

# GSK's RSVPreF3 OA Vaccine (AREXVY)

*AREXVY was approved by FDA on May 3, 2023, and is indicated for the prevention of LRTD caused by RSV in adults 60 and older, as a single dose.*

**ACIP June 21, 2023**

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Vice President, Scientific Affairs and Public Health



## Presentation Overview

### Efficacy and safety results over 2 full RSV seasons from pivotal Phase 3 Study

- 1 dose of AREXVY provides durable efficacy against RSV-associated LRTD over 2 full RSV seasons, including against severe RSV disease, in adults with underlying comorbidities, and across advancing ages
- 2<sup>nd</sup> dose 12 months after 1<sup>st</sup> dose does not appear to confer additional efficacy in overall population

### Immunogenicity and safety results from 2 co-administration trials with influenza vaccines (adjuvanted, high dose)

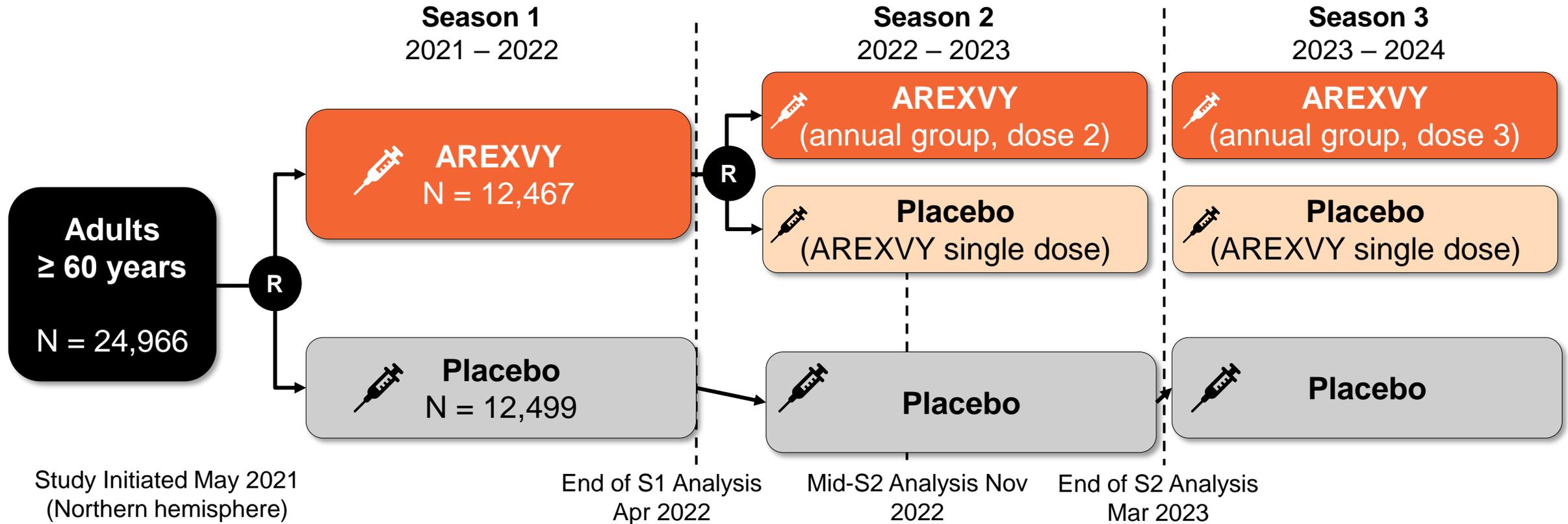
- AREXVY can be administered with all types of commonly used influenza vaccines

# Pivotal Efficacy and Safety Study (AReSVi-006): Results Through 2 Full RSV Seasons

Phase 3, randomized, placebo-controlled, multi-country study to demonstrate efficacy and safety of single and annual revaccination doses in adults 60 years and older

# Ongoing AReSVi-006 Phase 3 Trial Design

Randomized, placebo-controlled, observer-blind, multi-country efficacy study



**Confirmatory secondary endpoint: Evaluate efficacy of AREXVY in prevention of RSV\*-LRTD<sup>†</sup> in adults ≥ 60 YOA over 2 seasons, following a single dose of AREXVY and following annual revaccination dose**

- All RSV-LRTD cases adjudicated by independent external adjudication committee
- Success criterion: lower limit of 2-sided 97.5% CI for vaccine efficacy > 20%

# AReSVi-006 Case Definitions

## ARI

≥ 2 respiratory symptoms or signs  
OR  
 ≥ 1 respiratory and 1 systemic symptom or sign for at least 24 hours

### Systemic symptoms or signs

- Fever/feverishness
- Fatigue
- Body aches
- Headache
- Decreased appetite

### Respiratory symptoms or signs

#### Upper respiratory symptoms or signs

- Nasal congestion
- Sore throat

#### Lower respiratory symptoms

- Sputum
- Cough
- Dyspnea

#### Lower respiratory signs

- Wheezing
- Crackles/rhonchi
- Tachypnea
- Hypoxemia
- O2 supplement

## LRTD\*

≥ 2 lower respiratory symptoms or signs (≥ 1 sign)  
OR  
 ≥ 3 lower respiratory symptoms for at least 24 hours

#### Lower respiratory symptoms

- Sputum
- Cough
- Dyspnea

#### Lower respiratory signs

- Wheezing
- Crackles/rhonchi
- Tachypnea
- Hypoxemia
- O2 supplement

## Severe LRTD\*

≥ 2 lower respiratory signs  
OR  
 episode preventing normal, everyday activities

#### Lower respiratory signs

- Wheezing
- Crackles/rhonchi
- Tachypnea
- Hypoxemia
- O2 supplement

# AREXVY Produces Durable Vaccine Efficacy Against RSV-LRTD Over 2 Full Seasons

	Median Follow-Up (months)	AREXVY	Placebo			VE (95% CI)	VE (95% CI)
		Number of events				W/o season as covariate <sup>#</sup>	W/ season as covariate <sup>¶</sup>
<b>Single Dose</b>							
<b>Season 1*</b> VE 1	6.7	7 / 12,466	40 / 12,494			<b>82.6%</b> (57.9, 94.1)	<b>82.6%</b> (57.9, 94.1)
<b>Mid Season 2</b> Post dose 1	14	15 / 12,469	85 / 12,498			<b>80.9%<sup>#</sup></b> (66.7, 89.8)	<b>77.3%<sup>¶</sup></b> (60.2, 87.9)
<b>Season 2 Only</b> Post dose 2	6.4	20 / 4,991	91 / 10,031			<b>56.1%</b> (28.2, 74.4)	<b>56.1%</b> (28.2, 74.4)
<b>Season 1 + 2**</b>	18	30 / 12,469	139 / 12,498			<b>74.5%<sup>#</sup></b> (60.0, 84.5)	<b>67.2%<sup>¶</sup></b> (48.2, 80.0)
<b>Annual (2 doses, ~12 months apart)</b>							
<b>Season 2 Only</b> Post dose 2	6.4	20 / 4,966	91 / 10,031			<b>55.9%</b> (27.9, 74.3)	<b>55.9%</b> (27.9, 74.3)
<b>Seasons 1 + 2**</b>	18	30 / 12,469	139 / 12,498			<b>74.5%<sup>#</sup></b> (60.0, 84.4)	<b>67.1%<sup>¶</sup></b> (48.1, 80.0)

0 20 40 60 80 100

Modified exposed set

\*96.95% CI for VE 1; \*\*97.5% CI for Season 1 + 2

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# AREXVY Produces Durable Vaccine Efficacy Against RSV-Severe LRTD Over 2 Full Seasons

	Median Follow-Up (months)	AREXVY	Placebo			
		Number of events		VE (95% CI)	VE (95% CI)	
<b>Single Dose</b>				<i>W/o season as covariate<sup>#</sup></i>	<i>W/ season as covariate<sup>¶</sup></i>	
<b>Season 1*</b> VE 1	6.7	1 / 12,466	17 / 12,494		<b>94.1%</b> (62.4, 99.9)	<b>94.1%</b> (62.4, 99.9)
<b>Mid Season 2</b> Post dose 1	14	4 / 12,469	33 / 12,498		<b>86.8%<sup>#</sup></b> (63.0, 96.6)	<b>84.6%<sup>¶</sup></b> (56.4, 96.1)
<b>Season 2 Only</b> Post dose 2	6.4	5 / 4,991	28 / 10,031		<b>64.2%</b> (6.2, 89.2)	<b>64.2%</b> (6.2, 89.2)
<b>Season 1 + 2**</b>	18	7 / 12,469	48 / 12,498		<b>82.7%<sup>#</sup></b> (61.6, 93.4)	<b>78.8%<sup>¶</sup></b> (52.6, 92.0)
<b>Annual</b> (2 doses, ~12 months apart)						
<b>Season 2 Only</b> Post dose 2	6.4	5 / 4,966	28 / 10,031		<b>64.1%</b> (5.9, 89.2)	<b>64.1%</b> (5.9, 89.2)
<b>Seasons 1 + 2**</b>	18	7 / 12,469	48 / 12,498		<b>82.7%<sup>#</sup></b> (61.6, 93.4)	<b>78.8%<sup>¶</sup></b> (52.5, 92.0)

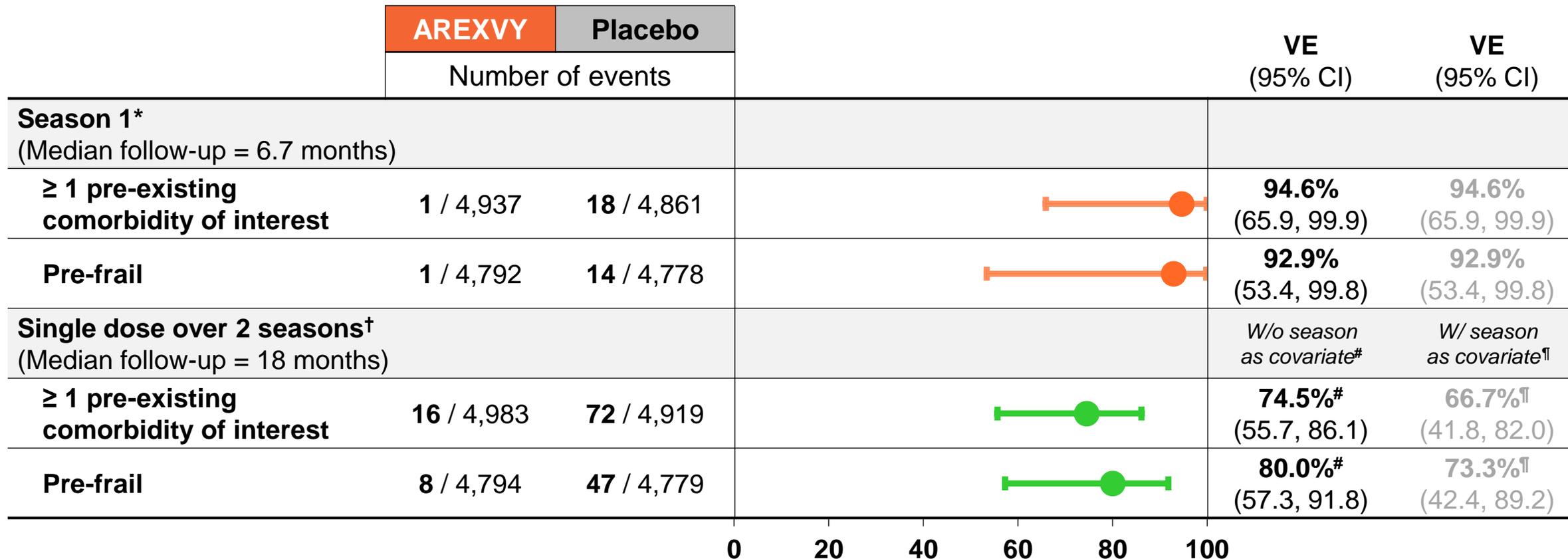
0 20 40 60 80 100

Modified exposed set

\*96.95% CI for VE 1; \*\*97.5% CI for Season 1 + 2

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# AREXVY Produces Durable Vaccine Efficacy Against RSV-LRTD in Vulnerable Populations Over 2 Full Seasons



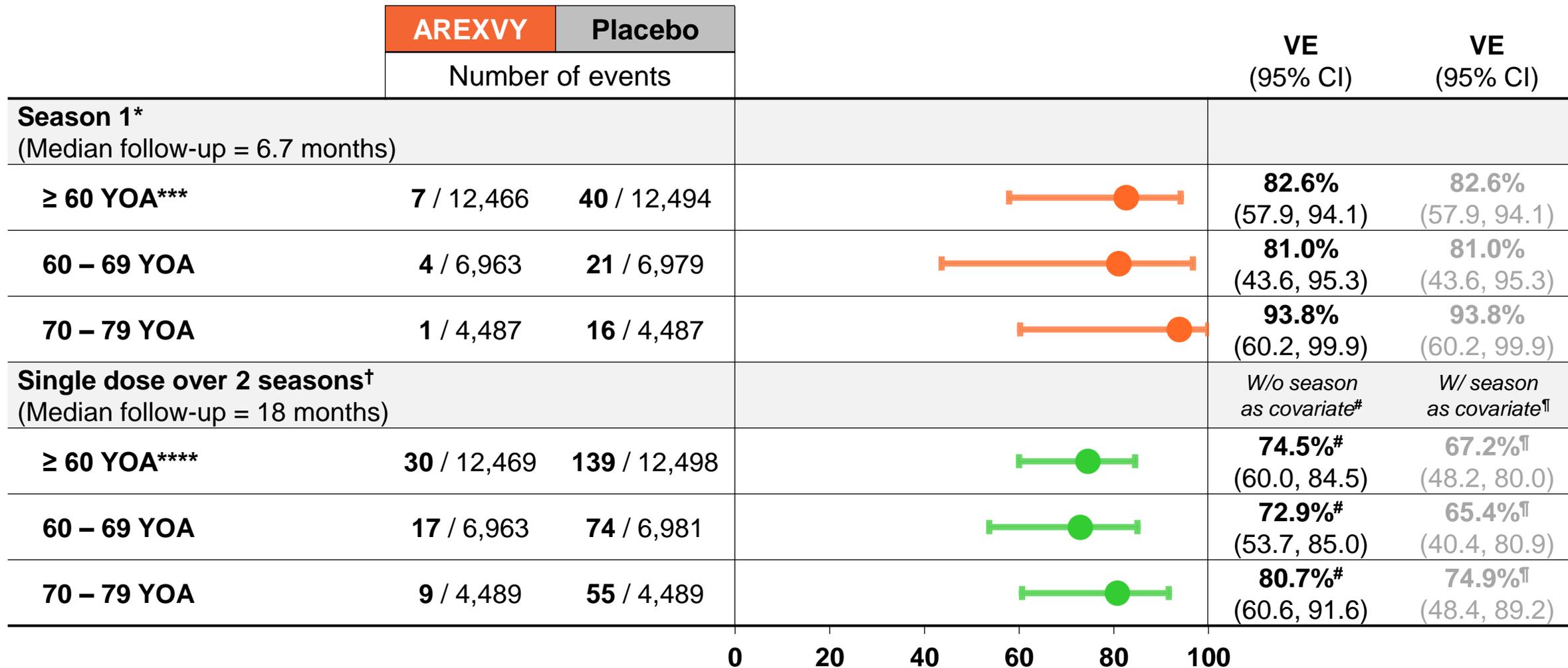
*Vaccine efficacy in frail participants cannot be concluded due to low number of cases accrued*

Comorbidities of interest include chronic obstructive pulmonary disease, asthma, any chronic respiratory or pulmonary disease, and chronic heart failure (cardiorespiratory condition) and diabetes mellitus type 1 or type 2 and advanced liver or renal disease (endocrine or metabolic condition)

\*April 2022 analysis; †From 15 days post Dose 1 up to end of Season 2 in Northern Hemisphere

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# AREXVY Produces Durable Vaccine Efficacy Against RSV LRTD Across Advancing Ages Over 2 Full Seasons

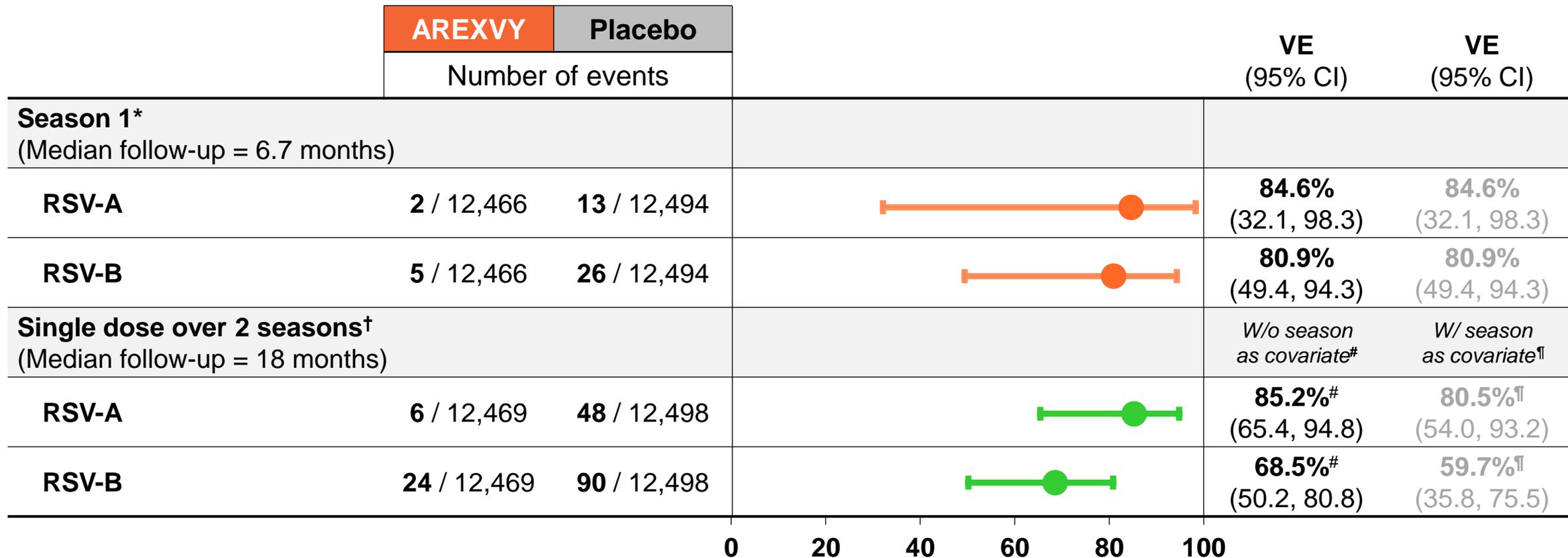


*Vaccine efficacy in adults ≥ 80 years of age cannot be concluded due to low number of cases accrued*

\*April 2022 analysis; \*\*\*96.95% CI; \*\*\*\*97.5% CI; YOA: years of age;

†From 15 days post Dose 1 up to end of Season 2 in Northern Hemisphere

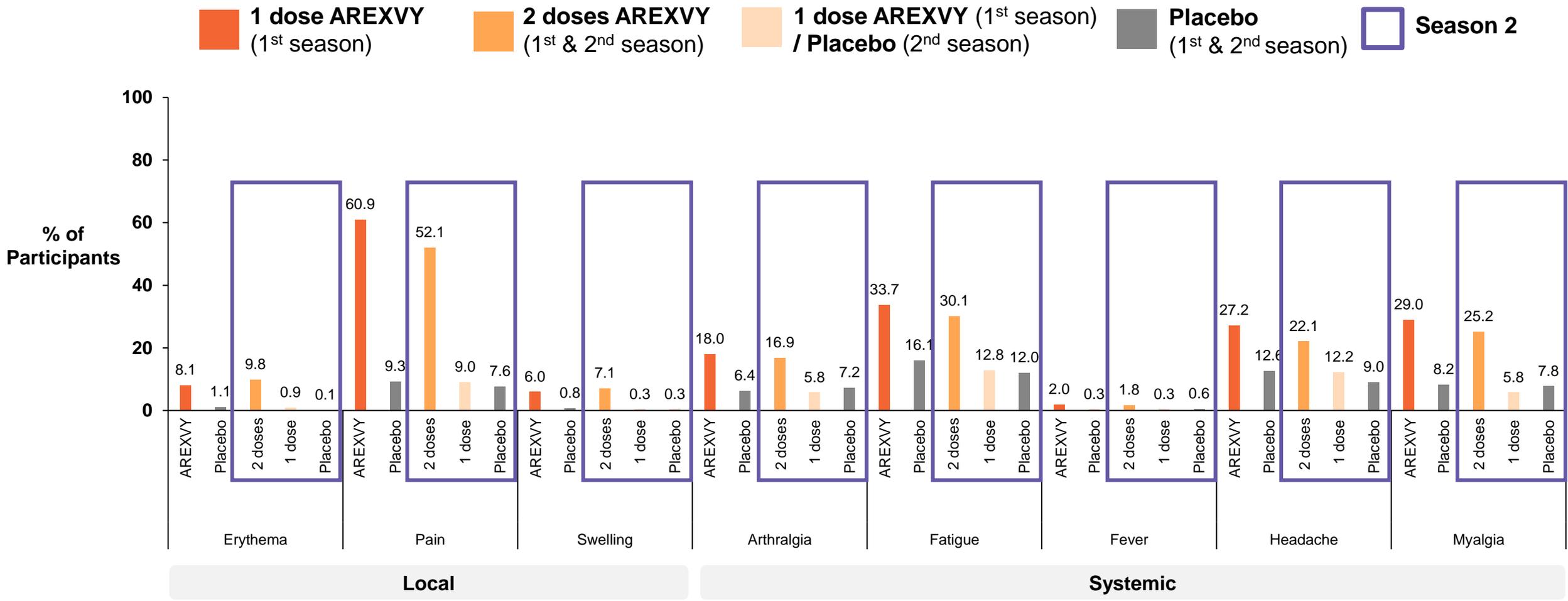
# AREXVY Produces Durable Vaccine Efficacy Against RSV-A LRTD and RSV-B LRTD Over 2 Full Seasons



\*April 2022 analysis; †From 15 days post Dose 1 up to end of Season 2 in Northern Hemisphere

# Reactogenicity Profile of 2<sup>nd</sup> Dose in Line with 1<sup>st</sup> Dose

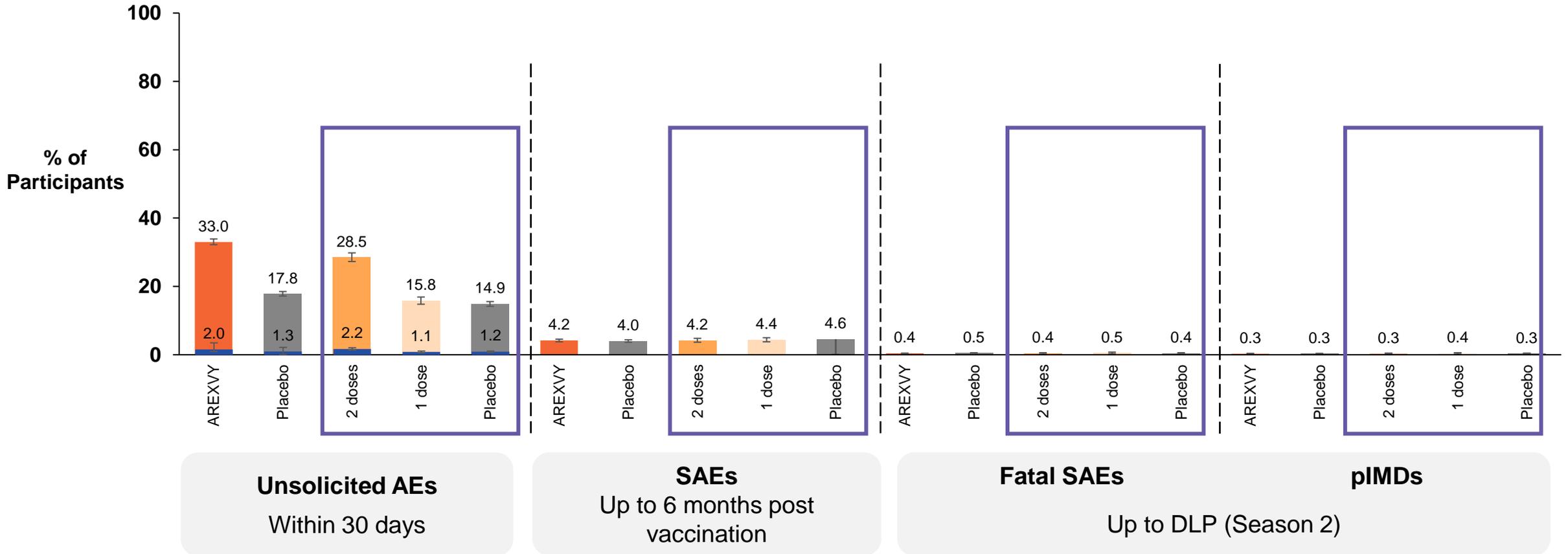
## Solicited AEs Reported Within 4 Days of Vaccination (Solicited Safety Set)



AREXVY Season 1 n=879; Placebo Season 1 n=878; 2 doses Season 2 n=326 (received AREXVY in Season 1 and Season 2);  
 1 dose Season 2 n=345 (received AREXVY in Season 1 and Placebo in Season 2);  
 Placebo Season 2 n=666 (received Placebo in Season 1 and Season 2)

# Safety Profile of 2<sup>nd</sup> Dose in Line with 1<sup>st</sup> Dose

Unsolicited AEs, SAEs, fatal SAEs, and pIMDs



**Unsolicited AEs**  
Within 30 days

**SAEs**  
Up to 6 months post vaccination

**Fatal SAEs**  
Up to DLP (Season 2)

**pIMDs**

AREXVY Season 1 n=12,467; Placebo Season 1 n=12,499; 2 doses Season 2 n=4,966 (received AREXVY in Season 1 and Season 2); 1 dose Season 2 n=4,991 (received AREXVY in Season 1 and Placebo in Season 2); Placebo Season 2 n=10,033 (received Placebo in Season 1 and Season 2)

DLP: data lock point; pIMD: potential immune-mediated disease

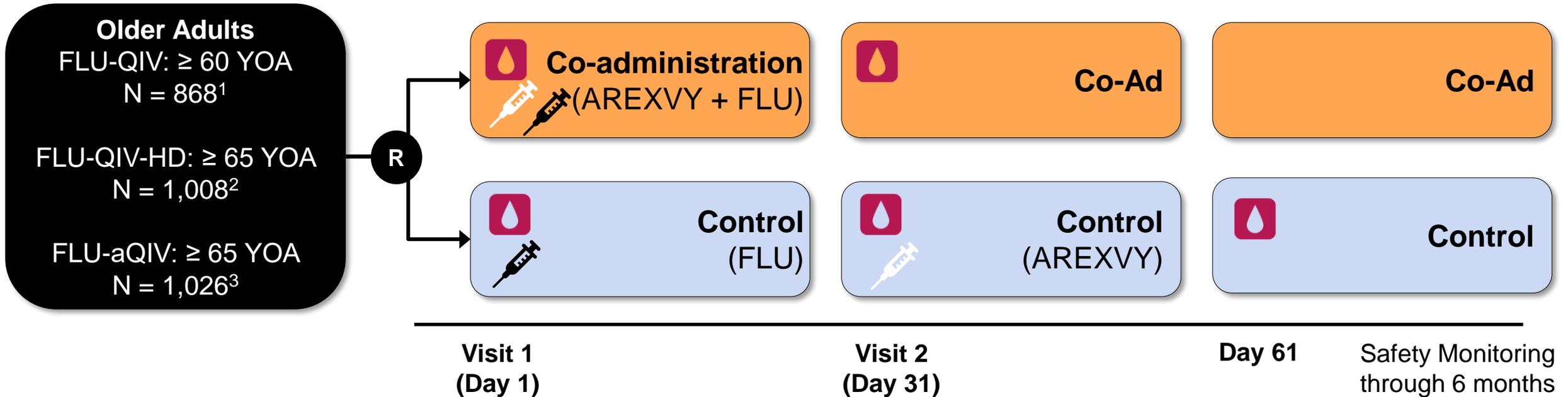
# Influenza Vaccine Co-administration Studies: Immunogenicity and Safety

Open-label, randomized, controlled, multi-country studies to evaluate immune response, safety, and reactogenicity of AREXVY when co-administered with influenza vaccines in adults aged 60 years and above (RSV OA=ADJ-007) or 65 years and above (RSV OA=ADJ-008 and RSV OA=ADJ-017)

# Phase 3 Influenza Vaccine Co-Administration Studies: Designs<sup>1-3</sup>

Open-label, randomized controlled studies evaluating immunogenicity, safety, and reactogenicity of AREXVY co-administered with:

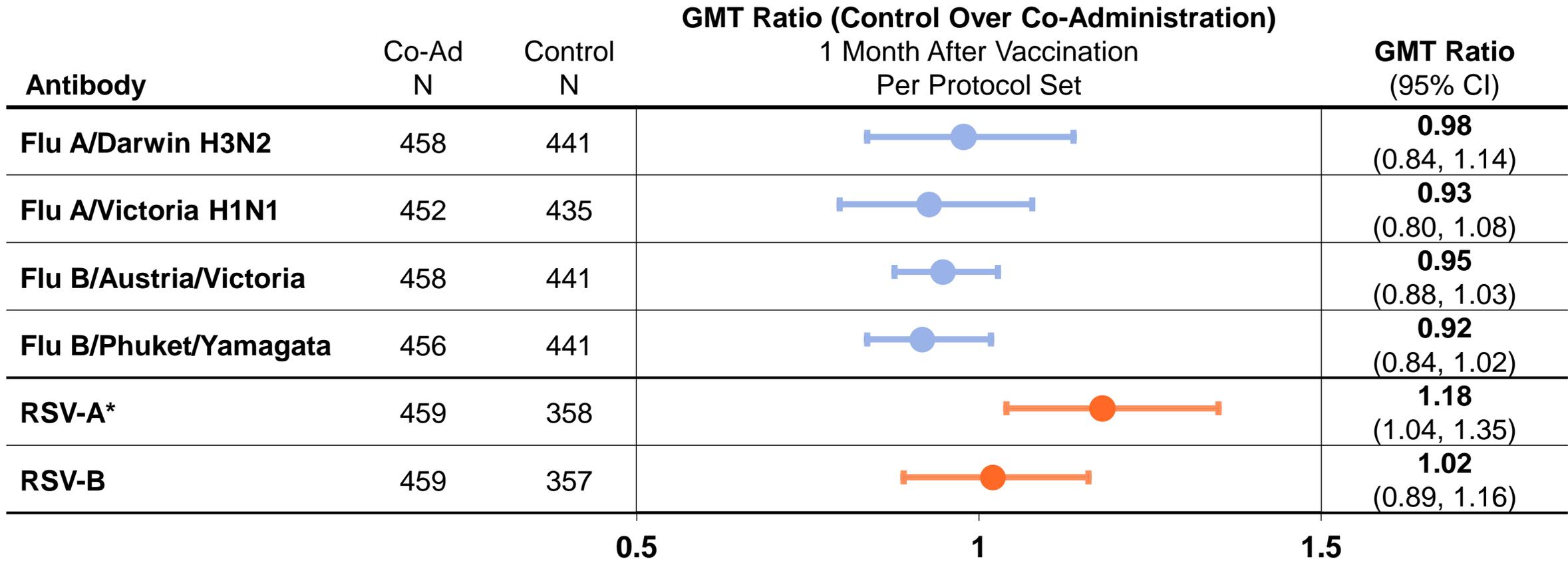
- FLU-QIV (RSV OA=ADJ-007; Southern hemisphere)<sup>1</sup>
- FLU-QIV-HD (RSV OA=ADJ-008; Northern hemisphere)<sup>2</sup>
- FLU-aQIV (RSV OA=ADJ-017; Europe)<sup>3</sup>



Co-Ad group: Participants receiving single dose of RSVPreF3 OA investigational vaccine and single dose of FLU vaccine at Visit 1. Control group: Participants receiving a single dose of FLU vaccine at Visit 1 (Day 1), followed by a single dose of the RSVPreF3 OA investigational vaccine at Visit 2. FLU-aQIV: adjuvanted quadrivalent influenza vaccine; FLU-QIV: quadrivalent influenza vaccine; FLU-QIV-HD: quadrivalent influenza vaccine-high dose. 1. ClinicalTrials.gov, 2022. NCT04841577. <https://clinicaltrials.gov/ct2/show/NCT04841577>; 2. ClinicalTrials.gov, 2023. NCT05559476. <https://clinicaltrials.gov/ct2/show/NCT05559476>;

3. ClinicalTrials.gov, 2023. NCT05568797. <https://clinicaltrials.gov/ct2/show/NCT05568797>. Accessed May 2023

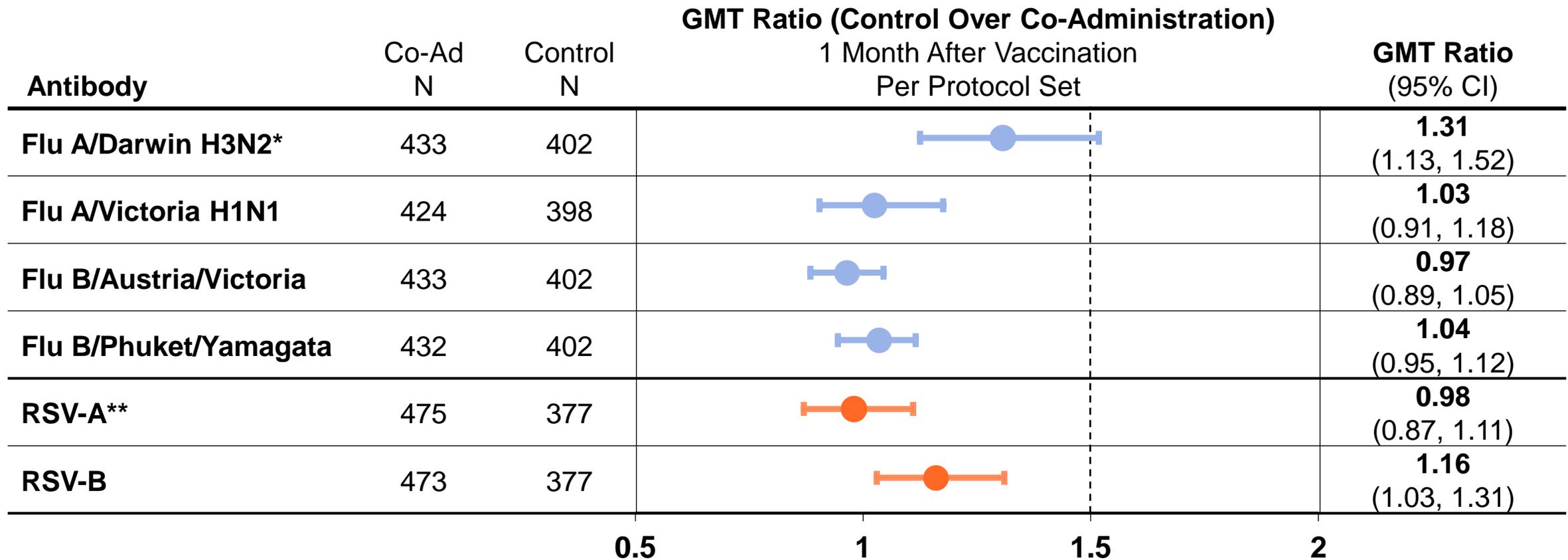
# Co-Administration of AREXVY and Licensed FLU-QIV-HD



**Success Criteria:** Upper limit ≤ 1.5 of 2-sided 95% CI for Group GMT Ratio (Control Group divided by Co-Ad Group) for RSV vaccine and for each of FLU vaccine strains

\*RSV-A preliminary, final results pending  
 Flu response evaluated using HI and RSV response evaluated using NAb (ED 60); HI: Hemagglutination

# Co-Administration of AREXVY and Licensed Flu-Adjuvanted QIV

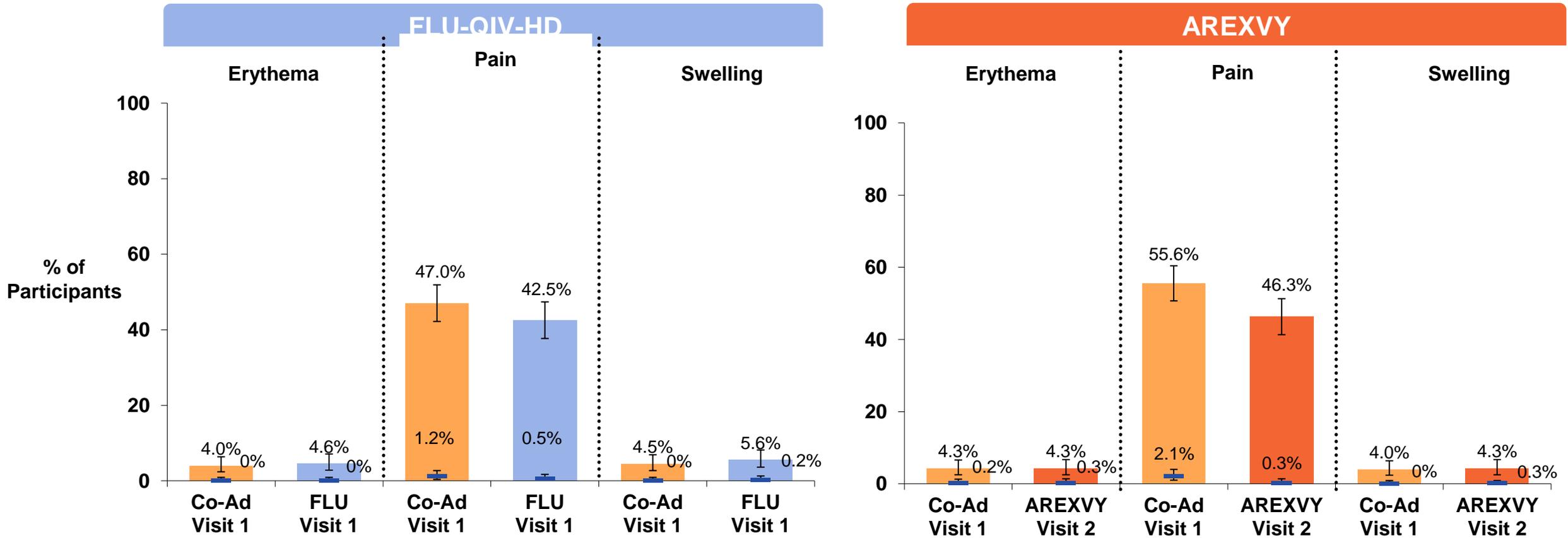


**Success Criteria:** Upper limit  $\leq 1.5$  of 2-sided 95% CI for Group GMT Ratio (Control Group divided by Co-Ad Group) for RSV vaccine and for each of FLU vaccine strains

\*Lower HI titers observed than expected, investigation ongoing; \*\*RSV-A preliminary, final results pending  
Flu response evaluated using HI and RSV response evaluated using NAb (ED 60); HI: Hemagglutination

# Modified Set: Solicited Local AEs Within 4 Days Post Vaccination

Co-Ad FLU AREXVY Grade 3

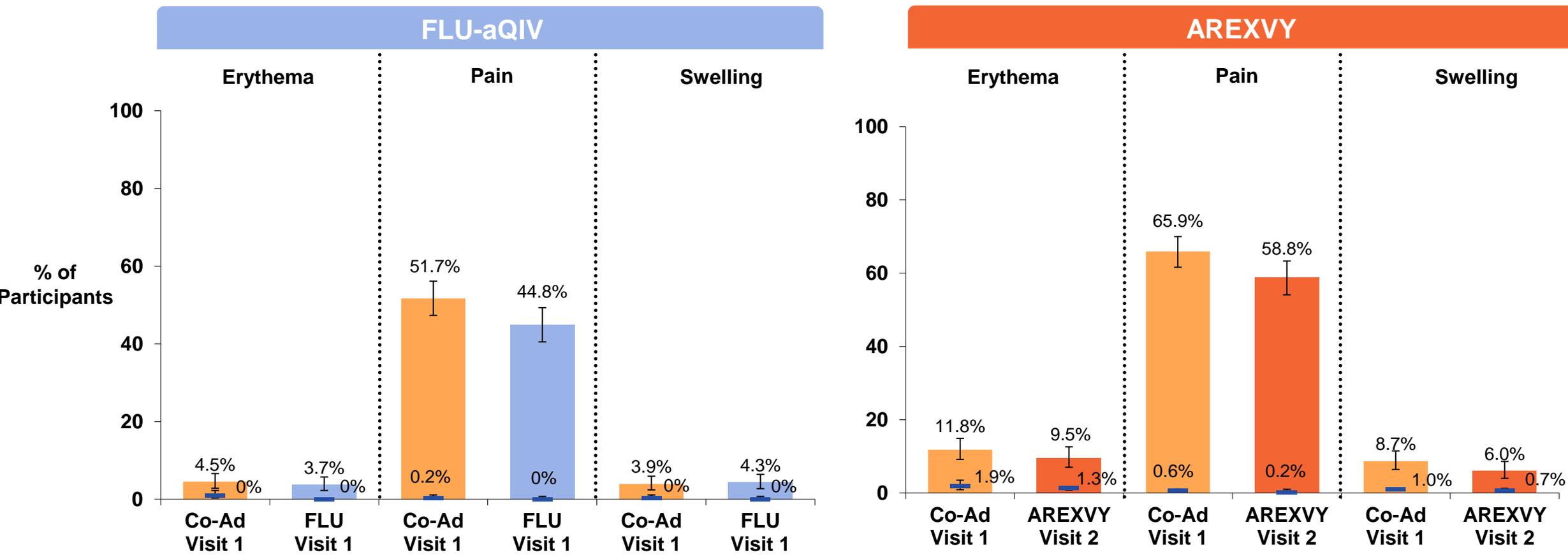


Grade 3: > 100 mm for erythema and swelling; Grade 3 pain: significant pain at rest; prevents normal everyday activities. Fever: temperature ≥ 38.0 C/100.4 F by any route (oral, axillary or tympanic); Grade 3 fever: > 39.0 C/102.2 F. Grade 3 headache, fatigue, myalgia, arthralgia: preventing normal activity

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# Exposed Set: Solicited Local AEs Within 7 Days Post Vaccination

■ Co-Ad 
 ■ FLU 
 ■ AREXVY 
 ■ Grade 3

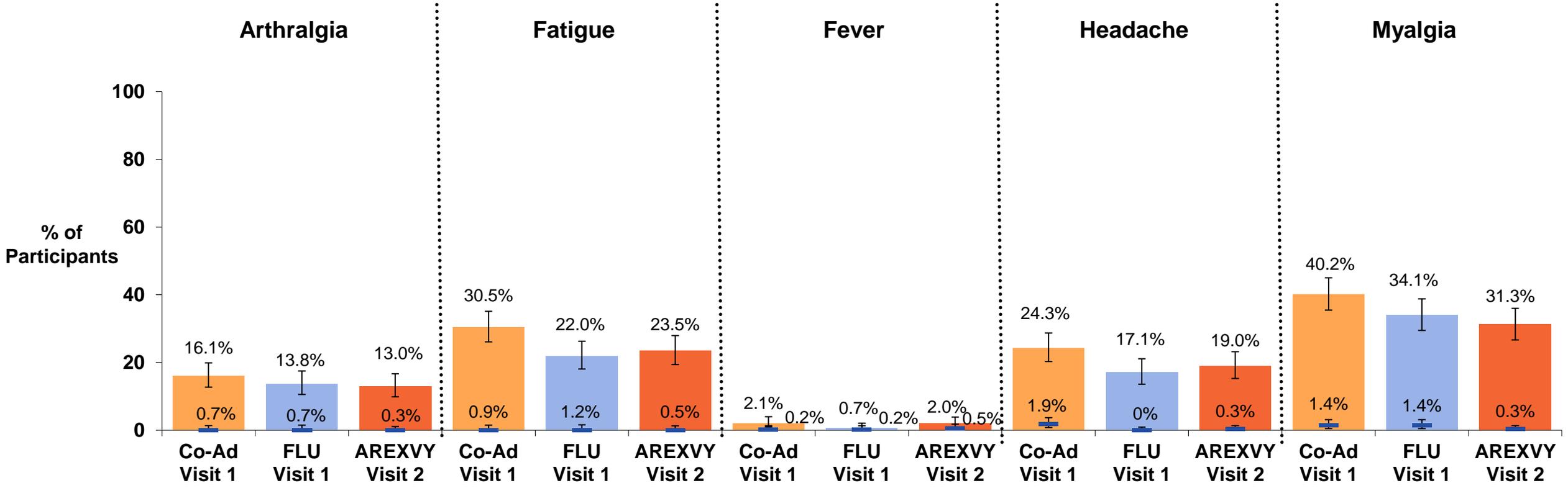


**Grade 3: > 100 mm for erythema and swelling; Grade 3 pain: significant pain at rest; prevents normal everyday activities. Fever: temperature  $\geq 38.0$  C/100.4 F by any route (oral, axillary or tympanic); Grade 3 fever: > 39.0 C/102.2 F. Grade 3 headache, fatigue, myalgia, arthralgia: preventing normal activity**

# Modified Set: Solicited Systemic AEs Within 4 Days Post Vaccination

Co-Ad FLU AREXVY Grade 3

## Solicited Systemic Adverse Events

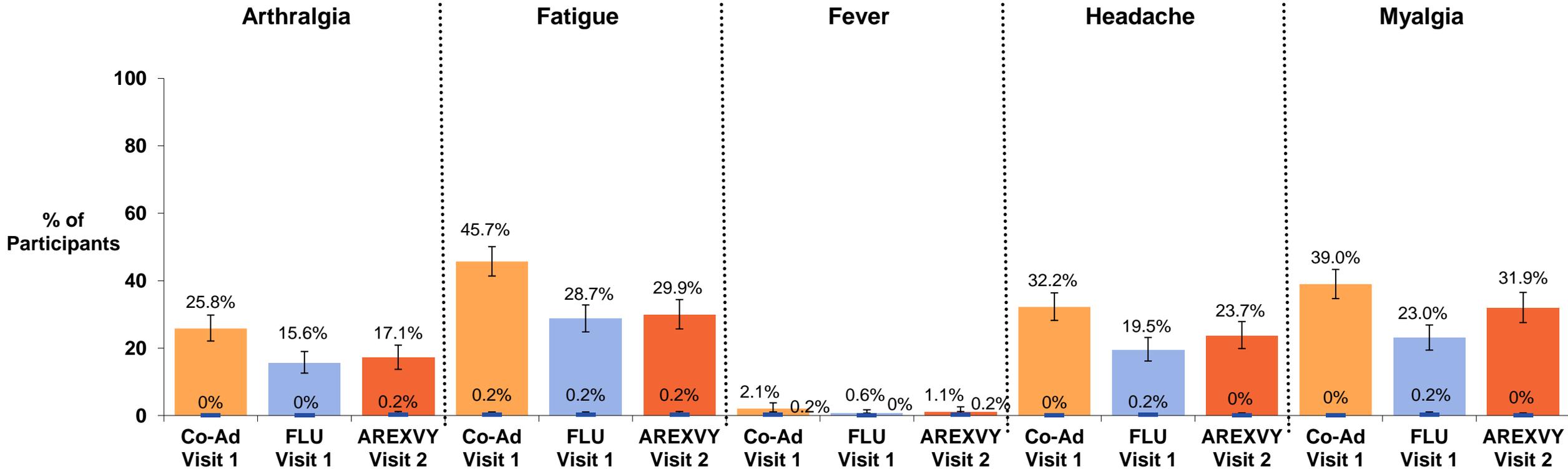


Grade 3: >100 mm for erythema and swelling. Grade 3 pain: significant pain at rest; prevents normal everyday activities.  
 Fever: temperature ≥ 38.0°C/100.4°F by any route (oral, axillary or tympanic); Grade 3 fever: > 39.0°C/102.2°F.  
 Grade 3 headache, fatigue, myalgia, arthralgia: preventing normal activity

# Exposed Set: Solicited Systemic AEs Within 7 Days Post Vaccination

■ Co-Ad 
 ■ FLU 
 ■ AREXVY 
 ■ Grade 3

## Solicited Systemic Adverse Events



Grade 3: >100 mm for erythema and swelling. Grade 3 pain: significant pain at rest; prevents normal everyday activities.

Fever: temperature  $\geq 38.0^{\circ}\text{C}/100.4^{\circ}\text{F}$  by any route (oral, axillary or tympanic); Grade 3 fever:  $> 39.0^{\circ}\text{C}/102.2^{\circ}\text{F}$ .

Grade 3 headache, fatigue, myalgia, arthralgia: preventing normal activity

## Summary of Findings

**1 dose of AREXVY provides durable efficacy against RSV-associated LRTD for 2 full RSV seasons, including against severe RSV disease, in adults with underlying comorbidities, and across advancing ages**

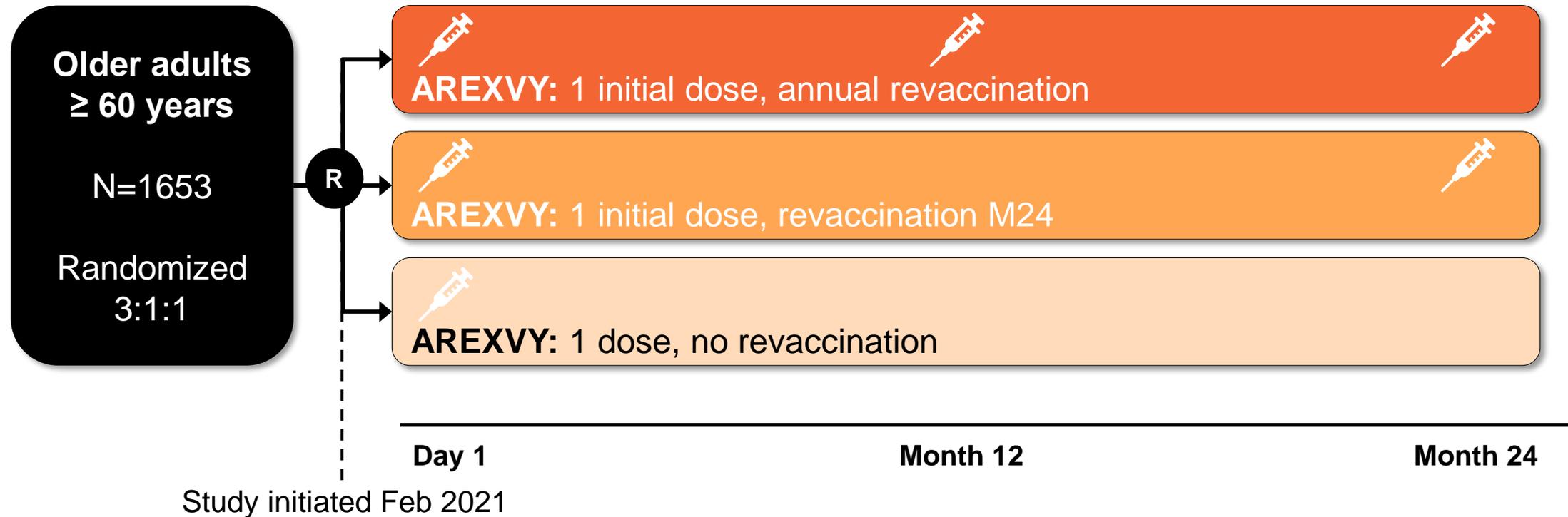
**Revaccination after 12 months does not appear to confer additional efficacy benefit for overall population; future data will inform optimal timing of revaccination**

**AREXVY can be administered with all types of commonly used influenza vaccines**

**Reactogenicity and safety profiles of 2<sup>nd</sup> dose in line with 1<sup>st</sup> dose; important for future revaccination consideration**

**Across all studies no new cases of GBS, ADEM, or other neuroinflammatory demyelinating disorders with additional exposure**

# AReSVi-004 Phase 3 Trial Design<sup>1</sup>



**Primary objective:** Evaluate humoral immune response following 1-dose primary schedule up to 12 months post-dose 1\*

**Key secondary objectives:** Evaluate humoral and CMI<sup>†</sup> responses following 1-dose primary schedule and revaccination doses, up to study end (Month 36)

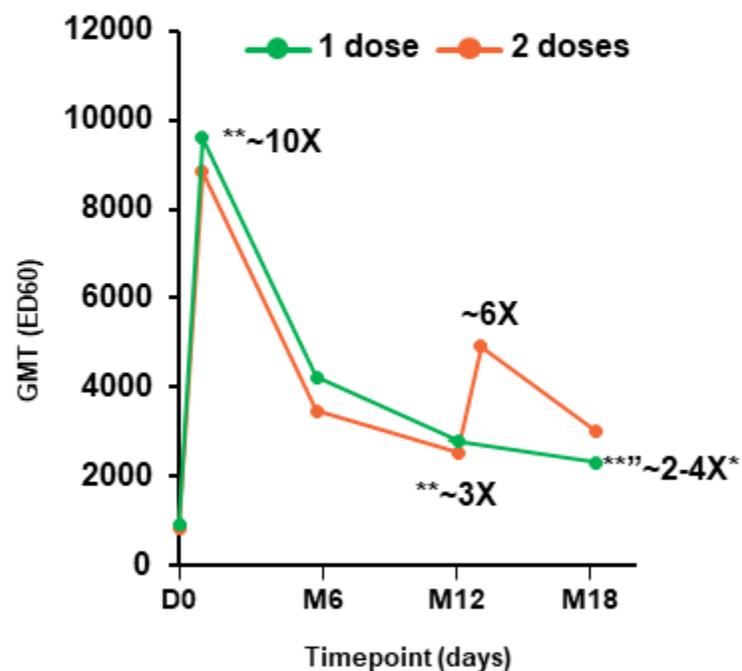
**Safety monitoring:** Throughout study

\*Primary endpoints: NAb geometric mean titers (RSV-A and RSV-B) at Day 1 (pre-vaccination), D31, M6, and M12 post-dose 1; <sup>†</sup>CMI response in terms of frequency of RSVPreF3-specific CD4+ and/or CD8+ T-cells expressing at least 2 activation markers. CD: cluster of differentiation; CMI: cell-mediated immune

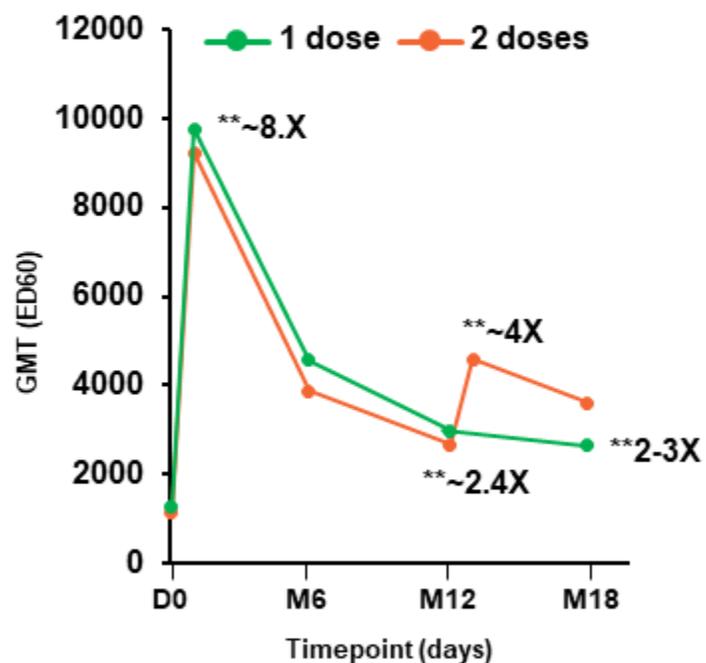
1. ClinicalTrials.gov. 2021. NCT04732871. <https://clinicaltrials.gov/ct2/show/NCT04732871> (accessed May 2023)

# Immunogenicity Overview Through Month 18 Post Vaccination

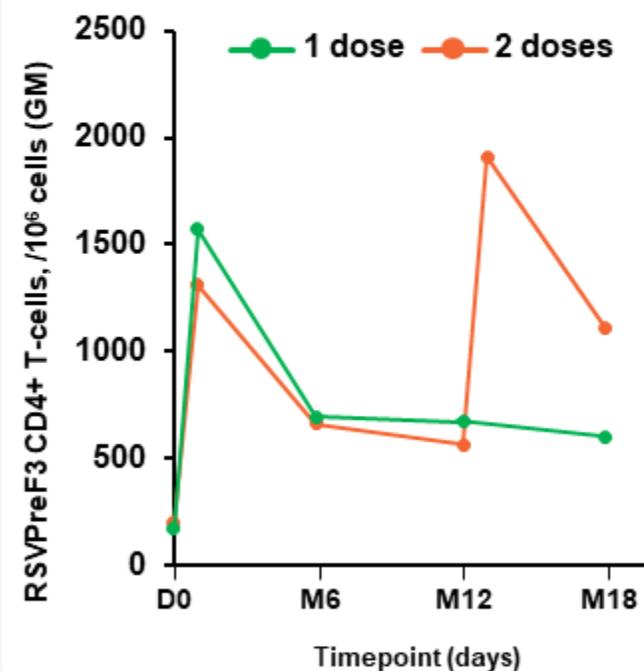
## RSV-A Serum Neutralization Titers



## RSV-B Serum Neutralization Titers



## RSVPreF3-specific CD4+ T-cells



\*RSV-A preliminary, final results pending

\*\*versus before vaccination 1; CD4+ T-cells expressing  $\geq 2$  activation markers including  $\geq 1$  cytokine among CD40L, 4-1BB, IL-2, TNF- $\alpha$ , IFN- $\gamma$ , IL-13, IL-17 (events/ $10^6$  cells; by intracellular staining). ED: Estimated Dilution; ED60: serum dilution inducing 60% inhibition in plaque-forming units; GMT: geometric mean titer; IL: interleukin; TNF: tumor necrosis factor