Update on Moderna's RSV Vaccine, mRESVIA (mRNA-1345), in Adults ≥60 Years of Age

Advisory Committee on Immunization Practices (ACIP)

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moderna

Licensure of mRESVIA, Moderna's RSV Vaccine (mRNA-1345) in United States

- FDA approval obtained May 31, 2024
- Indication/Presentation
  - For active immunization for the prevention of lower respiratory tract disease (LRTD) caused by respiratory syncytial virus (RSV) in adults 60 years of age and older
  - Single dose regimen
  - Prefilled syringe

Outline of Presentation

- Pivotal Phase 2/3 Trial
  - Brief review of study design
  - Update on safety
  - Update on efficacy
- 12-month revaccination data
  - Safety
  - Immunogenicity
- Summary

Pivotal Safety and Efficacy Study Design

Study 301

Population

- Healthy adults including those with chronic, stable medical conditions, and/or frailty
- ≥ 60 years of age
- 22 countries (both Northern and Southern Hemisphere)

Regimen and follow-up

- Single-dose regimen (1:1 50 µg RSV vaccine or saline placebo)
- 24-month follow-up

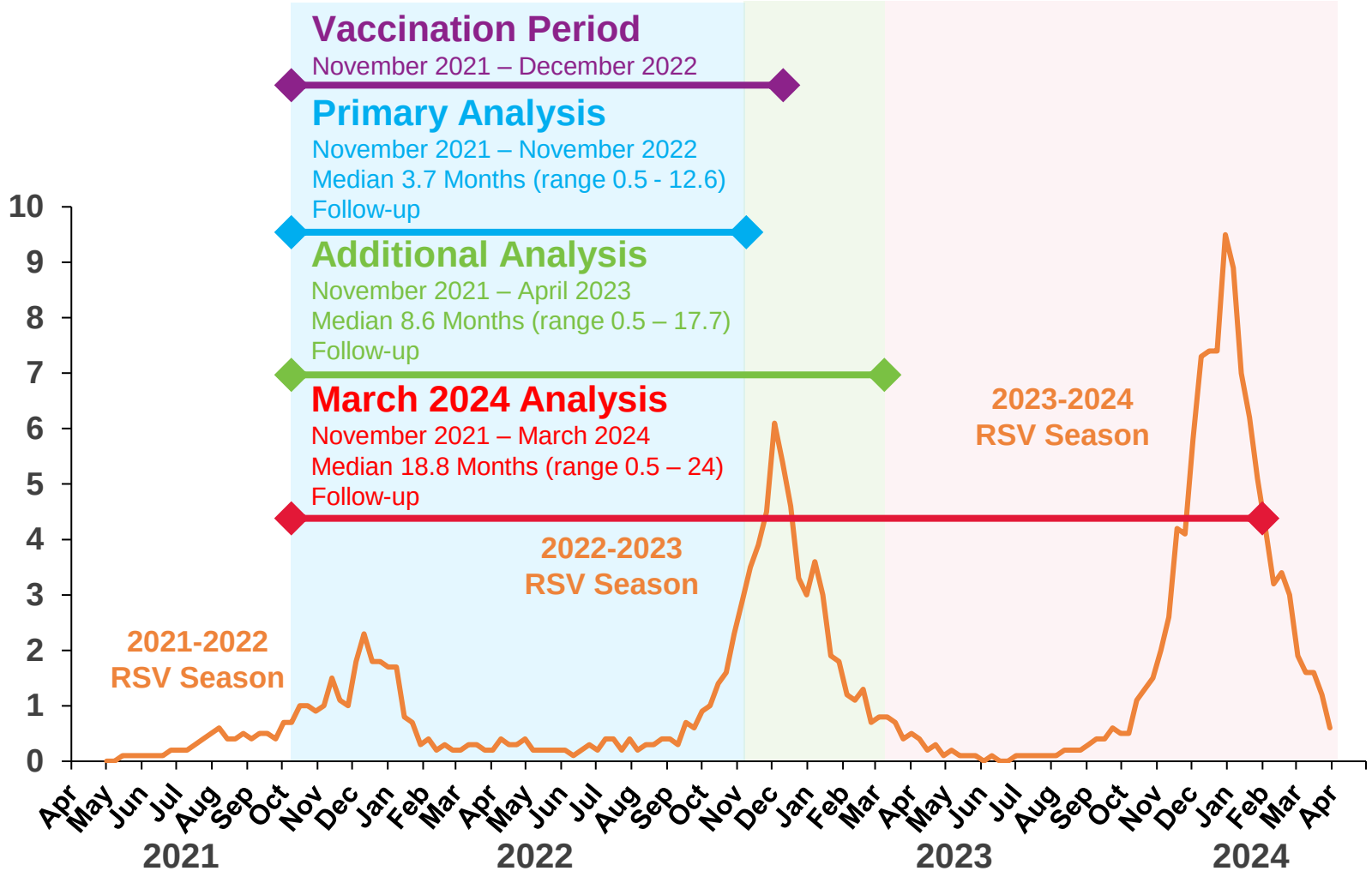
Stratified by

- Age (60 - 74 and ≥ 75 years)
- Presence or absence of congestive heart failure or chronic obstructive pulmonary disease

clinicaltrials.gov NCT05127434 https://clinicaltrials.gov/ct2/show/NCT05127434
Wilson et al *NEJM*, 2023.

Trial Analyses

US 2021-2023 RSV Hospitalization Rates (RSV-NET) in Adults ≥ 65 Years[1]



- RSV efficacy study conducted across 3 seasons
- >50% of participants enrolled in US
- **Primary Analysis:** Met success criteria
- **Additional Analysis:** >90% of participants followed for ≥ 6 months
- **March 2024 Analysis:** >90% of participants followed for ≥12 months

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

Timing of Vaccination and RSV Surveillance

Study 301

Vaccination

- COVID-19 pandemic precluded the assumption of standard RSV seasons
- Subjects vaccinated year-round for ~ 1 year (not limited to pre-RSV season)

Surveillance

- Active surveillance of >36,000 participants for RSV year-round (not limited to RSV seasons)
  - Included 2022/2023 and 2023/2024 high incidence RSV seasons[1]
    - Background rates in placebo recipients, 14 days - 24 months:
      - RSV-LRTD with ≥ 2 symptoms: 9.3 cases/1000 person years
      - RSV-LRTD with ≥ 3 symptoms: 3.7 cases/1000 person years
      - RSV-ARD: 16.4 cases/1000 person years
  - 683 confirmed RSV-ARD cases reported over 24 months

clinicaltrials.gov NCT05127434 https://clinicaltrials.gov/ct2/show/NCT05127434

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

Demographics of Study Participants

Study 301

Randomization Set Characteristic	RSV Vaccine (mRNA-1345) (N = 18,427)	Placebo (N = 18,387)
Median Age, years	**67**	**67**
Male, n (%)	9,410 (**51%**)	9,330 (**51%**)
Age Group, n (%)		
60 – 69 Years	11,437 (**62%**)	11,399 (**62%**)
70 – 79 Years	5,546 (**30%**)	5,534 (**30%**)
≥ 80 Years	1,444 (**8%**)	1,454 (**8%**)
Race/Ethnicity, n (%)		
White	11,311 (**61%**)	11,290 (**61%**)
Black or African American	2,204 (**12%**)	2,173 (**12%**)
Asian	2,151 (**12%**)	2,138 (**12%**)
Hispanic / Latino Ethnicity	6,117 (**33%**)	6,168 (**34%**)
Frailty Status (≥4 on Edmonton frail score)	3,862 (**21%**)	3,946 (**21%**)

Age, gender, race/ethnicity, and frailty status balanced between vaccine and placebo recipients
Race/ethnicity generally representative of US population

March 8, 2024 data cutoff

Prespecified Comorbidities among Study Population

Study 301 – Randomization Set

Randomization Set

	RSV Vaccine (mRNA-1345) (N = 18,427)	Placebo (N = 18,387)
≥1 Prespecified Comorbidity (%)	5,463 (30%)	5,357 (29%)
Chronic obstructive pulmonary disease (COPD)	1,097 (6%)	1,112 (6%)
Asthma	1,410 (8%)	1,365 (7%)
Chronic Respiratory Disease[1]	89 (0.5%)	84 (0.5%)
Diabetes	3,292 (18%)	3,207 (17%)
Congestive Heart Failure (CHF)	276 (2%)	268 (2%)
Advanced Liver Disease	49 (0.3%)	44 (0.2%)
Advanced Renal Disease	111 (0.6%)	127 (0.7%)

- ~30% of study participants with comorbidities
- Comorbidities balanced between vaccine and placebo recipients

1. Chronic respiratory disease includes chronic pulmonary fibrosis (idiopathic and otherwise), restrictive lung disease, asbestosis, bronchiectasis, cystic fibrosis, pulmonary hypertension, sarcoidosis, and history of tuberculosis

March 8, 2024 data cutoff

Safety Data

Study 301

Safety Set – March 8, 2024 data cutoff

Based on median of 18.8 months of follow-up

Unsolicited Adverse Events Within 28 Days After Injection, Regardless of Relationship to Vaccine/Placebo

Study 301

Safety Set	RSV Vaccine (mRNA-1345) (N = 18,369)	Placebo (N = 18,316)
All, n (%)	3,823 **(21%)**	3,467 **(19%)**
Serious	126 **(0.7%)**	114 **(0.6%)**
Fatal	2 **(<0.1%)**	6 **(<0.1%)**
Medically-Attended	1,664 **(9%)**	1,587 **(9%)**
Leading to Study Discontinuation	2 **(<0.1%)**	11 **(<0.1%)**
Severe/≥ Grade 3	138 **(0.8%)**	138 **(0.8%)**
Non-Serious	3,697 **(20%)**	3,353 **(18%)**
Any Adverse Event of Special Interest (AESI)	3 **(<0.1%)**	9 **(<0.1%)**

No imbalances in any categories between vaccine and placebo recipients

March 8, 2024 data cutoff

Adverse Events of Special Interest (AESI)

Study 301

Safety Set

- **Neurological Disorders**
  - No cases of acute disseminated encephalomyelitis (ADEM)
  - No safety concern with Guillain-Barre syndrome (3 unrelated cases reported >500 days postinjection [1 vaccine, 2 placebo])
  - No imbalance observed for other neurological disorders including Bell's palsy/facial paralysis
- **Cardiac Events**
  - No imbalance observed in cardiac arrhythmias such as atrial fibrillation
  - No confirmed cases of:
    - Acute myocarditis in vaccine recipients
    - Acute pericarditis in vaccine recipients with onset < 42 days

Efficacy Analyses

Study 301

Efficacy of mRNA-1345 Against RSV LRTD among Adults ≥ 60 Years

Study 301 – Primary and Additional Analyses

Per Protocol Analysis

	Primary Analysis (Case Driven)[1] *3.7 Months Median (range 0.5 - 12.6) Follow-up*			Additional Analysis[1] *8.6 Months Median (range 0.4 – 17.7) Follow-up*		
Cases, n (%)	RSV Vaccine (mRNA-1345) (N = 17,561)	Placebo (N = 17,503)	Vaccine Efficacy (%CI*)	RSV Vaccine (mRNA-1345) (N = 18,074)	Placebo (N = 18,010)	Vaccine Efficacy (% CI*)
RSV LRTD ≥ 2 symptoms	15 (0.09%)	70 (0.40%)	**78.7%** (62.8%, 87.9%)	48 (0.27%)	127 (0.71%)	**62.5%** (47.7%, 73.1%)
RSV LRTD ≥ 3 symptoms	5 (0.03%)	26 (0.15%)	**80.9%** (50.1%, 92.7%)	20 (0.11%)	51 (0.28%)	**61.1%** (34.7%, 76.8%)

- Vaccine protection continued through a high incidence RSV season (2022/2023)
- Lower bound of confidence interval continued to exceed 20%

1. US product insert mRESVIA

* For primary analysis, the alpha-adjusted 95.04% CI and 95.10% CI for RSV LRTD ≥ 2 symptoms and ≥ 3 symptoms are presented, respectively. For additional analysis, 95% CIs are presented. Efficacy based on hazard ratios

Efficacy of mRNA-1345 Against RSV LRTD among Adults ≥ 60 Years - 18 Month Analysis

Study 301 - Per Protocol Set

March 2024 Analysis

	Cases, n (%)		
	RSV Vaccine (mRNA-1345) (N = 18,181)	**Placebo** (N = 18,132)	**Vaccine Efficacy (%) (95% CI)**
RSV LRTD ≥ 2 symptoms	113 (0.6%)	225 (1.2%)	**50.3%** (37.5%, 60.7%)
RSV LRTD ≥ 3 symptoms	46 (0.3%)	91 (0.5%)	**49.9%** (27.8%, 65.6%)

- Vaccine protection continued over a longer period through high incidence 2022/2023 and 2023/2024 RSV seasons
- Lower bound of the confidence interval continued to exceed 20%

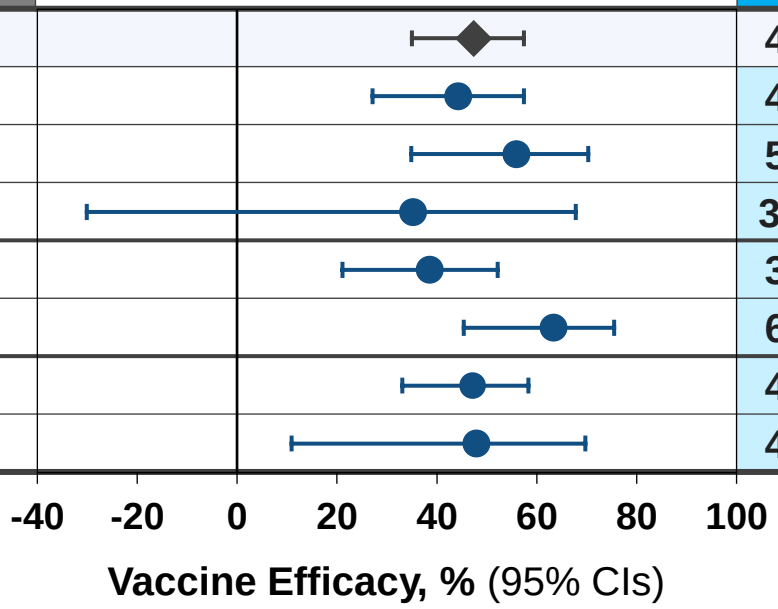
March 8, 2024 data cutoff

Efficacy based on incidence rates adjusted for person-time.

Efficacy of mRNA-1345 by Age, Comorbidities, and Frailty Against RSV LRTD ≥ 2 Symptoms

Study 301 - Per-Protocol Efficacy Set through 24 Months

RSV LRTD with ≥ 2 Symptoms		Numbers of Events: RSV Vaccine (mRNA-1345) (N = 18,181)	Numbers of Events: Placebo (N = 18,132)	Vaccine Efficacy (95% CI)
Overall		**132**/18,181	**248**/18,132	**47.4%** (35.0, 57.4)
Age	**60 – 69 Years**	**83**/11,269	**147**/11,238	**44.3%** (27.1, 57.4)
	70 – 79 Years	**36**/5,487	**81**/5,459	**56.0%** (34.9, 70.3)
	≥ 80 Years	**13**/1,425	**20**/1,435	**35.3%** (-30.1, 67.8)
Comorbidities	**No Comorbidities**	**99**/12,788	**160**/12,856	**38.6%** (21.1, 52.2)
	≥ 1 Comorbidities	**33**/5393	**88**/5276	**63.4%** (45.4, 75.5)
Frailty Status	**Fit** (0-3)	**106**/13,491	**197**/13,366	**47.2%** (33.1, 58.3)
	Vulnerable/Frail (≥ 4)	**20**/3802	**39**/3872	**48.0%** (10.9, 69.7)



- Case splits favorable for mRNA-1345 with respect to age, comorbidities, and frailty through 24 months

Comorbidities include COPD, CHF, asthma, chronic respiratory disease, diabetes, advanced liver disease, advanced renal disease
March 8, 2024 data cutoff

Efficacy of mRNA-1345 Against Severe LRTD Among Adults ≥ 60 Years

Study 301 - Post Hoc Analysis/Per Protocol Set

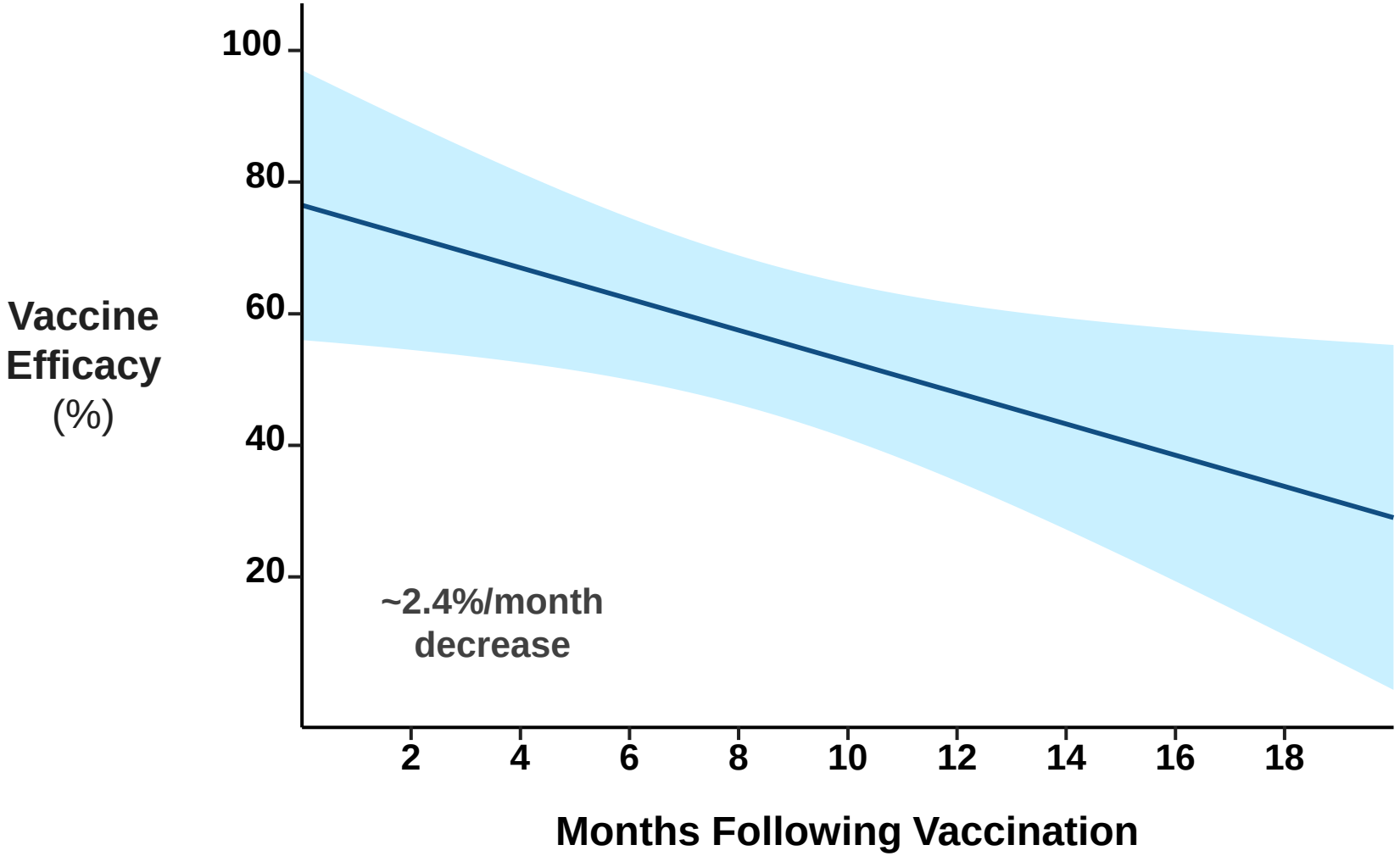
	Vaccine Efficacy (95% CI)		
	Primary Analysis *3.7 Months Median (0.5 - 12.6) Follow-up*	**Additional Analysis** *8.6 Months Median (0.4 – 17.7) Follow-up*	**March 2024 Analysis,** *18 Month*
RSV-LRTD Associated Shortness of Breath[1,2]	**86.7%** (41.9%, 97.0%)	**74.6%** (50.7%, 86.9%)	**56.7%** (33.1%, 72.6%)

- Shortness of breath is a key driver of seeking a higher level of care[1,2]
- Vaccine is efficacious in preventing shortness of breath associated with RSV-LRTD
- Too few hospitalizations to assess vaccine efficacy

1. Falsey et al NEJM, 2005; 2. Panozzo et al ESWI, 2023

Efficacy of mRNA-1345 Against RSV LRTD with ≥ 2 Symptoms Among Adults ≥ 60 Years Over Time

Study 301 – Post Hoc Analysis



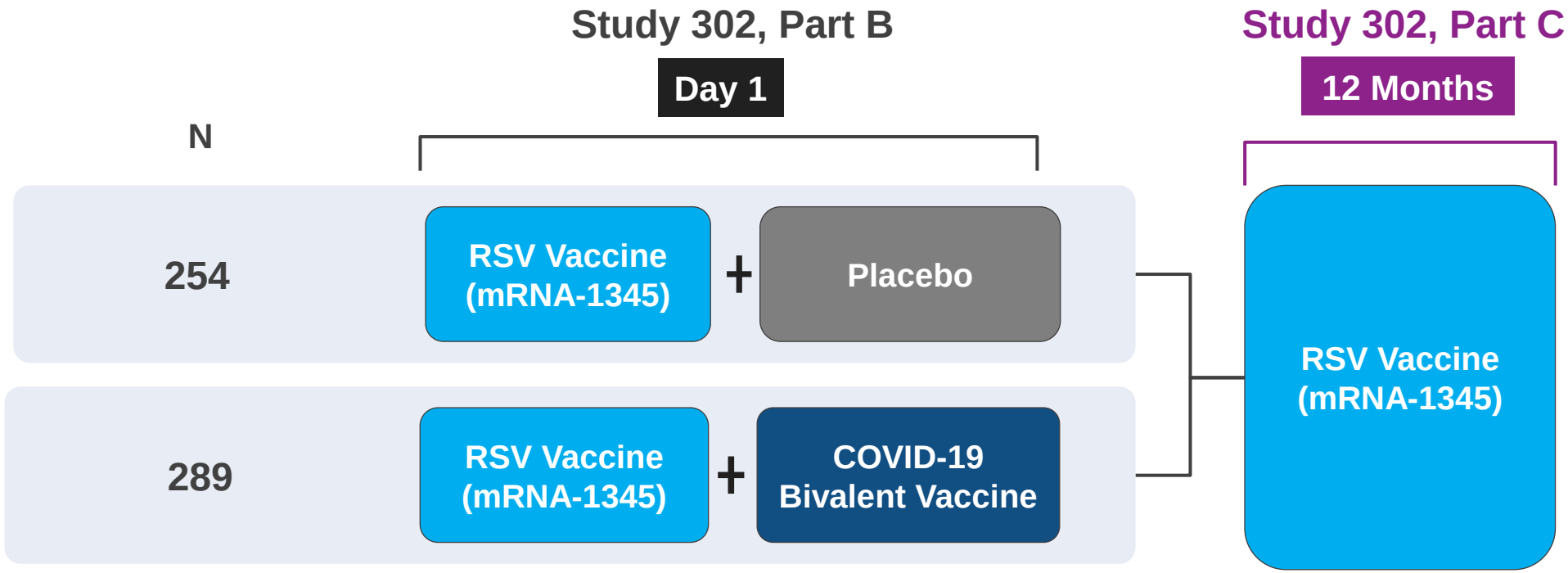
Weighted least square regression line and 95% CI (blue area) based on the bi-monthly VEs calculated using incidence rates adjusting person time over two-month periods

Persistence of RSV Antibody and Revaccination at 12 Months

Study 302

Vaccination Regimen

Study 302, Parts B & C



Participants from Study 302, Part B, were enrolled in Part C and revaccinated with RSV vaccine at 12 months

Safety Events of Interest – Revaccination at 12 Months with mRNA-1345

Study 302 C – Based on 2 Months Follow-up

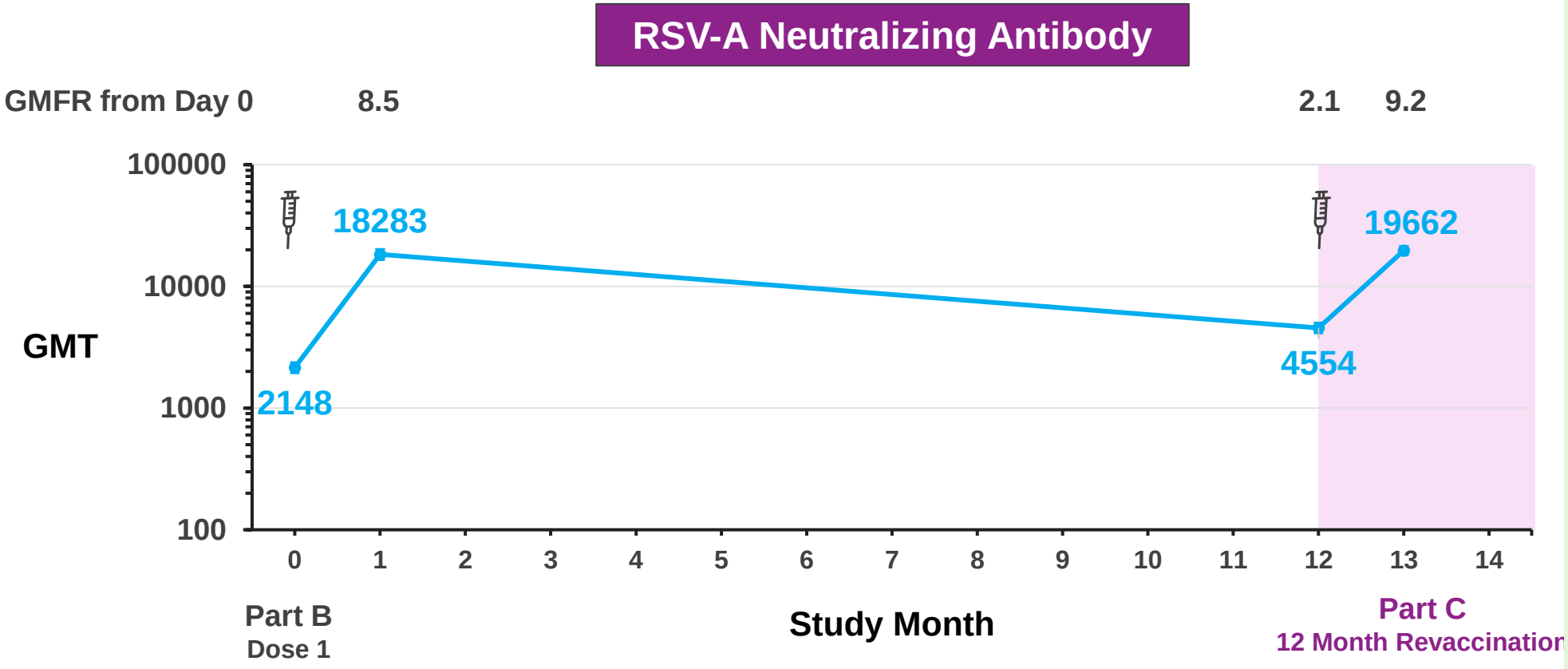
Safety Set

- No reports of:
  - Deaths, SAEs, or AESIs as assessed as related by the investigator
  - Anaphylaxis
  - Guillain Barre Syndrome
  - Acute disseminated encephalomyelitis (ADEM)
  - Bell's palsy/facial paralysis
  - Acute myocarditis or acute pericarditis

SAE – serious adverse event; AESI – adverse event of special interest
Dec 4, 2023 data cutoff

Durability of Neutralizing Antibody Responses Following Primary Dose and Revaccination at 12 Months with mRNA-1345

Study 302C – Adults ≥50 Years



GMR of revaccination vs first dose:

- **RSV-A - 1.08 (0.99, 1.17)**
- **RSV-B - 0.91 (0.84, 0.99)**

Non-inferiority criteria met (LB of 95% CI of GMR > 0.667) for RSV-A and RSV-B

- RSV-A and RSV-B neutralizing antibodies detectable at 12 months post-vaccination
- Revaccination with mRNA-1345 as soon as 1 year after primary vaccination elicits responses similar to that following primary vaccination
- Revaccination met pre-specified non-inferiority success criteria

SUMMARY

Summary
RSV Vaccine (mRNA-1345)

Safety	▪ Vaccine generally well tolerated in >19,700 adults ≥ 60 years vaccinated with 50 μg licensed dose ▪ No ADEM, no vaccine-related cases of GBS, or other safety concerns
Efficacy	▪ Efficacious through median of ~19 months follow-up ▪ Comparable efficacy in individuals ≥ 80-year-olds, with ≥ 1 comorbidity, and frail ▪ Shown to prevent severe RSV disease based on analysis of shortness of breath
Immunogenicity/ Revaccination	▪ Strong humoral and cellular immune responses[1] *(ACIP Feb 2024)* ▪ Neutralizing antibody detectable through 12 months post-vaccination ▪ Revaccination with mRNA-1345 as soon as 1 year after primary vaccination elicits responses similar to that following primary vaccination ▪ Revaccination well tolerated; no safety concerns
Concomitant Administration	▪ Pre-specified immunogenicity criteria met & and no new safety concerns observed with concomitant administration of mRNA-1345 with standard influenza & COVID-19 vaccines *(ACIP Feb 2024)*

[1] Goswami et al, *JID*, 2024

THANK YOU!

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