RSV Vaccine (mRNA-1345) Update:

- *Safety & Immunogenicity in 18-59 Year Olds at increased Risk for RSV Disease**
- *Revaccination of Adults at 12 or 24 Months**

ACIP

Frances Priddy, MD MPH

April 16, 2025



* mRESVIA has not been authorized for these indications

moderna

RSV Vaccine (mRNA-1345) Clinical Development

Efficacy, Immunogenicity, Safety, and Correlate of Protection

Adults ≥60 years
Study 301

Concomitant Administration with Standard Dose Influenza or COVID-19

Adults ≥50 years
Study 302 - Part A and B

Concomitant Administration with High Dose Influenza

Adults ≥65 years
Study 304

Safety and Immunogenicity in Adults at Increased Risk

Adults 18-59 years
Study 303 – Part A

12 Month Revaccination

Adults ≥50 years
Study 302 – Part C

24 Month Revaccination

Adults ≥60 years
Study 301 – Part B

Safety and Immunogenicity in Immunocompromised

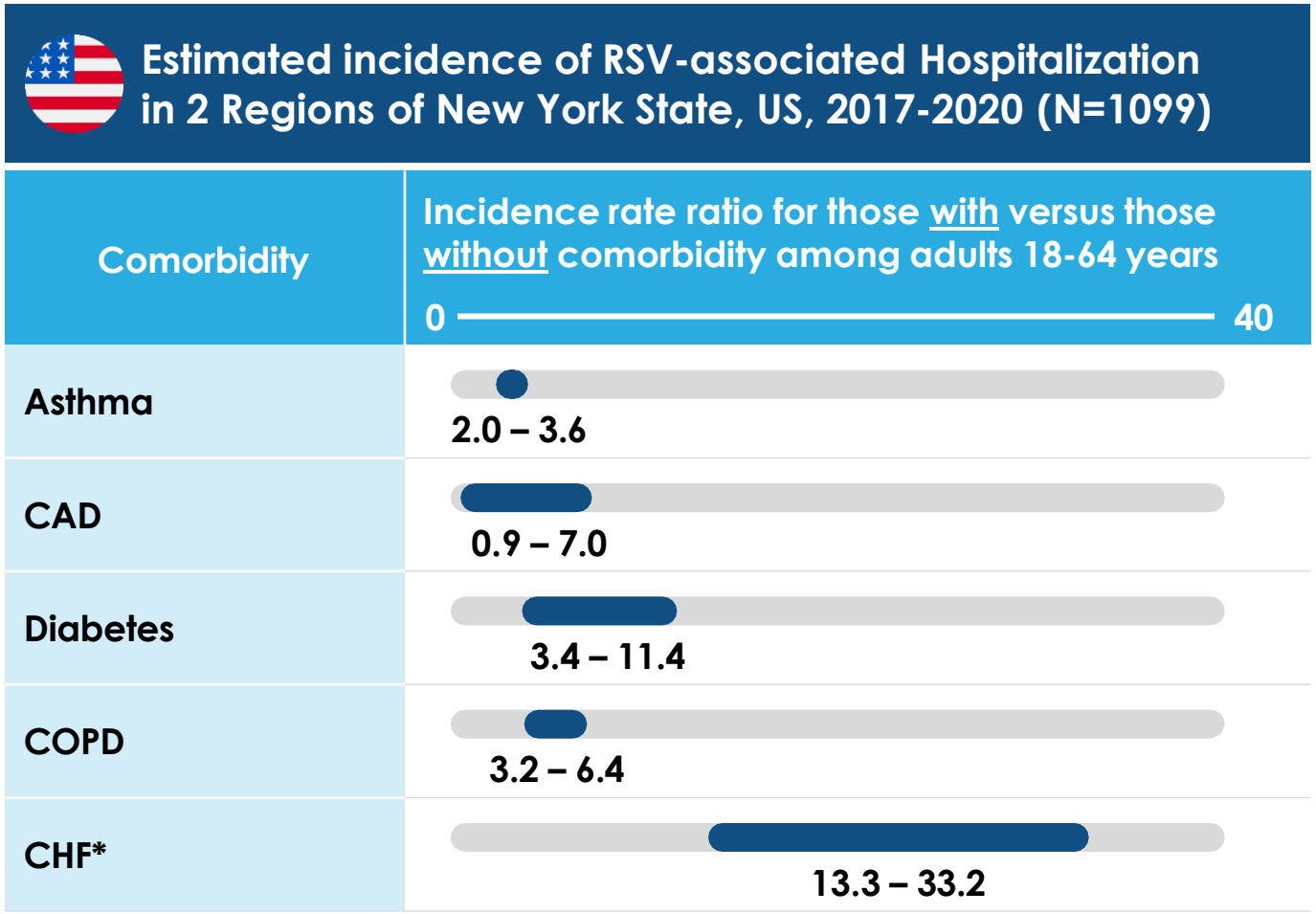
Adults with SOT ≥18 years
Study 303 – Part B

NCT05127434, NCT05330975, NCT06060457, NCT06067230

moderna

US Hospitalization Rates for RSV in 18-64 Year Olds with Underlying Conditions

Estimated incidence of RSV-associated Hospitalization in 2 Regions of New York State, US, 2017-2020 (N=1099)



RSV-NET Analysis –Adults Hospitalized with Laboratory Confirmed RSV 2016-2023 (N=16,575)

Adult RSV hospitalizations

- 37% in 18-64-year-olds
- 24% in 50-64-year-olds
  - 22% required ICU admission
  - 3% in-hospital mortality

CAD - coronary artery disease; CHF - congestive heart failure; COPD - chronic obstructive pulmonary disease; RSV - respiratory syncytial virus
*CHF age 20-59 years

Branche AR, et al. *Clin Infect Dis*. 2022.
Havers FP, et al. *JAMA Netw Open*. 2024.

moderna

mRNA-1345 in Adults,18-59 Years, at Increased Risk of RSV Disease

Study 303, Part A

ISIRV 2025

moderna

Study Design – Randomized Double-Blind Study in 18-59-Year-Old Adults at Increased Risk of RSV Disease

Study 303, Part A


United States


Canada


United Kingdom

Underlying Disease Category	mRNA-1345 Dose
Coronary Artery Disease (CAD) and/or Congestive Heart Failure (CHF)	50 µg N ~ 150
COPD, Persistent Asthma, Pulmonary Fibrosis, and/or Other Chronic Respiratory Diseases	50 µg N ~ 150
Diabetes Mellitus 1 or 2	50 µg N ~ 200

- Day 29 immunogenicity compared between this population and adults ≥60 years in pivotal efficacy trial
- Participants followed for 24 months

moderna

Key Study Objectives

Study 303, Part A

Primary Objectives

1. **Safety and tolerability of the vaccine in high-risk 18-59-year-olds**
2. **Compare RSV-A and RSV-B GMTs at Day 29 after a single dose of 50 µg in high-risk adults, 18-59 years, versus adults ≥60 years in the pivotal phase 2/3 efficacy trial**
   - *Criteria for Noninferiority: 95% CI of GMR LB > 0.667*

Secondary Objective

Comparison of seroresponse rates (SRR) of 50 µg high-risk 18-59 years olds vs 50 µg ≥ 60-year-olds in pivotal efficacy study

- *Criteria for Noninferiority: 95% CI of SRR difference LB > -10%*

LB – lower bound, CI – confidence interval; GMR – geometric mean ratio; SCR – seroconversion rate; SRR – seroresponse rate

moderna

Underlying Medical Conditions of Study Participants

Physician-documentation required for all underlying medical conditions

- **CAD**
- **CHF***
- **Chronic respiratory disease**
  - COPD*
  - Persistent asthma – requiring ≥1 maintenance medication
  - Pulmonary fibrosis
  - Other chronic lung disease
- **Stable type 1 or type 2 diabetes mellitus**
  - Controlled with ≥1 medication started 90 days prior to Day 1

CAD, coronary artery disease; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; RSV, respiratory syncytial virus.

*Severity of CHF and COPD assessed at baseline using NYHA Functional Classification for CHF (stage I, II, III, IV), or modified MRC Dyspnea Scale for COPD (stage 0,1,2,3,4)

moderna

Demographics of Study Participants

Study 303, Part A, Safety Set

Medical History Category	18-59 years N = 502	50-59 years N = 306
Median Age, years (range)	**53** (19-59)	**56** (50-59)
Female, n (%)	**269** (54%)	**158** (52%)
Race/Ethnicity, n (%)		
White	**401** (80%)	**238** (78%)
Black or African American	**85** (17%)	**64** (21%)
Asian	**4** (1%)	**2** (1%)
Hispanic / Latino Ethnicity	**140** (28%)	**88** (29%)

- Study population was racially/ethnically diverse

Sept 18, 2024 data cutoff

moderna

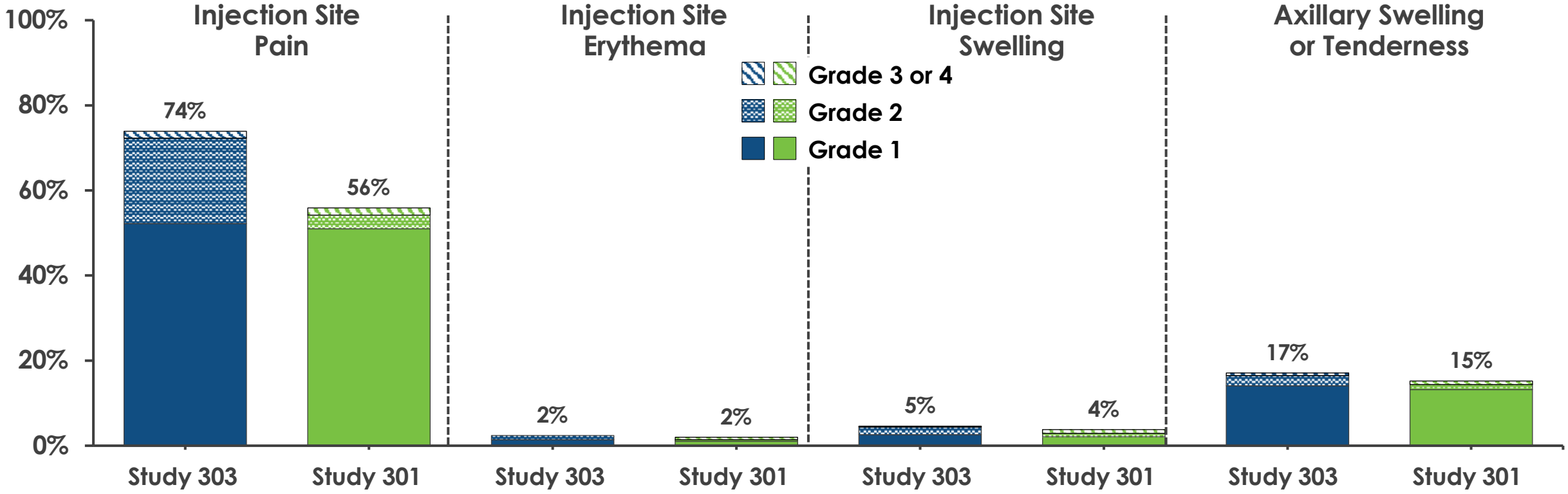
Safety – mRNA-1345 in Adults, 18-59 Years, at Increased Risk of RSV Disease

Study 303, Part A

moderna

Local Reactions - Vaccine Generally Well Tolerated in Adults, 18-59 Years, at Increased Risk for RSV Disease

Solicited Local Reactions within 7 Days of Injection compared to Older Adults ≥60 Years
Solicited Safety Set – Studies 303 Part A (N = 502) & 301 (N = 18,160)



- Injection site pain was more common among high-risk adults, 18-59 years, than adults ≥ 60 years
- Rates of other local reactions generally similar across age groups
- Mostly grade 1-2, onset days 1-2; median duration of 2 days; 1 grade 4 pain

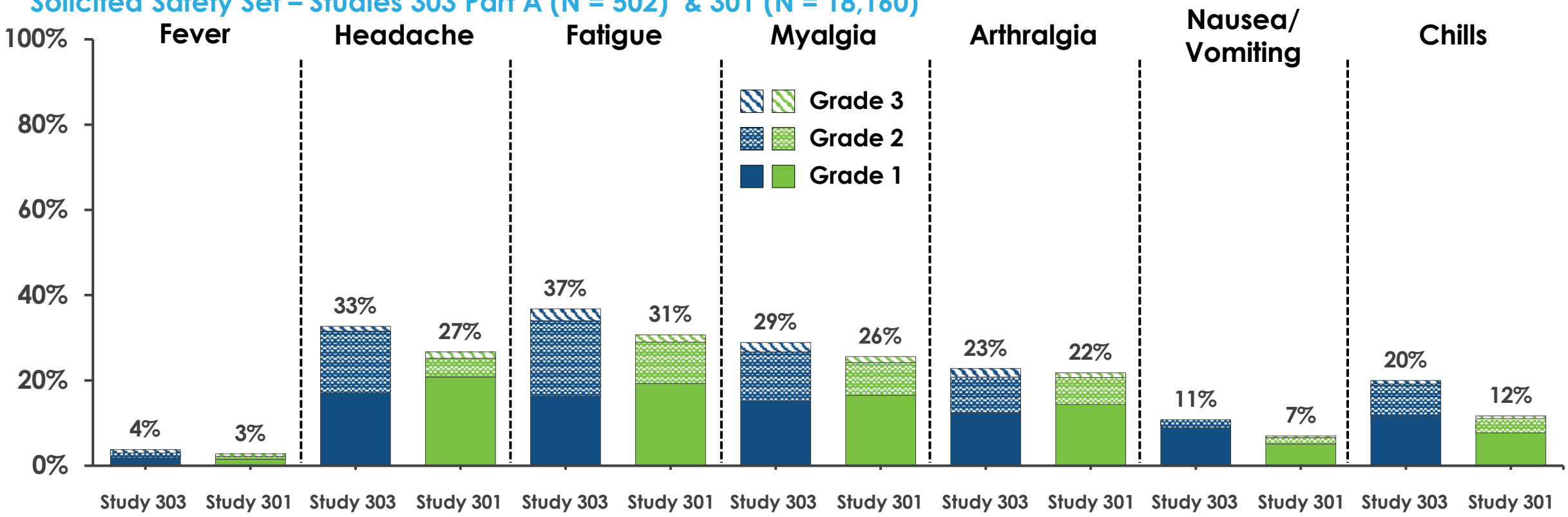
Sept 18, 2024 data cutoff - Study 303

moderna

Systemic Reactions - Vaccine Generally Well Tolerated in Adults, 18-59 Years, at Increased Risk for RSV Disease

Solicited Systemic Reactions within 7 Days of Injection compared to Older Adults ≥60 Years

Solicited Safety Set – Studies 303 Part A (N = 502) & 301 (N = 18,160)



- Rates of systemic reactions generally similar or slightly higher among 18-59-year-olds vs adults ≥60 years old
- Mostly grade 1-2, onset days 1-2; median duration of 2 days; no grade 4 reactions

Sept 18, 2024 data cutoff – Study 303

moderna

Unsolicited Adverse Events Within 28 Days After mRNA-1345 Regardless of Relationship to Study Vaccination

Study 303, Part A - Adults at Increased Risk of RSV – Safety Set

	mRNA-1345 18-59 years Total = 999	mRNA-1345 50-59 years N = 607
All, n (%)	**226** (22.6%)	**131** (21.6%)
Non-Serious	**224** (22.4%)	**129** (21.3%)
Serious	**2** (0.2%)*	**2** (0.3%)*
Fatal	**0**	**0**
Medically-Attended	**117** (11.7%)	**68** (11.2%)
Leading to Study Discontinuation	**0**	**0**
Severe	**2** (0.2%)*	**2** (0.3%)*
Any Adverse Event of Special Interest (AESI)	**0**	**0**

- No anaphylaxis, thrombocytopenia, Guillain-Barré syndrome, acute disseminated encephalomyelitis (ADEM), or acute myocarditis or acute pericarditis

Sept 18, 2024 data cutoff
30 µg, N=497; 50 µg, N=502
* 30 µg group, 50-59 year olds, unrelated to study injection by investigator: one case of pneumonia, one case of asthma exacerbation, both RSV RT-PCR negative

moderna

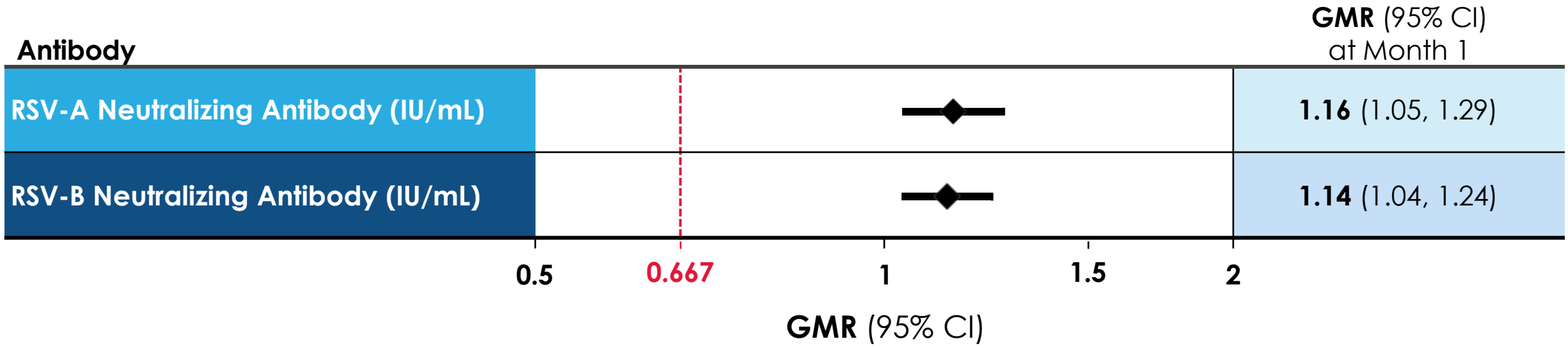
Immunogenicity – mRNA-1345 in Adults,18-59 Years, at Increased Risk of RSV Disease

Study 303, Part A

moderna

mRNA-1345 Vaccination (50 µg) in Adults,18-59 Years at Increased Risk of RSV Disease Meets Pre-Specified Noninferiority Criteria - RSV-A and RSV-B

Study 303, Part A & Study 301



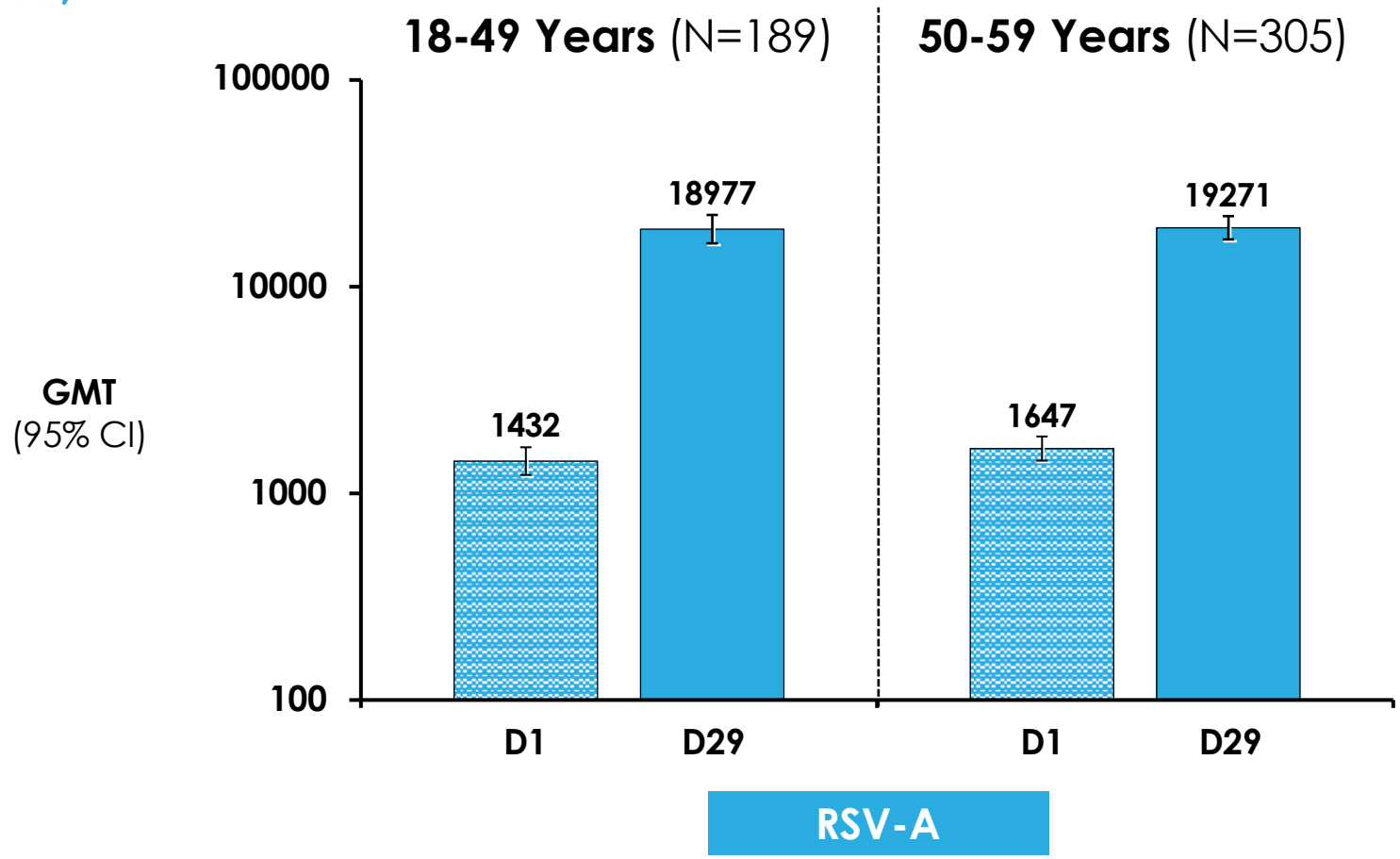
- All GMR non-inferiority criteria met (LB of the 2-sided 95% CI of GMR > 0.667) comparing 18-59-year-olds vs ≥60-year-olds in efficacy trial

GMR – Geometric mean ratio; Sept 18, 2024 data cutoff

moderna

RSV-A Neutralizing Antibody GMT after 50 µg of mRNA-1345 in Adults, 18-59 Years, at Increased Risk of RSV Disease, by Age

Study 303, Part A

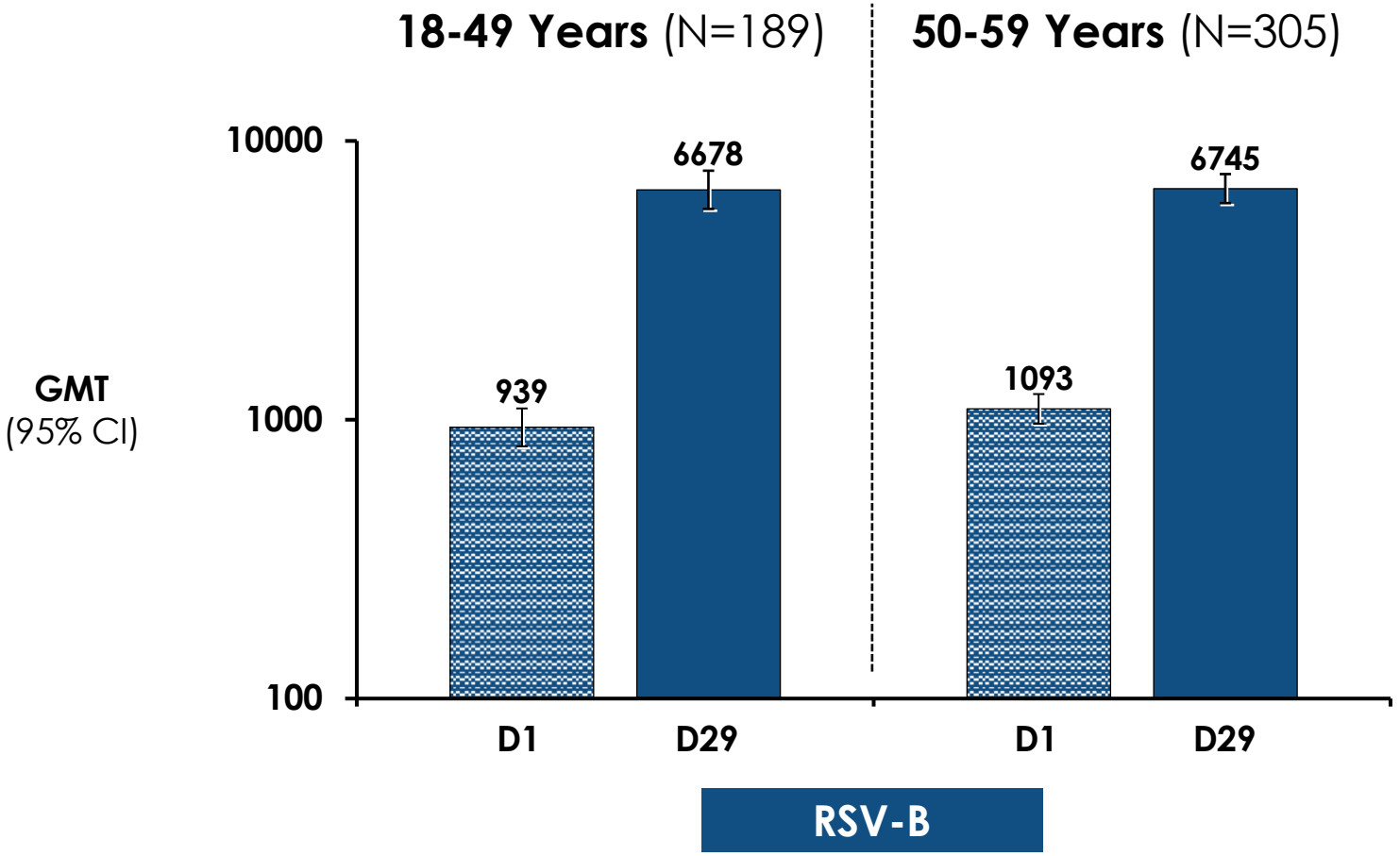


RSV-A GMT comparable between 18-49 and 50-59 year olds

moderna

RSV-B Neutralizing Antibody GMT after 50 µg of mRNA-1345 in Adults, 18-59 Years, at Increased Risk of RSV Disease, by Age

Study 303, Part A

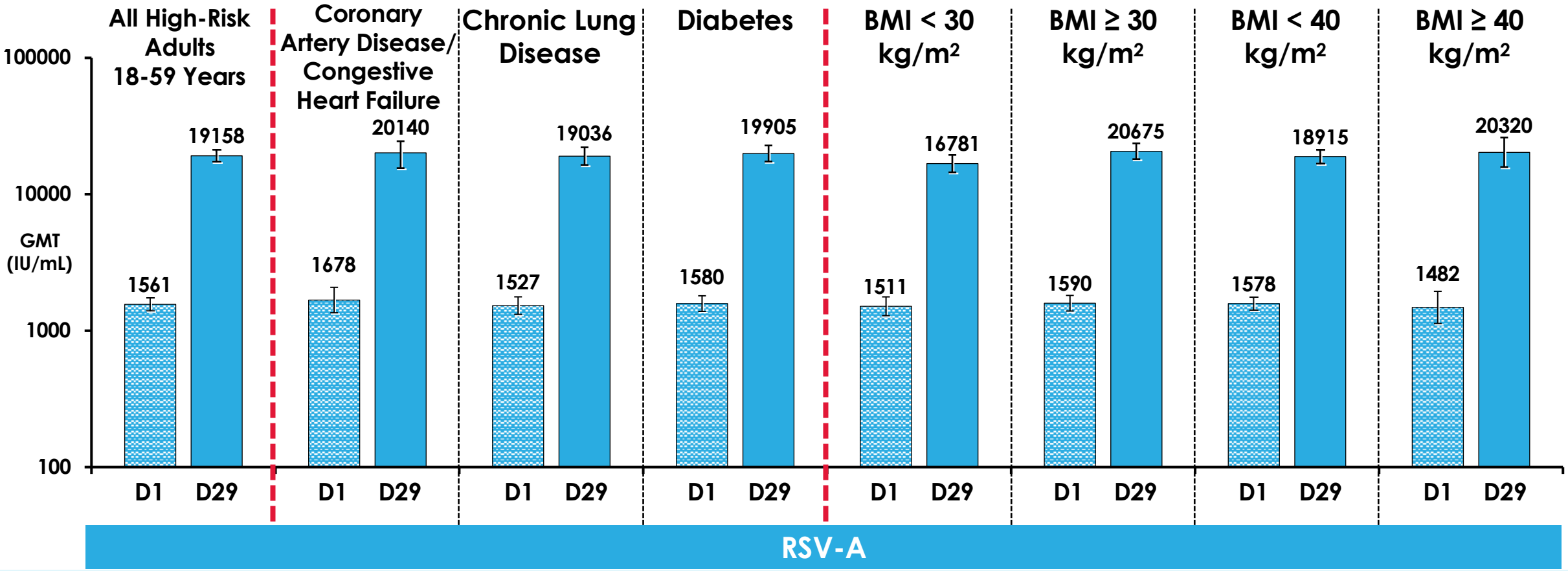


RSV-B GMT comparable between 18-49 and 50-59 year olds

moderna

RSV-A Neutralizing Antibody GMT after 50 µg of mRNA-1345 in Adults, 18-59 Years, at Increased Risk of RSV Disease by Primary Risk Factor and BMI

Study 303, Part A



- Individuals with medical risk factors for RSV show consistent RSV-A neutralizing antibody responses compared to entire study population; no impact of BMI on antibody response
- Similar results for RSV-B

GMT; Geometric Mean Titer

Summary – RSV Vaccine (mRNA-1345) in Adults, 18-59 Years, at Increased Risk of RSV Disease

Safety	• Vaccine generally well tolerated across all ages • No safety concerns identified (no reports of thrombocytopenia, GBS, ADEM, acute myocarditis and/or pericarditis)
Immunogenicity	• RSV-A & RSV-B immune responses non-inferior to adults ≥60 years in pivotal efficacy trial; similar efficacy inferred • Immunogenicity consistent across age groups, including 50-59 years, and underlying medical conditions
Public Health Impact	• Substantial burden of RSV-associated hospitalizations in adults, 18-59 years • mRNA-1345 has the potential to also protect adults, 18-59 years, at increased risk of severe RSV disease • Data under review by FDA; PDUFA date June 12, 2025

GBS – Guillain-Barré syndrome, ADEM – acute disseminated encephalomyelitis

moderna

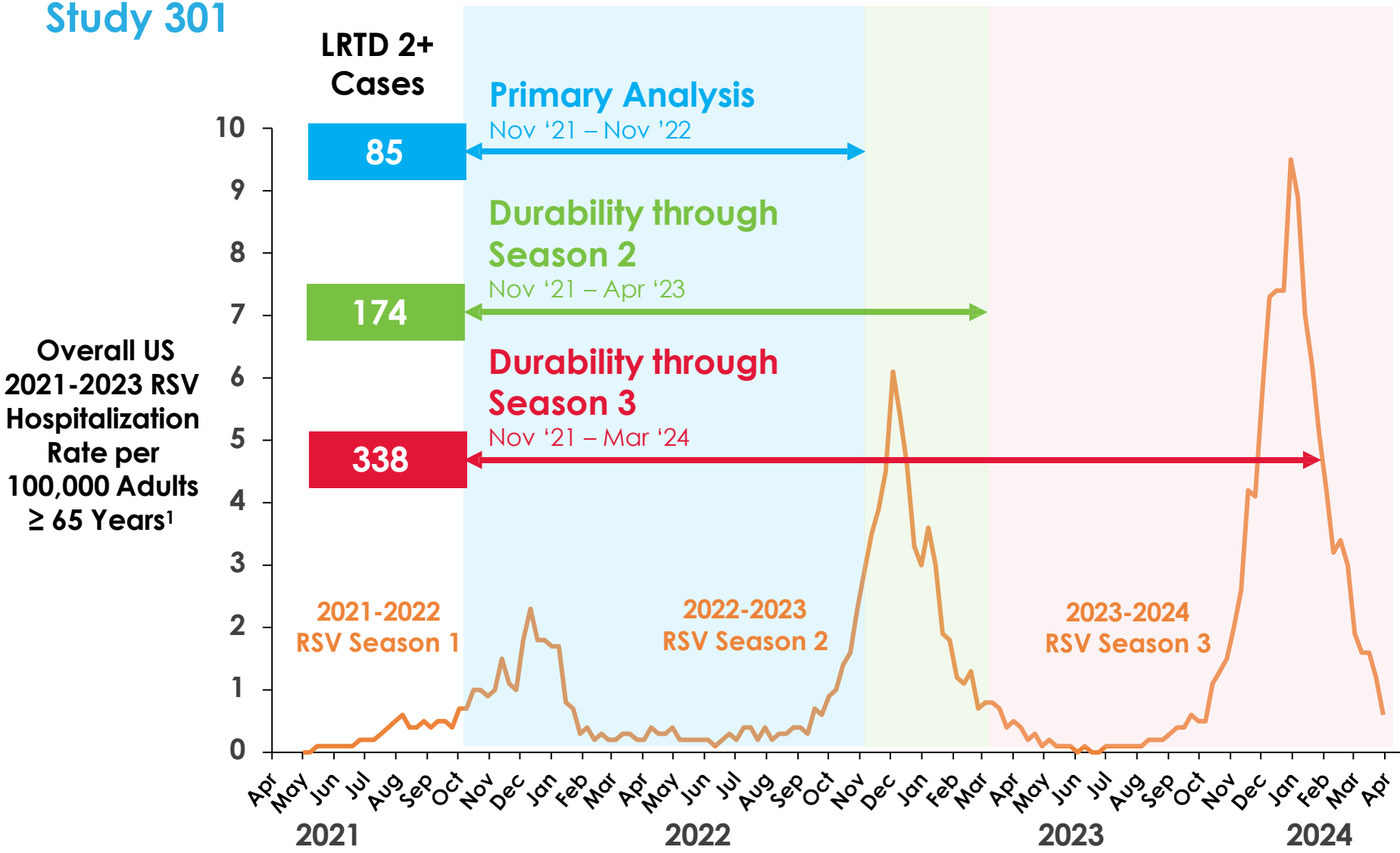
Revaccination of Healthy Adults at 12 or 24 Months

ESCMID 2025

moderna

RSV Case Accrual and Efficacy Analyses through 3 Seasons in the Phase 2/3 Pivotal Trial

Study 301



Efficacy[2]

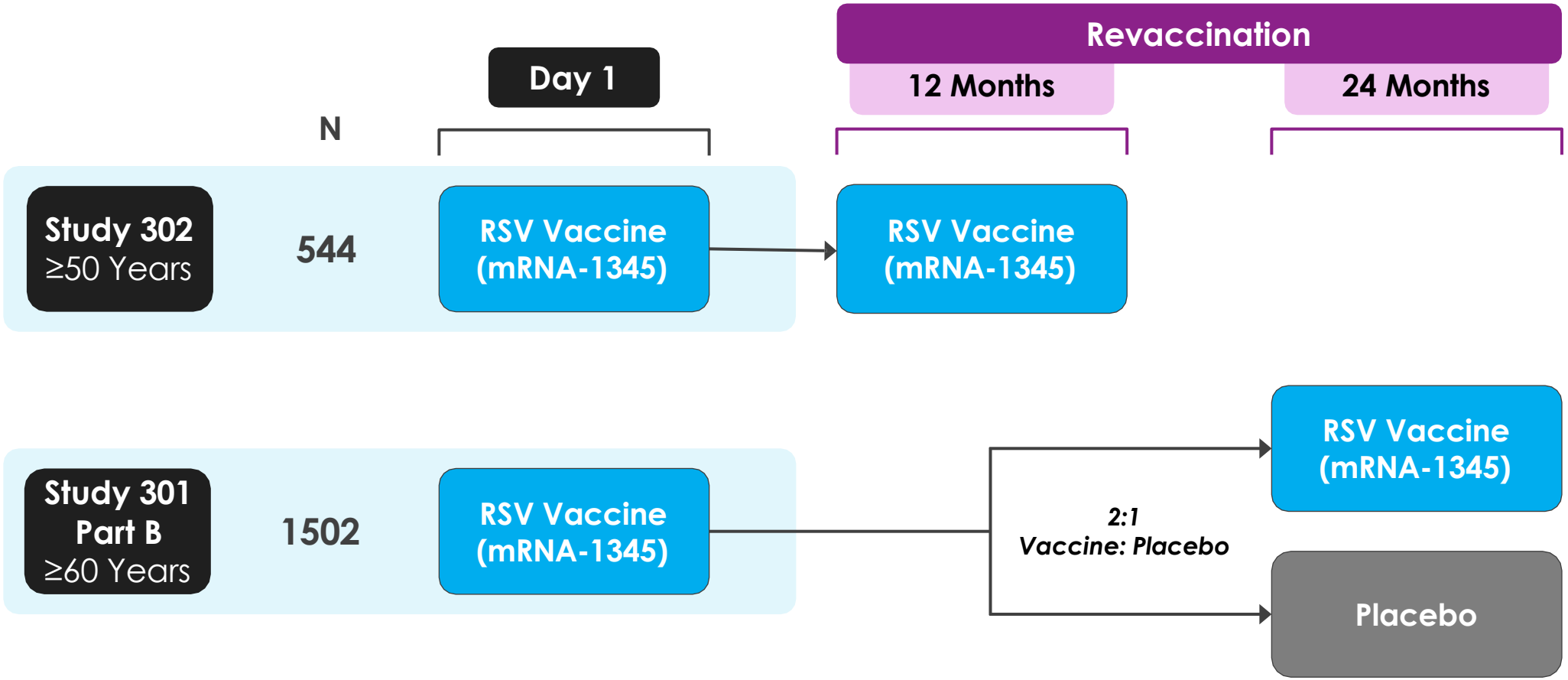
LRTD 2+	Severe RSV (shortness of breath)
78.7% (62.8%, 87.9%)	86.7% (41.9%, 97.0%)
62.5% (47.7%, 73.1%)	74.6% (50.7%, 86.9%)
50.3% (37.5%, 60.7%)	56.7% 33.1%, 72.6%)

1. CDC. Respiratory Syncytial Virus Hospitalization Surveillance Network (RSV-NET). https://www.cdc.gov/respiratory-viruses/data-research/dashboard/most-impacted-hospitalizations.html 2. Based on final FDA Package Insert

moderna

Vaccination Regimens – Revaccination Studies in Adults

Study 302 & Study 301 (50 µg)

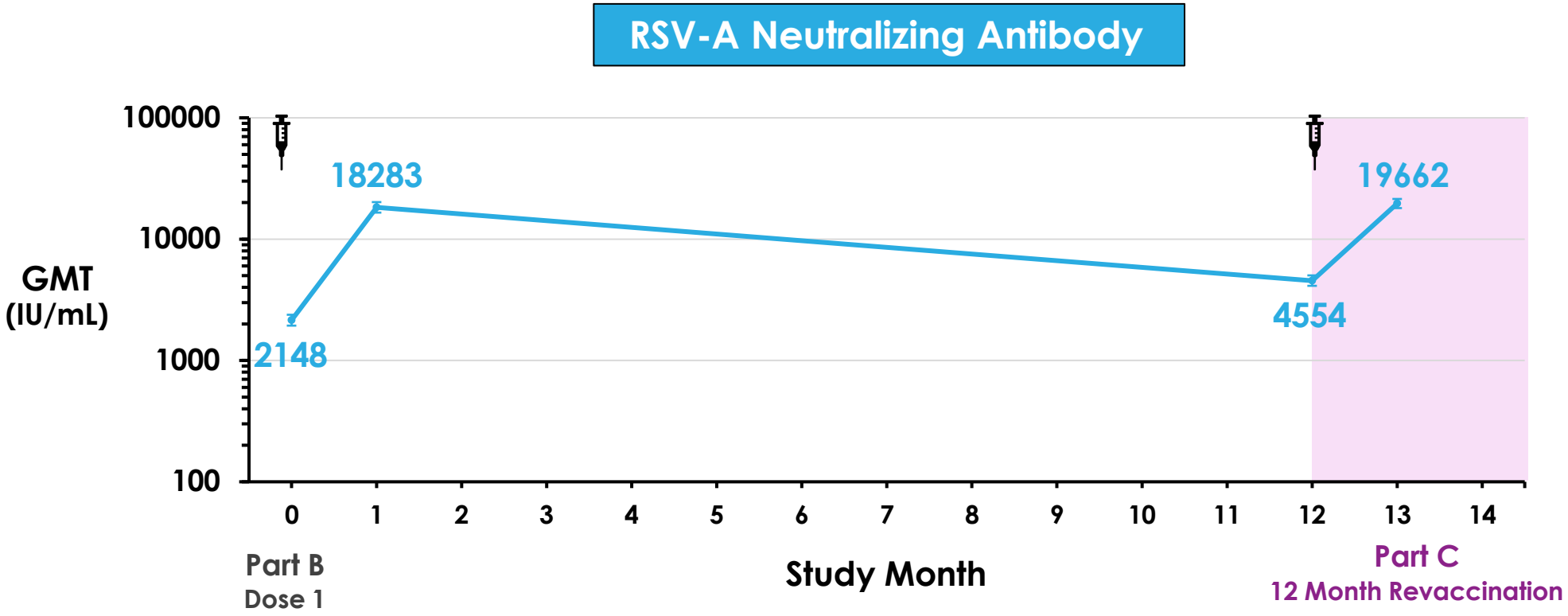


12-month data presented at June 2024 ACIP meeting

moderna

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

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)

moderna

24 Month Revaccination – Demographics of Study Participants

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/m²**	**317** (32%)

moderna

Safety – Revaccination at 24 Months

moderna

Safety - Revaccination at 24 Months with mRNA-1345

Study 301B, Adults ≥60 Years (N=998)

- **Revaccination generally well tolerated**
  - Local and systemic reactions were mainly Grade 1-2, with median onset on Day 2, and median 2-day duration
  - Comparable to reactogenicity after primary dose
- **No safety concerns identified**
- **No reports of:**
  - Deaths, SAEs, or AESIs as assessed as vaccine-related by the investigator
  - Anaphylaxis
  - Guillain Barre Syndrome
  - Acute disseminated encephalomyelitis (ADEM)
  - Acute myocarditis or acute pericarditis

SAE – serious adverse event; AESI – adverse event of special interest
End of study analysis (last subject last visit Oct 23, 2024)

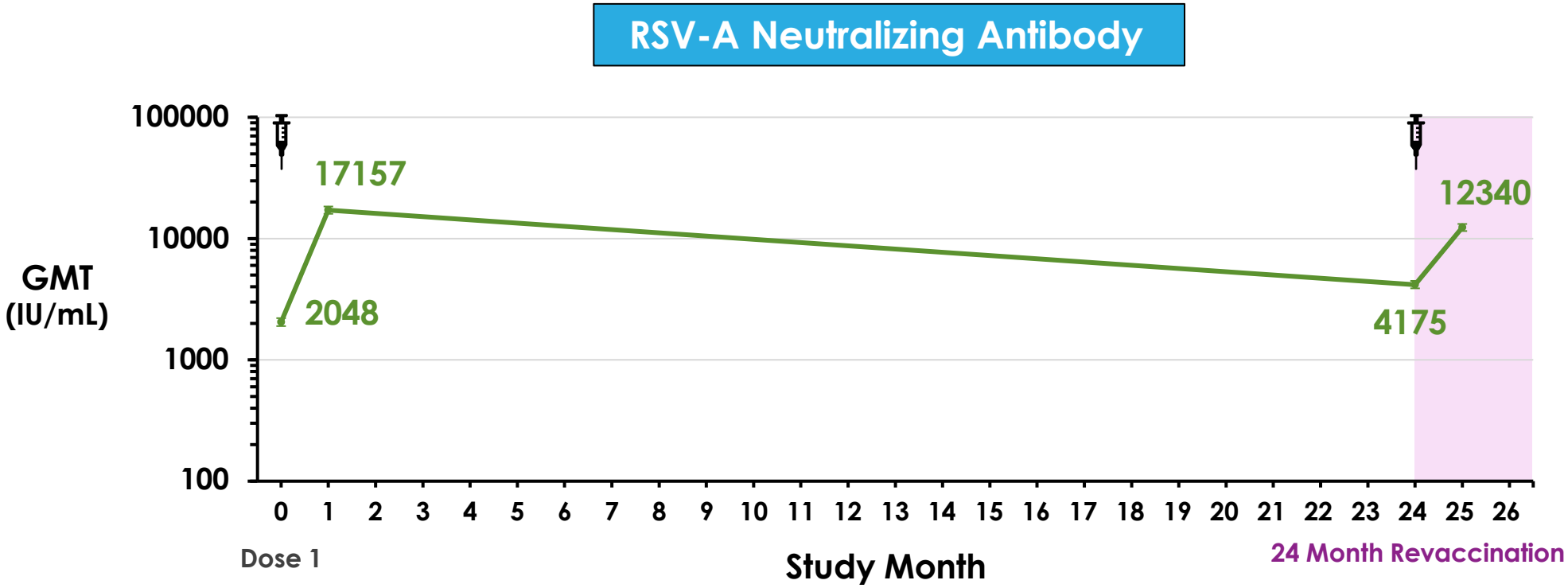
moderna

Immunogenicity – Revaccination at 24 Months

moderna

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

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



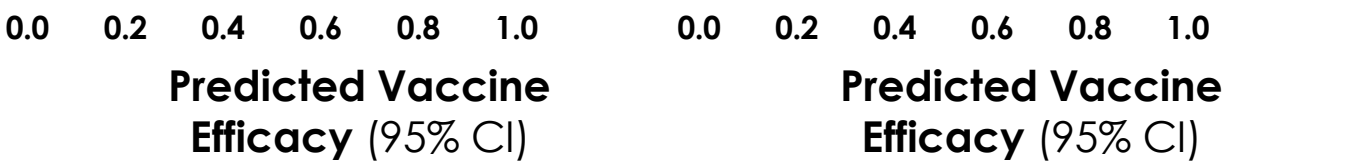
- RSV-A neutralizing antibodies detectable at 24 months post-vaccination
- Revaccination at 24 months after primary vaccination elicits responses similar to those following primary dose
- Revaccination met non-inferiority success criteria for RSV-A & RSV-B (LB of 95% CI of GMR > 0.667)

moderna

Predicted Vaccine Efficacy for the 12-Month Period Following 24 Month Revaccination with mRNA-1345

Study P301 Part B Per-Protocol Set ≥60 Years, N = 956

Neutralizing Antibody	Day 29 GMT After Revaccination	RSV-LRTD 2+	RSV-LRTD 3+
RSV-A (IU/mL)	**12382**	**60%** (43, 74)	**68%** (44, 84)
RSV-B (IU/mL)	**4024**	**58%** (40, 73)	**67%** (44, 84)



Correlate of protection model suggests revaccination restores vaccine efficacy

moderna

Summary – RSV Vaccine (mRNA-1345) Revaccination

Safety & Immunogenicity

- Revaccination generally well tolerated; no safety concerns identified
- 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

GBS – Guillain-Barré syndrome, ADEM – acute disseminated encephalomyelitis

moderna

THANK YOU!

- Investigators
- Study site personnel
- Laboratory personnel
- **Most importantly, the individuals who participated in these trials**

moderna