salud, Madrid, Spain; [14]NIHR Biomedical Research Centre, Oxford, UK; [15]The University of Chicago, Chicago, IL, USA; [16]The George Washington University, Washington, DC, USA; [17]Moderna, Inc., Cambridge, MA, USA; [18]Melanoma Institute Australia, The University of Sydney, Sydney, Mater and Royal North Shore Hospitals, NSW, Australia

Dr David James Pinato

Friday, October 17, 2025

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Background

- Checkpoint inhibition has revolutionized treatment of advanced melanoma; however, despite improvements in outcomes, the majority of patients will experience disease progression[1,2]
- mRNA-4359 is a lipid nanoparticle–encapsulated mRNA-based immune evasion–targeted cancer antigen therapy encoding epitopes of PD-L1 and IDO1 antigens[3]
- mRNA-4359 is designed to elicit T-cell responses against both tumor and immunosuppressive cells, resulting in direct tumor killing and rebalancing of the tumor microenvironment[3]
- An ongoing phase 1/2 trial (NCT05533697) is evaluating mRNA-4359 as monotherapy or in combination with pembrolizumab in patients with advanced solid tumors[3,4]
- We present clinical, safety, and translational data of mRNA-4359 plus pembrolizumab in the fully enrolled CPI-R/R melanoma cohort from the dose-confirmation portion of this ongoing study

CPI-R/R, checkpoint inhibitor–resistant/refractory; IDO1, indoleamine 2,3-dioxygenase 1; PD-1, programmed cell death protein 1; PD-L1, programmed cell death ligand 1.

1. Haist M, et al. *Cancer Metastasis Rev*. 2023;42:481–505; 2. Tiersma JF, et al. *Cancer Treat Rev*. 2024;129:102802; 3. Powderly JD, et al. *J Clin Oncol*. 2023;41:TPS2676; 4. Khattak MA, et al. *Ann Oncol*. 2024;35(Supplement 2):S521–S522.

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Study Design, Patient Disposition, and Baseline Characteristics

Arm 1b (dose confirmation) and pharmacodynamic arms

mRNA-4359 plus pembrolizumab[a]

- Previously treated, histologically confirmed locally advanced or metastatic **CPI-R/R melanoma** or NSCLC, with primary refractory or acquired resistance to CPI[b] (≥1 prior line of a PD-1/PD-L1 containing regimen), and with a tumor lesion amenable to biopsy at screening

29 participants with CPI-R/R melanoma enrolled

mRNA-4359 400 µg Q3W + pembro 400 mg Q6W	**mRNA-4359 1000 µg Q3W + pembro 400 mg Q6W**
14 received treatment	15 received treatment
1 completed both treatments **9 discontinued both treatments** PD (n = 6) AE (n =1) Death[c] (n = 1) Physician decision (n = 1)	**0 completed both treatments** **13 discontinued both treatments** PD (n = 12) Participant withdrawal (n = 1)
4 treatment ongoing Completed mRNA-4359 and pembro ongoing (n = 3) Pembro and mRNA-4359 ongoing (n = 1)	**2 treatment ongoing** Completed mRNA-4359 and pembro ongoing (n = 2)

Median follow-up time[a]: 19.9 (range 2.0–84.1) wk

	mRNA-4359 400 µg Q3W + pembro 400 mg Q6W (n = 14)	**mRNA-4359 1000 µg Q3W + pembro 400 mg Q6W (n = 15)**
Follow-up,[d] median (range), wk	22.5 (3.3–84.1)	10.4 (2.0–62.7)
Age, median (range), y	67 (49–83)	65 (29–79)
Male, n (%)	10 (71)	6 (40)
ECOG PS, n (%)		
0	9 (64)	12 (80)
1	5 (36)	3 (20)
PD-L1 TPS,[e] n (%)		
≥1%	6 (43)	4 (27)
<1%	6 (43)	7 (47)
Missing	2 (14)	4 (27)
CPI-R/R disease, n (%)	14 (100)	15 (100)
No. of prior therapy, median (range)	3 (1–8)	3 (1–7)

TPS, tumor proportion score. [a]Patients received treatment for 9 cycles, and afterwards, patients could continue with pembrolizumab for up to 2 years of total therapy. [b]Primary refractory resistance was defined as PD occurring within 6 months after the first dose of anti–PD-(L)1antibody; acquired resistance was defined as PD in setting of ongoing treatment occurring in patients who had confirmed objective response or prolonged SD. [c]Per autopsy, cause of death was mostly likely due to arrhythmia secondary to undiagnosed hypertrophic cardiomyopathy; melanoma disease response was pathologic complete response. [d]Defined as treatment initiation to earliest non-missing date of last known alive, death, or data cutoff. [e]PD-L1 testing was assessed centrally using PD-L1 IHC 22C3 pharmDx (Agilent, Santa Clara, CA). Data cutoff: February 28, 2025.

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mRNA-4359 + Pembrolizumab Demonstrated a Manageable Safety Profile

- mRNA-4359-related AEs were mostly grade 1/2 injection site reactions and self-limited systemic AEs (eg, fatigue, pyrexia, chills)
- Pembrolizumab AEs were consistent with its known safety profile
  - Pembrolizumab-related AEs occurred in 66% of patients (grade 3, 10%)
  - Pembrolizumab-related AEs with >10% incidence were fatigue (28%), diarrhea, (10%), pruritus (10%), and vomiting (10%)
- 13.8% of patients experienced immune-related AEs (eg, colitis, pancreatitis, gastritis, nephritis, and secondary adrenocortical insufficiency)
- No DLTs occurred for either dose level
- No grade 4 or 5 treatment-related AEs occurred

	mRNA-4359 400 µg Q3W + pembro 400 mg Q6W (n = 14)	mRNA-4359 1000 µg Q3W + pembro 400 mg Q6W (n = 15)
Duration of mRNA-4359 therapy, median (range), wk	12.5 (0.1–81.1)	6.1 (0.1–29.6)
Duration of pembro therapy, median (range), wk	10.1 (0.1–80.6)	5.9 (0.1–60.4)
mRNA-4359–related AEs, n (%)	14 (100)	12 (80)
Grade 3[a]	1 (7)[b]	1 (7)[c]
mRNA-4359–related AEs with incidence ≥20% in either cohort, n (%)		
Injection site pain	10 (71)	8 (53)
Fatigue	7 (50)	7 (47)
Pyrexia	7 (50)	4 (27)
Injection site erythema	4 (29)	1 (7)
Chills	3 (21)	2 (13)
Influenza-like illness	3 (21)	5 (33)
Vomiting	2 (14)	5 (33)
Decreased appetite	2 (14)	3 (20)
Nausea	2 (14)	3 (20)

[a]There were no grade 4 or 5 treatment-related AEs. [b]1 patient experienced grade 3 pulmonary embolism. [c]1 patient experienced grade 3 fatigue and increased blood lactic acid. Data cutoff: February 28, 2025.

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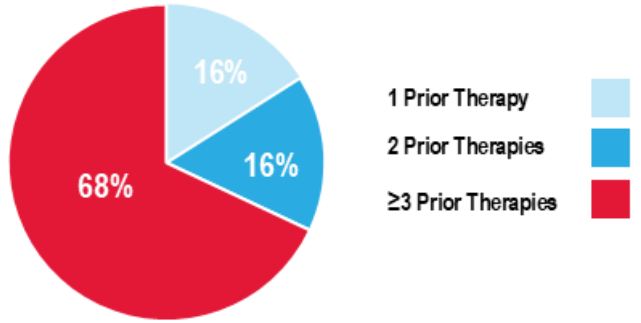
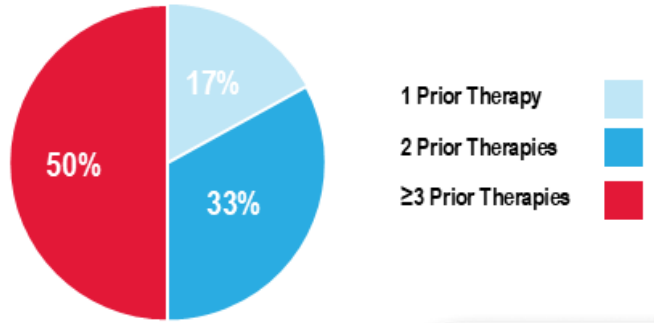
mRNA-4359 + Pembrolizumab Showed Antitumor Activity in Patients With CPI-R/R Melanoma

Evaluable patients	mRNA-4359 400 µg Q3W + pembro 400 mg Q6W (n = 13)	mRNA-4359 1000 µg Q3W + pembro 400 mg Q6W (n = 12)	All patients (N = 25)
ORR, % (95% CI)[a]	38 (14–68)	8 (0–39)	24 (9–45)
Best overall response, n (%)			
CR	0	1 (8)	1 (4)
PR	5 (38)	0	5 (20)
SD	5 (38)	4 (33)	9 (36)
PD	3 (23)	7 (58)	10 (40)
DCR, % (95% CI)[a]	77 (46–95)	42 (15–72)	60 (39–79)
DOR, median (95% CI),[b,c] wk	NR (NR–NR)	NR (NR–NR)	NR (NR–NR)

Number of Prior Therapies Among 25 Evaluable Patients



Number of Prior Therapies Among 6 Responders



CR complete response, NR, not reached. PR, partial response. [a]Based on the Clopper-Pearson exact test. [b]Based on Brookmeyer and Crowley methodology, using log-log transformation for calculating CIs. [c]The median follow-up duration of the 6 responders was 71 (range 38–84) wk by the data cutoff date. Data cutoff: February 28, 2025.

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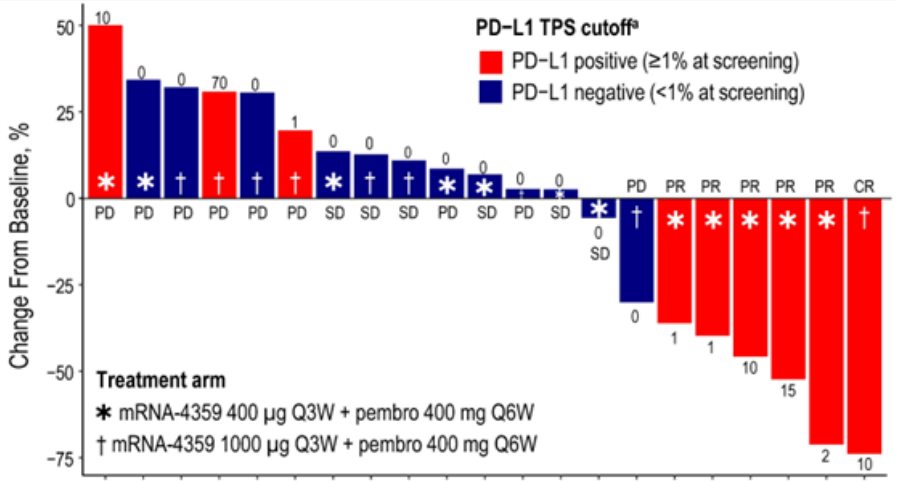
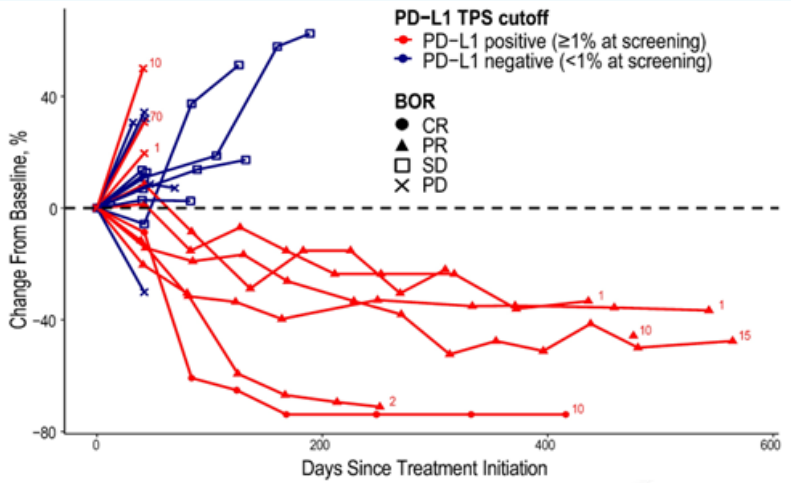
Responses Were Enriched in PD-L1–Positive Tumors (ORR, 67%), With Median Duration of Response Not Yet Reached, Indicating Encouraging Durability

Evaluable patients	Baseline PD-L1 TPS ≥1%			Baseline PD-L1 TPS <1%		
	mRNA-4359 400 µg Q3W + pembro 400 mg Q6W (n = 6)	mRNA-4359 1000 µg Q3W + pembro 400 mg Q6W (n = 3)	All patients (N = 9)	mRNA-4359 400 µg Q3W + pembro 400 mg Q6W (n = 6)	mRNA-4359 1000 µg Q3W + pembro 400 mg Q6W (n = 6)	All patients (N = 12)
ORR, % (95% CI)	83 (36–100)	33 (1–91)	67 (30–93)	0	0	0
DCR, % (95% CI)[b]	83 (36–100)	33 (1–91)	67 (30–93)	67 (22–96)	33 (4–78)	50 (21–79)

Best Percent Change From Baseline in Target Tumor Size



Tumor Responses Over Time[b]



BOR, best overall response. [a]Baseline PD-L1 TPS scores are displayed above or below each bar. [b]Baseline PD-L1 TPS scores in patients with PD-L1 positive tumors are displayed at the end of the line.
Data cutoff: February 28, 2025.

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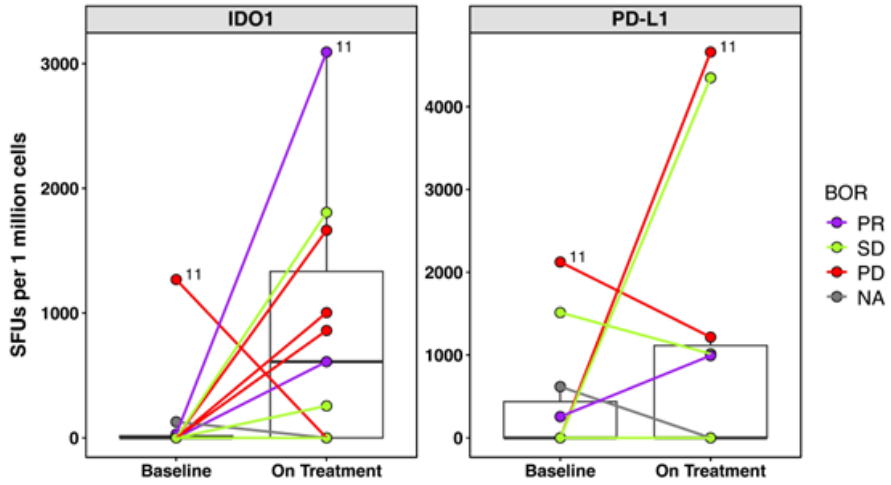
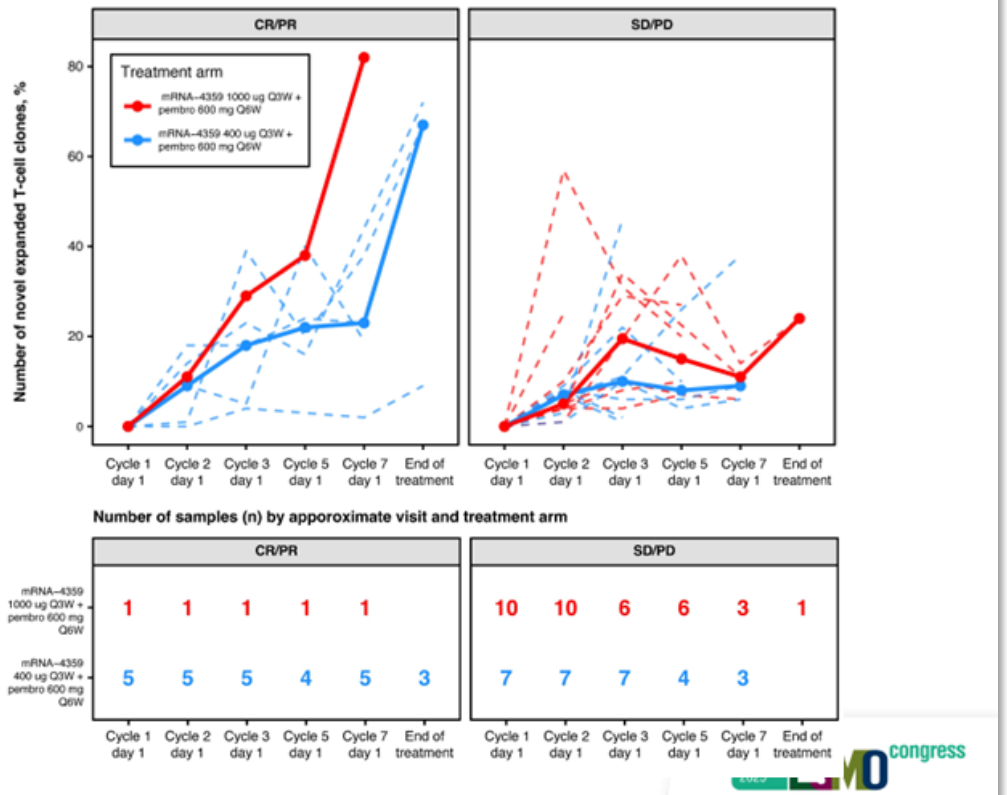
mRNA-4359 Demonstrated Biological Activity Through Specific T-Cell Responses and Novel Clonal Expansion in the Periphery

mRNA-4359 Elicited PD-L1- and IDO1-Specific T cell Responses in the Periphery[a]



Increase in Number of Novel Expanded TCR Clones in the Periphery with mRNA-4359 Treatment



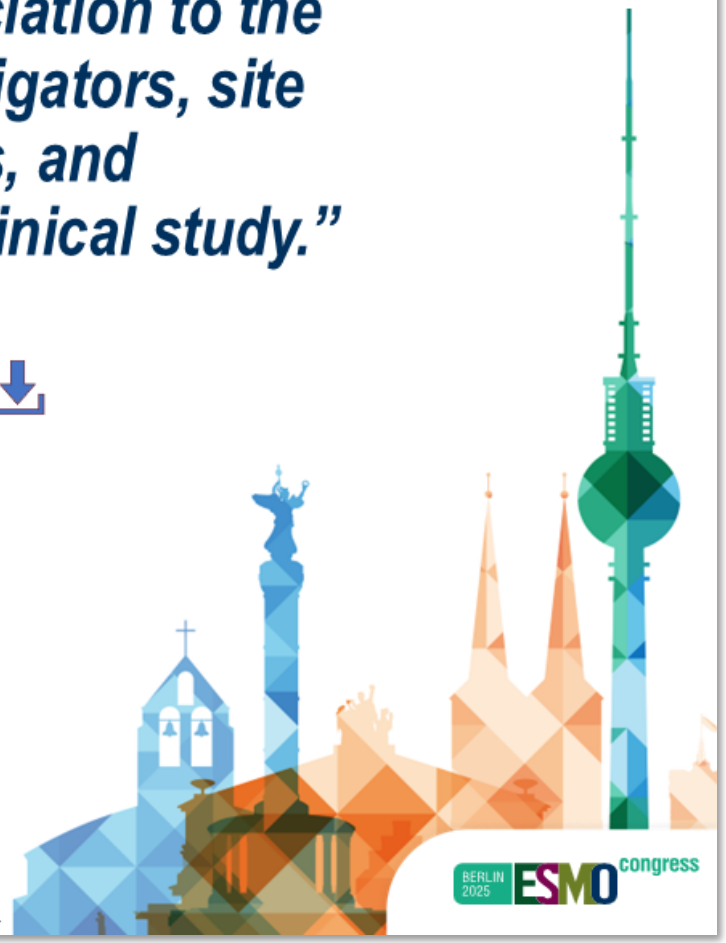
SFU, spot-forming unit; TCR, T cell receptor.

[a]On treatment responses were selected from the 'best' ELISpot response at different time points for each patient.

Presented by: David J. Pinato

"We wish to express our sincere appreciation to the study patients, their families, the investigators, site personnel, research teams, our vendors, and collaborators who contributed to this clinical study."

To download a copy of today's presentation



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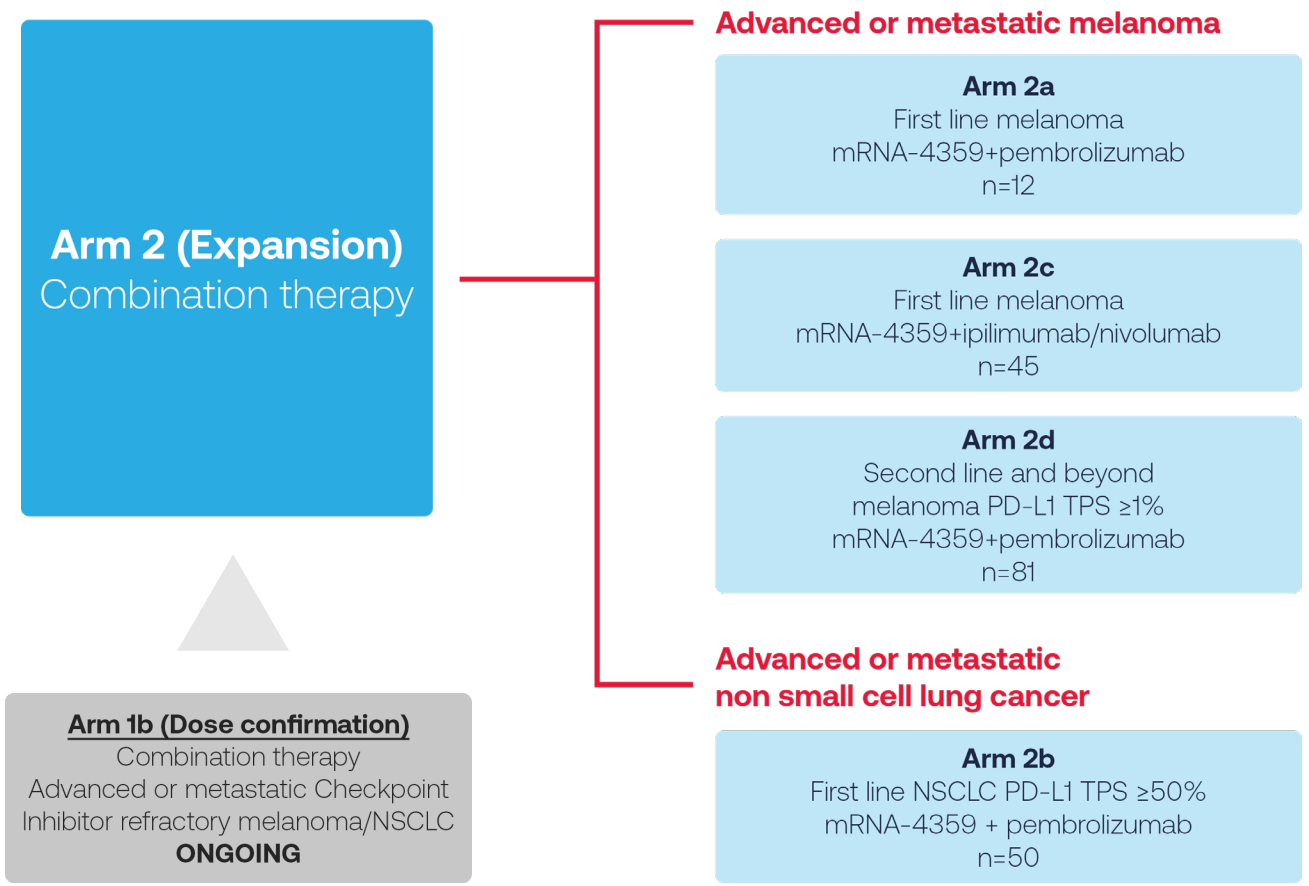
mRNA-4359 has advanced into a Phase 2 study with arms in metastatic melanoma and metastatic NSCLC



Key objectives

Primary endpoints

- Arms 2a-2c: Safety and tolerability of mRNA-4359
- Arm 2d: Objective response rate based on BICR per on RECIST v1.1

Secondary endpoints

- Arms 2a-2c: Objective response rate, disease control rate, duration of response, progression-free survival, all based investigator assessment per RECIST v1.1
- Arms 2a-2c: Percent change from baseline in T Cell profile in the tumor
- Arm 2d: Safety and tolerability of mRNA-4359
- Arm 2d: Duration of response, disease control rate, progression-free survival, all based on BICR per RECIST v1.1
- Arm 2d: Overall survival
- Arm 2d: Quality of Life

Abbreviations: BICR, Blinded Independent Central Review; RECIST v1.1, Response Evaluation Criteria in Solid Tumors Version 1.1

Early-stage oncology

Rose Loughlin, Ph.D.
Executive Vice President, Research

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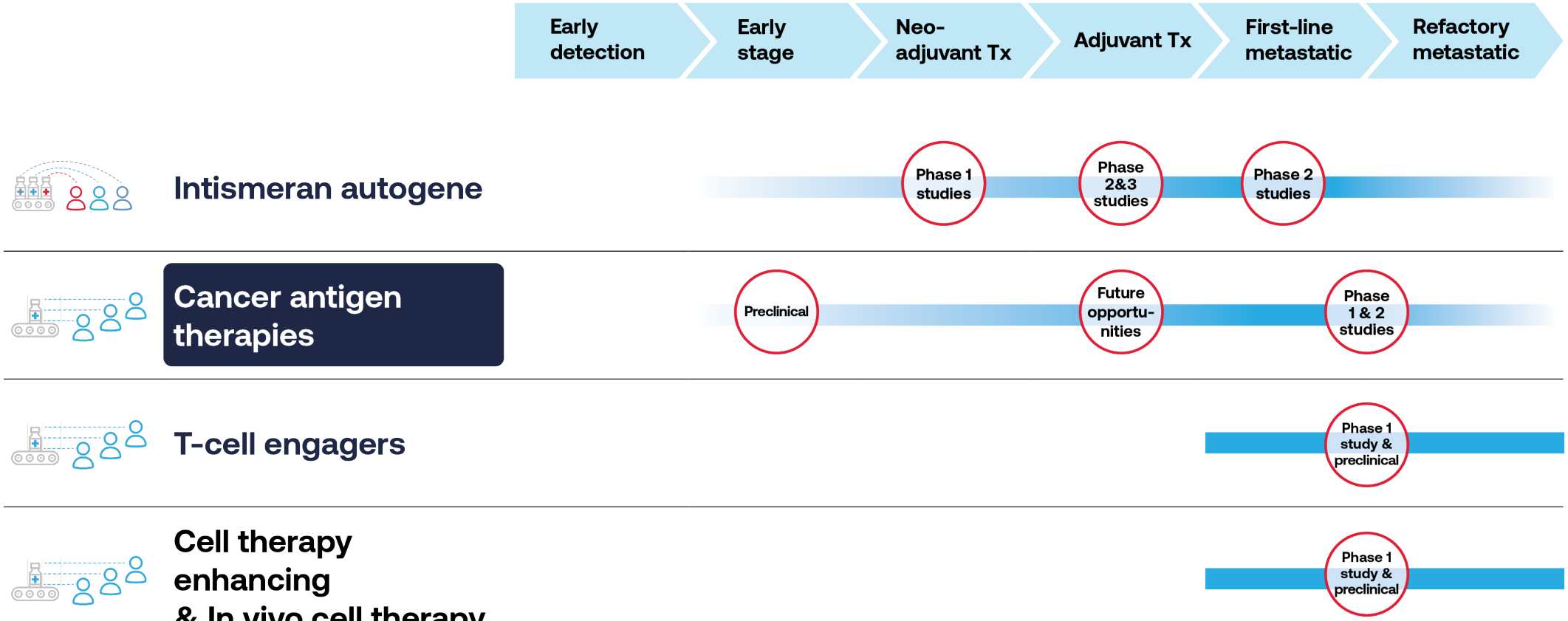
Moderna oncology research and development programs across cancer disease stages



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Three investigational off-the-shelf cancer antigen therapy candidates in development

Cancer antigen therapies

		Preclinical	Ph 1	Ph 2	Ph 3	Commercial
Advanced solid tumors	mRNA-4359					
Solid tumors	mRNA-4106					
Lynch Syndrome						

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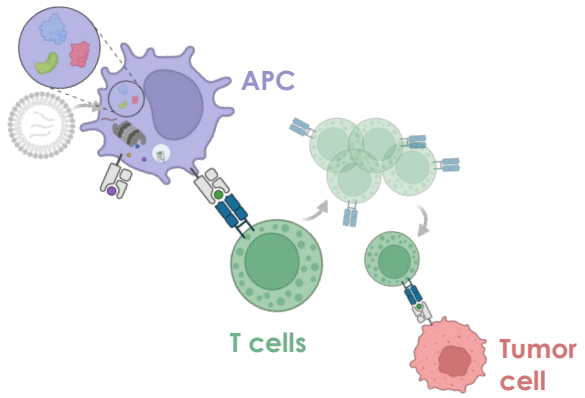
mRNA-4106 is a cancer antigen therapy offering broad coverage across tumor types

mRNA-4106



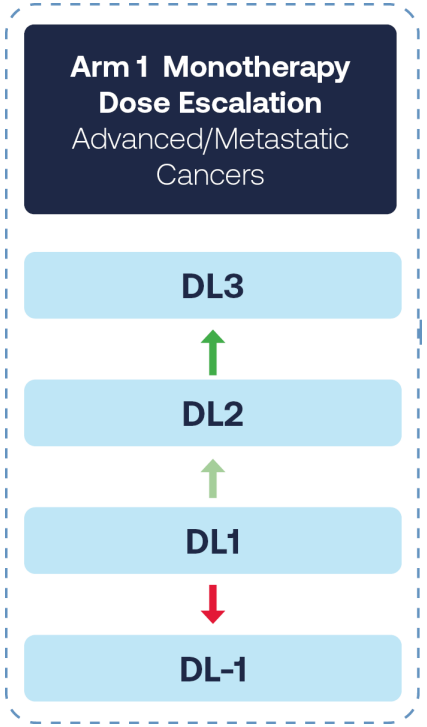
Harnessing T-cells with off-the-shelf cancer antigen therapies

- Encodes for multiple tumor targets
- Designed to broaden coverage across and within patients
- Applicable to multiple cancer types

Study design and key objectives

Primary Objective: safety/tolerability as monotherapy and in combination with checkpoint inhibitor therapy

Exploratory Objectives: Anti-tumor activity



Three investigational off-the-shelf cancer antigen therapy candidates in development

Cancer antigen therapies

		Preclinical	Ph 1	Ph 2	Ph 3	Commercial
Advanced solid tumors	mRNA-4359					
Solid tumors	mRNA-4106					
Lynch Syndrome						

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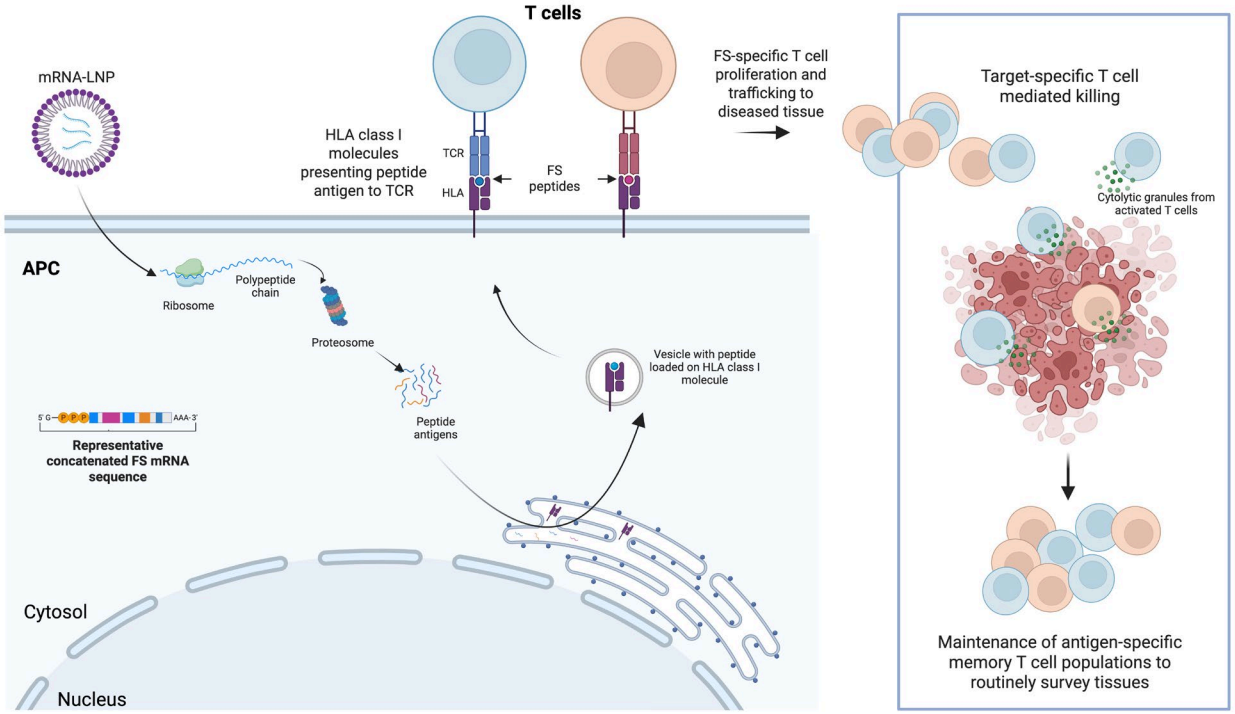
Cancer Antigen Therapy for patients with Lynch Syndrome



Abbreviations: APC = antigen presenting cell; FS = frameshift; HLA = human leucocyte antigen; LNP = lipid nanoparticle; mRNA = messenger ribonucleic acid; TCR = T-cell receptor

Cancer Antigen Therapy designed for preventive use in Lynch Syndrome patients

The clinical study will be conducted in collaboration with the University of Oxford

Phase 1/2 clinical trial planned for initiation in 2026

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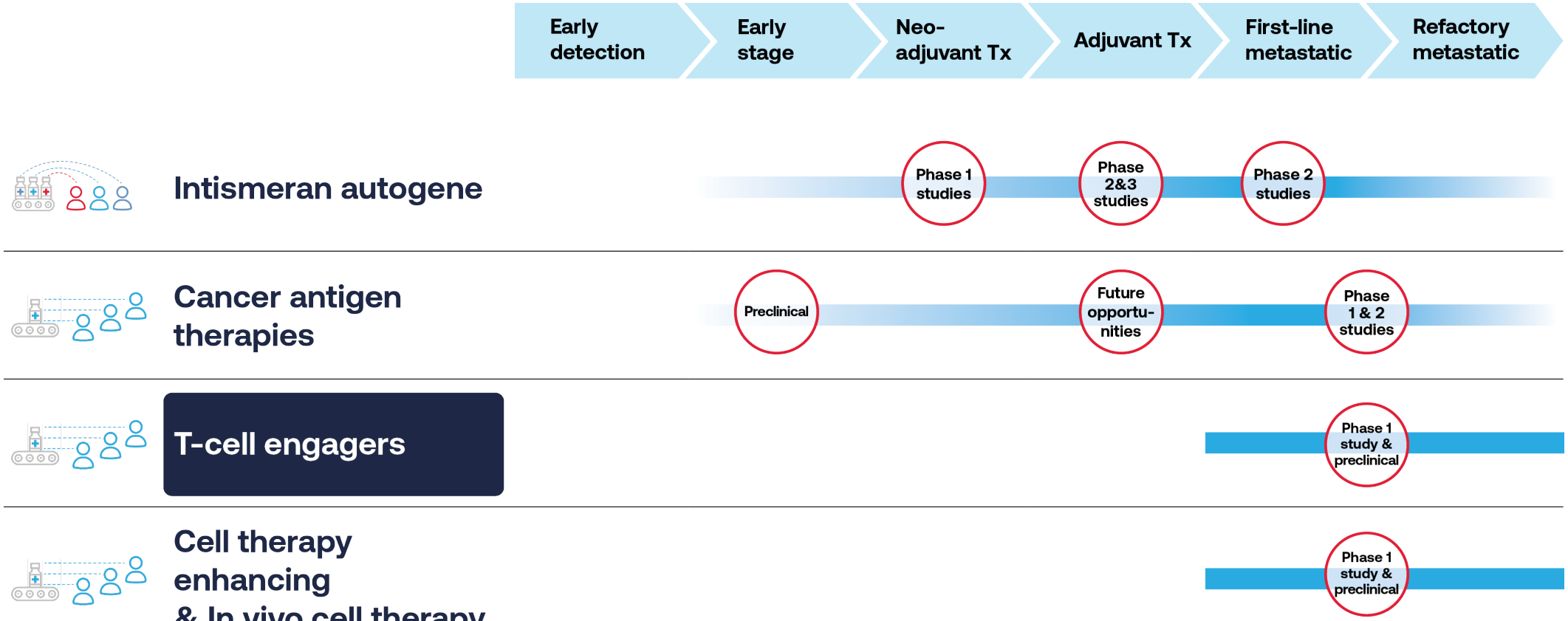
Moderna oncology research and development programs across cancer disease stages



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T cell engagers bind T cells and tumor antigens together to activate killing of cancer cells

T-cell engagers

		Preclinical	Ph 1	Ph 2	Ph 3	Commercial
Surface antigen T-cell engager - multiple myeloma	mRNA-2808					
Intracellular antigen T-cell engagers In partnership with Immatics	Preclinical					

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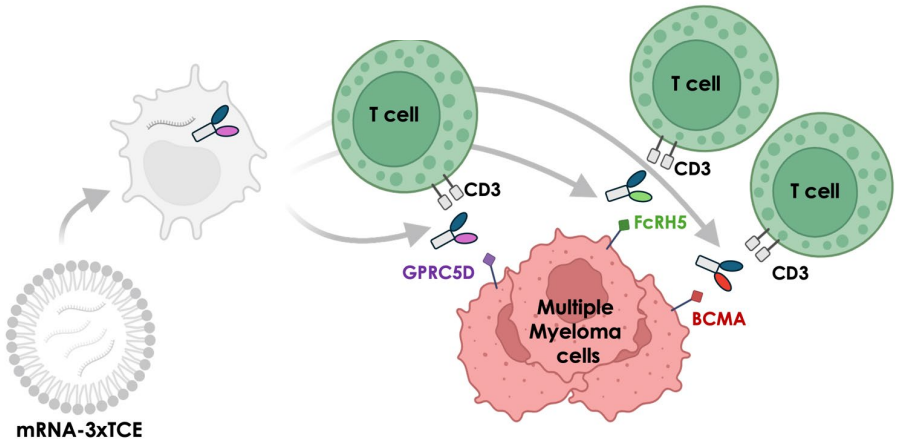
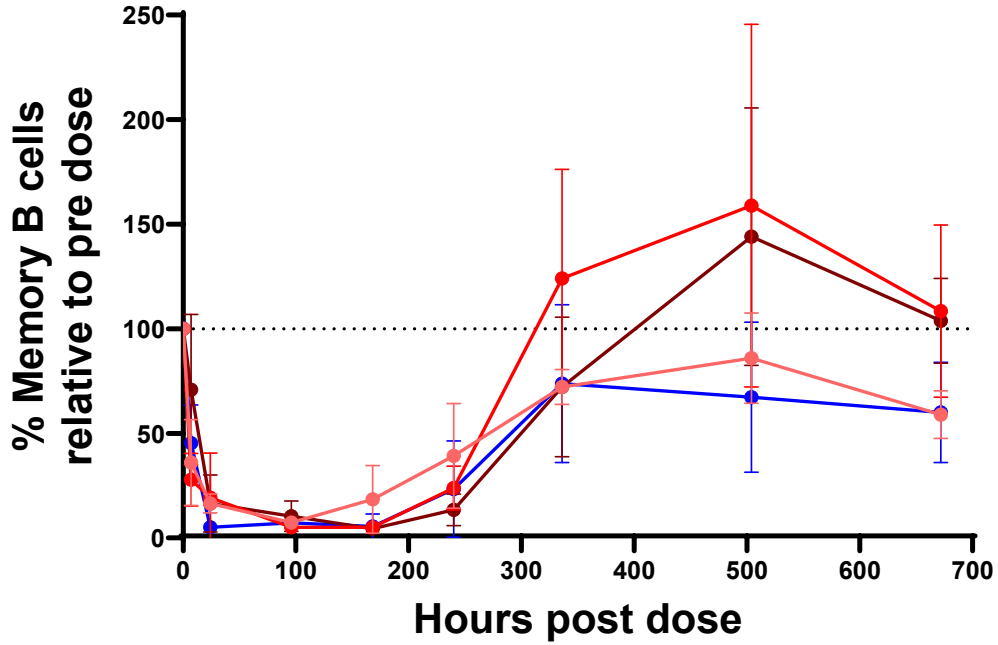
mRNA-2808 is a T Cell Engager targeting surface antigens in multiple myeloma

mRNA-2808



- Targets T-cell CD3 and tumor associated antigens (TAAs) that are present on the surface of the tumor
- Multiplexes to overcome antigen escape, well-established resistance mechanism
- Ability to multiplex other T-cell targets for co-stimulation

Memory B cell depletion

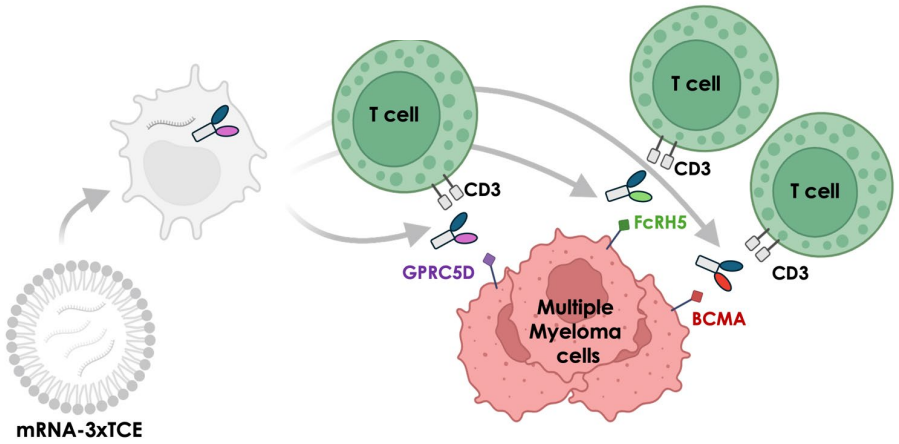


NHPs (n=4/group) received a single IV dose (0.125 mg/kg, 1 mg/kg, or 3 mg/kg) or subcutaneous (SC) injection (1 mg/kg)

ASH 2024

mRNA-2808 is currently dosing in a Phase 1/2 clinical study

mRNA-2808

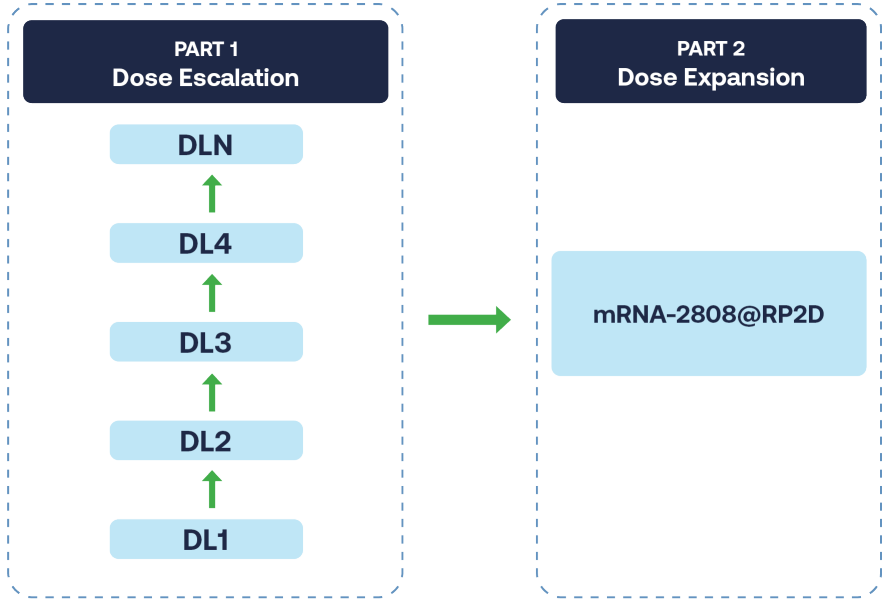


- Targets T-cell CD3 and tumor associated antigens (TAAs) that are present on the surface of the tumor
- Multiplexes to overcome antigen escape, well-established resistance mechanism
- Ability to multiplex other T-cell targets for co-stimulation

Phase 1/2 study design and key objectives

Primary endpoints: Safety, number of participants with dose limiting toxicity, number of participants with treatment-emergent adverse events

Secondary endpoints: Pharmacokinetics, pharmacodynamics, overall response rate by International Myeloma Working Group (IMWG), duration of response, progression-free survival



DL: dose level

T cell engagers bind T cells and tumor antigens together to activate killing of cancer cells

T-cell engagers

		Preclinical	Ph 1	Ph 2	Ph 3	Commercial
Surface antigen T-cell engager - multiple myeloma	mRNA-2808					
Intracellular antigen T-cell engagers In partnership with Immatics	Preclinical					

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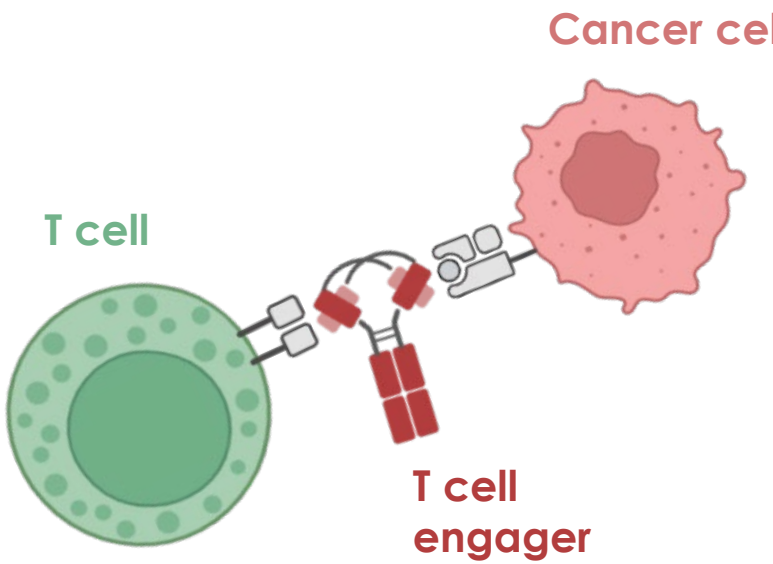
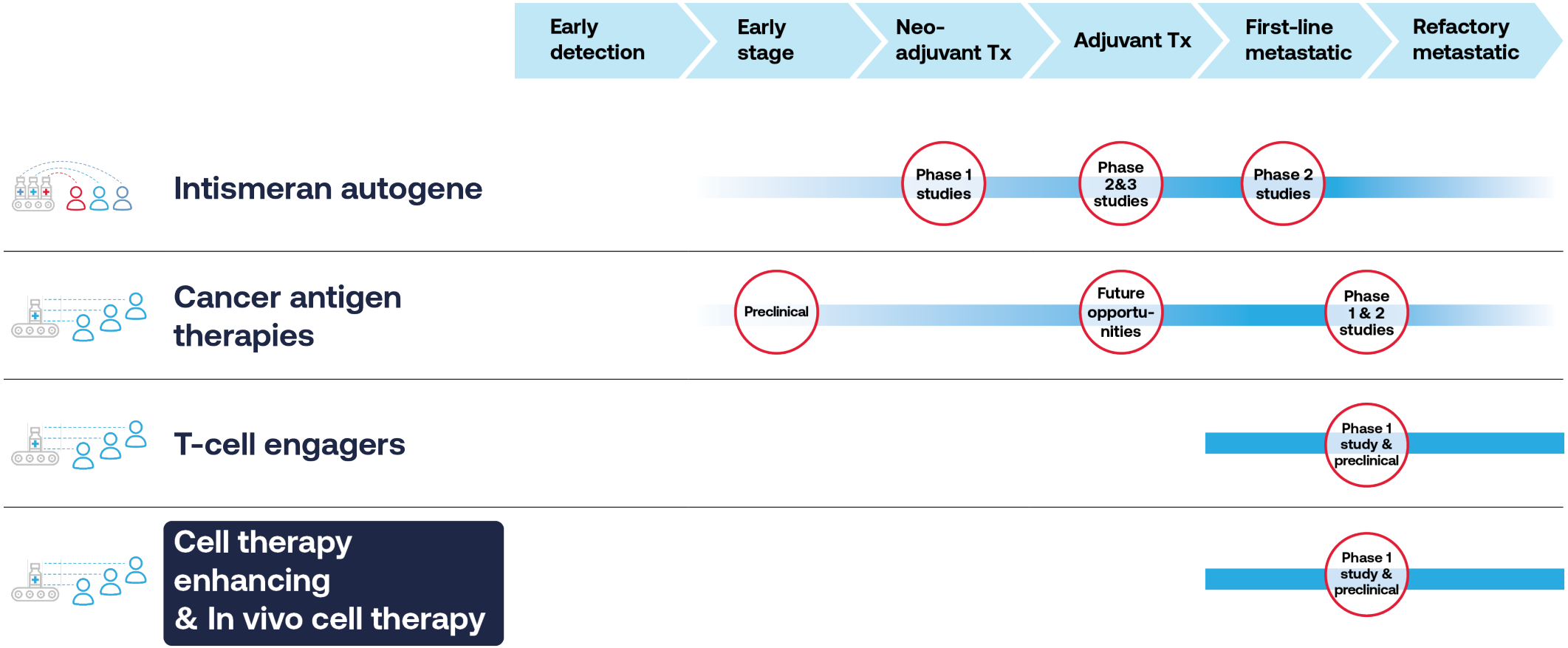
Intracellular antigen T-cell engagers in preclinical development



- Targets T-cells and tumor-specific antigens that are processed and displayed as peptides by MHC
- Ability to multiplex to provide more coverage of intracellular proteins as well as across different HLA subtypes
- In partnership with Immatics

Moderna oncology research and development programs across cancer disease stages



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Multiple approaches engineer patients' cells to fight cancer

Cell therapy enhancing & In vivo cell therapy

		Preclinical	Ph 1	Ph 2	Ph 3	Commercial
Solid tumors In partnership with Immatics	mRNA-4203 + anzu-cel (IMA203)					
CAR-T						
CAR-M						

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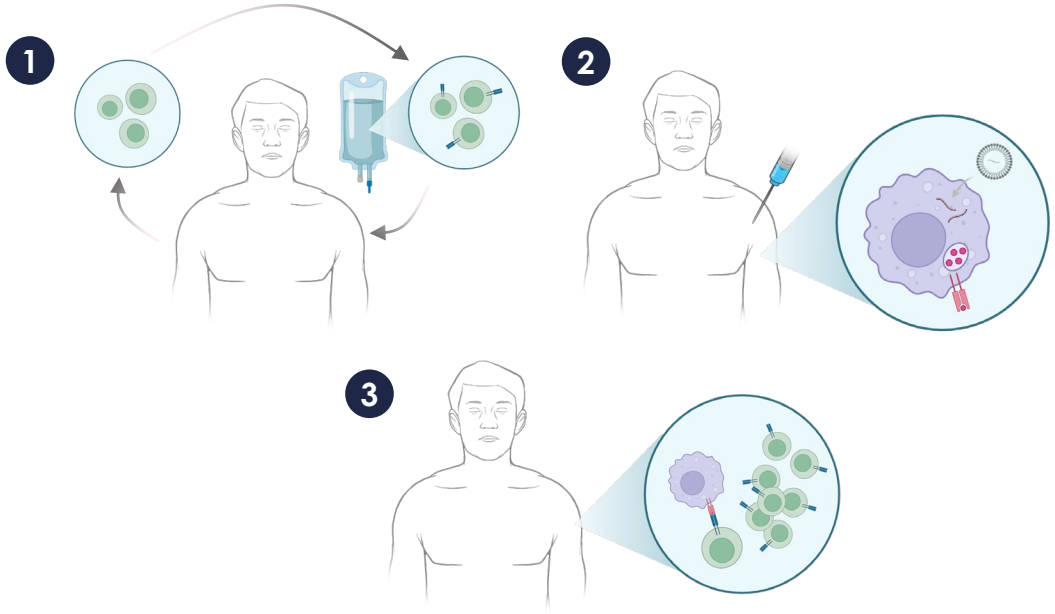
mRNA-4203 is a cell therapy enhancer in a Phase 1 study

mRNA-4203 + anzu-cel (IMA203)

In partnership with Immatics



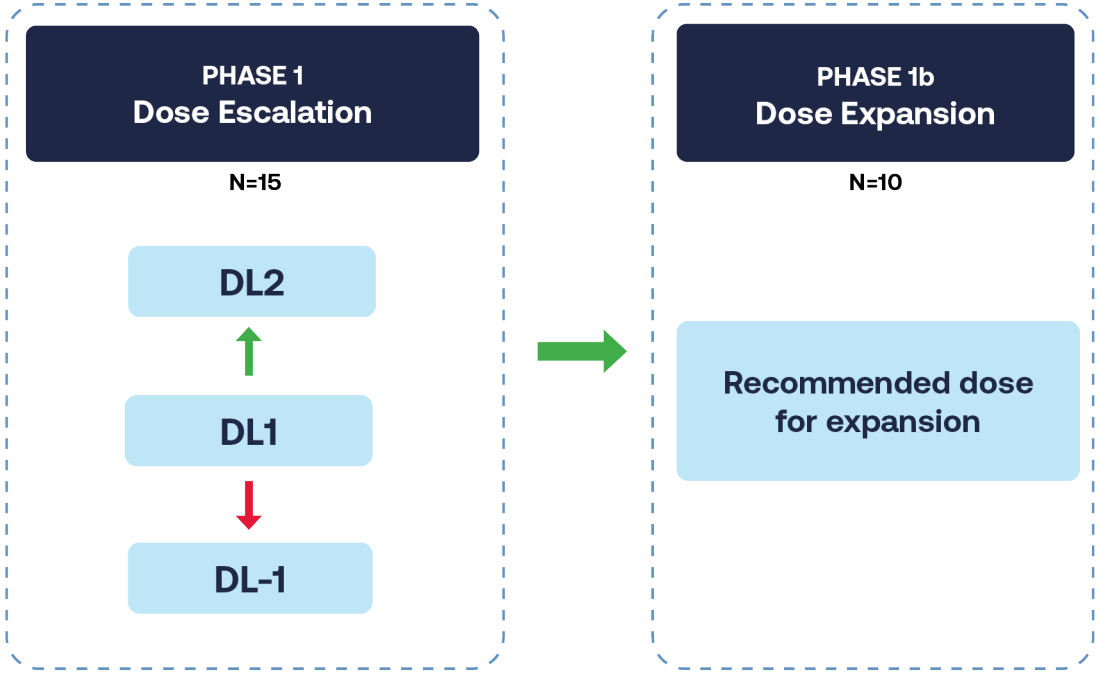
Cell therapy-enhancing antigen therapy

Encodes for the target of an *ex vivo* cell therapy to enhance the persistence and efficacy of the cell therapy

Phase 1 study design and key objectives

Primary endpoints: Safety, determine recommended dose expansion

Secondary endpoints: Evaluate anti-tumor activity of IMA203 in combination with mRNA-4203 and evaluate the pharmacokinetics of TCR-engineered T cells in combination with mRNA-4203



DL: dose level

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Multiple approaches engineer patients' cells to fight cancer

Cell therapy enhancing & In vivo cell therapy

		Preclinical	Ph 1	Ph 2	Ph 3	Commercial
Solid tumors In partnership with Immatics	mRNA-4203 + anzu-cel (IMA203)					
CAR-T						
CAR-M						

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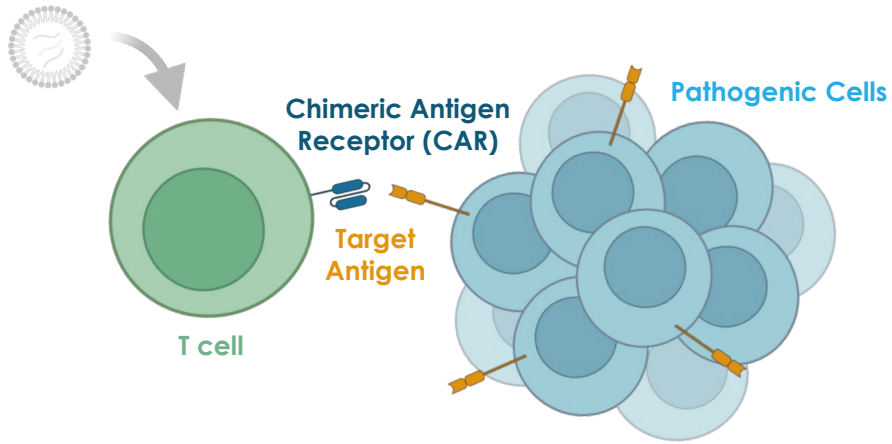
CAR-T candidates currently in preclinical development

Leverages mRNA-LNP technology to transfect T-cells for in vivo CAR-T cell therapy

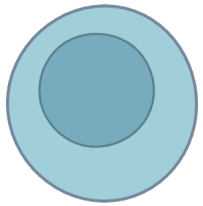
In vivo CAR-T eliminates the need for harsh preconditioning and complex, costly manufacturing required for ex vivo CAR-T

Mechanism of Action



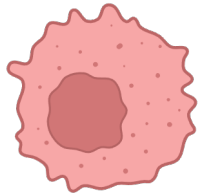
LNPs deliver mRNA into T cells, enabling them to express CARs that recognize and kill pathogenic cells

Therapeutic Applications



Pathogenic B cells

Autoimmune: Potential to treat a wide range of autoimmune diseases through reset of B cell immunity



Tumor cells

Oncology: Engineer CAR-T cells to target tumor cells to drive anti-tumor activity

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Multiple approaches engineer patients' cells to fight cancer

Cell therapy enhancing & In vivo cell therapy

		Preclinical	Ph 1	Ph 2	Ph 3	Commercial
Solid tumors In partnership with Immatics	mRNA-4203 + anzu-cel (IMA203)					
CAR-T						
CAR-M						

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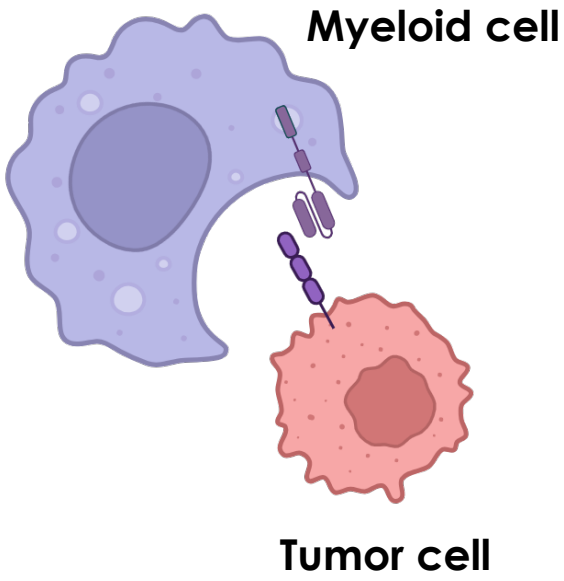
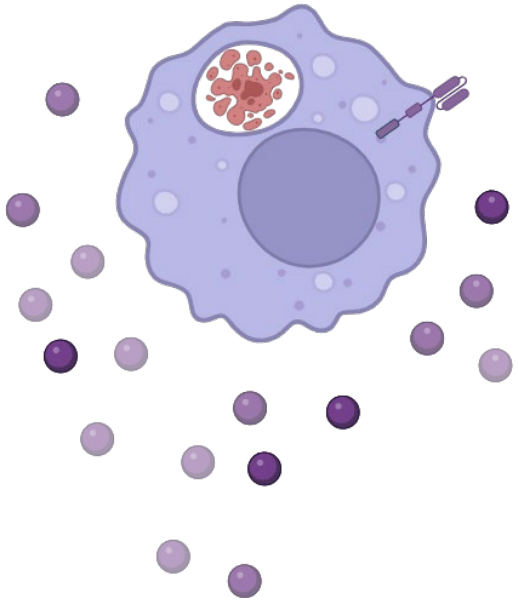
CAR-M candidates currently in preclinical development

Leverages mRNA-LNP technology to transfect myeloid cells for in vivo CAR-M cell therapy

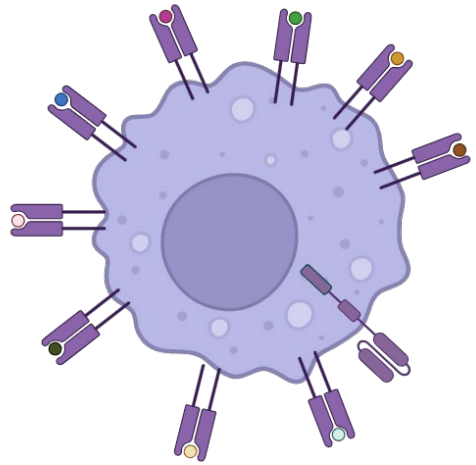
1 **Tumor cell phagocytosis**



2 **Secretion of pro-inflammatory factors**



3 **Presentation of diverse cancer antigens**



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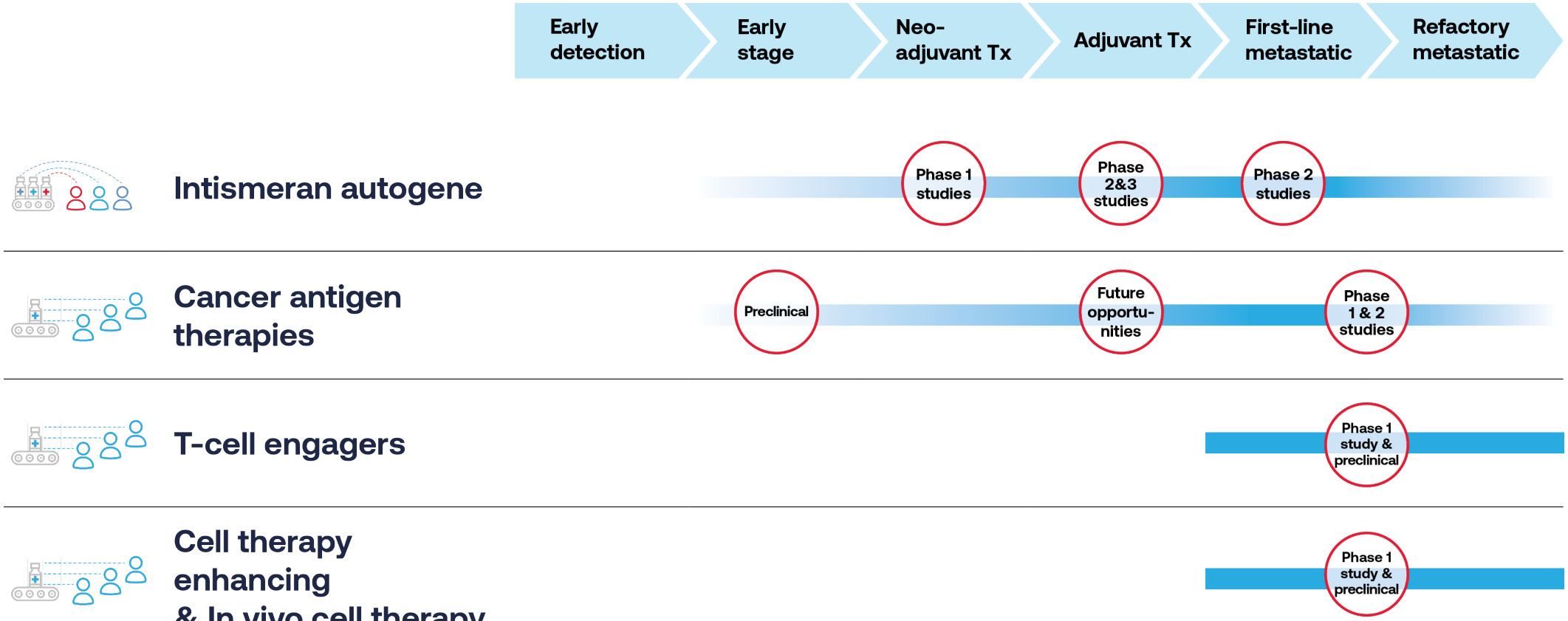
Moderna oncology research and development programs across cancer disease stages



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Rare disease therapeutics portfolio

Rituparna Das, MD
Vice President, Clinical Development Head,
Respiratory and Rare Diseases

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PA

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Propionic Acidemia (PA) is a Rare Metabolic Disorder Primarily Affecting Newborns and Infants That Causes Significant Morbidity and Mortality[1]

PA is caused by a deficiency in the propionyl–CoA carboxylase (PCC) enzyme[1,2]

Estimated global prevalence is 0.29 to 4.24 per 100,000 newborns[3]

Pathogenic variants in the PCC enzyme subunit genes *PCCA* and *PCCB* result in PCC enzyme deficiency and the accumulation of toxic metabolites[2]

PA is a multisystemic disease with neurologic, cardiac, endocrine, and immunologic manifestations[1,2,4]

Characterized by metabolic decompensation events (MDEs), which can be life-threatening

No approved therapies treat the underlying PCC enzyme deficiency

Current disease management involves dietary protein restriction and liver transplantation[4,5]

1. Fraser JL, et al. *Curr Opin Pediatr.* 2016;28:682–693; 2. Haijes HA, et al. *J Inherit Metab Dis.* 2019;42:745–761; 3. Almasi T, et al. *Orphanet J Rare Dis.* 2019;14(1):40; 4. Forny P, et al. *J Inherit Metab Dis.* 2021;44:566–592; 5. Jurecki E, et al. *Mol Genet Metab.* 2019;126:341–354; 6. Koeberl D, et al. *Nature*. 2024;630(8017):E13.

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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

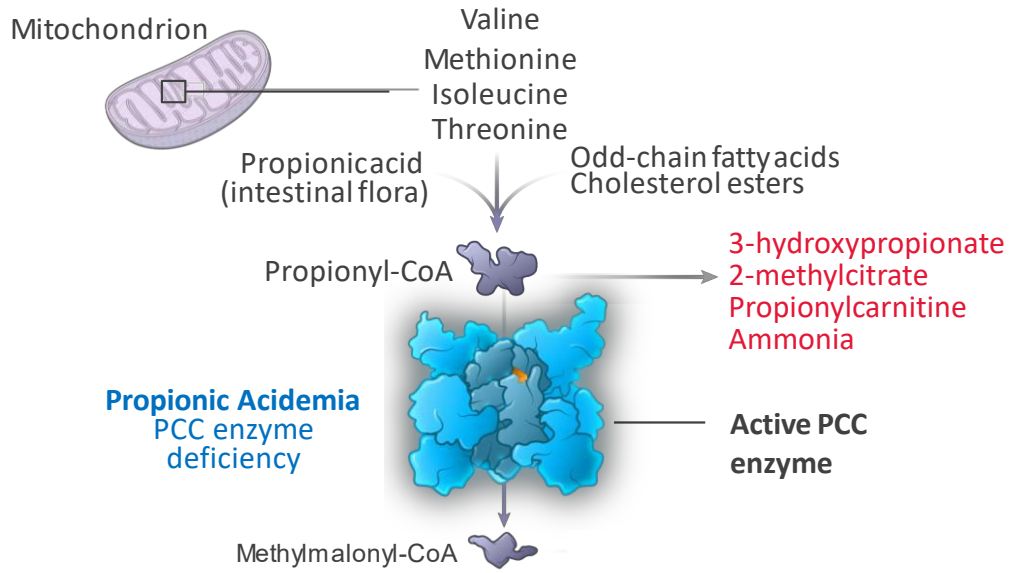


Figure adapted from Koeberl D, et al[6]

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 is an Investigational Therapy Encoding the Missing PCC Enzyme Subunits[1]

mRNA-3927 can address the underlying cause of PA

- mRNA-3927 is a novel, lipid nanoparticle–encapsulated, mRNA-based intravenous (IV) therapy[1]
- By encoding the normal PCCA and PCCB subunit proteins, it is hypothesized to restore PCC enzyme activity in the liver[1,2]

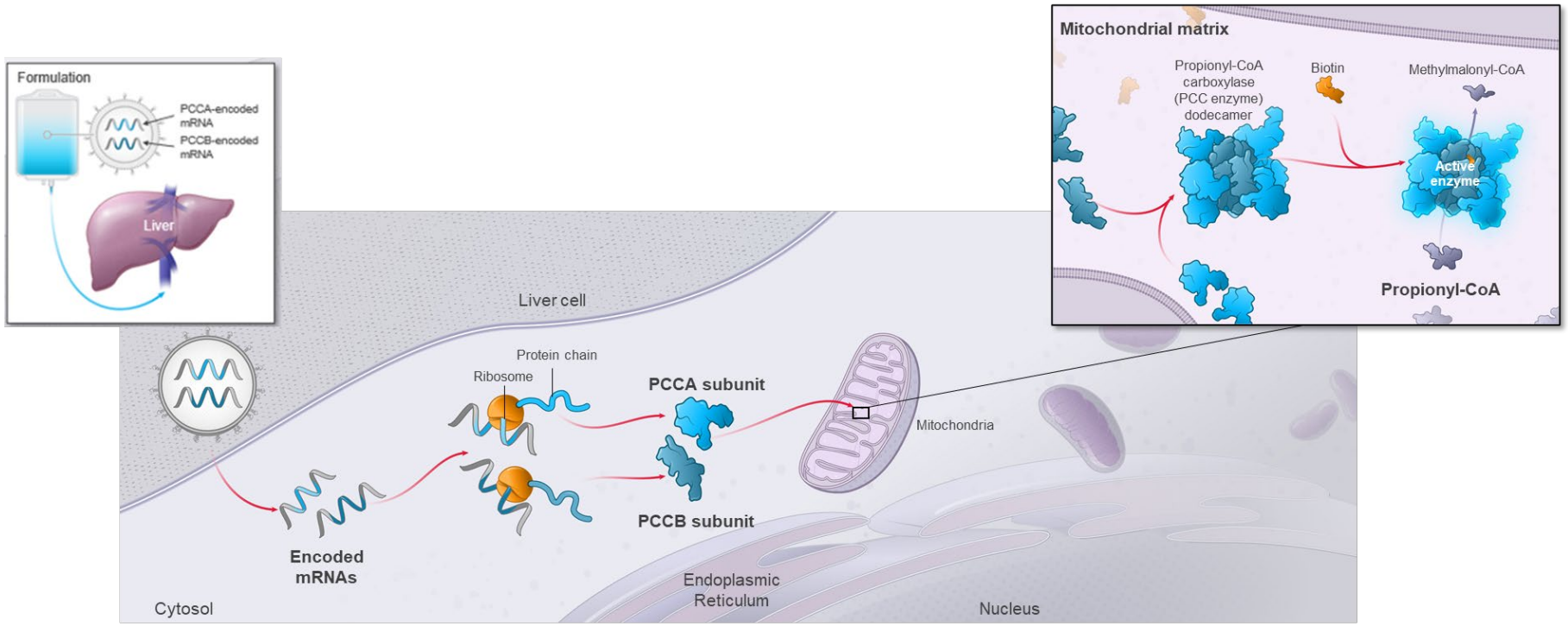


Figure adapted from Baek R, et al[3]

1. Koeberl D, et al. *Nature*. 2024;630(8017):E13; 2. Jiang L, et al. *Nat Commun*. 2020;11:5339; 3. Baek R, et al. *Nat Commun*. 2024;15(1):3804.

Open-Label, 3-Part, Phase 1/2 and Long-term Extension (EXT) Trials Ongoing to Evaluate mRNA-3927 in Participants with PA

PARAMOUNT: a global, phase 1/2, open-label study of mRNA-3927 (NCT04159103; mRNA-3927-P101)

Phase 1/2, open-label, extension study of mRNA-3927 (NCT05130437; mRNA-3927-P101-EXT)

Primary Endpoints

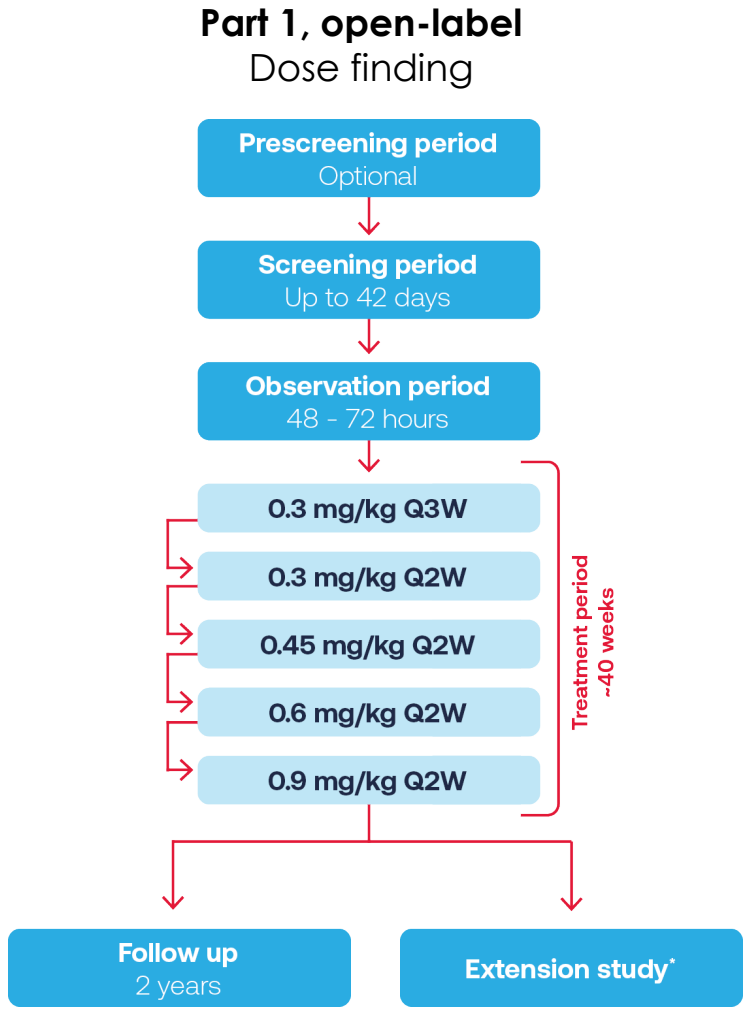
Safety and tolerability

Key Exploratory Endpoints

Change in frequency of MDEs

Dosing (N=≤43; 5 cohorts)

- Weight-based IV dosing
- Q2W or Q3W for ≤10 doses of mRNA-3927
- 14-day dose-limiting window after dose 1 for each participant



Eligibility Criteria for Enrollment in Part 1

Key Inclusion Criteria

- Confirmed diagnosis of PA by molecular genetic testing (biallelic *PCCA* and/or *PCCB* variants)
- Part 1: ≥1 year of age at the time of consent/assent

Key Exclusion Criteria

- Laboratory abnormalities achieving exclusionary thresholds
- eGFR <30 mL/min/1.73 m^2 or chronic dialysis
- QTc >480 msec using Bazett's correction
- Grade 3 or 4 heart failure
- History of or planned organ transplant
- Major surgical procedure within ≤30 days of screening

eGFR, estimated glomerular filtration rate; QTc, corrected QT interval.

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Participant Demographics and Baseline Characteristics

- By database cutoff (June 30, 2025), 20 participants were enrolled in Part 1; 18 completed treatment and 2 discontinued
- Of the 17 participants who entered the extension study, 10 were continuing treatment, 2 entered follow-up, and 5 discontinued

	0.3 mg/kg Q3W (n=4)	0.3 mg/kg Q2W (n=3)	0.45 mg/kg Q2W (n=3)	0.6 mg/kg Q2W (n=6)	0.9 mg/kg Q2W (n=4)	Total (N=20)
Age at time of informed consent, y						
Mean (SD)	15.7 (10.4)	4.0 (3.7)	6.9 (7.4)	11.6 (9.1)	14.2 (9.1)	11.1 (8.7)
Min, max	5.2, 26.8	1.5, 8.3	1.6, 15.3	1.3, 21.4	1.4, 22.5	1.3, 26.8
Age group at time of informed consent, n (%)						
1 to <2 y	0	1 (33.3)	1 (33.3)	2 (33.3)	1 (25.0)	5 (25.0)
2 to <12 y	2 (50.0)	2 (66.7)	1 (33.3)	1 (16.7)	0	6 (30.0)
12 to <18 y	0	0	1 (33.3)	1 (16.7)	2 (50.0)	4 (20.0)
≥18 y	2 (50.0)	0	0	2 (33.3)	1 (25.0)	5 (25.0)
Sex, n (%)						
Male	2 (50.0)	0	2 (66.7)	5 (83.3)	3 (75.0)	12 (60.0)
Female	2 (50.0)	3 (100.0)	1 (33.3)	1 (16.7)	1 (25.0)	8 (40.0)
Age at time of disease onset, mo						
n	4	3	3	6	4	20
Mean (SD)	0.3 (0.5)	0.0 (0.0)[a]	0.3 (0.6)	0.5 (1.2)	4.8 (9.5)	1.2 (4.3)

Data cutoff: 30 June 2025

SD, standard deviation.
[a]Age ranged from birth to <1 month of age.

mRNA-3927 Was Well Tolerated and Had a Manageable Safety Profile[a]

	0.3 mg/kg Q3W (n=4)	0.3 mg/kg Q2W (n=5)	0.45 mg/kg Q2W (n=3)	0.6 mg/kg Q2W (n=15)	0.9 mg/kg Q2W (n=5)	Total (N=20)[b]
Total no. of doses administered	86	140	91	506	176	999
Number of doses with IRR, n (%)	14 (16.3)	0	0	20 (4.0)	11 (6.3)	45 (4.5)
Total patient-years[c]	5.38	5.81	3.82	21.23	6.92	43.16
Total no. of TEAEs[d]	143	139	57	380	94	813
Participants with TEAEs, n (%)	3 (75.0)	5 (100.0)	3 (100.0)	15 (100.0)	5 (100.0)	19 (95.0)
DLTs[e]	0	0	0	0	0	0
Serious TEAEs	2 (50.0)	3 (60.0)	1 (33.3)	12 (80.0)	4 (80.0)	15 (75.0)
Grade 3 or 4 TEAEs	2 (50.0)	3 (60.0)	2 (66.7)	11 (73.3)	4 (80.0)	14 (70.0)
Leading to discontinuation	0	0	0	2 (13.3)	0	2 (10.0)
Total no. of treatment-related TEAEs	42	2	1	53	28	126
Participants with treatment-related TEAEs, n (%)[f]	3 (75.0)	1 (20.0)	1 (33.3)	7 (46.7)	3 (60.0)	14 (70.0)
Serious treatment-related TEAEs	0	0	0	3 (20.0)	2 (40.0)	5 (25.0)
Grade 3 treatment-related TEAEs[f]	0	0	0	2 (13.3)	2 (40.0)	4 (20.0)
Participants with IRRs,[g] n (%)[h]	3 (75.0)	0	0	6 (40.0)	3 (60.0)	11 (55.0)
Participants with hypersensitivity reactions, n (%)[i]	1 (25.0)	0	0	2 (13.3)	1 (20.0)	4 (20.0)

Data cutoff: 30 June 2025

AE, adverse event; DLT, dose-limiting toxicity; IRR, infusion-related reaction; TEAE, treatment-emergent AE.
Participants who switched dose levels during treatment are depicted by the current dose level when an AE occurred.
[a]Part 1 participant data from the P101 primary study and the extension study. [b]N is the total number of participants who received ≥1 dose at each dose level. [c]Length of exposure to mRNA-3927 treatment in days divided by 365.25. [d]Any event not present before exposure to mRNA-3927 or already present that worsened in intensity or increased in frequency after exposure to mRNA-3927. [e]Defined as grade ≥3 treatment-related TEAEs observed ≤14 days of the first mRNA-3927 dose. [f]No participants in any cohort had grade 4 treatment-related TEAEs. [g]Reactions related to the infusion of mRNA-3927 observed during or ≤24 hours after the initiation of infusion. [h]All IRRs were grade 3 or lower and resolved with conservative management, including stopping the infusion and administering acetaminophen. [i]All hypersensitivity reaction events were grade 1 or 2.

Most Frequently Occurring TEAEs[a,b]

n (%)/# events	0.3 mg/kg Q3W (n=4)	0.3 mg/kg Q2W (n=5)	0.45 mg/kg Q2W (n=3)	0.6 mg/kg Q2W (n=15)	0.9 mg/kg Q2W (n=5)	Total (N=20)[c]
Pyrexia	3 (75.0)/10	4 (80.0)/8	1 (33.3)/1	8 (53.3)/15	3 (60.0)/4	15 (75.0)/38
Vomiting	1 (25.0)/25	4 (80.0)/25	1 (33.3)/7	11 (73.3)/59	3 (60.0)/8	13 (65.0)/124
Diarrhea	2 (50.0)/4	4 (80.0)/4	1 (33.3)/2	5 (33.3)/9	4 (80.0)/4	11 (55.0)/23
Cough	1 (25.0)/2	2 (40.0)/4	1 (33.3)/1	4 (26.7)/10	3 (60.0)/8	9 (45.0)/25
Rhinorrhea	0	3 (60.0)/5	1 (33.3)/1	6 (40.0)/7	1 (20.0)/2	9 (45.0)/15
Upper respiratory tract infection	2 (50.0)/3	3 (60.0)/5	1 (33.3)/1	6 (40.0)/13	0	9 (45.0)/22
Metabolic disorder	2 (50.0)/7	1 (20.0)/5	0	7 (46.7)/17	2 (40.0)/6	8 (40.0)/35
Rash	1 (25.0)/2	0	0	4 (26.7)/4	2 (40.0)/3	7 (35.0)/9
Chills	2 (50.0)/5	0	0	5 (33.3)/9	1 (20.0)/3	6 (30.0)/17
COVID-19	1 (25.0)/1	3 (60.0)/4	0	1 (6.7)/1	1 (20.0)/1	6 (30.0)/7
Diaper dermatitis	1 (25.0)/1	2 (40.0)/6	0	4 (26.7)/8	0	6 (30.0)/15
Gastroenteritis	1 (25.0)/1	0	0	5 (33.3)/5	0	6 (30.0)/6
Lethargy	0	2 (40.0)/2	0	4 (26.7)/5	0	6 (30.0)/7
Nasopharyngitis	0	1 (20.0)/1	1 (33.3)/3	3 (20.0)/4	2 (40.0)/2	6 (30.0)/10
Tachycardia	1 (25.0)/1	0	0	3 (20.0)/4	2 (40.0)/4	6 (30.0)/9

Data cutoff: 30 June 2025

Participants who switched dose levels during treatment are depicted by the current dose level when an AE occurred.
[a]Part 1 participant data from the P101 primary study and the extension study. [b]TEAEs occurring in ≥30% of the total participant population. [c]N is the total number of participants who received ≥1 dose at each dose level.

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PA: Overall Phase 1/ 2 clinical experience

As of June 30, 2025, 22 participants have been dosed in part 1

- 13 participants have >1 year of dosing
- 43.6 cumulative patient-years of experience on study drug
- Longest duration of treatment is 3.1 years and median duration 1.45 years
- Over 999 intravenous doses administered; No dose limiting toxicities (DLT's) occurred
- Study is ongoing; dose was defined at 0.6mg/kg with an option to increase or decrease per protocol
- The majority of participants have elected to continue on Open Label Extension (OLE) Study

1 Patient had a history of recurrent pancreatitis prior to enrollment

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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

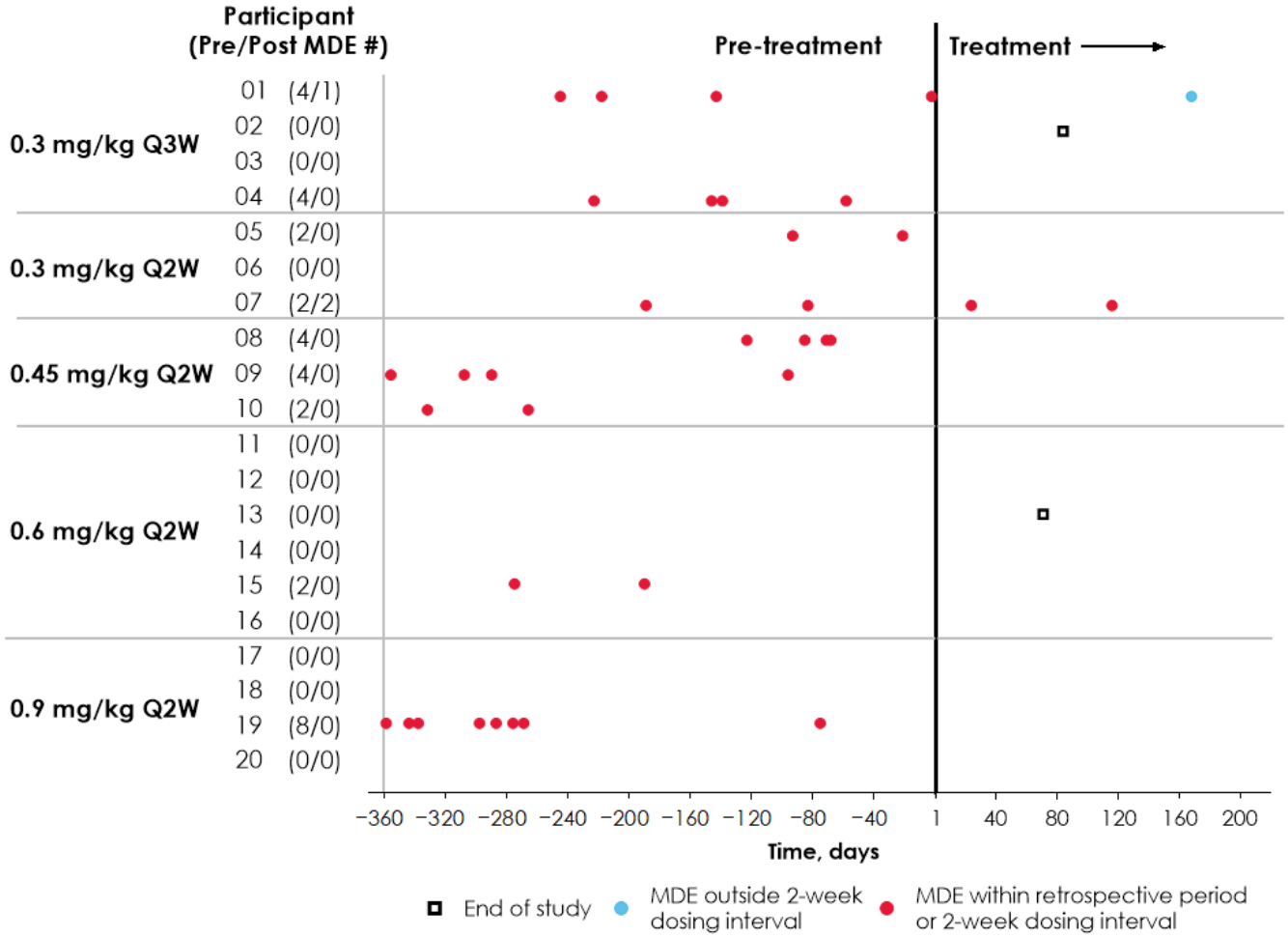
Identification and measurement of MDEs

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

Treatment with 10 Doses of mRNA-3927 Resulted in a Sustained Reduction in MDEs[a] (Final P101/Part 1 Data)



[a]Investigator-reported MDEs were defined as either metabolic acidosis with elevated anion gap or acute hyperammonemia, both of which require medical intervention to establish anabolism.

Treatment with mRNA-3927 Resulted in a Significant Reduction in MDE Risk

- **Treatment with mRNA-3927 showed a 76% relative risk reduction in MDEs**
- **Participants receiving doses ≥0.6 mg/kg Q2W had an 83% relative risk reduction in MDEs, suggesting that mRNA-3927 has a dose-dependent treatment effect**

MDE[a] Rates Pre-treatment and During Treatment[b] in Participants With ≥1 Pre-Treatment MDE

	<0.6 mg/kg	≥0.6 mg/kg	Overall
Annualized MDE rate,[c] LS mean (SE)			
Pretreatment	2.97 (0.383)	4.61 (3.916)	3.34 (0.633)
Treatment	0.82 (0.378)	0.77 (0.181)	0.81 (0.307)
Relative risk vs pretreatment period, 95% CI	0.28 (0.083–0.917)	0.17 (0.038–0.752)	0.24 (0.087–0.668)
Unadjusted *P* value	0.0390	0.0260	0.0122

Data cutoff: 30 June 2025

CI, confidence interval; LS, least squares; SE, standard error.
[a]Investigator-reported MDEs were defined as either metabolic acidosis with elevated anion gap or acute hyperammonemia, both of which require medical intervention to establish anabolism.
[b]Part 1 participant data from the P101 primary study and the extension study. [c]Defined as a participant's total number of MDEs divided by the length of the defined period.

PA summary

Safety

- mRNA-3927 was well tolerated at the doses administered, with no DLTs
- All IRRs were grade 3 or lower and resolved with conservative management

Efficacy

- mRNA-3927 treatment continued to demonstrate sustained reduction in MDE rates, with clinical benefit highest for participants receiving doses ≥0.6 mg/kg Q2W
- Findings from this analysis support further clinical development of mRNA-3927 at a dose of 0.6 mg/kg for the treatment of patients with PA

Next steps

- Registrational study (part 2) ongoing; Target enrollment reached
- Infant dose-finding study (part 3) is ongoing

MMA

Methylmalonic Acidemia (MMA)

MMA

- Onset typically occurring early in life[1]
- Associated with acute metabolic decompensation events (MDEs) and chronic toxicity[1,2]

Only symptomatic treatment available[1]

- Protein-restricted diet
- Levocarnitine supplementation
- Liver and/or kidney transplantation

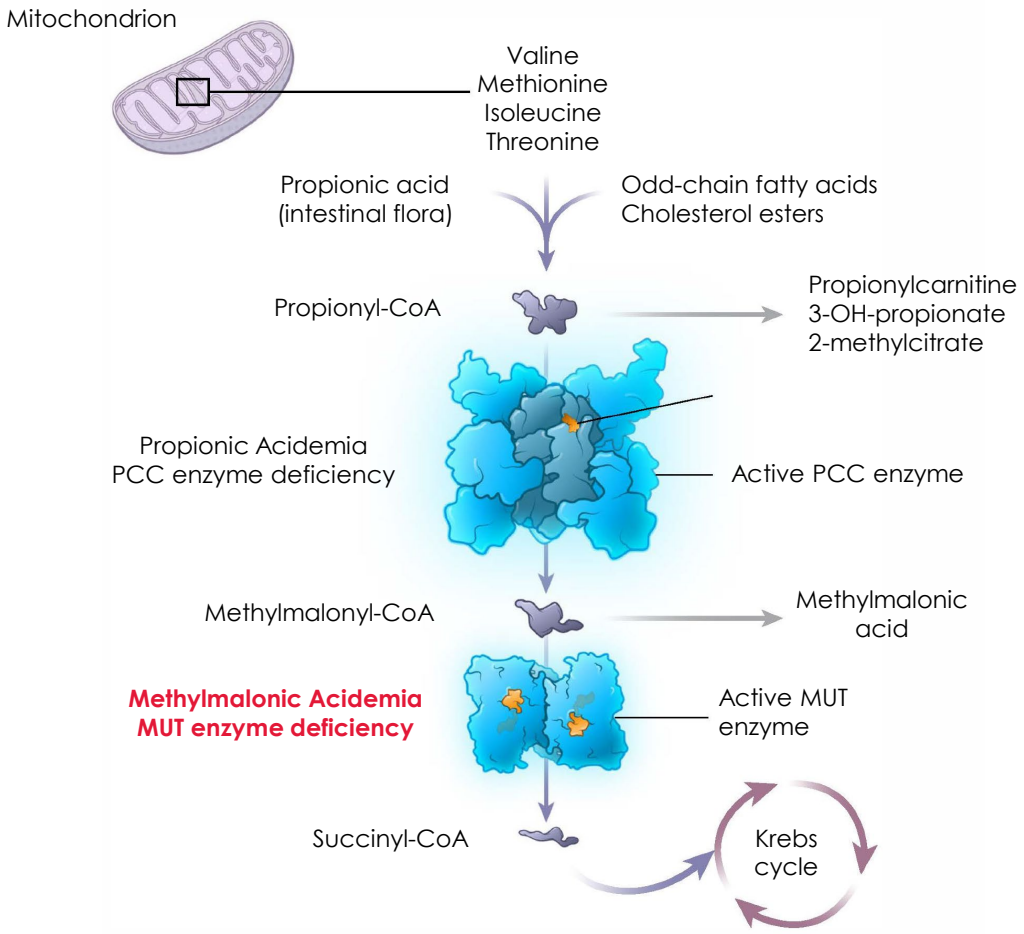
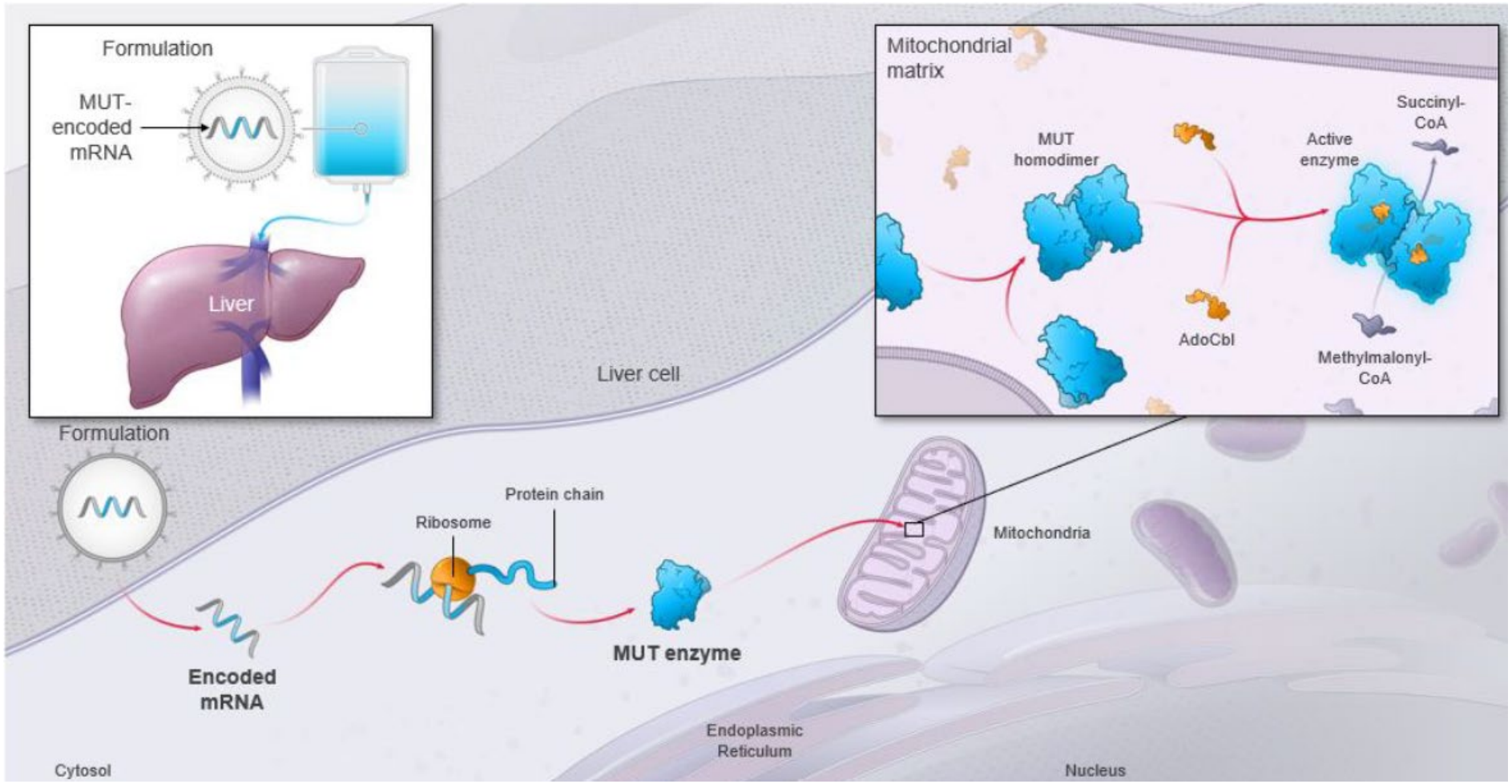


Figure adapted from Koeberl D, et al[3]

1. Almási T, et al. *Orphanet J Rare Dis*. 2019;14(1):84; 2. Forny P, et al. *J Inherit Metab Dis*. 2021;44(3):566–592; 3. Koeberl D, et al. *Nature*. 2024 Jun;630(8017):E13.

Addressing the Cause of MMA: mRNA-3705 Encoding the MUT Enzyme[1]



AdoCbl, cofactor adenosylcobalamin.
Figure adapted from Baek R, et al[1]

1. Baek R, et al. *Nat Commun*. 2024;15(1):3804.

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Phase 1/2 Study Evaluating Safety and Pharmacology of mRNA-3705 in Participants With MUT-Deficient MMA

A first-in-human, global, phase 1/2 study of mRNA-3705 (Parts 1–3; NCT04899310; mRNA-3705-P101)

Phase 1/2, open-label, extension study of mRNA-3705 (NCT05295433; mRNA-3705-P101-EXT)

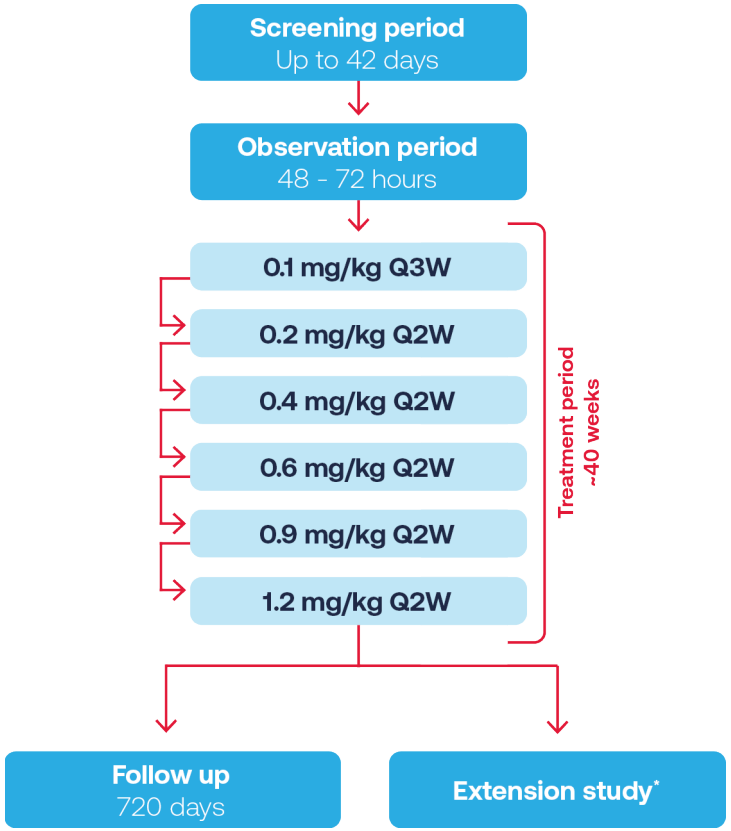
Objective

To assess safety, tolerability, pharmacokinetics, and pharmacodynamics of mRNA-3705

Dosing (N≤36; 6 cohorts)

- Weight based IV dosing
- Q2W or Q3W for ≤10 doses of mRNA-3705
- 14-day dose-limiting window after dose 1 for each participant

Part 1, open-label
Dose optimization



Q2W, every 2 weeks; Q3W, every 3 weeks.
[a]Participants enrolled the extension study receive the same dose of mRNA-3705 as received in Part 1.

Eligibility Criteria for Enrollment in Part 1

Key Inclusion Criteria

- Diagnosis of isolated MMA due to MUT deficiency confirmed by molecular genetic testing
- ≥1 year of age
- Body weight of ≥11.0 kg
- Blood vitamin B12 level ≥lower limit of normal

Key Exclusion Criteria

- Diagnosis of isolated MMA cblA, cblB, or cblD enzymatic subtypes or methylmalonyl-CoA epimerase deficiency or combined MMA with homocystinuria
- Laboratory abnormalities achieving exclusionary thresholds
- eGFR <30 mL/min/1.73 m2 or chronic dialysis
- QTc >480 msec using Bazett's correction
- Previously received gene therapy for the treatment of MMA
- History of or planned organ transplant

eGFR, estimated glomerular filtration rate; QTc, corrected QT interval.

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Participant Demographics and Baseline Characteristics

- By database cutoff (July 31, 2025), 18 participants were enrolled in 6 countries worldwide

	0.1 mg/kg Q3W (n=3)	0.2 mg/kg Q2W (n=3)	0.4 mg/kg Q2W (n=3)	0.6 mg/kg Q2W (n=3)	0.9 mg/kg Q2W (n=3)	1.2 mg/kg Q2W (n=3)	Total (N=18)
Age							
Age at enrollment, median (range), y	12.2 (4.5–14.4)	2.7 (2.5–39.5)	7.8 (5.8–16.0)	18.8 (4.3–32.3)	6.1 (3.1–8.5)	5.7 (2.8–10.3)	7.0 (2.5–39.5)
Age at disease onset, median (range), mo	0 (0–0)	0 (0–1)	3.0 (0–10.0)	8.0 (0–117.0)	0 (0–52.0)	0 (0–8.0)	0 (0–117.0)
Sex							
Female, n (%)	2 (67)	2 (67)	2 (67)	1(33)	0 (0)	1(33)	8 (44)
Weight							
Weight, median (range), kg	25.2 (19.5–40.7)	13.2 (12.2–57.1)	22.6 (16.2–53.4)	60.1 (16.3–66.0)	22.5 (17.0–23.2)	25.2 (12.0–47.7)	22.9 (12.0–66.0)
Phenotype							
mut^0, n (%)	3 (100)	3 (100)	3 (100)	2 (67)	2 (67)	2 (67)	15 (83)
mut$^-$, n (%)	0 (0)	0 (0)	0 (0)	1 (33)	1 (33)	1 (33)	3 (17)

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The Safety Profile of mRNA-3705 was Manageable[a]

- Median treatment duration was 99.6 weeks (range, 48.3–118.4 weeks)
- All 18 participants continued mRNA-3705 dosing in the extension study; 3 subsequently discontinued due to reasons not related to safety

	0.1 mg/kg Q3W (n=3)	0.2 mg/kg Q2W (n=3)	0.4 mg/kg Q2W (n=7)[b]	0.6 mg/kg Q2W (n=3)	0.9 mg/kg Q2W (n=10)[b]	1.2 mg/kg Q2W (n=8)[b]	Total (N=18)[c]
Total no. of doses administered	90	105	249	141	163	117	865
Total patient-years[d]	5.64	4.22	9.86	5.52	6.40	4.53	36.17
Total no. of TEAEs	48	101	83	91	89	97	509
Participants with TEAEs, n (%)[e]	3 (100)	3 (100)	7 (100)	3 (100)	10 (100)	8 (100)	18 (100)
DLTs[e]	0	0	0	0	0	0	0
Serious TEAEs	2 (66.7)	3 (100)	2 (28.6)	2 (66.7)	1 (10.0)	4 (50.0)	11 (61.1)
Grade 3 TEAEs	3 (100)	3 (100)	2 (28.6)	2 (66.7)	0 (0)	3 (37.5)	10 (55.6)
Total no. of TRAEs	2	4	19	14	45	28	112
Participants with TRAEs, n (%)[e]	2 (66.7)	2 (66.7)	4 (57.1)	3 (100)	6 (60.0)	5 (62.5)	14 (77.8)
Serious TRAEs	0 (0)	1 (33.3)	1 (14.3)	0 (0)	0 (0)	0 (0)	2 (11.1)
Grade 3 TRAEs	1 (33.3)	0 (0)	1 (14.3)	0 (0)	0 (0)	0 (0)	1 (5.6)
Participants with suspected IRRs, n (%)	2 (66.7)	2 (66.7)	4 (57.1)	3 (100)	6 (60.0)	5 (62.5)	14 (77.8)

AE, adverse event; DLT, dose-limiting toxicity; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event.
[a]Includes participants from Part 1 and the extension study. [b]n is inclusive of participants with dose escalation in the extension study, including 4 participants who received 0.4 mg/kg Q2W, 7 who received 0.9 mg/kg Q2W, and 5 who received 1.2 mg/kg Q2W in the extension study. [c]N is the total number of participants in the study. [d]Length of exposure to mRNA-3705 in days divided by 365.25. [e]There were no participants in any cohort with DLTs, TEAEs or TRAEs leading to treatment discontinuation, or grade 4 or 5 TEAEs or TRAEs.

MMA: Overall Phase 1/ 2 clinical experience

As of July 31, 2025, 18 participants have been dosed

- 36.2 cumulative patient-years of experience on study drug
- 865 doses administered; no dose limiting toxicities have occurred
- Longest duration of treatment is 2.3 years and median duration 1.92 years
- mRNA-3705 was well tolerated in participants with MUT-deficient MMA in this phase 1/2 study
- All participants continued mRNA-3705 dosing in the extension study

1 Patient had a history of recurrent pancreatitis prior to enrollment

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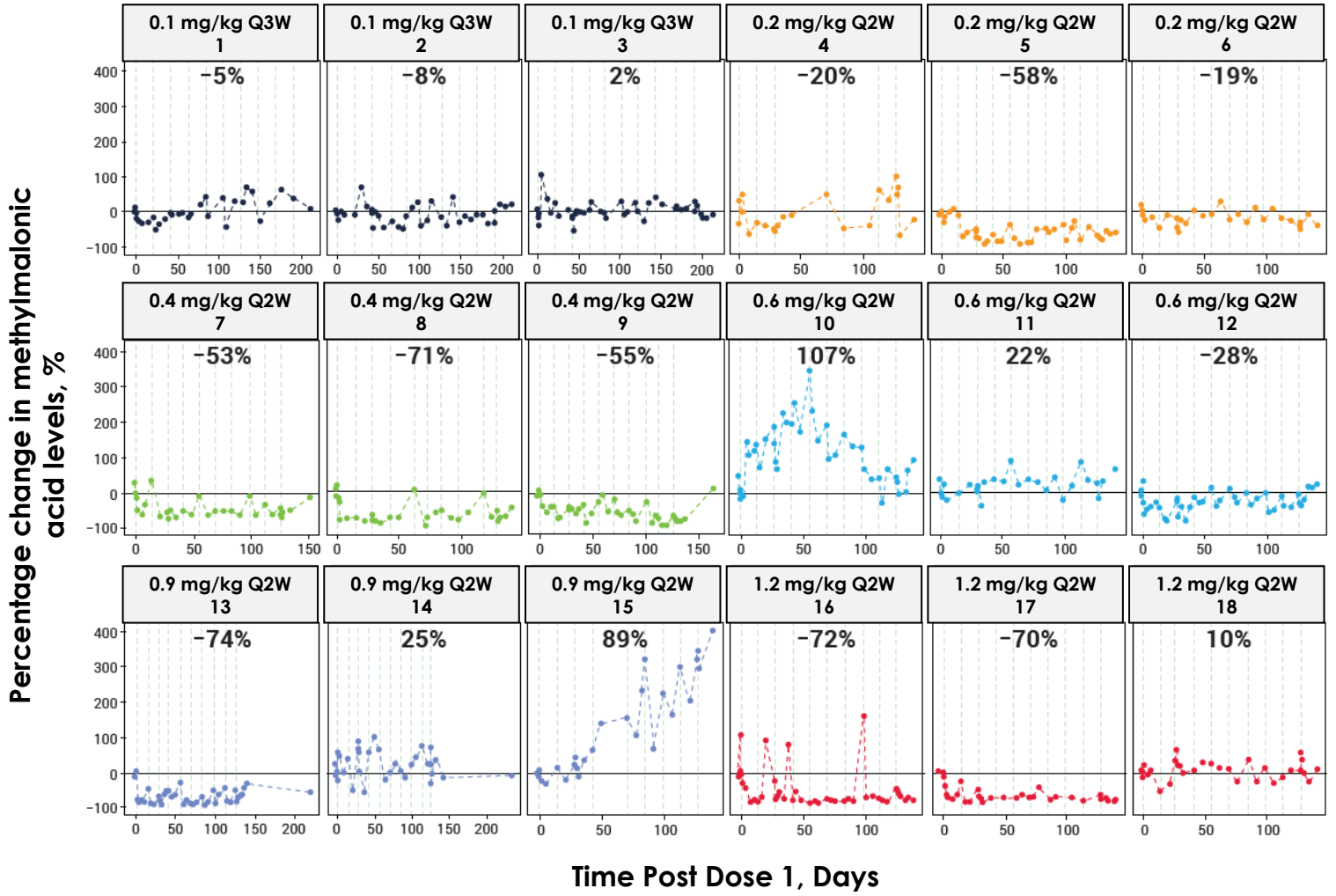
mRNA-3705 Decreases Methylmalonic Acid Levels[a]

Reductions in plasma methylmalonic acid levels of ≥50% from baseline were observed in half of participants treated with mRNA-3705 ≥0.4 mg/kg Q2W

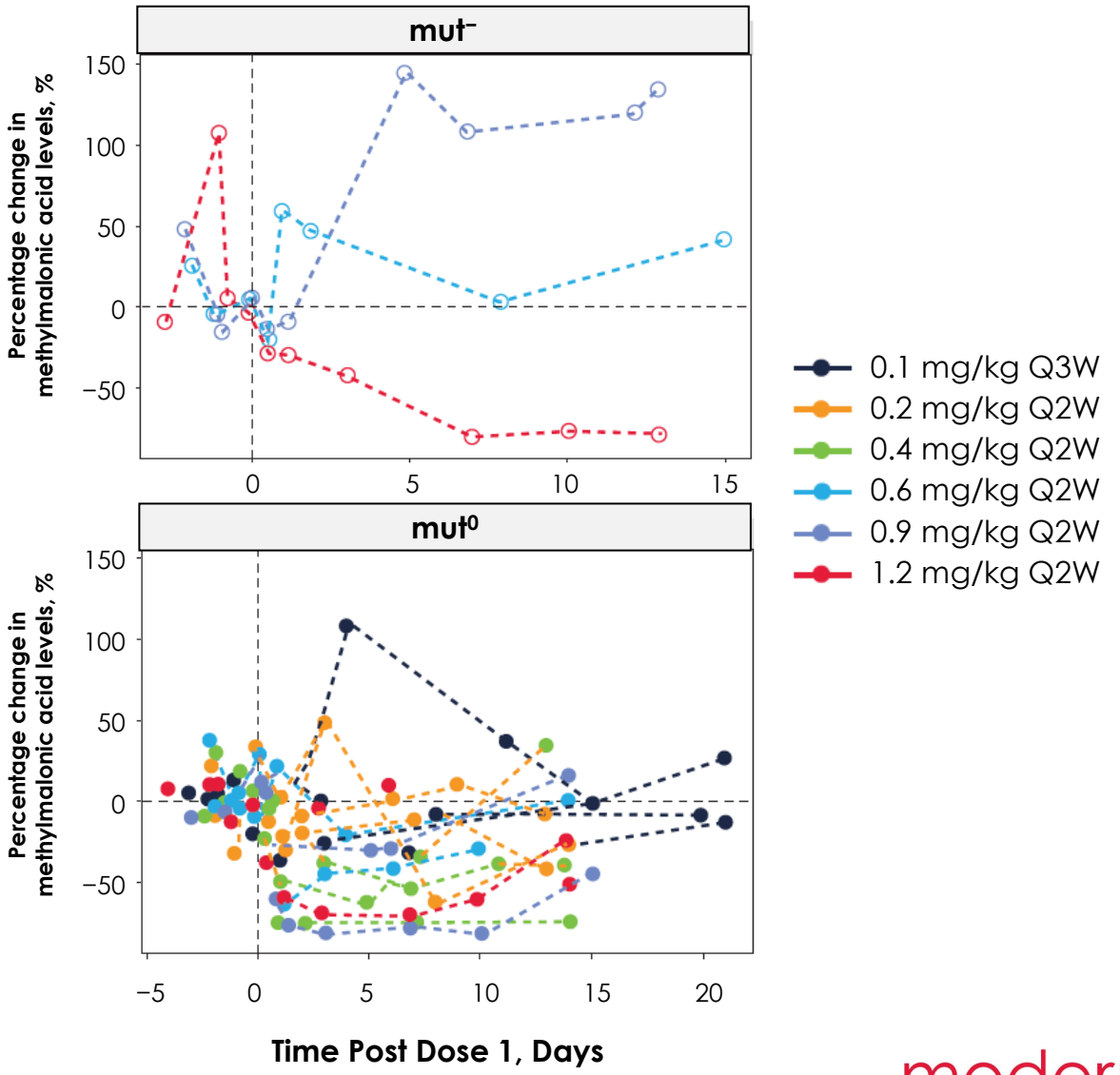


Median percentage change from baseline for each participant is shown in black text, and the vertical dashed lines represent doses administered.
[a]Includes participants from Part 1.

mRNA-3705 Decreases MMA-Related Biomarkers[a]

- Dose-dependent reductions in plasma methylmalonic acid levels from baseline observed after first dose of mRNA-3705, particularly in participants with mut^0 phenotype

- mRNA-3705 reduced other MMA-related biomarkers (2-methylcitrate, 3-hydroxypropionic acid, and propionyl glycine), indicating improved propionate catabolism



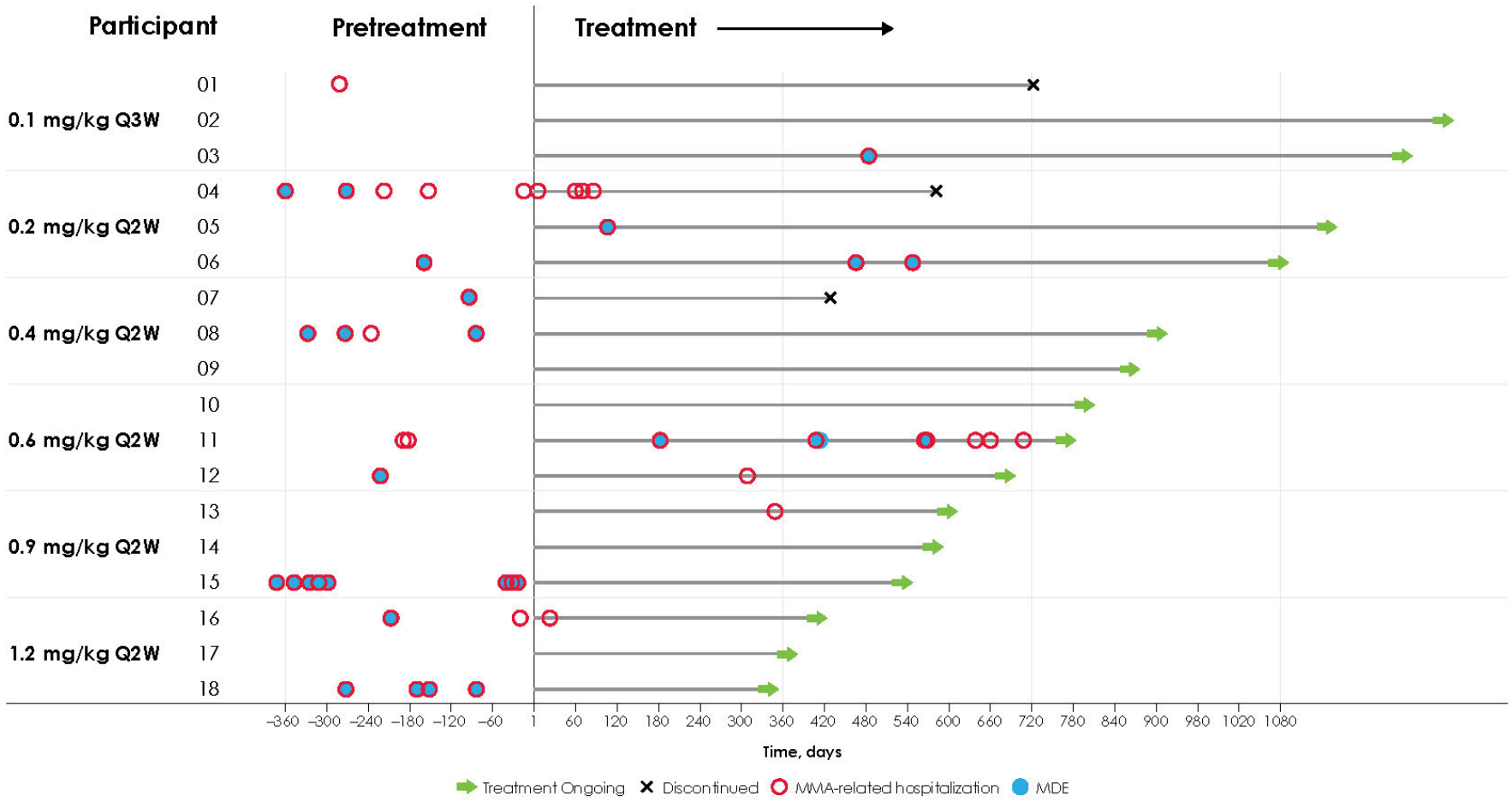
[a]Includes participants from Part 1.

MMA-Related Hospitalizations and MDEs[a]

Treatment with **mRNA-3705 ≥0.4 mg/kg Q2W** showed

- **75% relative risk reduction in MMA-related hospitalizations** vs pre-treatment (relative risk, 0.25; 95% CI, 0.054–1.176)
- **91% relative risk reduction in MDEs** (relative risk, 0.09; 95% CI, 0.007–1.213)

MMA-related hospitalizations and MDEs[b]



[a]Includes participants from Part 1 and the extension study. [b]Investigator reported.

MMA-Related Hospitalizations and MDEs[a]

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- **75% relative risk reduction in MMA-related hospitalizations** vs pre-treatment (relative risk, 0.25; 95% CI, 0.054–1.176)
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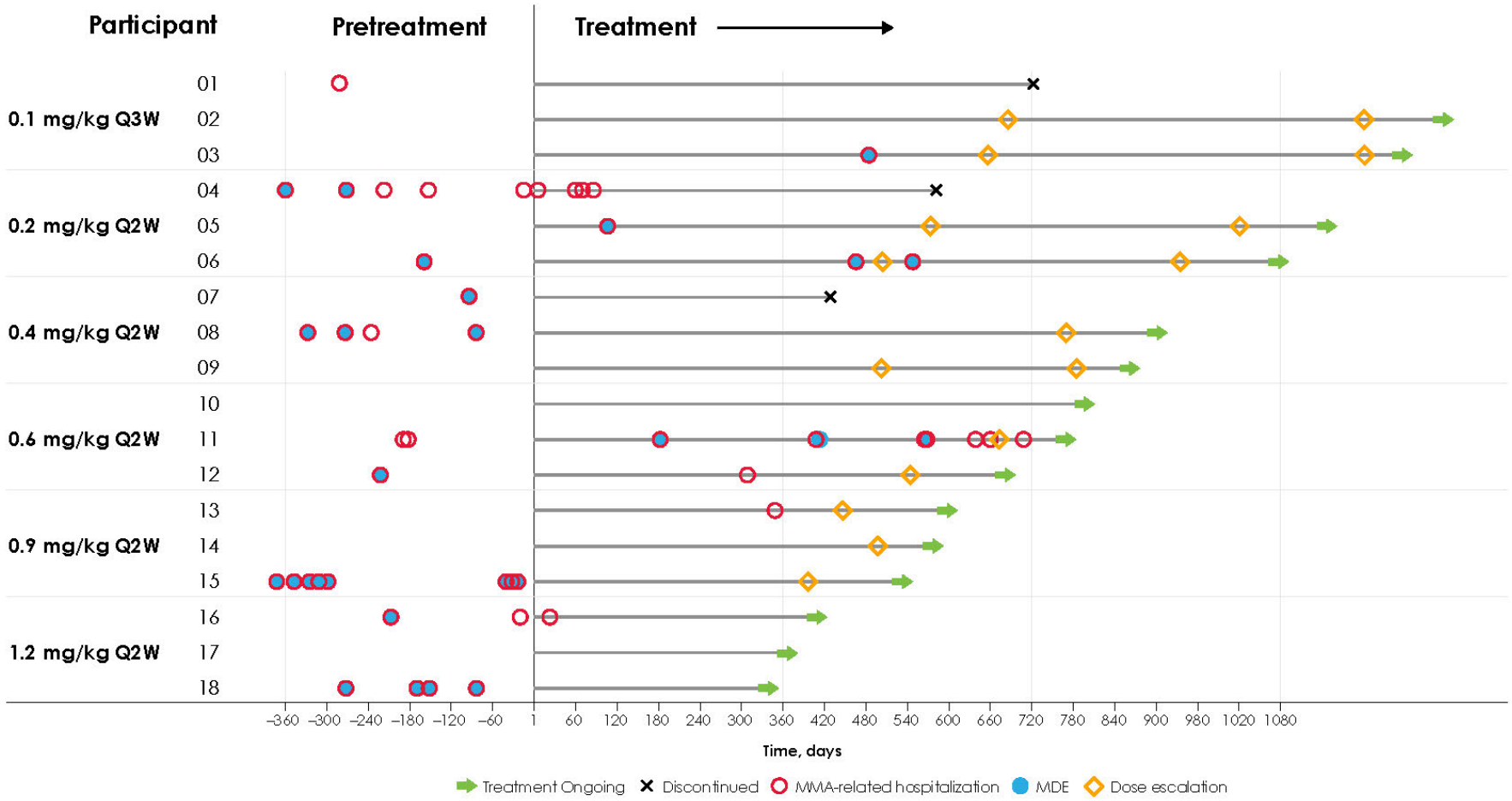
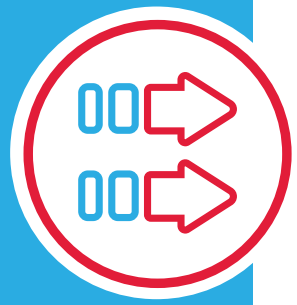
MMA-related hospitalizations and MDEs[b]



[a]Includes participants from Part 1 and the extension study. [b]Investigator reported.

MMA summary

Safety	• mRNA-3705 was well tolerated in participants with MUT-deficient MMA in this phase 1/2 study • No dose-limiting toxicities and no treatment-emergent adverse events leading to treatment discontinuation
Biomarker/ Efficacy	• Reductions in disease-related biomarkers with mRNA-3705 indicated improved propionate catabolism • Reductions in clinical events (MMA-related hospitalizations and metabolic decompensation events) with mRNA-3705 at doses ≥0.4 mg/kg Q2W
Next steps	• Registrational study expected to start in 2026



Looking forward

Stéphane Bancel
Chief Executive Officer

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Near-term strategy

Build a **large seasonal vaccine franchise** for high-risk populations

Marketed products

- spikevax™ COVID-19 Vaccine, mRNA
- mNEXSPIKE® COVID-19 Vaccine, mRNA
- mRESVIA® (Respiratory Syncytial Virus Vaccine)

Expected launches

- Flu
- Flu + COVID
- Norovirus

Invest cash generated into **oncology and rare disease therapeutics**

Oncology

Intismeran

- Adjuvant melanoma
- Adjuvant NSCLC
- Adjuvant NSCLC non-pCR post neoadjuvant
- Adjuvant renal cell carcinoma
- Adjuvant MIBC
- Adjuvant NMIBC
- Metastatic melanoma
- Metastatic NSCLC

- mRNA-4359
- mRNA-4106
- mRNA-4203
- mRNA-2808

Rare disease

- PA
- MMA

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Key takeaways

Poised to deliver up to 10% revenue growth in 2026
with multiple growth opportunities in 2027 and beyond

Driving gross margin expansion over coming years
(10%+ over 3 years)

Evolving R&D investments to diversify further
into oncology

Reducing 2027 projected cash costs
to $3.5-3.9 billion and targeting 2028 cash breakeven

Confident in strong financial framework
with enhanced liquidity

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Our mission

Deliver the greatest possible impact to **people** through mRNA **medicines**

moderna®

Q&A