Meeting of the Advisory Committee on Immunization Practices (ACIP)

Centers for Disease Control and Prevention

April 16, 2025

Susan Gerber, MD

Medical Director

GSK

AREXVY Indications and Updates

AREXVY is indicated for active immunization for prevention of lower respiratory tract disease (LRTD) caused by RSV in

- Individuals **≥ 60 YOA**
- Individuals **50-59 YOA** at increased risk for LRTD caused by RSV

~ 11 million AREXVY doses administered in US through March*

*Up to March 2025; YOA, years of age; LRTD: lower respiratory tract disease

FDA, 2024. AREXVY Prescribing Information (PI); https://www.fda.gov/media/167805/download (URL accessed January 2025)

Clinical Development

Key Studies in Current US Clinical Development Plan

Pivotal efficacy in ≥ 60 YOA

- AReSVi-006
- **Complete**

Safety, immunogenicity, persistence and revaccination in ≥ 60 YOA

- RSV OA=ADJ-012
- Ongoing
- Extension of AReSVi-006

Safety, immunogenicity, persistence and revaccination in ≥ 60 YOA

- AReSVi-004
- Ongoing

Co-administration[7–12]

- **COVID-19 mRNA** vaccine (RSV OA=ADJ-013; Ongoing)
- **PCV20** (RSV OA=ADJ-019; **Complete**)
- **HZ/su** (RSV OA=ADJ-020; **Complete**)
- **FLU-QIV** (RSV OA=ADJ-007; **Complete**)
- **FLU-aQIV** (RSV OA=ADJ-017; **Complete**)
- **FLU-QIV-HD** (RSV OA=ADJ-008; **Complete**)

Immunogenicity & safety in 50-59 YOA (incl. AIR)

- RSV OA=ADJ-018
- **Complete**

Immunogenicity & safety in 18-49 YOA AIR

- RSV OA=ADJ-025
- Ongoing

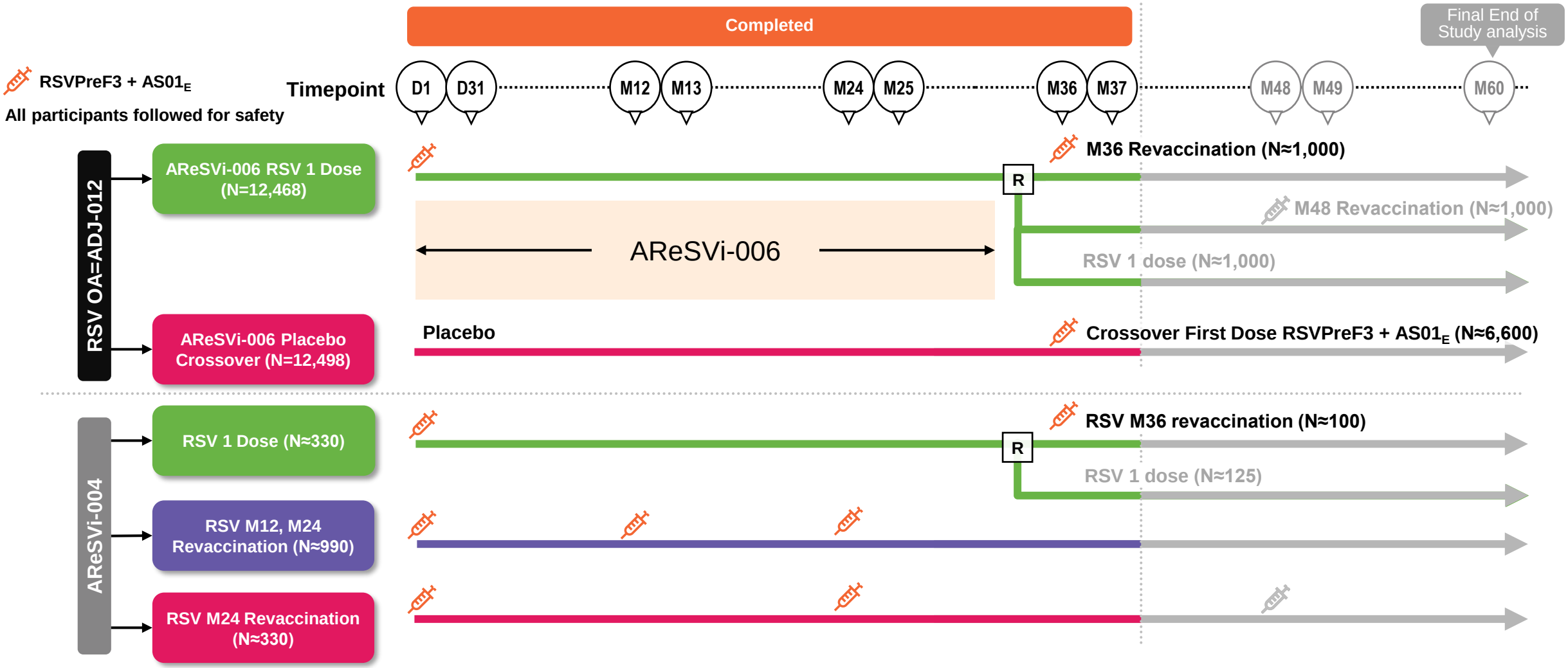
Immunogenicity & safety in Immunocompromised ≥ 18 YOA (lung and kidney SOT)

- RSV OA=ADJ-023
- Ongoing

Phase 2b **Phase 3**

AIR, at increased risk; FLU-aQIV, adjuvanted quadrivalent influenza vaccine; FLU-QIV, quadrivalent influenza vaccine; FLU-QIV-HD, high-dose quadrivalent influenza vaccine; HZ/su, herpes zoster recombinant subunit vaccine; PCV20, 20-valent pneumococcal conjugate vaccine; SOT, solid organ transplant; YOA, years of age;All studies ClinicalTrials.gov; All URLs accessed February 2025

Immunogenicity of AREXVY in Adults ≥ 60 YOA Evaluated in Two Complementary Trials



All studies available on clinicaltrials.gov; All URLs accessed April 2025.

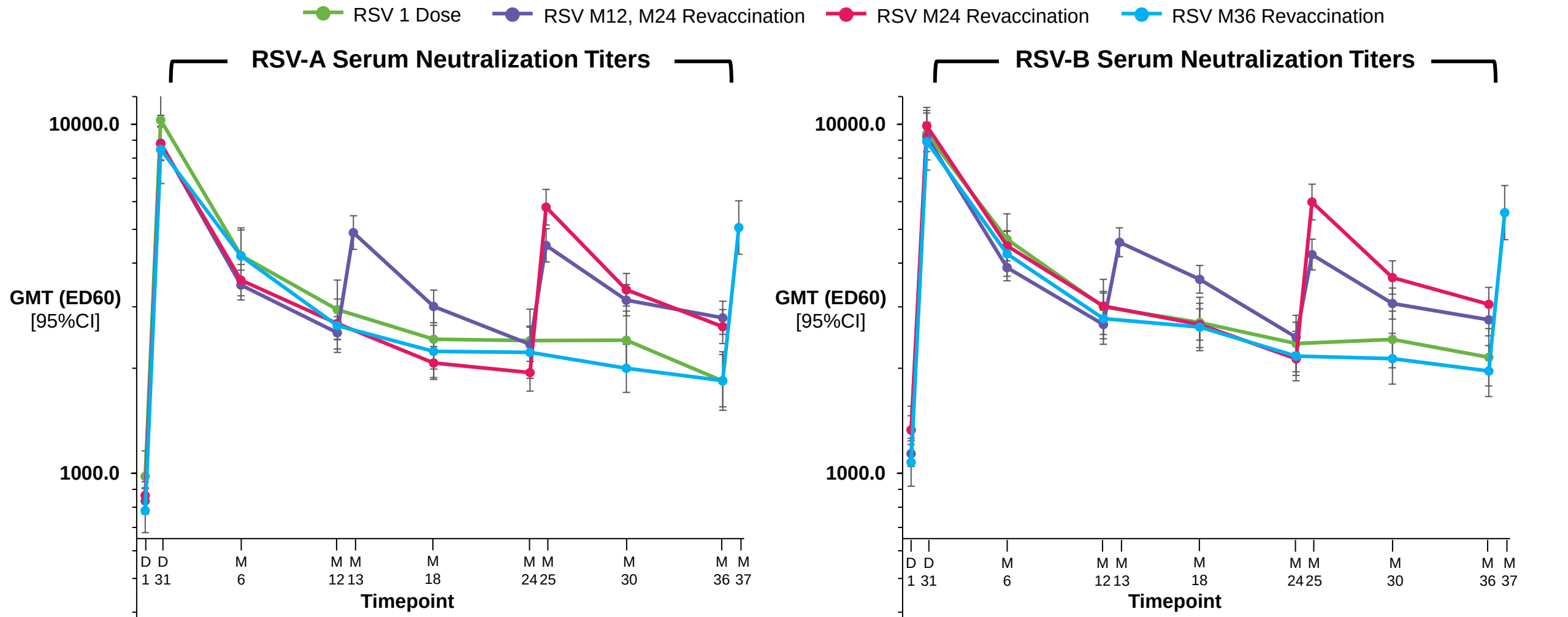
AReSVi-004: Immunogenicity and Persistence of Single Dose of AREXVY Vaccine and Different Revaccination Schedules in Adults ≥ 60 YOA

Randomized, open-label, multi-country study (NCT04732871)

Preliminary updated results

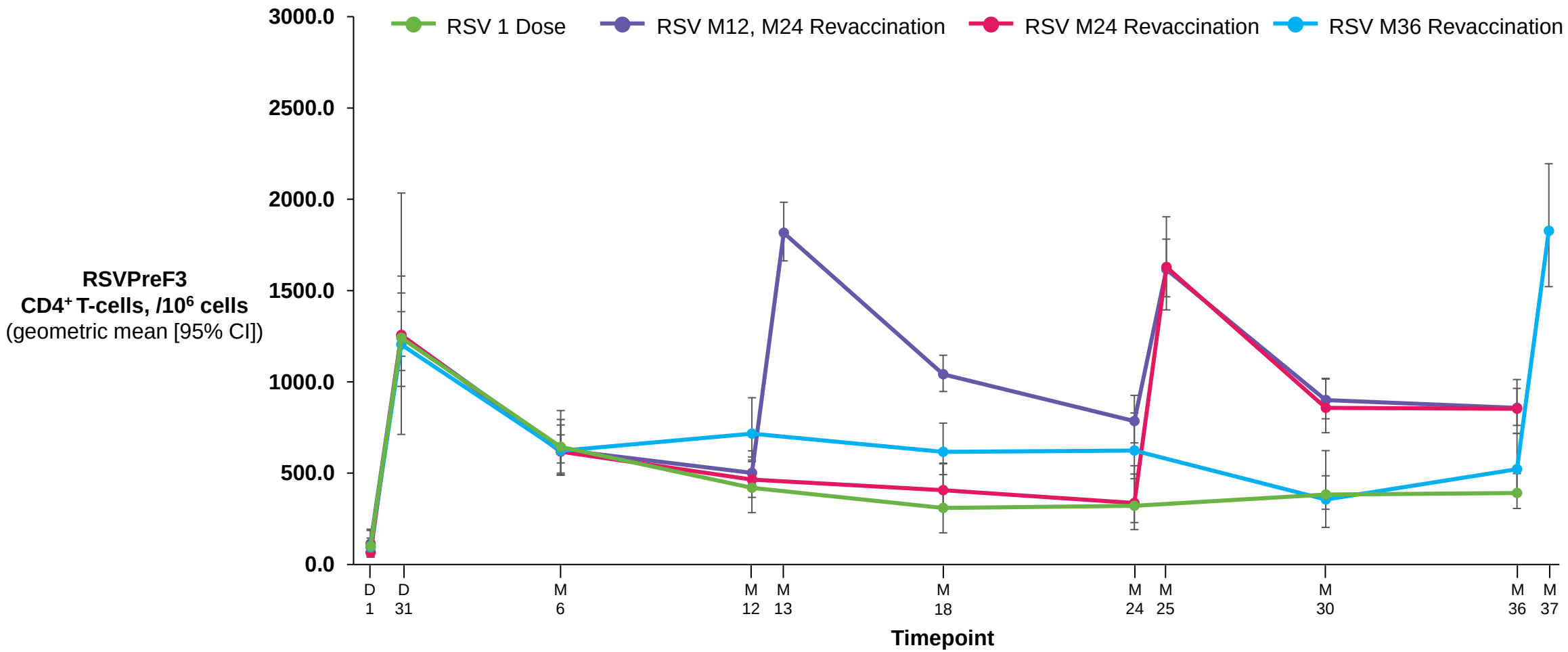
Presentation by GSK at ACIP April 16, 2025

RSV-A and RSV-B Neutralizing Antibody Titers After 12-, 24-, and 36-Month Vaccination Intervals



RSV 1 dose (N=112-121): Participants receiving single dose (Dose 1) of RSVPreF3 + AS01$_E$ at Day 1; RSV M12, M24 revaccination (N=247-341): Participants receiving first dose (Dose 1) of RSVPreF3 + AS01$_E$ at Day 1, followed by revaccination doses at 12 months and 24 months post Dose 1; RSV M24 revaccination (N=223-318): Participants receiving first dose (Dose 1) of RSVPreF3 + AS01$_E$ at Day 1 followed by revaccination dose at 24 months post Dose 1; RSV M36 Revaccination (N=98-107): Participants receiving first dose (Dose 1) of RSVPreF3 + AS01$_E$ at Day 1, followed by revaccination dose at 36 months post Dose 1. ED, estimated dilution; GMT, geometric mean titer

RSVPreF3-Specific CD4+ T-Cells*: Consistent Responses Post Each Vaccination Dose



*Expressing ≥ 2 activation markers including ≥ 1 cytokine among CD40L, 4-1BB, IL-2, TNF-a, IFN-g, IL-13, IL-17; RSV 1 dose (N=31-42): Participants receiving single dose (Dose 1) of RSVPreF3 + $AS01_E$ at Day 1; RSV M12, M24 revaccination (N=215-286): Participants receiving first dose (Dose 1) of RSVPreF3 + $AS01_E$ at Day 1, followed by revaccination doses at 12 months and 24 months post Dose 1; RSV M24 revaccination (N=68-88): Participants receiving first dose (Dose 1) of RSVPreF3 + $AS01_E$ at Day 1 followed by revaccination dose at 24 months post Dose 1; RSV M36 Revaccination (N=31-37): Participants receiving first dose (Dose 1) of RSVPreF3 + $AS01_E$ at Day 1, followed by revaccination dose at 36 months post Dose 1.

CD, cluster of differentiation; IL, interleukin; NAb, neutralizing antibody; TNF, tumor necrosis factor

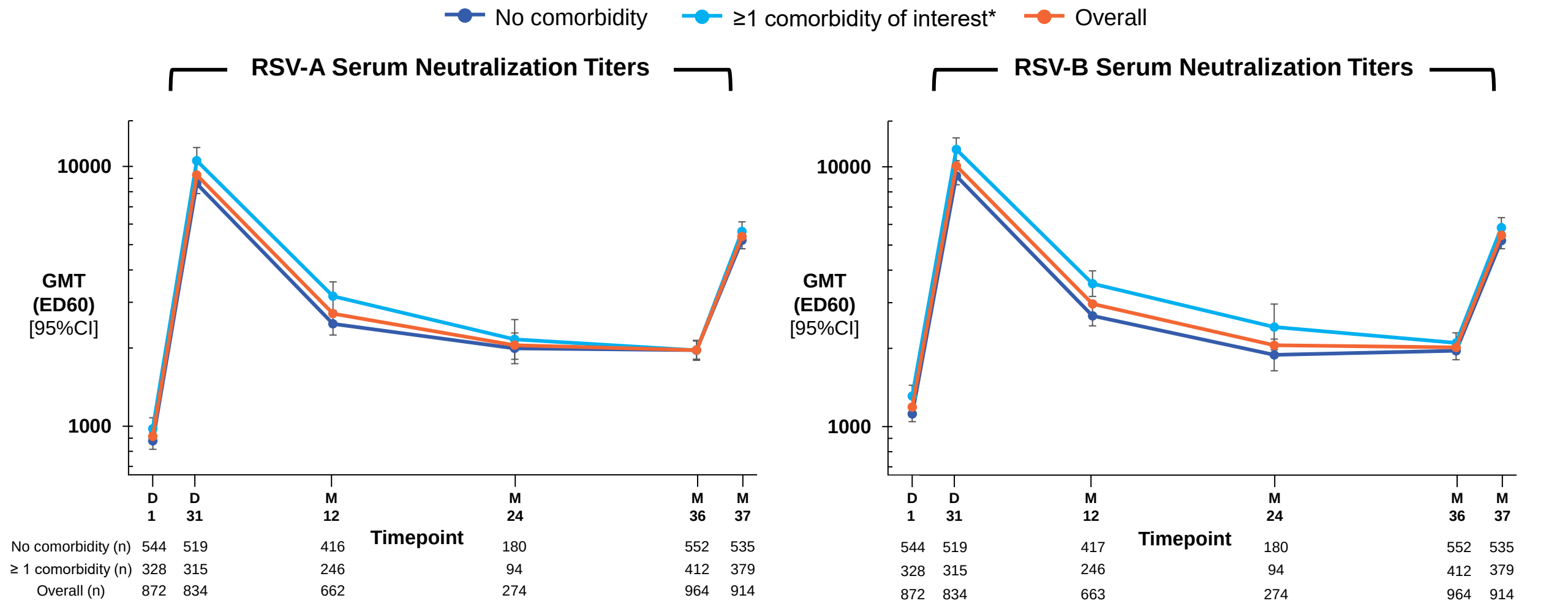
RSV OA=ADJ-012: Immunogenicity of Different Revaccination Schedules and Persistence of a Single Dose of AREXVY Vaccine in Adults Aged ≥ 60 YOA Who Participated in Pivotal AReSVi-006 Efficacy Study

Open-label extension and crossover study (NCT06534892)

Preliminary results

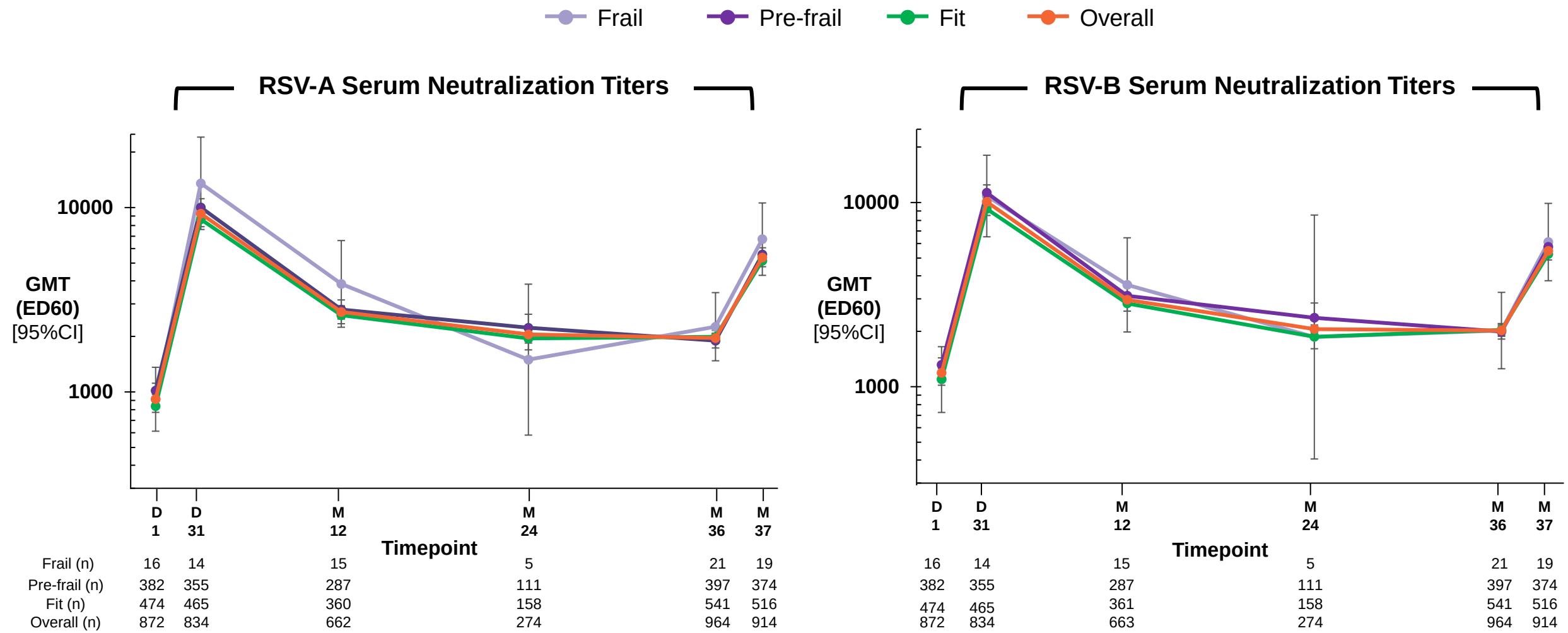
Presentation by GSK at ACIP April 16, 2025

RSV-A and RSV-B NAb Titers After Initial Dose and 36-Month Revaccination Similar Regardless of Comorbidities of Interest*



*COPD, asthma, any chronic respiratory/pulmonary disease, diabetes type 1 or type 2, chronic heart failure, advanced liver or renal disease; ED, estimated dilution; GMT, geometric mean titer; NAb, neutralizing antibody; 1. Unpublished data; 2. Feldman RG et al. *Clin Infect Dis* 2024; Day 1 to M12: All participants who received one dose of RSVPreF3 + $AS01_E$ in AReSVi-006 (Immunosubset); M24: All participants randomized into RSV_1dose group (Immunosubset) in AReSVi-006 who did not receive additional doses of vaccine;
M36 - M37: All participants who received second dose of RSVPreF3 + $AS01_E$ approximately 36 Months post-primary dose

RSV-A and RSV-B NAb Titers After Initial Dose and 36-Month Revaccination Similar Regardless of Frailty Status



	D 1	D 31	M 12	M 24	M 36	M 37
Frail (n)	16	14	15	5	21	19
Pre-frail (n)	382	355	287	111	397	374
Fit (n)	474	465	360	158	541	516
Overall (n)	872	834	662	274	964	914

	D 1	D 31	M 12	M 24	M 36	M 37
Frail (n)	16	14	15	5	21	19
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Overall (n)	872	834	663	274	964	914

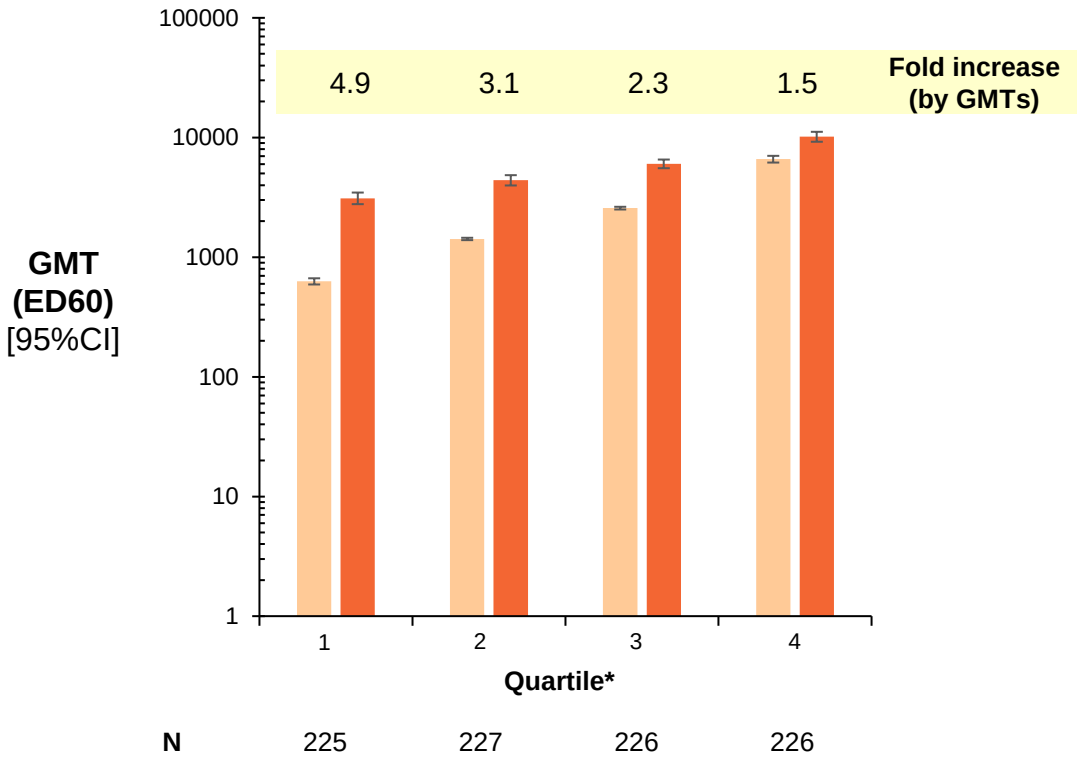
ED, estimated dilution; GMT, geometric mean titer; NAb, neutralizing antibody; Unpublished data; Day 1 to M12: All participants who received one dose of adjuvanted RSVPreF3 vaccine in RSV OA=ADJ-006 (Immunosubset); M24: All participants randomized into the RSV_1dose group (Immunosubset) in RSV OA=ADJ-006 who did not receive additional doses of vaccine; M36 - M37: All participants who received a second dose of adjuvanted RSVPreF3 vaccine approximately 36 Months post-primary dose

Increase in RSV-A and RSV-B NAb Titers Following Revaccination with AREXVY at 36 Months Across Pre-Revaccination Levels

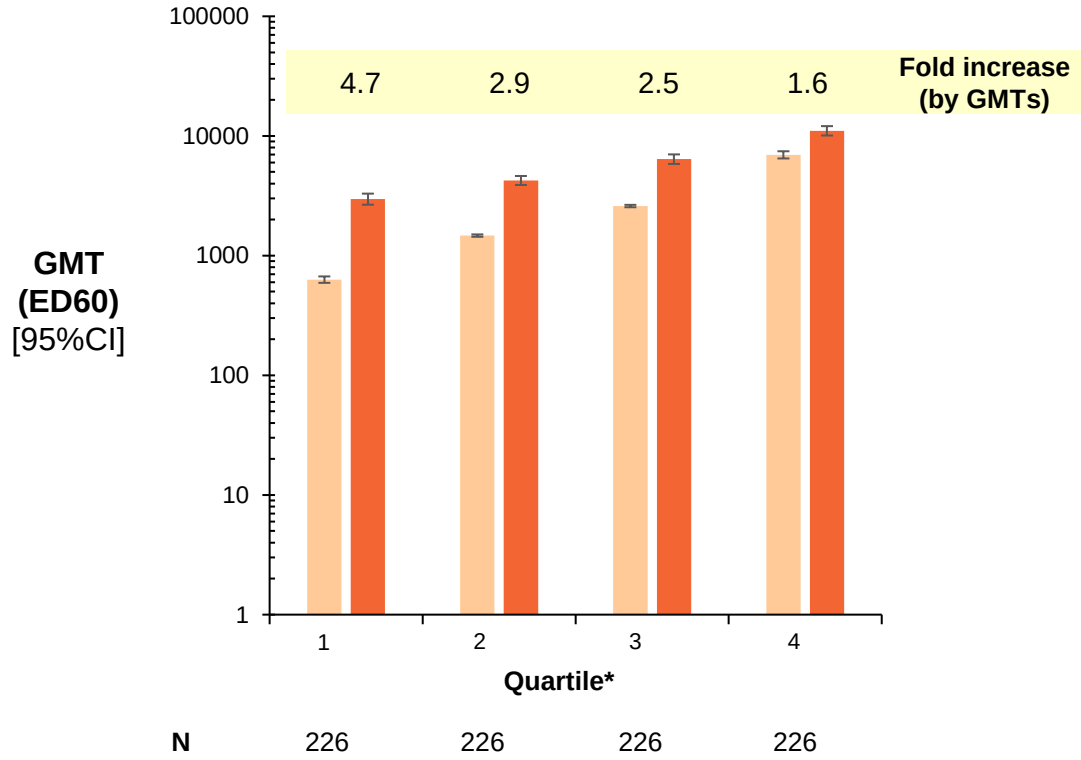
Pre-revaccination (Month 36)

Post-revaccination (Month 37)

RSV-A Serum Neutralization Titers



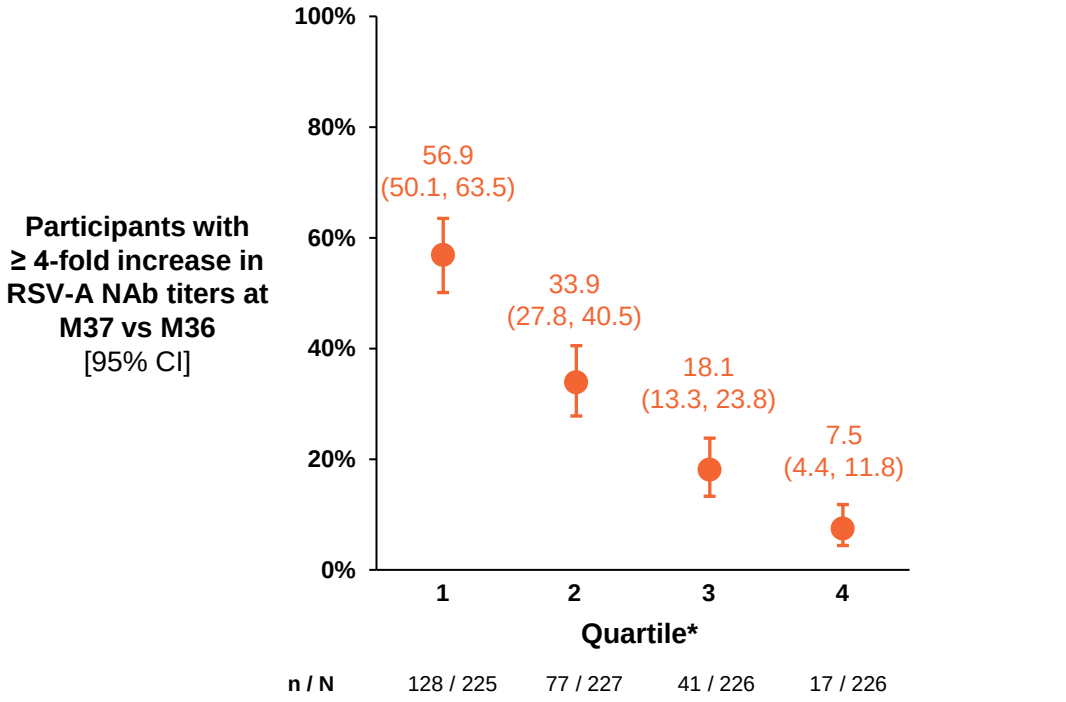
RSV-B Serum Neutralization Titers



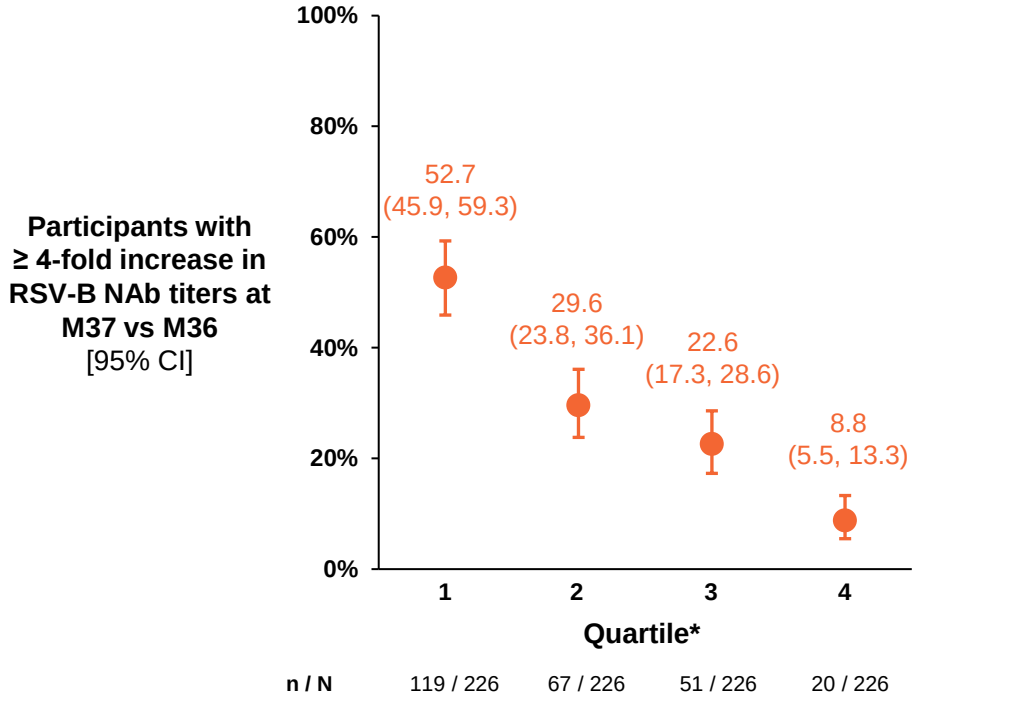
*Participants grouped into quartiles depending on pre-revaccination NAb titers. Participants in quartile 1 had lowest pre-revaccination NAb and those in quartile 4 had highest; Participants receiving first dose (Dose 1) of RSVPreF3 + AS01$_E$ at Day 1 (in AReSVi-006 study) followed by revaccination dose at 36 months post Dose 1 (in RSV OA=ADJ-012 study); ED, estimated dilution; GMT, geometric mean titer; NAb, neutralizing antibody
Unpublished data

Lower Pre-Revaccination RSV-A and RSV-B NAb Titers Associated with Higher Seroresponse Rates (≥ 4-Fold Increase) After Revaccination at 36 Months

RSV-A Serum Neutralization Titers



RSV-B Serum Neutralization Titers



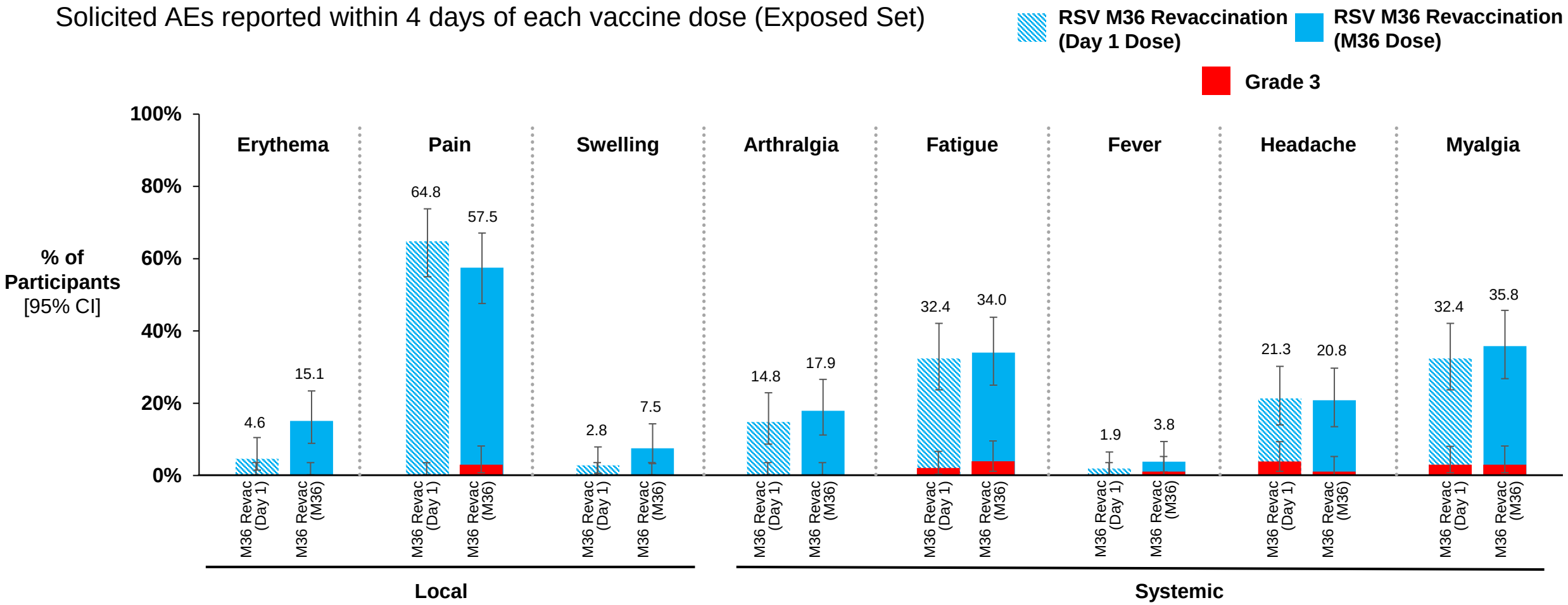
*Participants grouped into quartiles depending on pre-revaccination NAb titers. Participants in quartile 1 had lowest pre-revaccination NAb and those in quartile 4 had highest; Participants receiving first dose (Dose 1) of RSVPreF3 + AS01$_E$ at Day 1 (in AReSVi-006 study) followed by revaccination dose at 36 months post Dose 1 (in RSV OA=ADJ-012 study); NAb, neutralizing antibody

AReSVi-004 and RSV OA=ADJ-012: Safety Results

Preliminary updated results

Safety and Reactogenicity Profile in Individuals Revaccinated at Month 36 Similar to First Dose

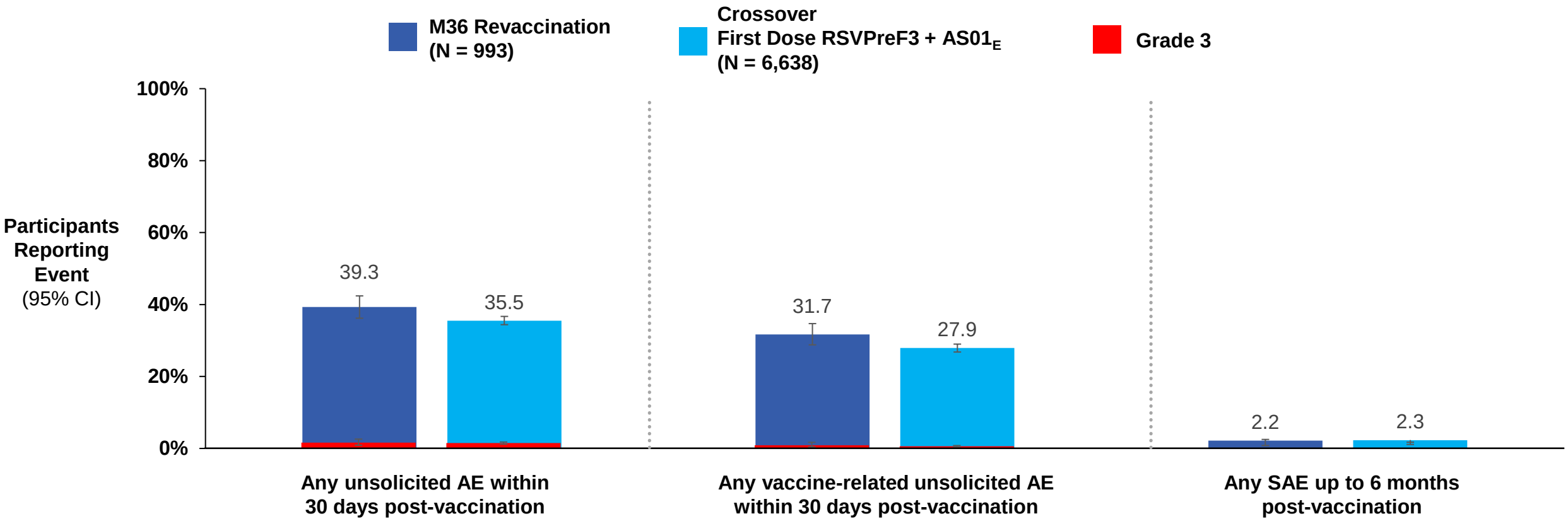
Solicited AEs reported within 4 days of each vaccine dose (Exposed Set)



Unsolicited AEs, SAEs, Fatal SAEs and pIMDs of individuals who were revaccinated at Month 36 also similar to those vaccinated at Day 1

RSV 36M revaccination: Participants receiving the first dose (Day 1 Dose) of RSVPreF3 + AS01$_E$ at Day 1 followed by a revaccination dose at 36 months (M36 Dose) post-Dose 1.
Grade 3: >100 mm for erythema and swelling; significant pain at rest, prevents normal everyday activities for pain; prevents normal activity for headache, fatigue, myalgia, and arthralgia; >39.0°C (102.2°F) for fever. AE, adverse event; SAE, serious adverse event; pIMD, potential immune-mediated disease

Safety Profile of Revaccination at Month 36 Similar to First-Vaccination Dose in Crossover Group



- Safety profile after revaccination of AREXVY acceptable and consistent with first dose in RSV OA=ADJ-012
- No events of GBS or ADEM reported in RSV OA=ADJ-012

*Solicited AEs not collected in RSV OA=ADJ-012

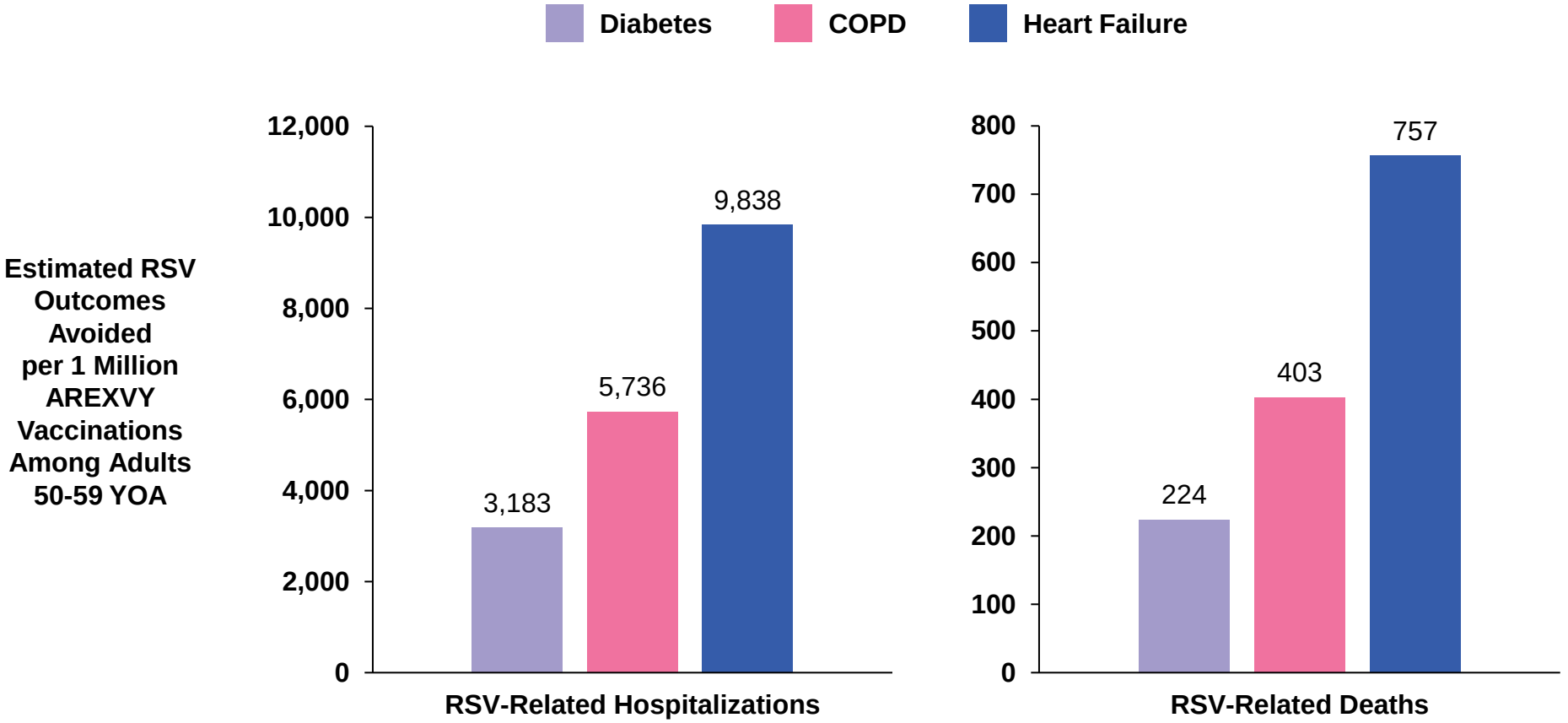
Summary: AReSVi-004 and RSV OA=ADJ-012

Robust humoral and cellular immune responses observed with AREXVY revaccination

- Humoral immune responses similar among participants with ≥ 1 comorbidity of interest or frailty status compared to overall population
- RSV neutralizing antibody responses observed after revaccination at 36-month interval similar to RSV neutralizing antibody responses after revaccination at 24-month interval
- The lower the pre-revaccination RSV-A and RSV-B neutralizing titers, the higher the seroresponse rates after revaccination at 36 months

Safety and reactogenicity of revaccination is similar as compared with first dose

RSV Outcomes Estimated to be Avoided with Vaccination vs No Vaccination Over 3 Years Based on Vaccine Efficacy Results from AReSVi-006 (30.6-Month Median Follow Up)



Estimates are based on GSK modeling that synthesized multiple published and public sources, and involved assumptions to inform certain parameters, including variability in RSV-related mortality by age. Key references for model inputs include: Singer et al., Poster Presentation at RSV Symposium 2025; La et al., Human Vaccines & Immunotherapeutics, 2024; Branche et al., Clin Infect Dis, 2022; McLaughlin et al., Open Forum Infect Dis, 2022; Tseng et al., J Infect Dis, 2020; Ison et al., Poster Presentation at CHEST 2024.
COPD = chronic obstructive pulmonary disease; YOA = years of age

Conclusion

Evidence to support revaccination with AREXVY

- Robust humoral and cellular immune responses following revaccination at 24 and 36-month intervals
- Lower pre-revaccination titers elicit higher seroresponse rates after revaccination
- Safety and reactogenicity of revaccination is similar as compared with first dose

Real world vaccine effectiveness data, along with ongoing immunogenicity studies, will inform optimal revaccination timing

~13 million US adults 50-59 YOA at risk for severe RSV disease

- Over 3 years, vaccination with AREXVY* may help prevent an estimated
  - ~3,218 hospitalizations in individuals with **heart failure**
  - ~8,638 hospitalizations in individuals with **COPD**
  - ~8,164 hospitalizations in individuals with **diabetes**

*Based on GSK modeling 46.2% uptake = flu vaccine uptake in group

Meeting of the Advisory Committee on Immunization Practices (ACIP)

Centers for Disease Control and Prevention

April 16, 2025

Susan Gerber, MD

Medical Director

GSK

AREXVY Indication

AREXVY is a vaccine indicated for active immunization for the prevention of lower respiratory tract disease (LRTD) caused by respiratory syncytial virus (RSV) in:

- individuals 60 years of age and older;
- individuals 50 through 59 years of age who are at increased risk for LRTD caused by RSV

AREXVY Important Safety Information

- AREXVY is contraindicated in anyone with a history of a severe allergic reaction (eg, anaphylaxis) to any component of AREXVY
- The results of a postmarketing observational study suggest an increased risk of Guillain-Barré syndrome during the 42 days following vaccination with AREXVY
- Appropriate medical treatment must be immediately available to manage potential anaphylactic reactions following administration of AREXVY
- Syncope (fainting) may occur in association with administration of injectable vaccines, including AREXVY. Procedures should be in place to avoid injury from fainting
- Immunocompromised persons, including those receiving immunosuppressive therapy, may have a diminished immune response to AREXVY
- In adults 60 years of age and older, the most commonly reported adverse reactions (≥10%) were injection site pain (60.9%), fatigue (33.6%), myalgia (28.9%), headache (27.2%), and arthralgia (18.1%)
- In adults 50 through 59 years of age, the most commonly reported adverse reactions (≥10%) were injection site pain (75.8%), fatigue (39.8%), myalgia (35.6%), headache (31.7%), arthralgia (23.4%), erythema (13.2%), and swelling (10.4%)
- There are no data on the use of AREXVY in pregnant or breastfeeding individuals. AREXVY is not approved for use in persons <50 years of age
- Vaccination with AREXVY may not result in protection of all vaccine recipients