Safety and immunogenicity of mRNA-1345 RSV revaccination at least 12 months following primary vaccination with a licensed protein subunit RSV vaccine

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Disclosures and Acknowledgments

- Mihir Desai, Shraddha Mehta, Aghogho Okparavero, Zhantao Lin, and Frances Priddy are employees of Moderna, Inc., and hold stock/stock options in the company. Archana Kapoor was an employee of Moderna, Inc., and held stock/stock options in the company. All relevant financial disclosures have been mitigated. All other authors have no conflicts of interest to declare.
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The Case for Revaccination Against Respiratory Syncytial Virus

- Respiratory syncytial virus (RSV) is a common respiratory pathogen that causes significant global disease burden each year, including among older adults[1-3]
- RSV vaccines are currently licensed as a single dose in adults; however, like natural infection, protection provided by vaccination is not expected to be lifelong
- Vaccine effectiveness declines over time, with reduced protection observed by the second RSV season across clinical trials and real-world studies[4,5]
  - Real-world effectiveness studies (primarily US-based) show declining protection following a single RSV vaccine dose, with effectiveness against RSV-related hospitalization of 67% to 83% within 6 months, declining to 42% after ≥12 months[6]
- Declining effectiveness is more pronounced in immunocompromised individuals[7]

1. Testaert H, et al. *Clin Microbiol Infect*. 2021;27(6):897-903. 2. Savic M, et al. *Influenza Other Respir Viruses*. 2023;17(1):e13031. 3. Shi T, et al. *J Infect Dis*. 2020;222(suppl 7):S577-S583; 4. Kelleher K, et al. *Ther Adv Vaccines Immunother*. 2025;13:25151355241310601. 5. Trusinska D, et al. *Lancet Reg Health Eur*. 2026;64:101623. 6. Link-Gelles R, et al. 221. *Open Forum Infect Dis*. 2026;13(suppl 1):ofaf695.079. 7. Bajema KL, et al. *JAMA Intern Med*. 2026;186(1):78-88.

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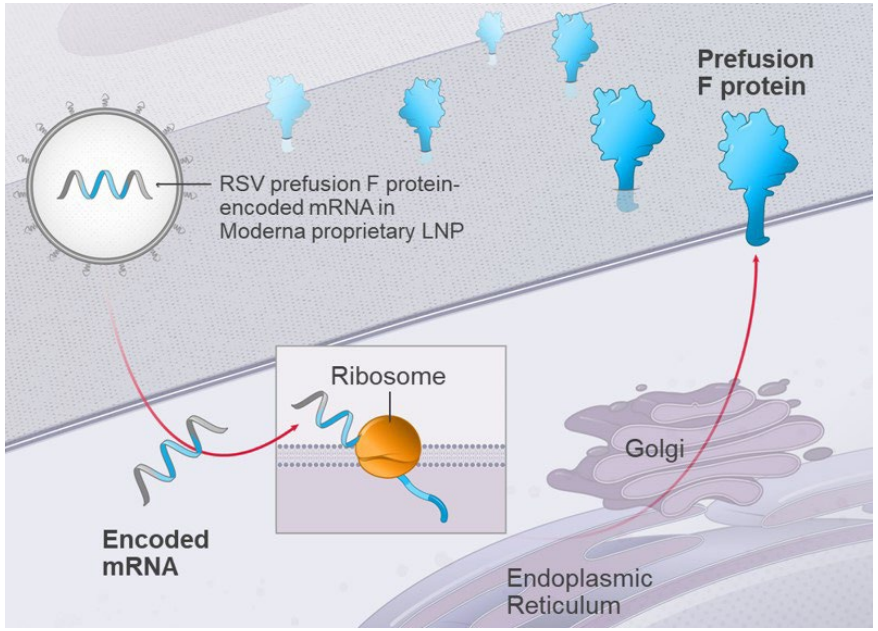
Clinical Background for mRNA-1345

- mRNA-1345 (mRESVIA; Moderna, Inc.) is an mRNA vaccine approved in multiple regions for the prevention of RSV-LRTD in adults aged ≥60 years and in adults aged 18 to 59 years who are at increased risk for RSV-LRTD
- RSV neutralizing antibody responses are correlated with vaccine efficacy, with higher titers associated with greater protection[1]
  - Immunobridging of RSV neutralizing antibody responses to the pivotal Phase 2/3 efficacy study supported approval in adults aged 18 to 59 years at increased risk[2]
- Homologous revaccination with mRNA-1345 at 12 or 24 months has demonstrated noninferior RSV nAb responses in Phase 3 studies[3,4]
- Here, we present interim findings from an ongoing heterologous revaccination study with mRNA-1345



mRNA-1345 (mRESVIA) is an **mRNA-based, LNP-encapsulated RSV vaccine** encoding membrane-anchored **RSV F** glycoprotein in the **prefusion** conformation

LNP, lipid nanoparticle; LRTD, lower respiratory tract disease; nAb, neutralizing antibody; RSV, respiratory syncytial virus.

1. Ma C, et al. *Nat Commun*. 2025;16(1):6118. 2. Mayer EF, et al. *Clin Infect Dis*. 2026;81(6):e708-e716. doi:10.1093/cid/ciaf292. 3. Goswami J, et al. *Clin Infect Dis*. Published online September 23, 2025. doi:10.1093/cid/ciaf515. 4. Desai M, et al. P5040. Presented at the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) Global Congress; 11-15 April 2025; Vienna, Austria.

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Study Design

Phase 3, Open-Label Revaccination Study with mRNA-1345 in Adults Aged ≥60 Years at Least 12 Months Following Primary Vaccination with a Licensed Protein Subunit RSV Vaccine (NCT07117487)

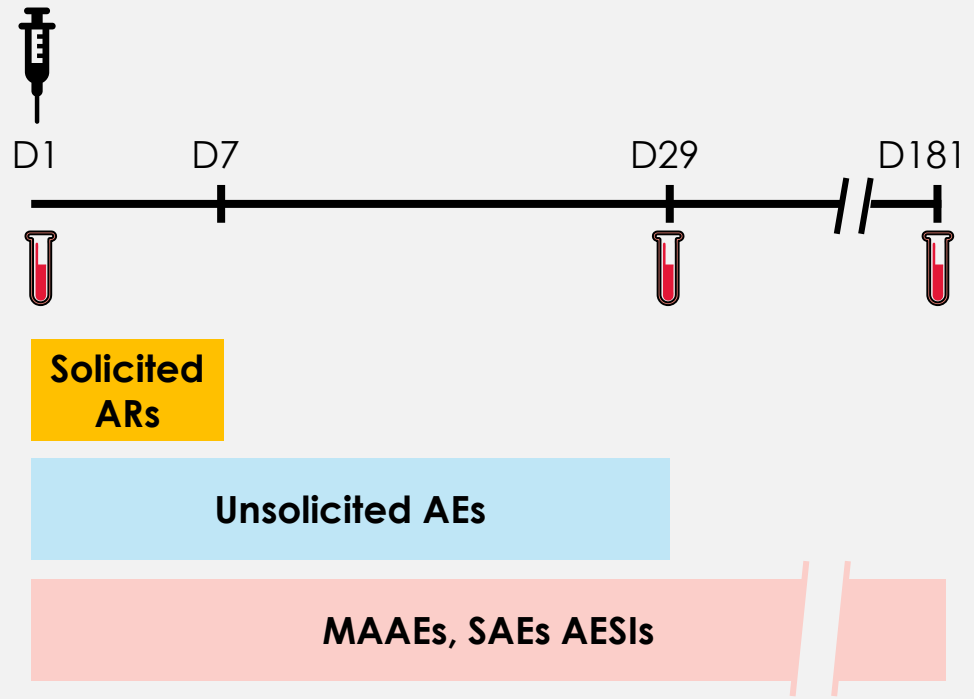
Design
Open-label study

Number of participants
~500 participants ≥60 years of age at least 12 months after primary vaccination with a protein-based RSV vaccine

Vaccination schedule
Revaccination with mRNA-1345

Duration:
6 months
Enrollment initiation: August 2025

Site locations
Multicenter, US only



AE, adverse event; AESI, adverse event of special interest; AR, adverse reaction; D, day; MAAE, medically attended adverse event; RSV, respiratory syncytial virus; SAE, serious adverse event.

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Study Objectives and Endpoints

Safety

Primary Objective

- To evaluate the safety and tolerability of revaccination with mRNA-1345 50 µg administered ≥12 months after a licensed RSV protein subunit vaccine in adults ≥60 years

Primary Endpoints

- Solicited local and systemic ARs through 7 days post-revaccination
- Unsolicited AEs through 28 days post-revaccination
- MAAEs, AESIs, SAEs, and AEs leading to discontinuation from Day 1 through EOS

Immunogenicity

Primary Objective

- To evaluate the immunogenicity of revaccination with mRNA-1345 50 µg administered ≥12 months after a licensed RSV protein subunit vaccine in adults ≥60 years

Primary Endpoints

- GMTs of RSV-A and RSV-B nAbs at Day 29

AE, adverse event; AESI, adverse event of special interest; AR, adverse reaction; EOS, end of study; GMT, geometric mean titer; MAAE, medically attended adverse event; nAb, neutralizing antibody; RSV, respiratory syncytial virus; SAE, serious adverse event.

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Demographics and Baseline Characteristics

Safety Set

		mRNA-1345 50 µg (N = 506)
Median age, years		70.0
Female, n (%)		**300** (59.3)
Age group, n (%)	**60-74 years**	**397** (78.5)
	≥75 years	**109** (21.5)
Race/ethnicity, n (%)	**White**	**435** (86.0)
	Black or African American	**57** (11.3)
	Asian	**5** (1.0)
	Hispanic/Latino ethnicity	**180** (35.6)
≥1 Comorbidity of interest (associated with high risk of RSV-LRTD)		**275** (54.3)
Brand of primary dose RSV vaccine Received, n (%)	**RSVpreF AS01E (Arexvy, GSK)**	**373** (73.7)
	RSVpreF bivalent (Abrysvo, Pfizer)	**133** (26.3)
Median time on study from injection (days) (Min/Max)		**59.0** (24, 80)
Median time from primary dose To study injection (days) (Min, Max)		**637.0** (365, 743)

LRTD, lower respiratory tract disease; Max, maximum; Min, minimum; preF, prefusion; RSV, respiratory syncytial virus.
Data cutoff: 24 October 2025.
Comorbidity of interest: asthma, chronic kidney disease, chronic liver disease, chronic respiratory disease, cystic fibrosis, diabetes mellitus (type 1 and 2), cardiac conditions, neurological conditions (limited to amyotrophic lateral sclerosis and muscular dystrophy), morbid obesity (body mass index ≥40 kg/m^2), and hemoglobinopathies.

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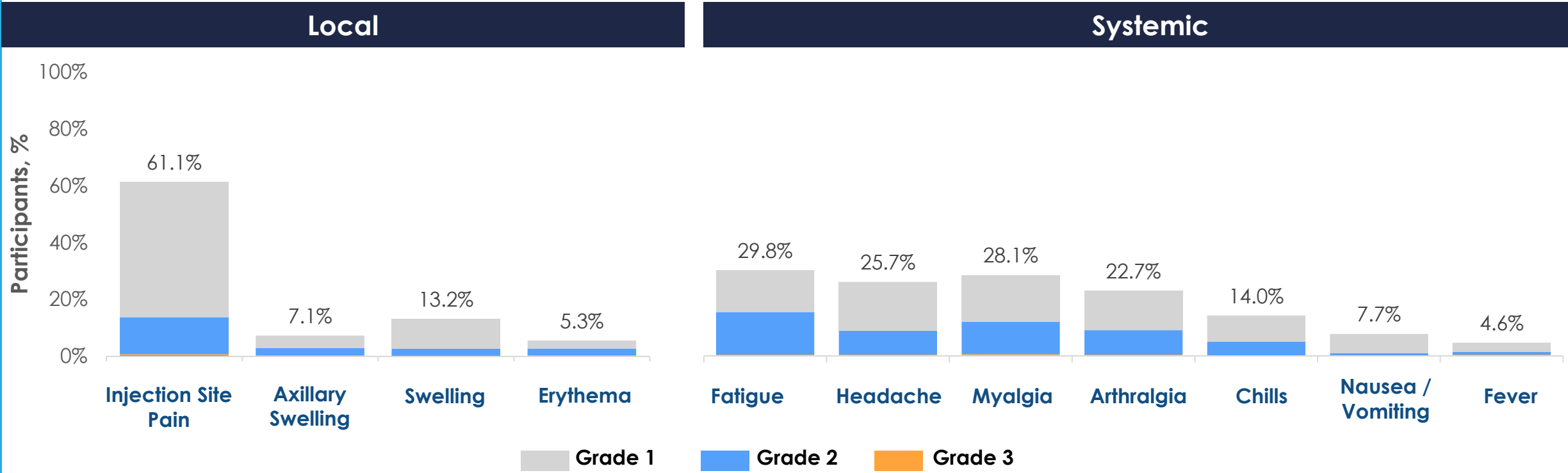
Safety

Solicited Adverse Reactions within 7 Days After mRNA-1345 Injection

Solicited Safety Set



- Solicited adverse reactions were mostly grade 1-2, with no grade 4 solicited adverse reactions reported
- Median onset was Day 2, with a median duration of 2 days
- Injection site pain was the most common local adverse reaction
- Fatigue, myalgia, headache, and arthralgia were the most common systemic adverse reactions
- Reactogenicity following revaccination with mRNA-1345 was generally similar by brand of primary RSV vaccine received

Data cutoff: 24 October 2025.

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Overall Summary of Unsolicited AEs Up to DCO

Safety Set

	mRNA-1345 50 µg (N = 506)			
	Unsolicited AEs up to 28 days, n (%)		Unsolicited AEs up to DCO, n (%)	
	Any AE	Related to Study Injection	Any AE	Related to Study Injection
All unsolicited AEs, n (%)[a]	30 (**5.9**)	2 (0.4)	--	--
Serious	2 (0.4)	0	4 (**0.8**)	0
Fatal	0	0	0	0
Medically attended	10 (**2.0**)	0	14 (**2.8**)	0
Leading to study discontinuation	0	0	0	0
Severe (grade ≥3)	0	0	1 (**0.2**)	0
Any AE of Special Interest	0	0	0	0

- Safety findings were consistent with the established safety and reactogenicity profile of mRNA-1345 and were generally similar by brand of primary RSV vaccine received

AE, adverse event; DCO, data cutoff, EOS, end of study; RSV, respiratory syncytial virus.
[a]Up to DCO columns summarize specified AE categories collected beyond Day 28, therefore an overall "All unsolicited AEs" row through DCO/EOS is not applicable.

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Immunogenicity

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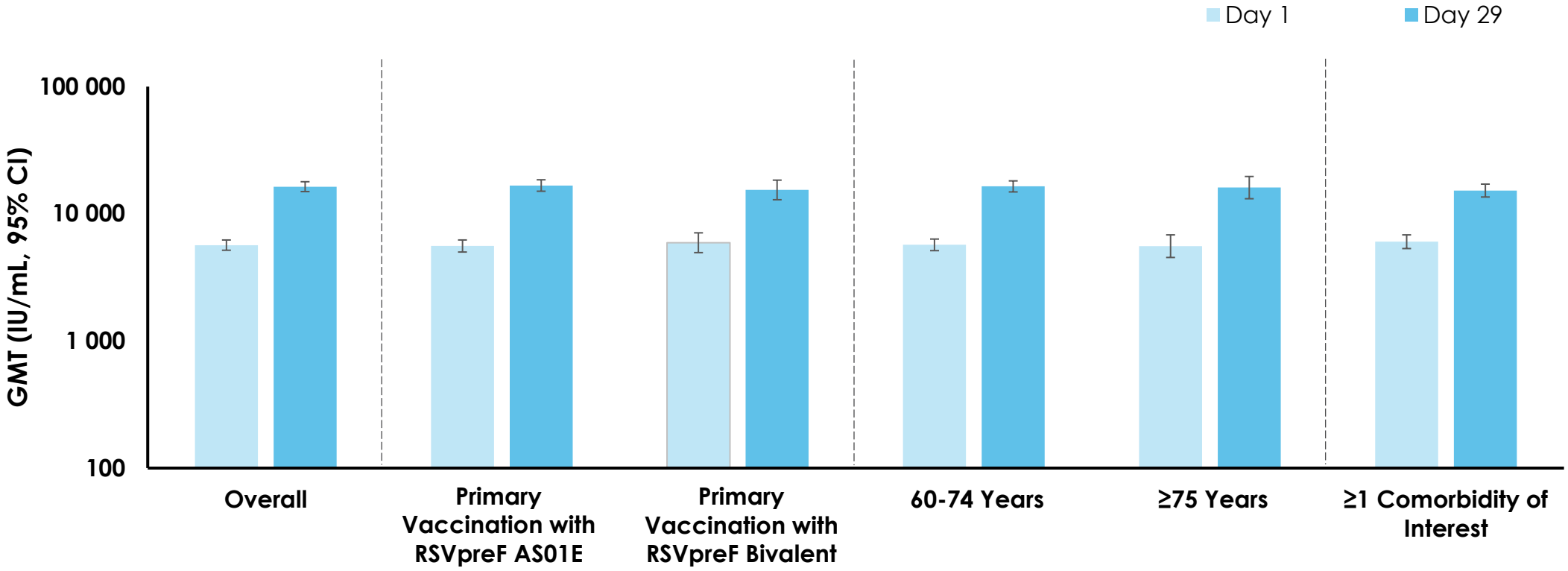
Summary of Overall and Subgroups for RSV-A Neutralizing Antibodies Pre and Post mRNA-1345

Per-Protocol Immunogenicity Set



- Day 29 RSV-A nAb responses demonstrate that heterologous revaccination with mRNA-1345 administered ≥12 months after primary vaccination elicited robust increases in titers
- Responses were consistent across subgroups, including by brand of primary RSV vaccine received, age group, and comorbidity of interest

CI, confidence interval; GMT, geometric mean titer; nAb, neutralizing antibody; RSV, respiratory syncytial virus.

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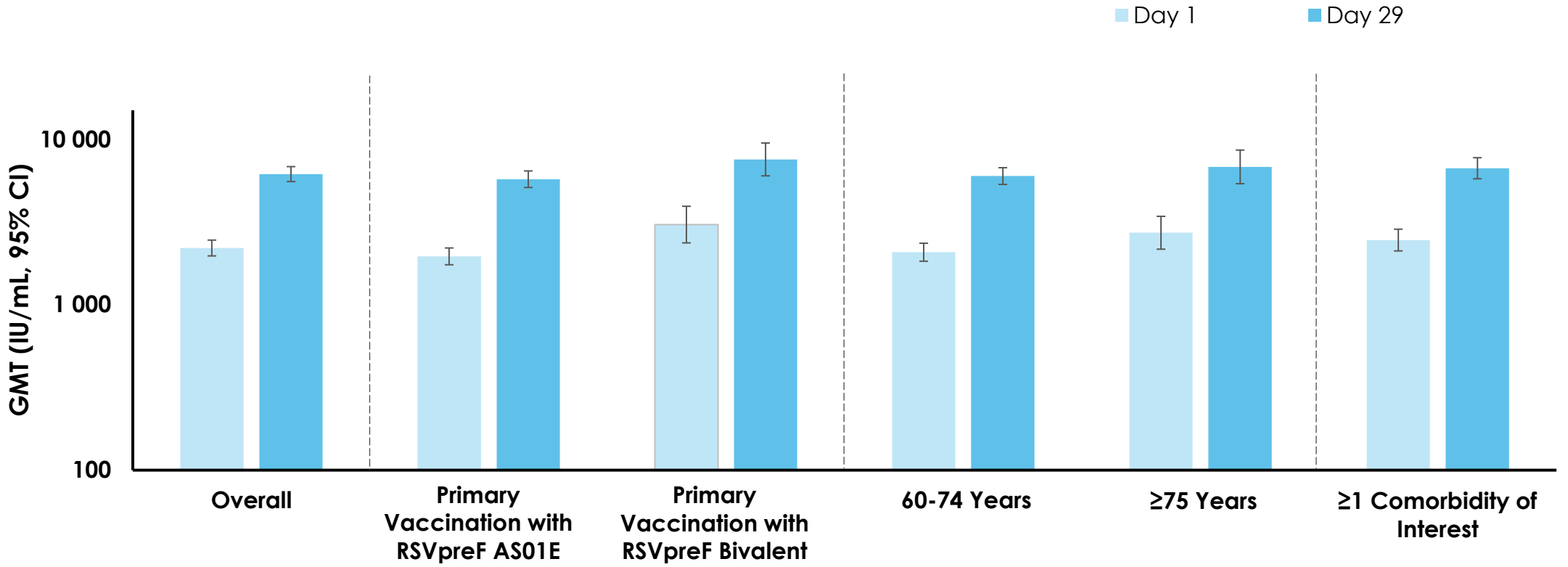
Summary of RSV-B Neutralizing Antibodies by Brand of Primary RSV Vaccine, Age Group, and Comorbidity Status

Per-Protocol Immunogenicity Set



- Consistent with RSV-A nAb responses, Day 29 RSV B nAbs demonstrate that heterologous revaccination with mRNA-1345 elicits robust nAb responses

CI, confidence interval; GMT, geometric mean titer; nAb, neutralizing antibody; RSV, respiratory syncytial virus.

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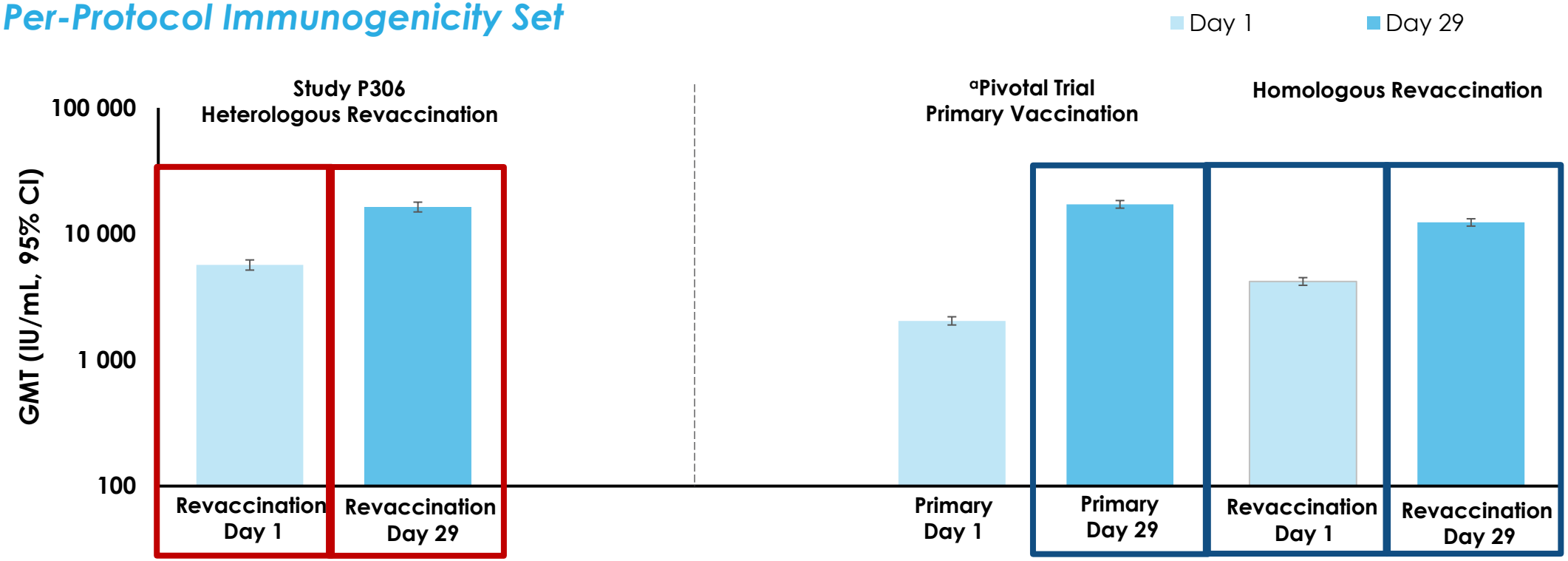
Post Hoc Analysis: RSV-A Neutralizing Antibody Response Pre and Post mRNA-1345 Heterologous and Homologous Revaccination

Per-Protocol Immunogenicity Set



- Findings were evaluated in the context of a subset of participants from the pivotal efficacy study who were revaccinated at 24 months
- At Revaccination Day 1, over a comparable median interval, RSV neutralizing antibody titers were similar irrespective of the brand of primary RSV vaccine received
- Heterologous revaccination with mRNA-1345 demonstrated similar Day 29 responses to primary and homologous revaccination

[a]Primary vaccination titers from a subset of participants from the pivotal efficacy trial that were revaccinated with mRNA-1345 at 24 months
CI, confidence interval; GMT, geometric mean titer; RSV, respiratory syncytial virus.

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Post Hoc Comparison of Day 29 Neutralizing Antibody Responses: Heterologous Revaccination vs Primary Vaccination

Per-Protocol Immunogenicity Set

	[a]Primary Vaccination (Pivotal Trial, Day 29) mRNA-1345 50 µg			Heterologous Revaccination (Day 29) mRNA-1345 50 µg			GMR (Revaccination vs Primary, Day 29)	
	N	GMT	GMT (95% CI)	N	GMT	GMT (95% CI)	GMR	95% CI
RSV-A nAb (IU/mL)	955	17157.48	(16040.06, 18352.75)	473	16336.01	(14845.24, 17976.49)	0.952	(0.847, 1.070)
RSV-B nAb (IU/mL)	952	5673.73	(5290.08, 6085.20)	491	6168.59	(5595.60, 6800.25)	1.087	(0.964, 1.226)

LB of 95% CI >0.667

- In a post hoc analysis, the lower bound of 95% confidence interval of the geometric mean ratio was greater than the standard noninferiority margin (GMR LB>0.667)

[a]Primary vaccination titers from a subset of participants from the pivotal efficacy trial that were revaccinated with mRNA-1345 at 24 months
CI, confidence interval; GMR, geometric mean ratio; GMT, geometric mean titer; LB, lower bound; nAb, neutralizing antibody; RSV, respiratory syncytial virus.
GMT and GMR were derived using an analysis of variance (ANOVA) model.

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Conclusions

Safety

- Heterologous revaccination with mRNA-1345 was well-tolerated, with no safety concerns identified
- Safety and reactogenicity were consistent with the established profile of mRNA-1345 and did not differ by brand of primary RSV vaccine received

Immunogenicity

- Heterologous revaccination with mRNA-1345 elicited robust increases in RSV-A and RSV-B neutralizing antibody titers at Day 29
- Efficacy of revaccination with mRNA-1345 after a protein subunit RSV vaccine is anticipated to be restored to that of primary vaccination based on a post hoc analysis

RSV, respiratory syncytial virus.

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Thank you

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