RSVpreF Older Adults

Clinical Development Program Updates

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Presentation to ACIP

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RSVpreF Older Adult – Clinical Development Program Updates

ABRYSVO™ (Respiratory Syncytial Virus Vaccine)

FDA Approval on 5/31/2023

Indication

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

Additional Clinical Trial Data

- RENOIR – End-of-Season 1 and Mid-Season 2 analyses
- RSVpreF/influenza vaccine coadministration study

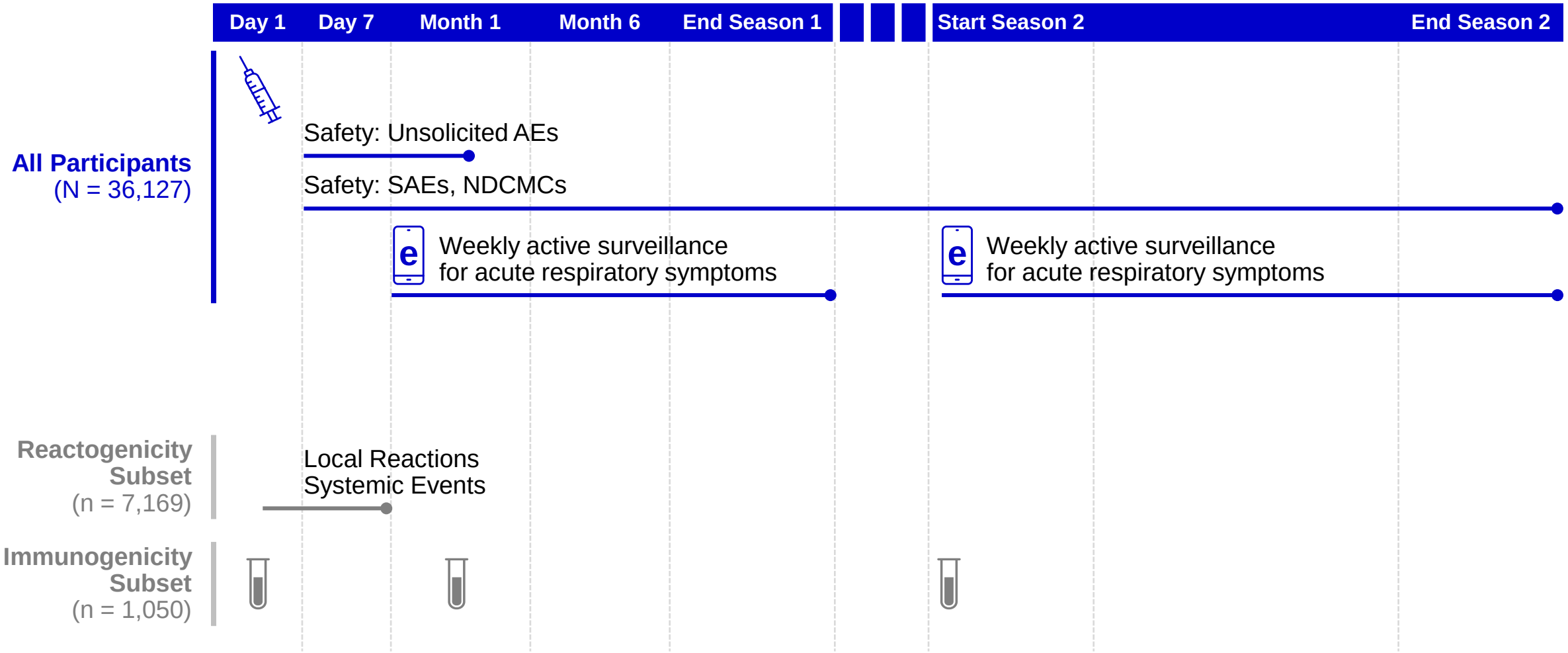
RENOIR
– Phase 3 safety and efficacy study in adults ≥ 60 years of age

38,863 participants enrolled
Healthy or with stable chronic conditions

Randomized 1:1 to receive
RSVpreF 120 µg or placebo

Stratified by age group
60–69 years | 70–79 years | ≥ 80 years

RENOIR Study Design



AE, adverse event; NDCMC, newly diagnosed chronic medical condition; SAE, serious adverse event

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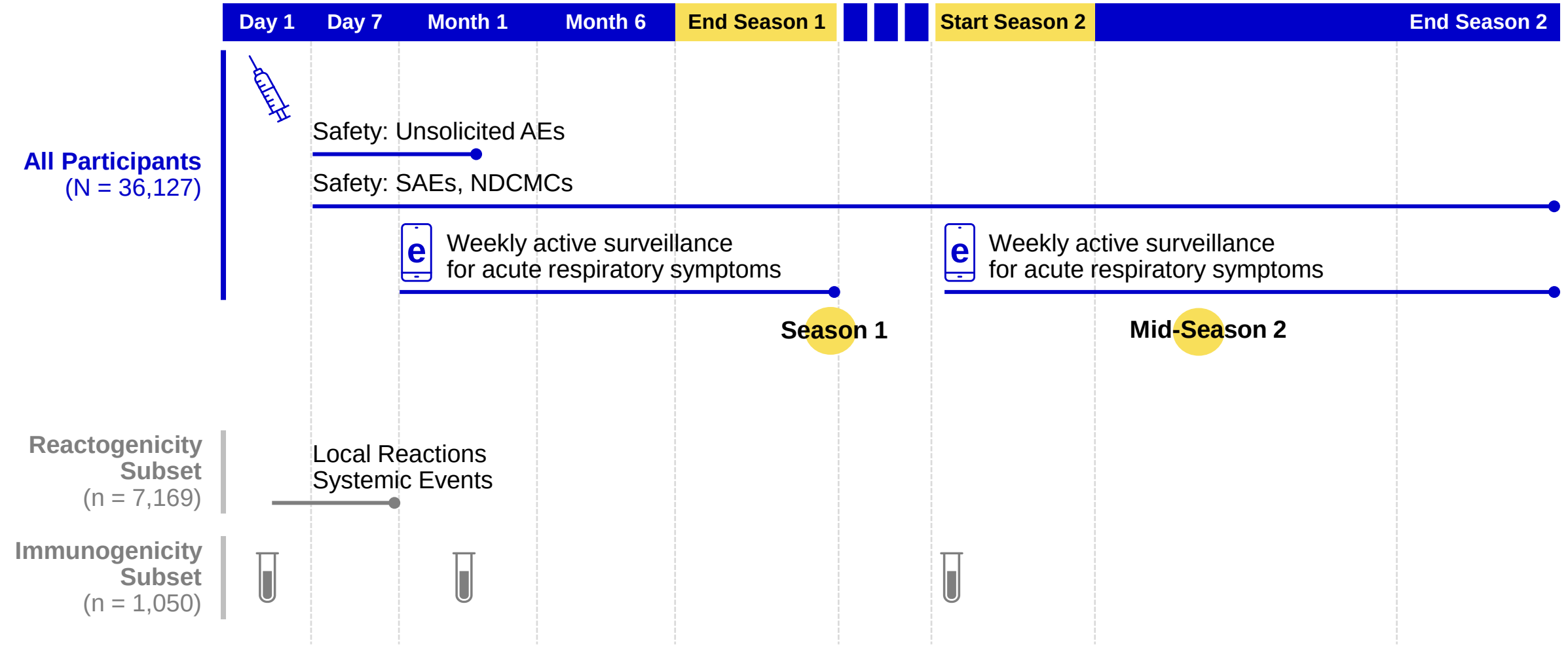

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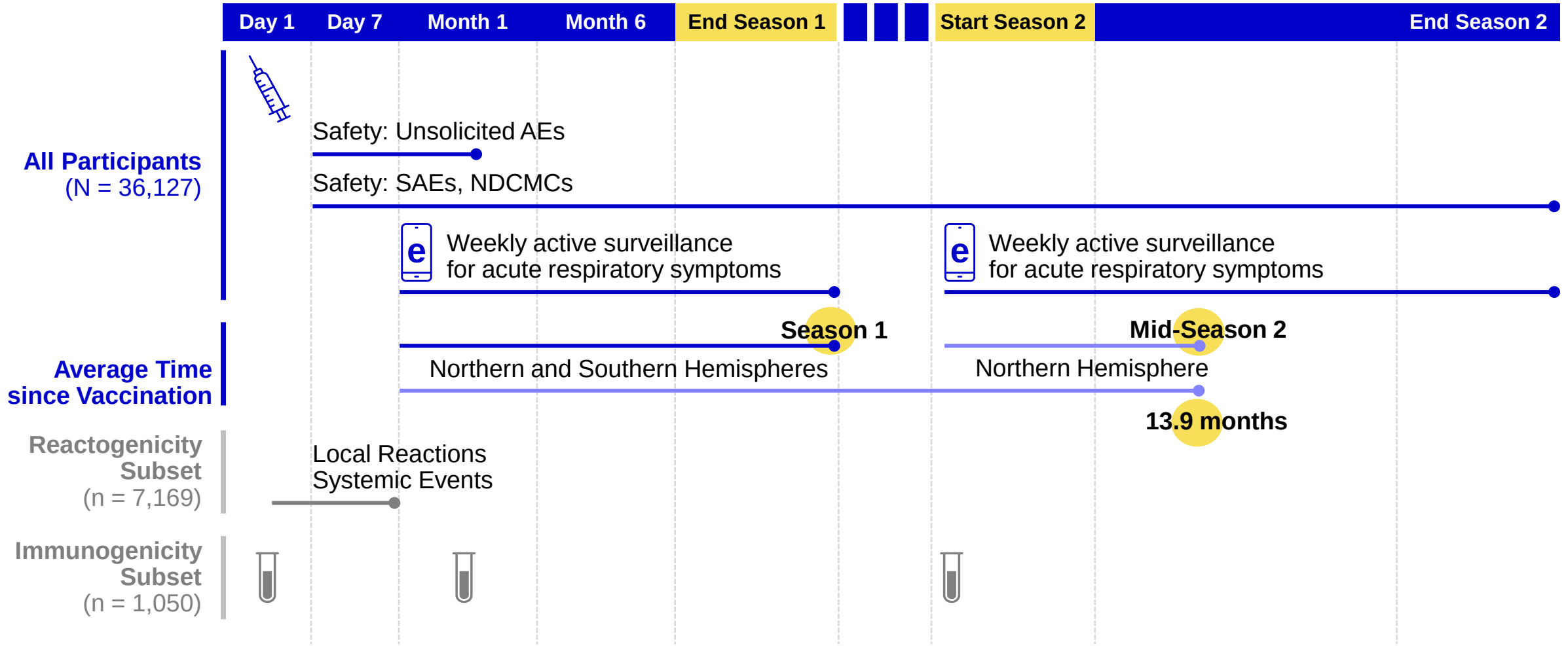

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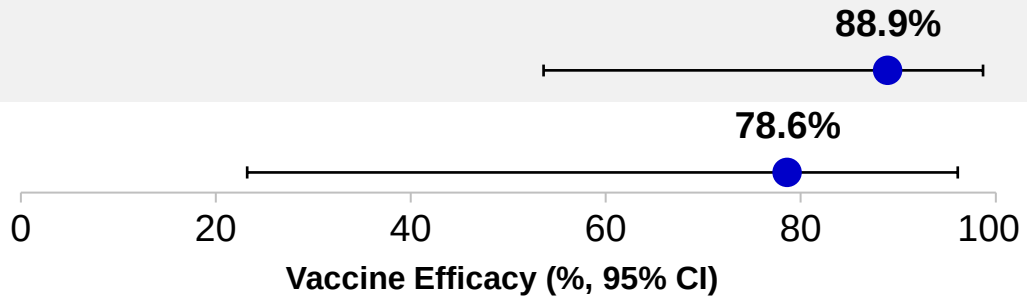
Efficacy against RSV-LRTD – Demonstrated through Mid-Season 2 Analysis

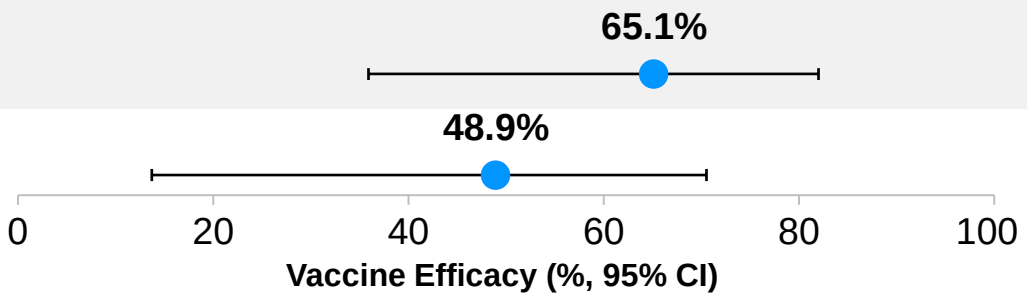
RSV-LRTD with ≥ 3 symptoms

	Number of Events	
	RSVpreF	Placebo
Season 1 (N = 36,127)	2	18
Mid-Season 2 (n = 20,019)	3	14



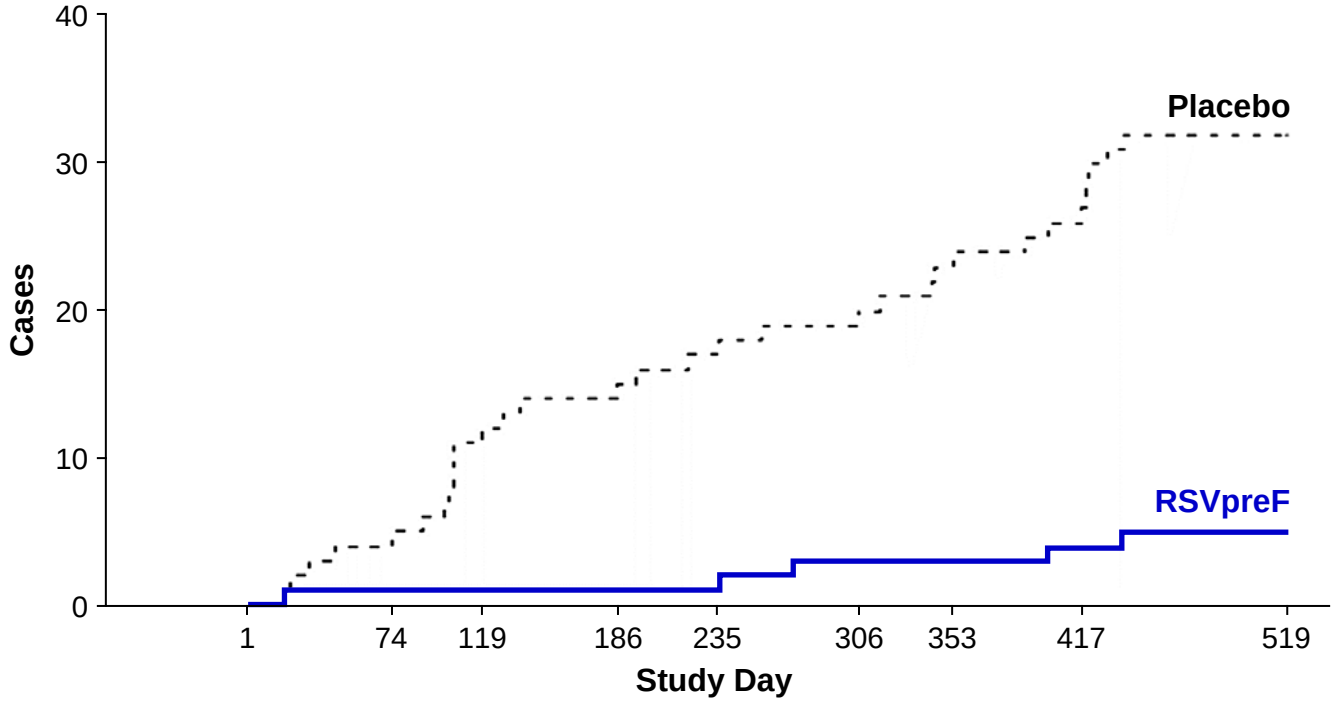
RSV-LRTD with ≥ 2 symptoms

	Number of Events	
	RSVpreF	Placebo
Season 1 (N = 36,127)	15	43
Mid-Season 2 (n = 20,019)	23	45



Mid-Season 2 includes Northern Hemisphere only (US, Canada, Finland) through January 31, 2023

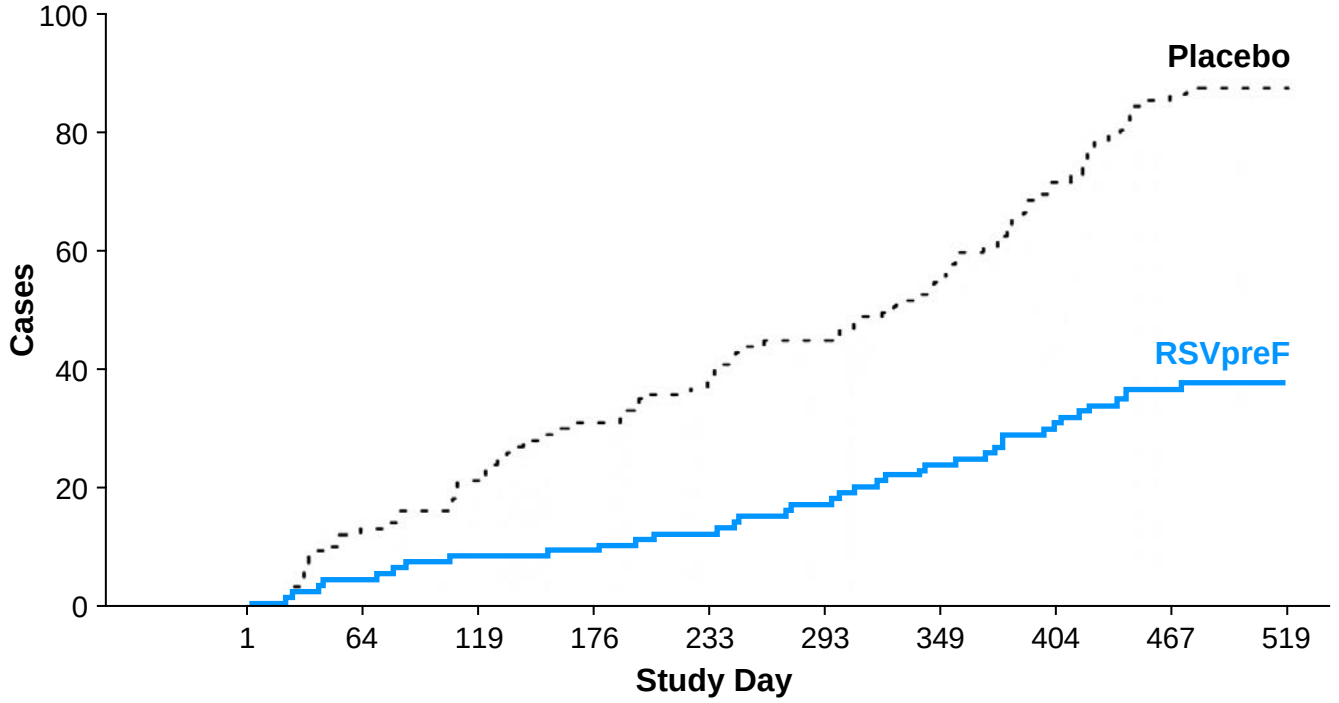
Persistent VE against RSV-LRTD with ≥ 3 Symptoms through Mid-Season 2



Cumulative Events									
RSVpreF	0	1	1	1	2	3	3	4	5
Placebo	0	5	12	15	17	20	24	27	32

RSV-LRTD, lower respiratory tract disease due to RSV; RSV, respiratory syncytial virus; VE, vaccine efficacy.

Persistent VE against RSV-LRTD with ≥ 2 Symptoms through Mid-Season 2



Cumulative Events										
RSVpreF	0	5	8	10	12	18	24	31	38	38
Placebo	0	13	23	31	40	45	57	72	87	88

RSV-LRTD, lower respiratory tract disease due to RSV; RSV, respiratory syncytial virus; VE, vaccine efficacy.

Adverse Events, by Category, from Vaccination through 1-Month Follow Up Visit and through Data Cutoff (31Jan2023): Safety Population

	RSVpreF N = 18,575		Placebo N = 18,288	
Adverse Event Category	**n (%)**	**(95% CI)**	**n (%)**	**(95% CI)**
From Vaccination through 1-Month Follow-Up Visit				
Any Event	**1,976 (10.6)**	**(10.2, 11.1)**	**1,897 (10.4)**	**(9.9, 10.8)**
Related	**259 (1.4)**	**(1.2, 1.6)**	**178 (1.0)**	**(0.8, 1.1)**
Immediate AE	**37 (0.2)**	**(0.1, 0.3)**	**33 (0.2)**	**(0.1, 0.3)**
Severe or life-threatening	**102 (0.5)**	**(0.4, 0.7)**	**95 (0.5)**	**(0.4, 0.6)**
From Vaccination through 31Jan2023				
NDCMC	806 (4.3)	(4.1, 4.6)	825 (4.5)	(4.2, 4.8)
SAE	790 (4.3)	(4.0, 4.6)	746 (4.1)	(3.8, 4.4)
Related SAE	3 (<0.1)	(0.0, 0.1)	0	(0.0, 0.0)
AE leading to withdrawal	12 (<0.1)	(0.0, 0.1)	11 (<0.1)	(0.0, 0.1)
AE leading to death	100 (0.5)	(0.4, 0.7)	104 (0.6)	(0.5, 0.7)

Any reactogenicity reported as adverse events (from either reactogenicity subset or non-reactogenicity subset) during the specified time period are included in this table.
Immediate AE refers to an AE reported in the 30-minute post-vaccination observation period.
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RSVpreF/influenza vaccine coadministration study

RSVpreF/SIIV Coadministration in Adults ≥ 65 Years of Age

Phase 3 Study Design and Key Procedures

- Placebo-controlled, double-blind study
- Assessing safety and immunogenicity (non-inferiority)
- Australia (31 sites)
- ~1,400 healthy participants ≥ 65 years of age
- Randomized 1:1
- SIIV: Fluad Quadrivalent
- Timeframe: April 13, 2022 – October 12, 2022

SIIV, seasonal inactivated influenza vaccine

Demographics

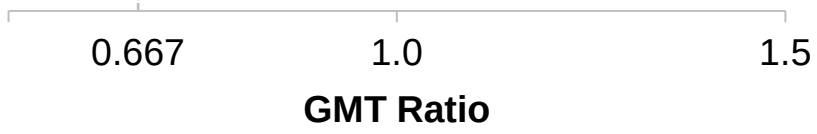
	Coadministration (RSVpreF + SIIV) / Placebo (N = 703) n (%)	Sequential Administration (Placebo + SIIV) / RSVpreF (N = 696) n (%)	Total (N = 1,399) n (%)
Sex			
Female	398 (56.6)	372 (53.4)	770 (55.0)
Age at Visit 1 (years)			
Mean (SD)	70.7 (4.7)	70.7 (4.7)	70.7 (4.7)
Median	70.0	70.0	70.0
Min, max	(65, 91)	(65, 88)	(65, 91)
Age group at Visit 1			
65-74 years	567 (80.7)	559 (80.3)	1126 (80.5)
≥ 75 years	136 (19.3)	137 (19.7)	273 (19.5)
Race			
White	669 (95.2)	665 (95.5)	1,334 (95.4)
Asian	22 (3.1)	21 (3.0)	43 (3.1)
Multiracial	4 (0.6)	1 (0.1)	5 (0.4)
Other	4 (0.6)	4 (0.5)	8 (0.6)
Not reported or unknown	4 (0.6)	5 (0.7)	9 (0.6)

SIIV, seasonal inactivated influenza vaccine

Non-inferiority Demonstrated by SIIV HAI and RSV Neutralizing Titer GMRs

Geometric Mean Ratios with 95% CIs – Evaluable RSV Immunogenicity Population and Evaluable SIIV Immunogenicity Population

Comparison, by SIIV/RSV Subgroup	GMR (95% CI)
SIIV: HAI: H1N1 A/Victoria	0.86 (0.769, 0.963)
SIIV: HAI: H3N2 A/Darwin	0.77 (0.680, 0.866)
SIIV: HAI: B/Austria	0.90 (0.789, 1.019)
SIIV: HAI: B/Phuket	0.87 (0.779, 0.964)
RSVpreF: NT: RSV A	0.86 (0.785, 0.951)
RSVpreF: NT: RSV B	0.85 (0.766, 0.943)



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GMRs and 2-sided confidence intervals (CIs) calculated by exponentiating the mean difference of the logarithms of the titers (coadministration minus sequential-administration) and corresponding confidence intervals (CIs) (based on Student's t distribution).

GMR, geometric mean ratio; GMT, geometric mean titer; HAI, hemagglutination inhibition assay; NT, neutralizing titer; RSV, respiratory syncytial virus

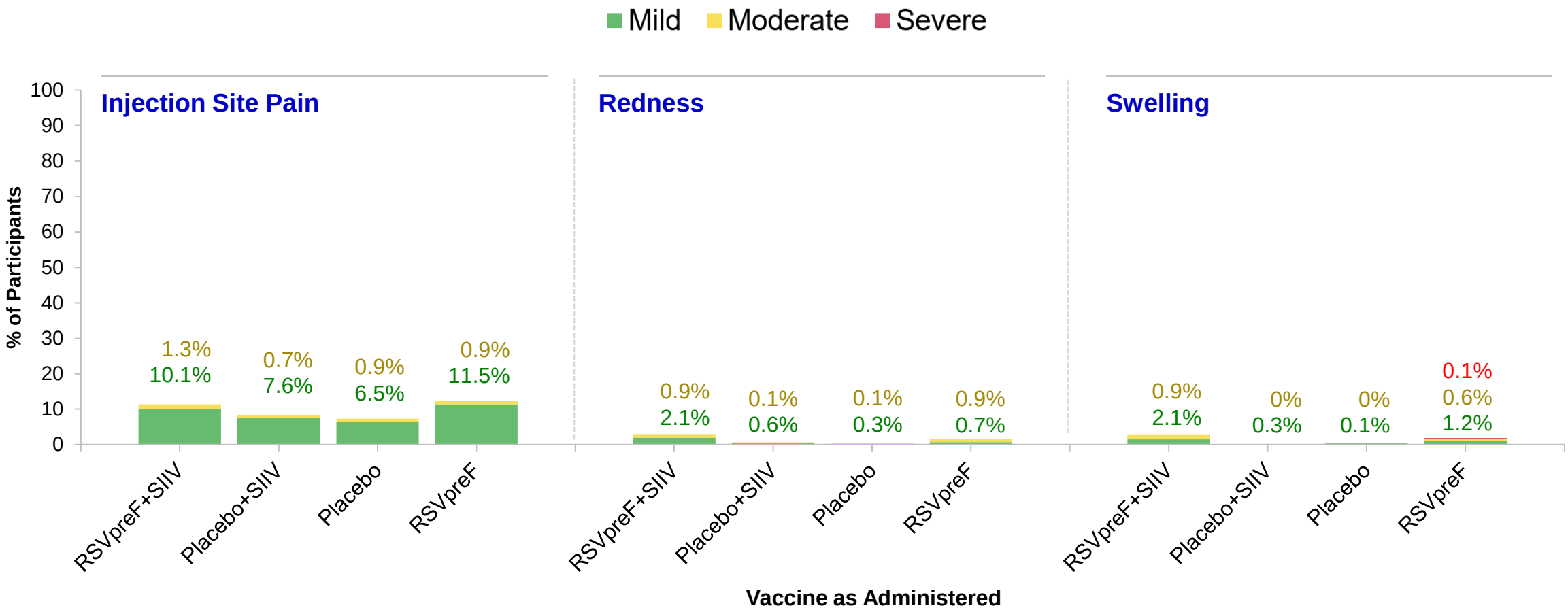
Similar HAI Titer Seroprotection and Seroconversion at 1 Month in Coadministration and Sequential Administration Groups

	Coadministration (RSVpreF + SIIV)/Placebo		Sequential Administration (Placebo + SIIV)/RSVpreF	
Serostatus, Strain	**%**	**(95% CI)**	**%**	**(95% CI)**
Seroprotection[1]				
1 month after vaccination				
H1N1 A/Victoria	**91.6**	(89.3, 93.6)	**94.3**	(92.3, 95.9)
H3N2 A/Darwin	**87.9**	(85.2, 90.3)	**91.0**	(88.6, 93.0)
B/Austria	**85.3**	(82.4, 87.9)	**89.5**	(87.0, 91.7)
B/Phuket	**88.4**	(85.7, 90.7)	**92.6**	(90.4, 94.4)
Seroconversion[2]				
H1N1 A/Victoria	**36.6**	(32.9, 40.3)	**43.9**	(40.1, 47.7)
H3N2 A/Darwin	**58.8**	(55.0, 62.6)	**62.6**	(58.9, 66.3)
B/Austria	**39.5**	(35.8, 43.3)	**47.3**	(43.5, 51.1)
B/Phuket	**25.3**	(22.1, 28.8)	**28.0**	(24.6, 31.5)

[1]Seroprotection: HAI titer ≥ 1:40

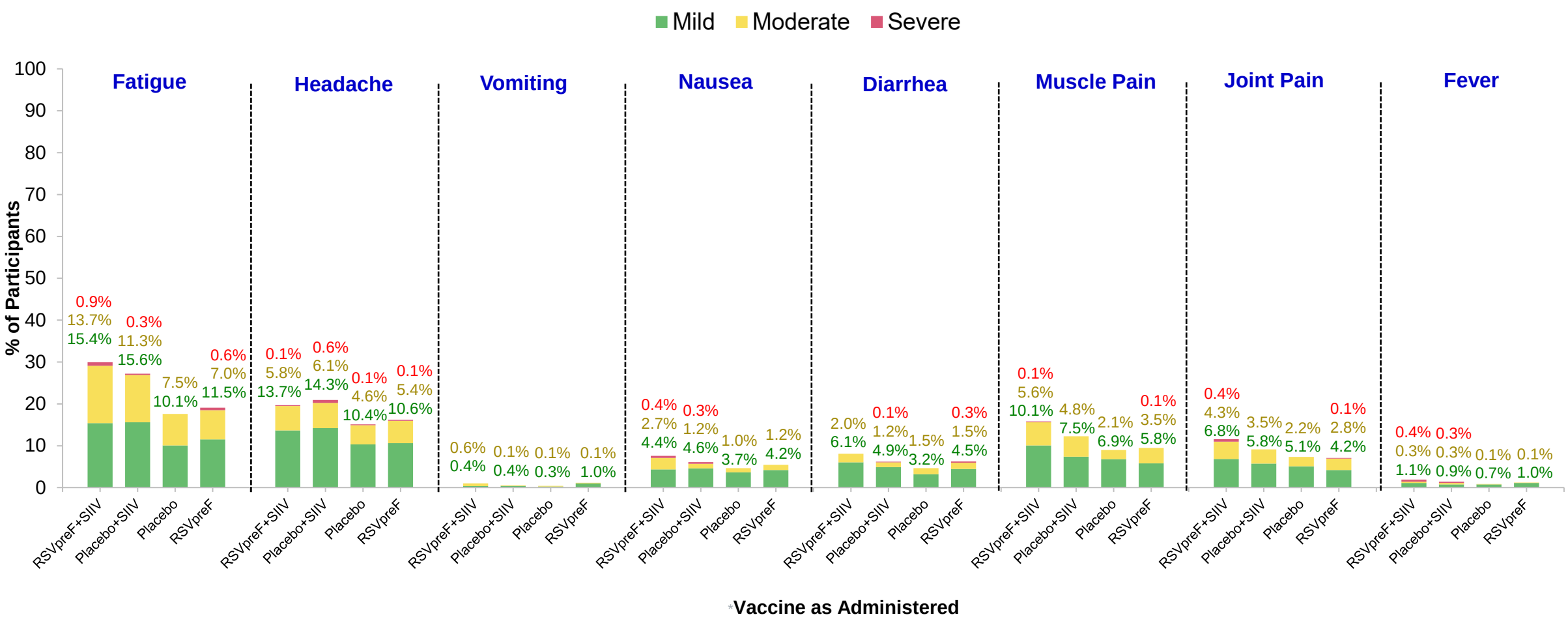
[2]Seroconversion: ≥ 4-fold rise from before to after receipt of SIIV if the HAI titer is ≥1:10 before SIIV or if the after SIIV HAI titer is ≥ 1:40 where the before SIIV is <1:10

Local Reactions Mostly Mild or Moderate



Participants reporting local reactions by maximum severity within 7 days after each vaccination
Local reactions evaluated on the arm receiving RSVpreF/placebo; no assessment of local reactogenicity at SIIV injection site.
Local reactions after RSVpreF had median onset 2 to 3 days after vaccination and median duration of 1 to 2 days
Only 1 severe local reaction reported (swelling), in the sequential administration group at Visit 2
SIIV, seasonal inactivated influenza vaccine

Systemic Events Mostly Mild or Moderate



Participants reporting systemic events by maximum severity within 7 days after each vaccination
Systemic events after RSVpreF+SIIV had median onset 2 to 4 days after vaccination and median duration of 1 to 2 days
SIIV, seasonal inactivated influenza vaccine

Adverse Events, by Category, within One Month after Vaccination: Safety Population

Adverse Event Category	RSVpreF+SIIV (N = 703) n (%)	Placebo+SIIV (N = 695) n (%)	Placebo (N = 689) n (%)	RSVpreF (N = 691) n (%)
Any event	154 (21.9)	134 (19.3)	117 (17.0)	115 (16.6)
Related	9 (1.3)	3 (0.4)	3 (0.4)	5 (0.7)
Serious	8 (1.1)	6 (0.9)	2 (0.3)	5 (0.7)
Related	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Death	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)
Immediate	3 (0.4)	1 (0.1)	1 (0.1)	0 (0.0)

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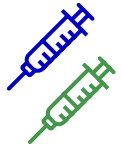
RSVpreF Older Adult Clinical Development Program Updates – Conclusions

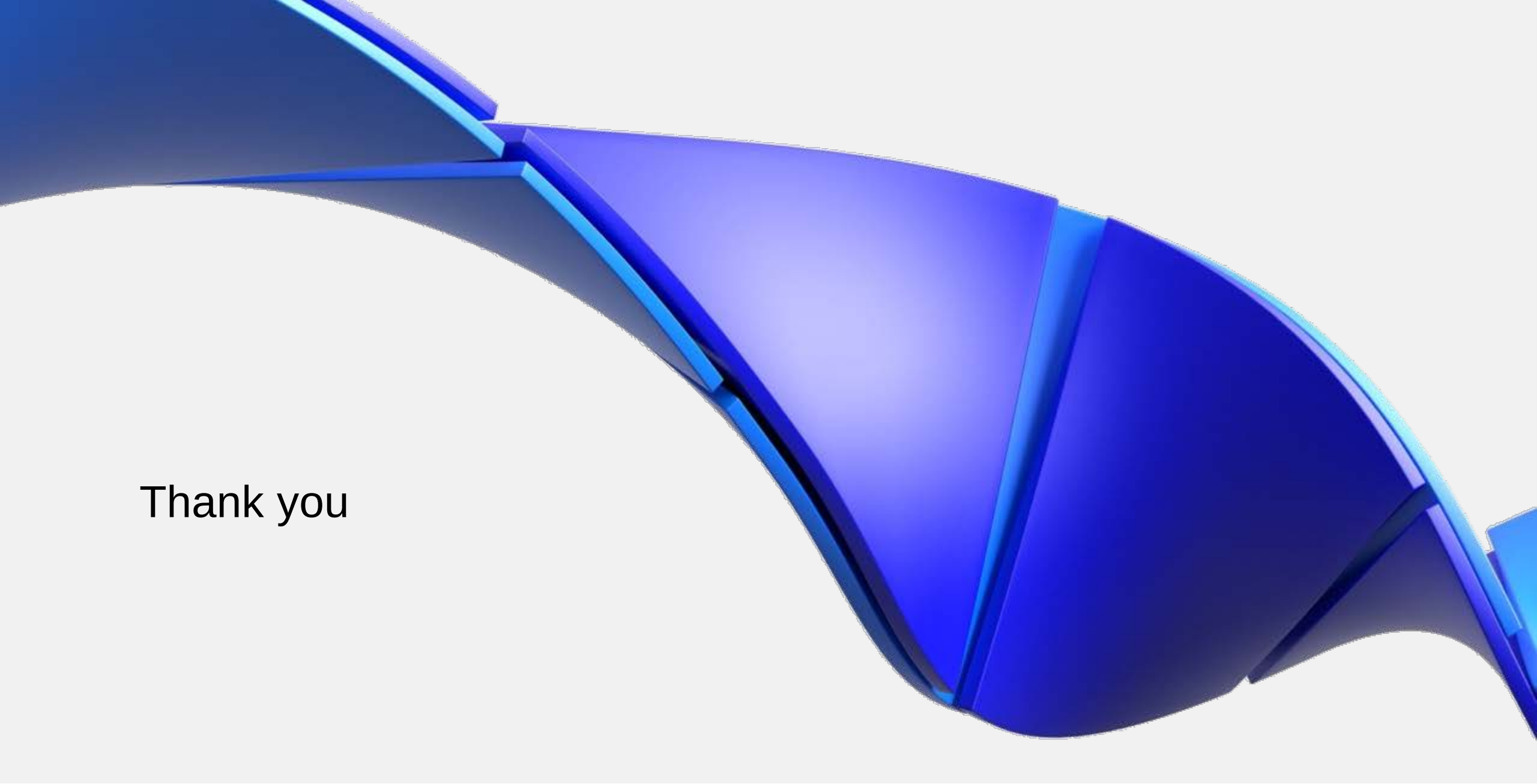
RENOIR Phase 3 Pivotal Efficacy – Season 1 and Mid-Season 2

- Favorable overall safety profile of RSVpreF
- RSVpreF remained efficacious in prevention of RSV-LRTD
  - Through end of season 1
  - In mid-season 2
  - Average 13.9 months of follow up since vaccination



RSVpreF Coadministration with Influenza Vaccine

- RSVpreF safe and well tolerated when coadministered with influenza vaccine
- Non-inferior immune responses when RSVpreF coadministered with influenza vaccine



Thank you