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Bivalent RSV Prefusion F Vaccine in Adults ≥60 Years of Age

Vaccines and Related Biological Products Advisory Committee

February 28, 2023

Introduction

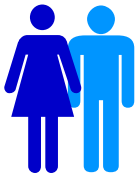
Alejandra Gurtman, MD, FIDSA

Vice President,
Vaccine Research and Development

Bivalent RSV Prefusion F Vaccine

Proposed Indication:

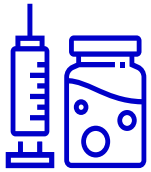
Prevention of acute respiratory disease and lower respiratory tract disease caused by respiratory syncytial virus (RSV)



Individuals 60 years of age and older

DOSE LEVEL

- 120 µg without an adjuvant
- Dose contains 60 µg dose of each prefusion protein antigen, in a 0.5 mL injection



PRESENTATION

- Single dose 2 mL vial
- 1 mL Pre-filled syringe
- Vial adaptor

STORAGE

- Refrigeration at 2°C to 8°C (36°F to 46°F)
- After reconstitution: 15ºC to 30ºC (used within 4 hours of reconstitution)

Presentation Agenda

- Unmet Medical Need and Clinical Development Plan
- Safety
- Efficacy
- Pharmacovigilance & Surveillance
- Benefit-Risk & Conclusions

RSV Can Cause Serious Illness Yet Often Underrecognized

RSV infection is common[1]

- Nearly all children infected before age of 2 years
- Repeat infections can occur throughout life
- Typically causes cold-like symptoms

Some at higher risk for serious illness from RSV[2,3]

- Infants
- Children and younger adults with certain conditions
- Older adults

Annual burden: U.S. adults 65 years and older [4,5,6,7]

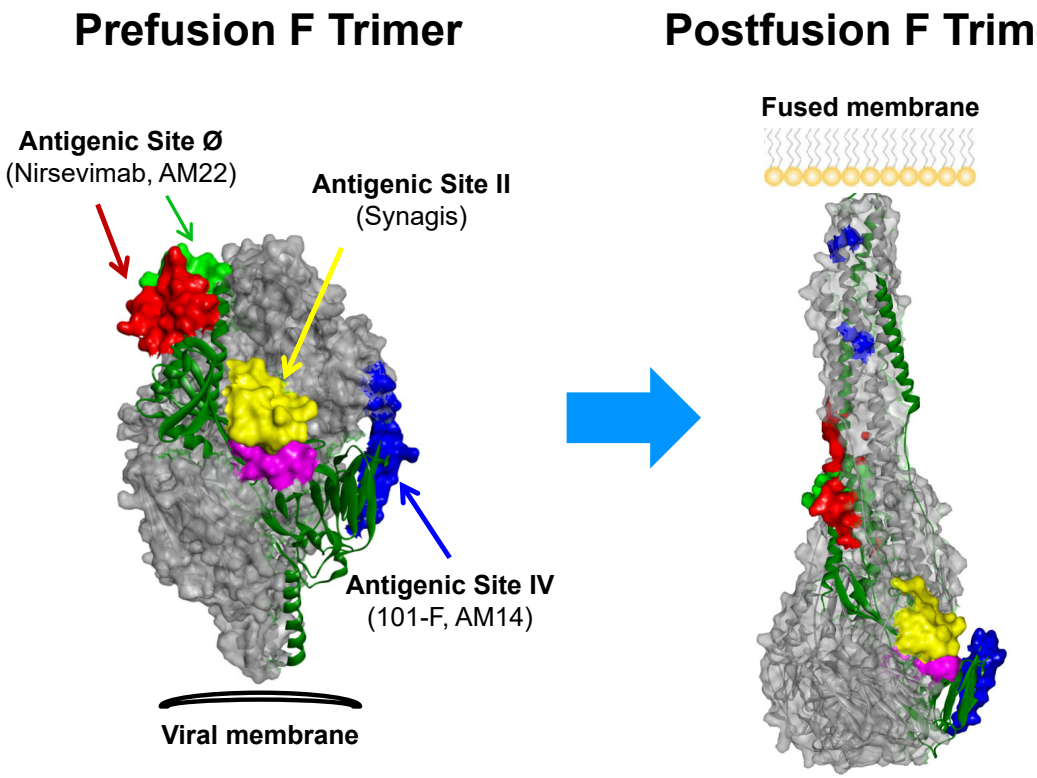
- 60,000–160,000 hospitalizations
- 6,000–13,000 deaths

Treatment: Supportive care[8]

No approved targeted prevention options to date

1. https//www.cdc.gov/rsv/about/transmission.html (accessed on 27-Jan-2023). 2. https://www.cdc.gov/rsv/high-risk/infants-young-children.html (accessed on 27-Jan-2023).
3 https://www.cdc.gov/rsv/high-risk/older-adults.html (accessed on 27-Jan-2023). 4. McLaughlin JM, et al. Open Forum Infect Dis. 2022;9(7):ofac300. 5. Thompson WW, et al. JAMA. 2003;289(2):179-86. 6. Hansen CL, et al. *JAMA Netw Open.* 2022;5(2):e220527. 7. CDC. ACIP Adult RSV Work Group Considerations. 2022. https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2022-10-19-20/04-RSV-Adults-Melgar-508.pdf. (accessed on: 14-Jan-2023). 8. https://www.cdc.gov/rsv/about/symptoms.html. (accessed on: 14-Jan-2023).

Groundbreaking Structural Work by NIH Elucidated that RSV F on the Virus Exists as an Unstable Prefusion Form

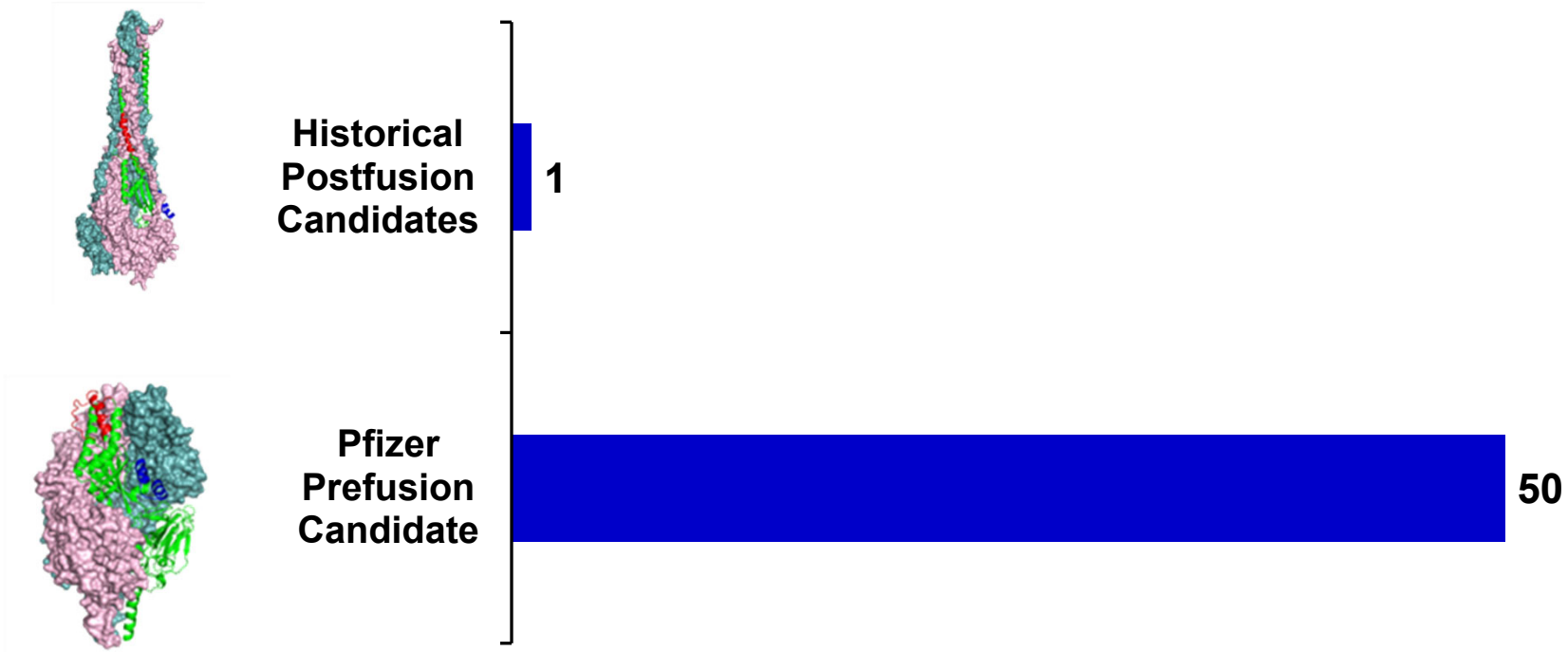


- **Only prefusion F can bind host cells for RSV to infect**
- **Antibodies specific to the prefusion form are most effective at blocking virus infection**

McLellan et al. *Science*, Nov 2013
NIH=National Institutes of Health

Structural Engineering Enabled Superior Vaccine Immunogenicity

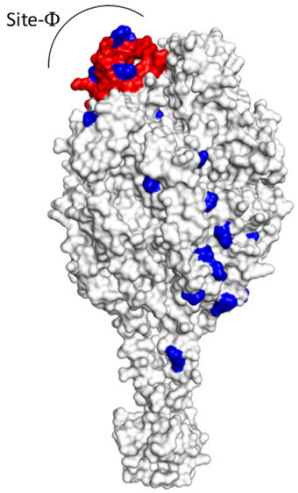
Fold Difference in RSV Neutralization in Preclinical Non-human Primate Studies



Rhesus macaques (n=7/group) received 2 doses of each vaccine candidate at 30 mcg dose level with aluminum hydroxide.
RSV A 50% neutralizing titers at 2 weeks post Dose 2 were normalized against the GMT for the postfusion group.

Rationale for Bivalent Stabilized RSV Prefusion F Vaccine

RSV F subgroup A and B amino acid sequence differences (shown in blue) cluster in prefusion-specific sites



Balanced neutralizing responses against both RSV A and RSV B observed with bivalent prefusion F-based vaccine in contrast with other monovalent investigational RSV prefusion F-based vaccines

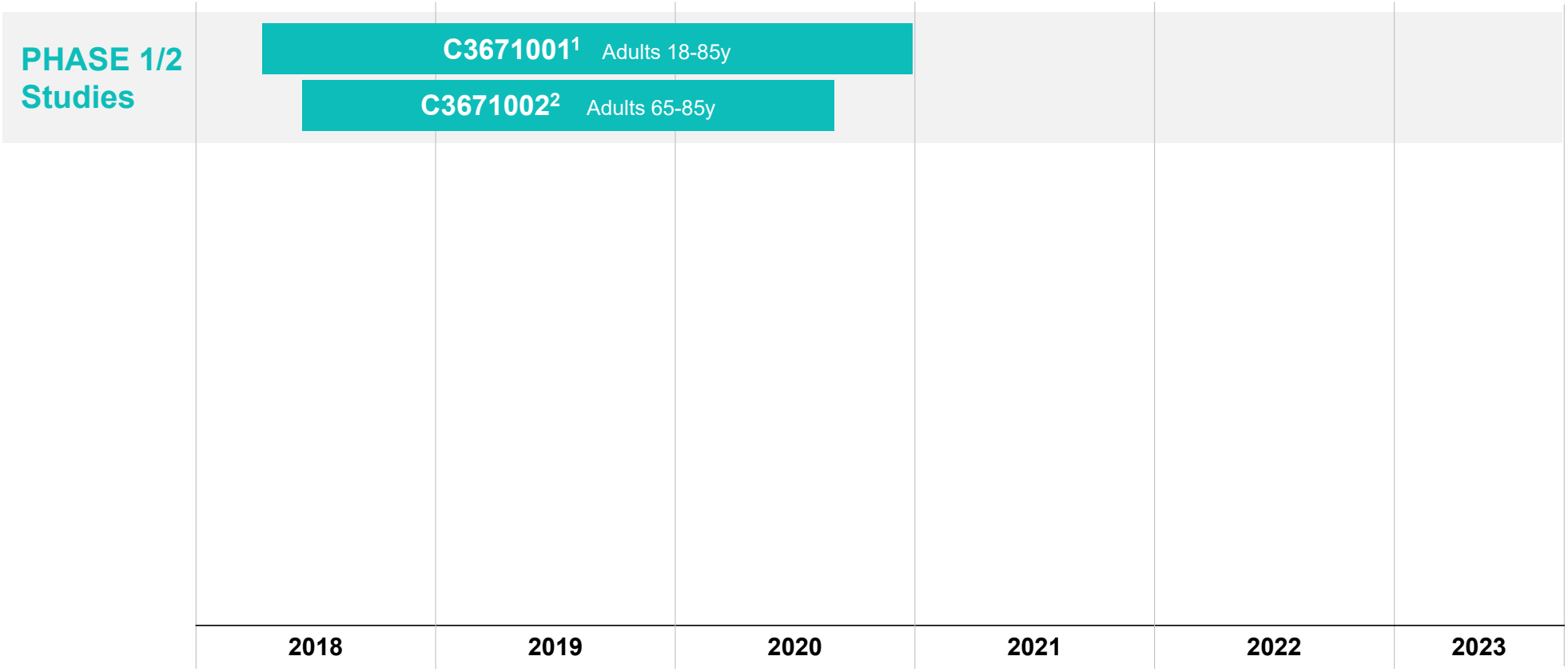
Ontario (RSV A) and Buenos Aires (RSV B) remain dominant genotypes and are the basis of Pfizer's RSVpreF bivalent vaccine

RSV subgroup dominance can vary over time

Both subgroup viruses are associated with severe disease

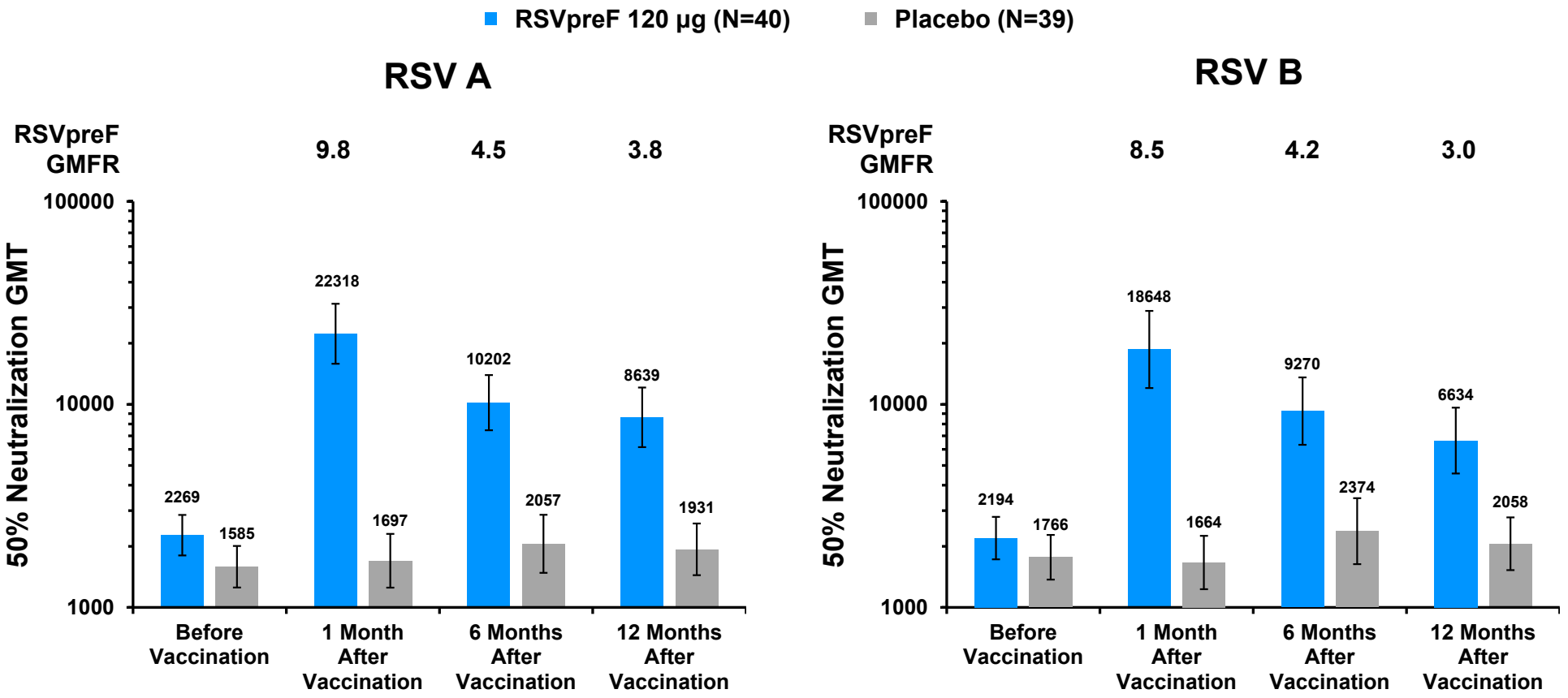
Crank et al, Science 2019, 365:505-9; Hall et al,. *J Infect Dis* 1990; 162:1283-90 Langedijk et al., *Rev Med Virol.* 2021;e2284. https://doi.org/10.1002/rmv.2284

Pfizer's RSVpreF Older Adult Clinical Development Program



1. A Study to Describe the Safety and Immunogenicity of a RSV Vaccine in Healthy Adults. NCT03529773; 2. A Study to Evaluate the Safety and Immunogenicity of an Adjuvanted RSV Vaccine in Healthy Older Adults. NCT03572062; 3. Schmoele-Thoma B et al. Vaccine Efficacy in Adults in a Respiratory Syncytial Virus Challenge Study. *N Engl J Med* 2022; 386:2377-89. 4. Clinical Lot Consistency for RSVpreF in a Population of Healthy Adults 18 to ≤ 49 Years of Age. NCT05096208; 5. Safety and Immunogenicity of RSVpreF Coadministered with SIIV in Adults ≥ 65 Years of Age. NCT05301322; 6. Study to Evaluate the Efficacy, Immunogenicity, and Safety of RSVpreF in Adults (RENOIR). NCT05035212

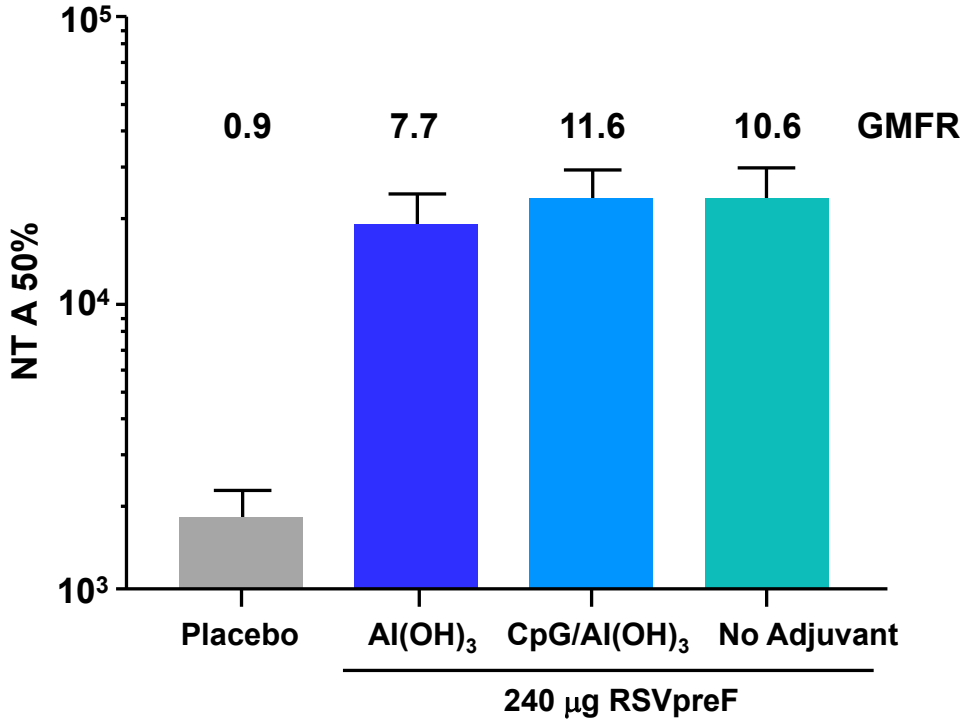
RSV Neutralizing Titer GMFRs at 1, 6, and 12 months After Vaccination Compared with Pre-vaccination for RSV Subgroups A and B in Participants 65–85 Years of Age



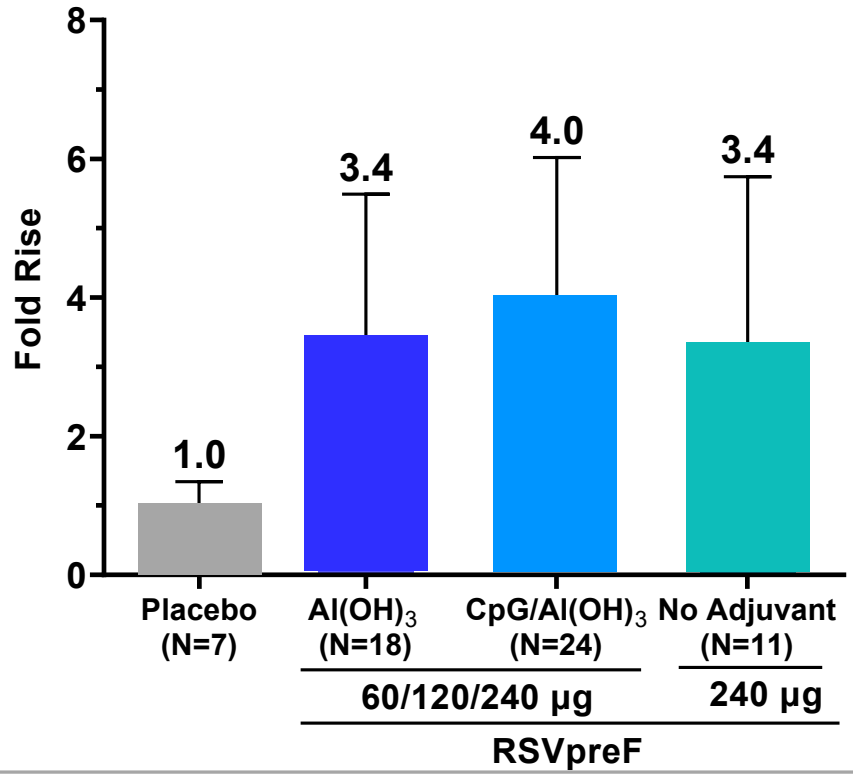
GMFR=Geometric Mean Fold Rise, GMT=Geometric Mean Titer

CpG – No Benefit For Antibody or T-cell Responses

RSV Neutralizing Antibody

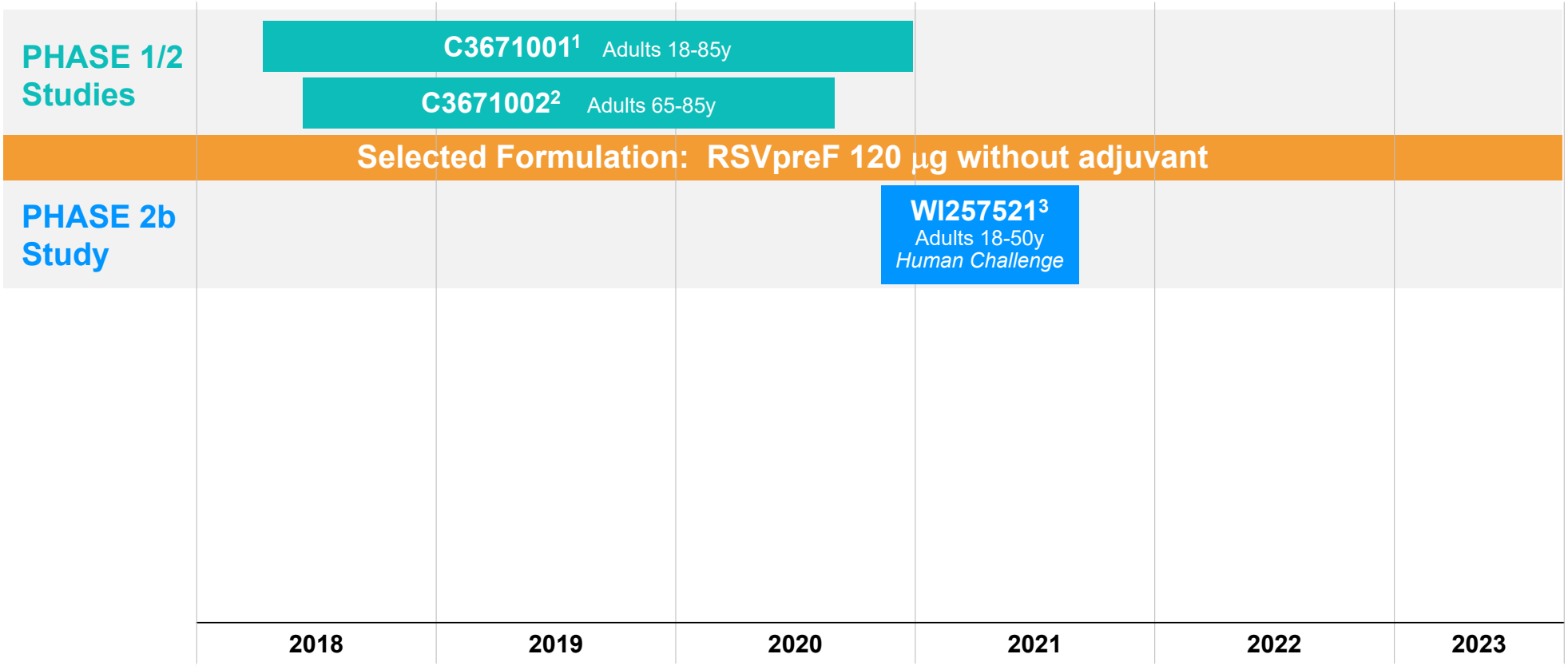


IFN-γ T-cell ELISpot



All data are 1 month post-vaccination. Geometric mean with 95% CI. Fold rise/GMFR, relative to baseline. $Al(OH)_3$=Aluminum hydroxide; CpG=Cytosine phosphodiester Guanine

Pfizer's RSVpreF Older Adult Clinical Development Program



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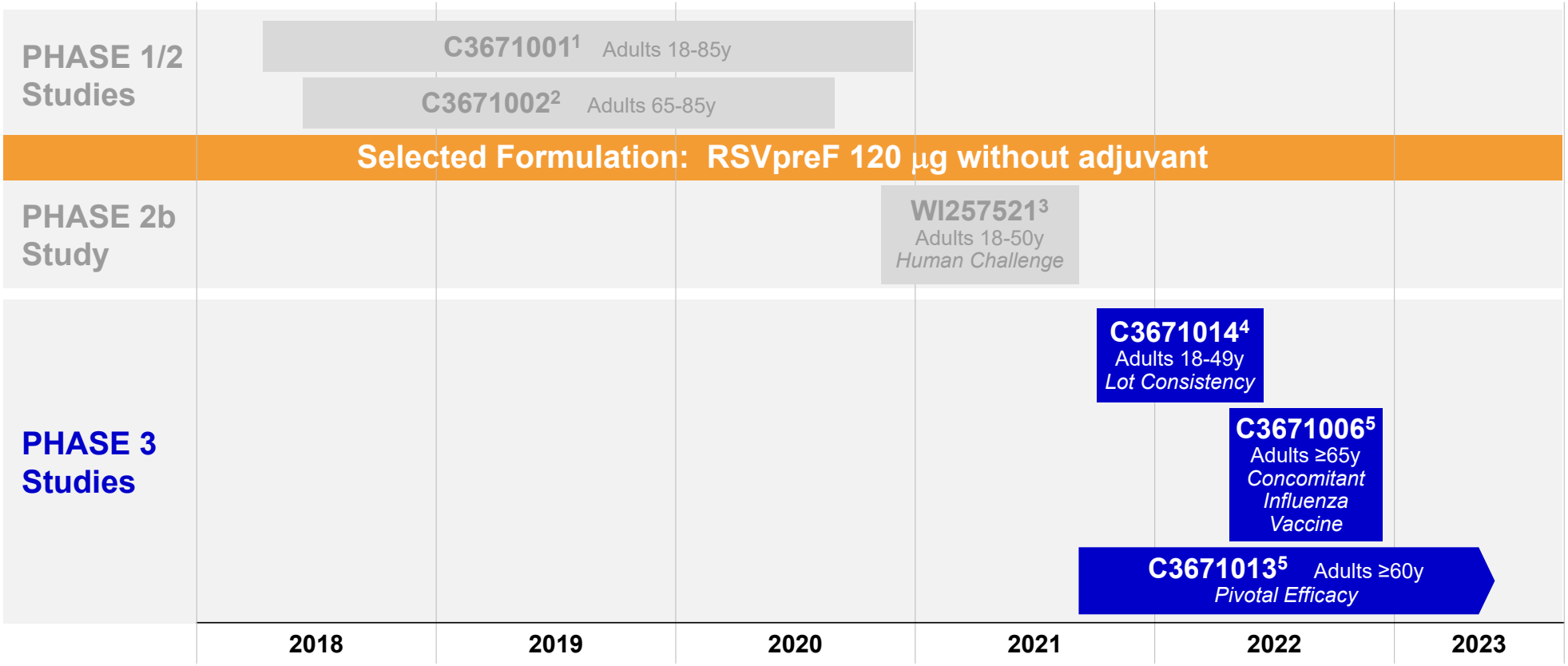
RSVpreF 120 µg (Non Adjuvanted) was Highly Efficacious Against Symptomatic and Asymptomatic RSV Infection

Efficacy Endpoints	RSVpreF N=31 % (n)	Placebo N=31 % (n)	Difference VE (95% CI)
RT-PCR confirmed symptomatic RSV infection (detectable viral RNA on at least 2 consecutive days)	6 (2)	48 (15)	**86.7% (53.8, 96.5)**
RT-PCR confirmed symptomatic RSV infection (quantifiable viral RNA on at least 2 consecutive days)	0	42 (13)	**100% (72.8, 100)**
RT-PCR confirmed infection (≥LLOQ) regardless of symptoms	13 (4)	52 (16)	**75.0% (38.4, 90.6)**

LLOQ, lower limit of quantification; RT-PCR, reverse transcription-polymerase chain reaction;

Pfizer's RSVpreF Older Adult Clinical Development Program



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Summary of Early RSVpreF Studies

- **RSVpreF induced high neutralizing titers and the addition of aluminum or CPG provided no immunological benefit**
- **High efficacy against symptomatic illness in a RSV human challenge study**
- **Bivalent, unadjuvanted RSVpreF subunit vaccine has a good tolerability and safety profile**

Renoir

Pfizer

(The **R**SV vaccine **E**fficacy study i**N** **O**lder adults **I**mmunized against **R**SV disease)

A Phase 3 Study to Evaluate the Efficacy, Immunogenicity, and Safety of Respiratory Syncytial Virus (RSV) Prefusion F Subunit Vaccine in Adults

RENOIR Study Design I

240 study sites in 7 countries

- Argentina
- Canada
- Finland
- Japan
- Netherlands
- South Africa
- United States

Up to **45,000** participants
Adults **≥ 60 years**

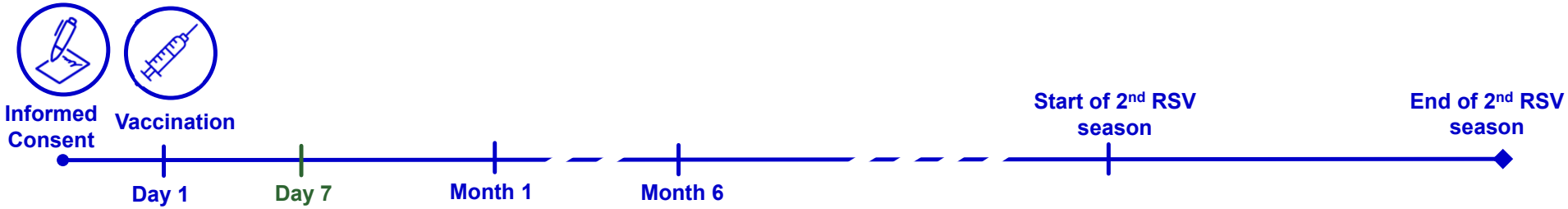
Randomized 1:1 to receive
RSVpreF 120 µg or placebo

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

Study Population
Healthy or with stable chronic conditions

Two Season Study
Followed RSV season in each country

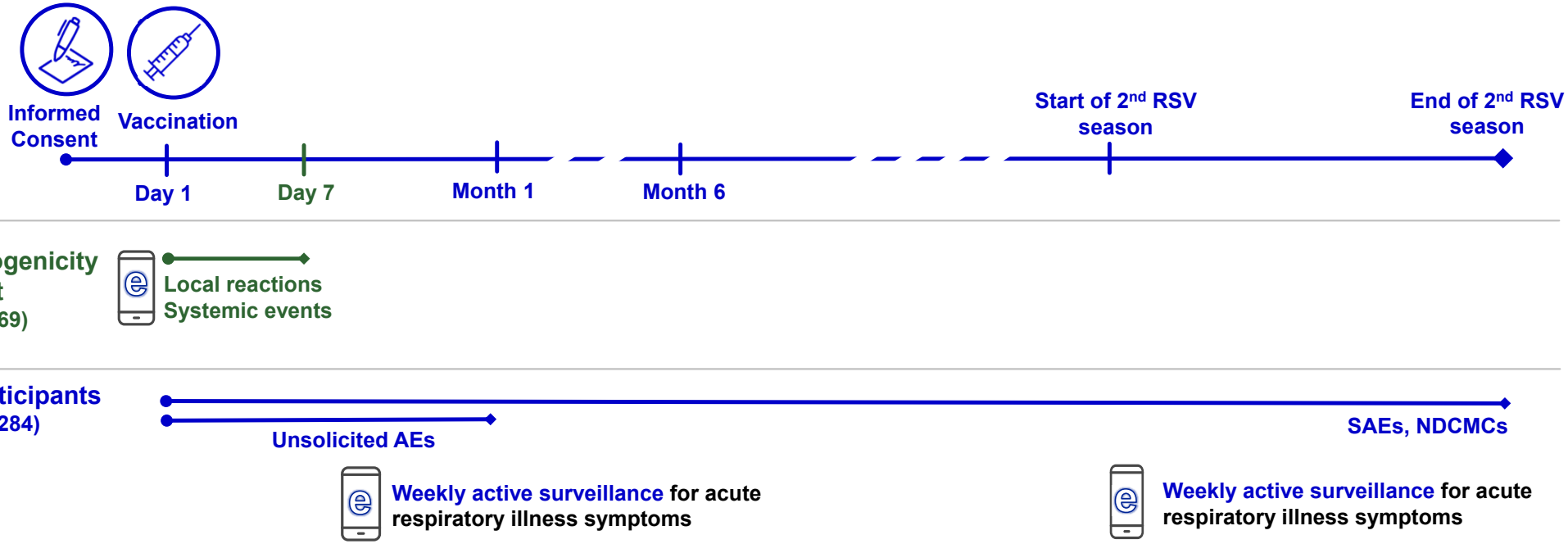
RENOIR Study Design II



Reactogenicity Subset
(N ~ 7,169)

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

RENOIR Study Design II



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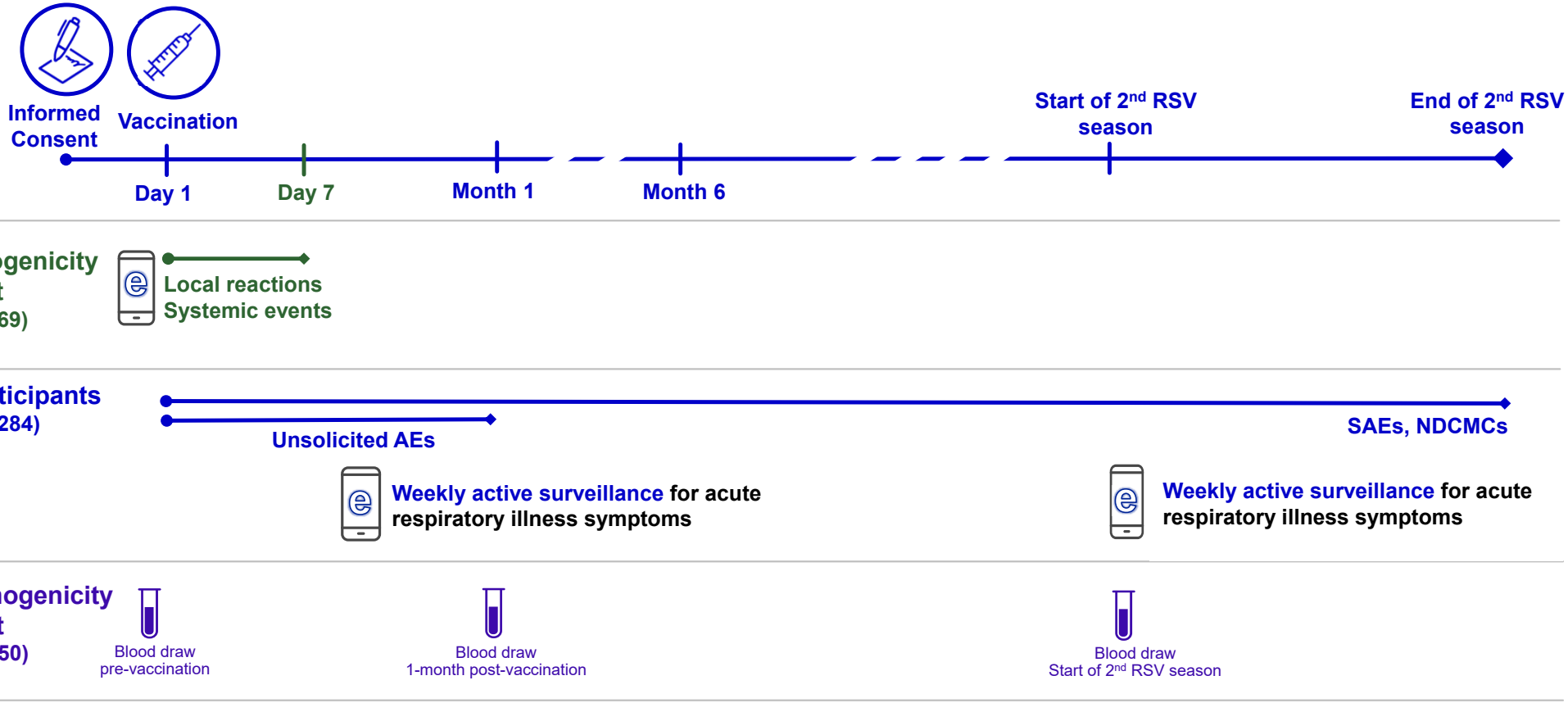

Immunogenicity results not presented today.
Abbreviations: AE, adverse event; NDCMC, newly diagnosed chronic medical condition; SAE, serious adverse event

Phase 3 Study Objectives

Safety

- **Describe the safety profile of RSVpreF**
  - Local reactions and systemic events within 7 days post-vaccination
  - AEs through 1-month post-vaccination
  - SAEs and NDCMCs throughout study

1. Includes LRTI-RSV involving ≥ 2 signs/symptoms and LRTI-RSV involving ≥ 3 signs/symptoms

AE, adverse event; ARI, acute respiratory illness; LRTI, lower respiratory tract illness; NDCMC, newly diagnosed chronic medical condition; RSV, respiratory syncytial virus; SAE, serious adverse event; sLRTI, severe lower respiratory tract illness; VE, vaccine efficacy

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- **Describe the safety profile of RSVpreF**
  - Local reactions and systemic events within 7 days post-vaccination
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Primary Efficacy

- **Prevention of LRTI-RSV in the 1st RSV season**
  - VE of 1st episode LRTI-RSV involving ≥ 2 signs/symptoms in 1st RSV season
  - VE of 1st episode LRTI-RSV involving ≥ 3 signs/symptoms in 1st RSV season

1. Includes LRTI-RSV involving ≥ 2 signs/symptoms and LRTI-RSV involving ≥ 3 signs/symptoms

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Primary Efficacy

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  - VE of 1st episode LRTI-RSV involving ≥ 2 signs/symptoms in 1st RSV season
  - VE of 1st episode LRTI-RSV involving ≥ 3 signs/symptoms in 1st RSV season

Secondary Efficacy

- **Prevention of ARI-RSV in 1st season**
  - VE of 1st episode ARI-RSV in 1st season
- **Prevention of RSV-sLRTI in the 1st RSV season**
- **Prevention of LRTI-RSV[1], ARI-RSV, sLRTI-RSV in 2nd RSV season**
- **Prevention of LRTI-RSV[1], ARI-RSV, sLRTI-RSV across 2 RSV seasons**

1. Includes LRTI-RSV involving ≥ 2 signs/symptoms and LRTI-RSV involving ≥ 3 signs/symptoms

AE, adverse event; ARI, acute respiratory illness; LRTI, lower respiratory tract illness; NDCMC, newly diagnosed chronic medical condition; RSV, respiratory syncytial virus; SAE, serious adverse event; sLRTI, severe lower respiratory tract illness; VE, vaccine efficacy

RENOIR: Statistical Considerations

- **Preplanned interim analysis (IA), per protocol**
- **Agreement with regulatory agencies on licensure criteria**
  - VE: lower bound of confidence interval >20%
  - Case definitions (LRTI-RSV, ARI-RSV, sLRTI-RSV) agreed upon with regulatory agencies
- **Type I error adjustment for IA**

RSV, respiratory syncytial virus; ARI, acute respiratory illness; LRTI, lower respiratory tract illness; sLRTI, severe lower respiratory tract illness; VE, vaccine efficacy

ARI Symptom Surveillance

Weekly active surveillance for ARI symptoms
Symptoms trigger nasal swab and possibly a visit

Acute Respiratory Illness (ARI)

1 or more of these symptoms (**new or worsened from baseline**), lasting more than 1 day

Nasal discharge	Nasal congestion	Sore throat	Cough	Sputum production	Wheezing	Shortness of breath

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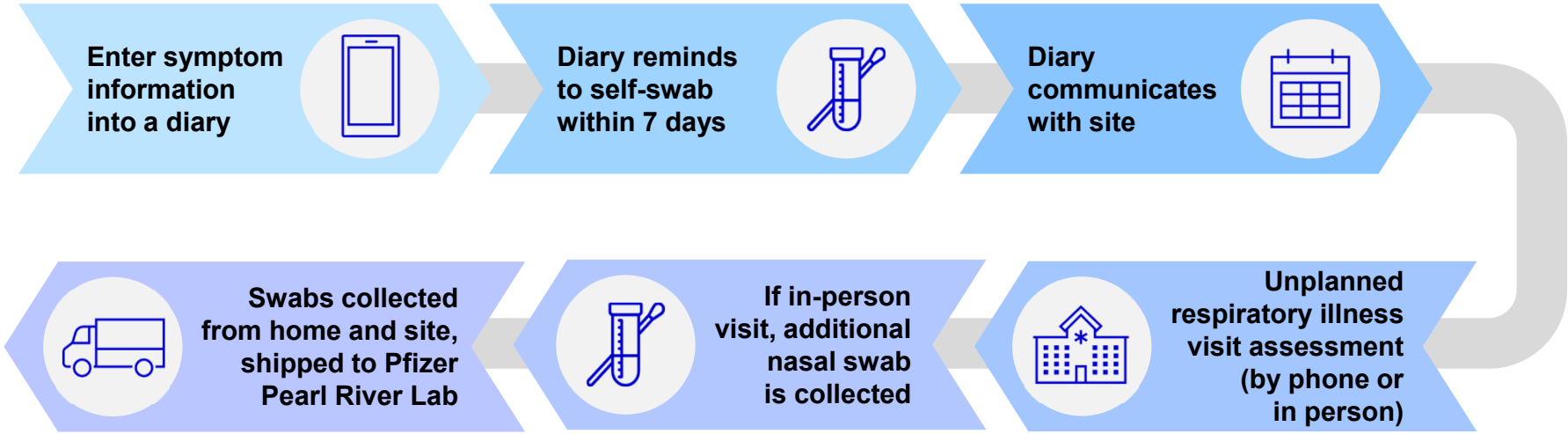

Key Study Definitions

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- Nasal discharge
- Nasal congestion
- Sore throat
- Cough
- Sputum production
- Wheezing
- Shortness of breath

Lower Respiratory Tract Illness (LRTI)

- Cough
- Sputum production
- Wheezing
- Shortness of breath
- Tachypnea

ARI with ≥2 or ≥3 lower respiratory tract signs/symptoms (new or worsened)

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ARI with ≥2 or ≥3 lower respiratory tract signs/symptoms (new or worsened)

Severe LRTI (sLRTI)

LRTI criteria plus at least 1 of the following:

- **Hospitalization** due to LRTI
- New/increased **oxygen supplementation**
- New/increased **mechanical ventilation** (including CPAP)

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- New/increased **oxygen supplementation**
- New/increased **mechanical ventilation** (including CPAP)

Positive validated RT-PCR in central laboratory

- **ARI-RSV**
- **LRTI-RSV**
- **sLRTI-RSV**

RENOIR Results

Demographic Characteristics
Safety Population

	RSVpreF 120 µg N = 17,215 n (%)	Placebo N = 17,069 n (%)	Total N = 34,284 n (%)
Sex			
Female	8,415 (48.9)	8,468 (49.6)	16,883 (49.2)
Race[1]			
White	13,475 (78.3)	13,360 (78.3)	26,835 (78.3)
Black or African American	2,206 (12.8)	2,207 (12.9)	4,413 (12.9)
Asian	1,352 (7.9)	1,333 (7.8)	2,685 (7.8)
Ethnicity			
Hispanic/Latino	6,384 (37.1)	6,260 (36.7)	12,644 (36.9)
Age at Vaccination			
<60 Years[2]	1 (<0.1)	0	1 (<0.1)
60-69 Years	10,756 (62.5)	10,680 (62.6)	21,436 (62.5)
70-79 Years	**5,488 (31.9)**	**5,431 (31.8)**	**10,919 (31.8)**
≥80 Years	**970 (5.6)**	**958 (5.6)**	**1,928 (5.6)**
Mean (SD)	68.3 (6.14)	68.3 (6.18)	68.3 (6.16)
Median (min, max)	67.0 (59, 95)	67.0 (60, 97)	67.0 (59, 97)

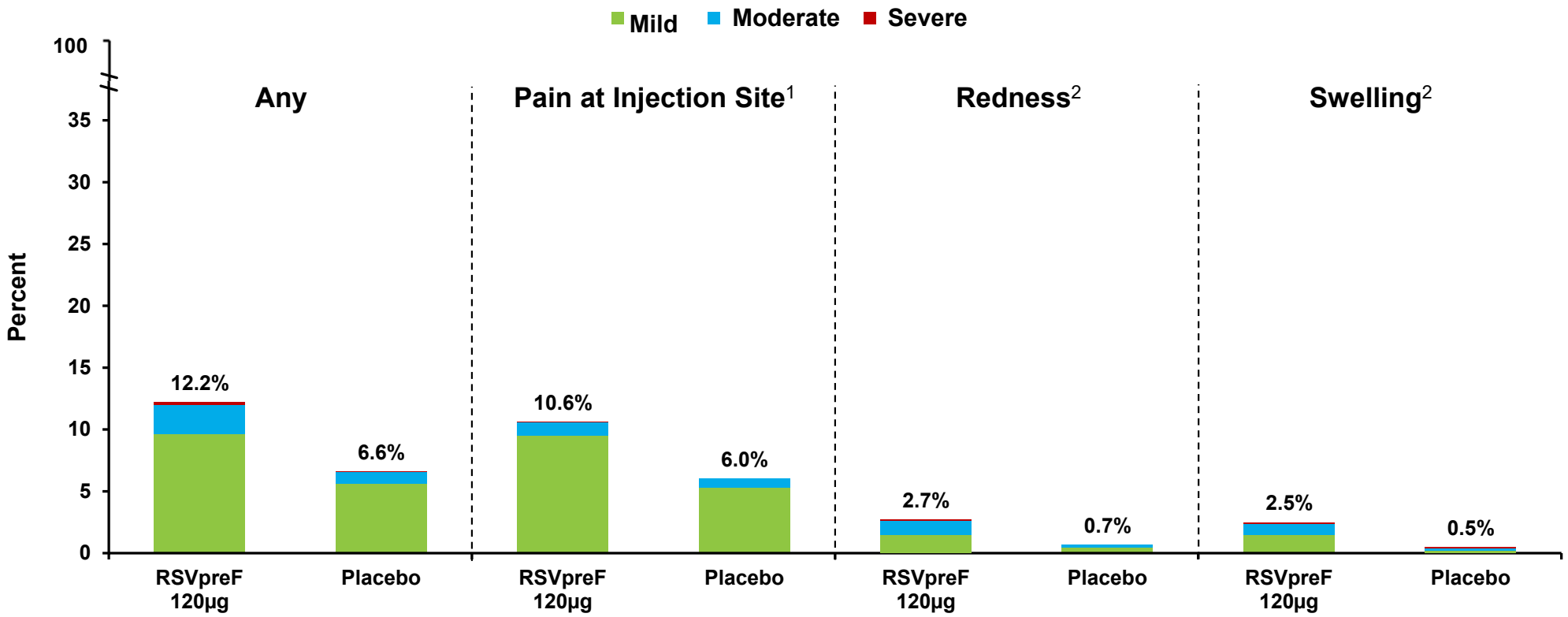
1. Race was recorded as unknown in 0.2% in each group; race was not reported in 0.3% of each group. <0.5% were Native American /Native Alaskan or Native Hawaii/Pacific Islander.
2. One participant enrolled at age <60 years; because this participant received vaccine, the participant is included in the safety reporting.

Baseline Characteristics – Prespecified Significant Conditions
Safety Population

	RSVpreF 120 µg N 17,215 n (%)	Placebo N = 17,069 n (%)	Total N = 34,284 n (%)
With ≥1 prespecified high risk condition	8,867 (51.5)	8,831 (51.7)	17,698 (51.6)
Heart disease	2,221 (12.9)	2,233 (13.1)	4,454 (13.0)
Lung disease	1,956 (11.4)	2,040 (12.0)	3,996 (11.7)
With ≥1 chronic cardiopulmonary condition	2,595 (15.1)	2,640 (15.5)	5,235 (15.3)
Asthma	1,541 (9.0)	1,508 (8.8)	3,049 (8.9)
Chronic obstructive pulmonary disease (COPD)	1,012 (5.9)	1,080 (6.3)	2,092 (6.1)
Congestive heart failure (CHF)	293 (1.7)	307 (1.8)	600 (1.8)
Diabetes	3,224 (18.7)	3,284 (19.2)	6,508 (19.0)
Liver disease	335 (1.9)	329 (1.9)	664 (1.9)
Renal disease	502 (2.9)	459 (2.7)	961 (2.8)
Current tobacco use	2,642 (15.3)	2,571 (15.1)	5,213 (15.2)

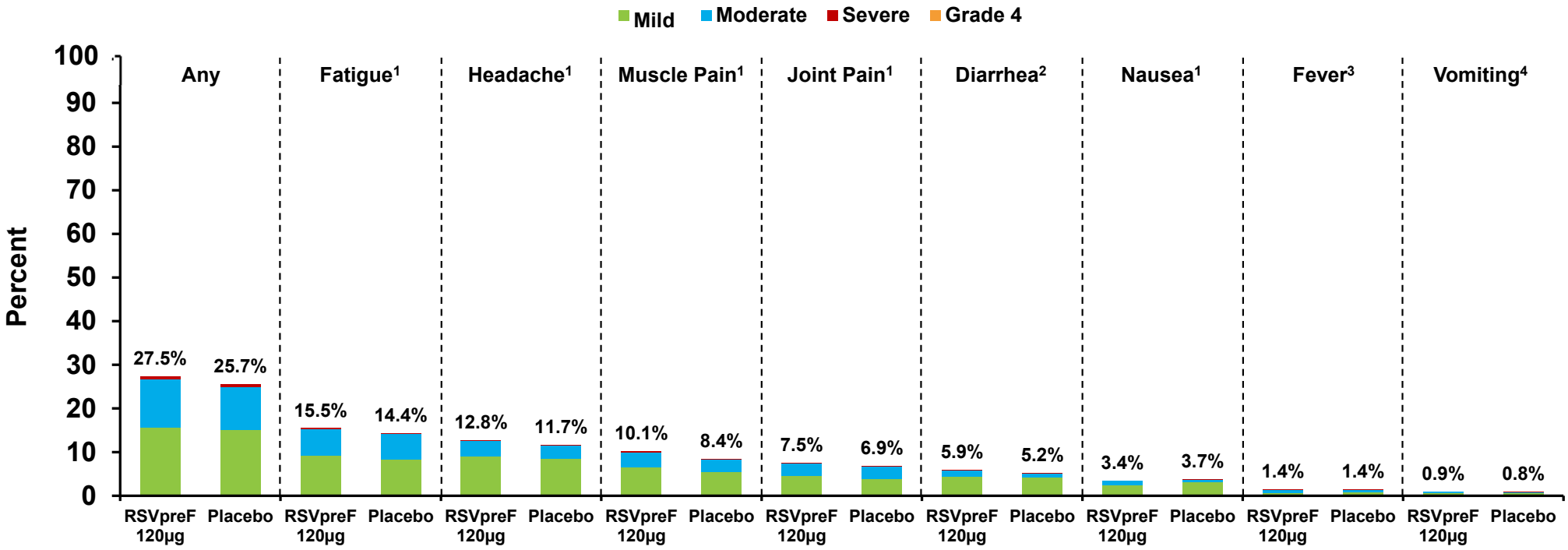
Safety

Local Reactions, by Maximum Severity, Within 7 Days After Vaccination



1Severity definition: mild = no interference with daily activity; moderate = some interference with daily activity; severe = prevents daily activity
2Severity definition: mild = >2-5 cm, moderate = >5-10 cm; severe = >10 cm
RSVpreF N = 3619-3621; placebo N = 3532-3539

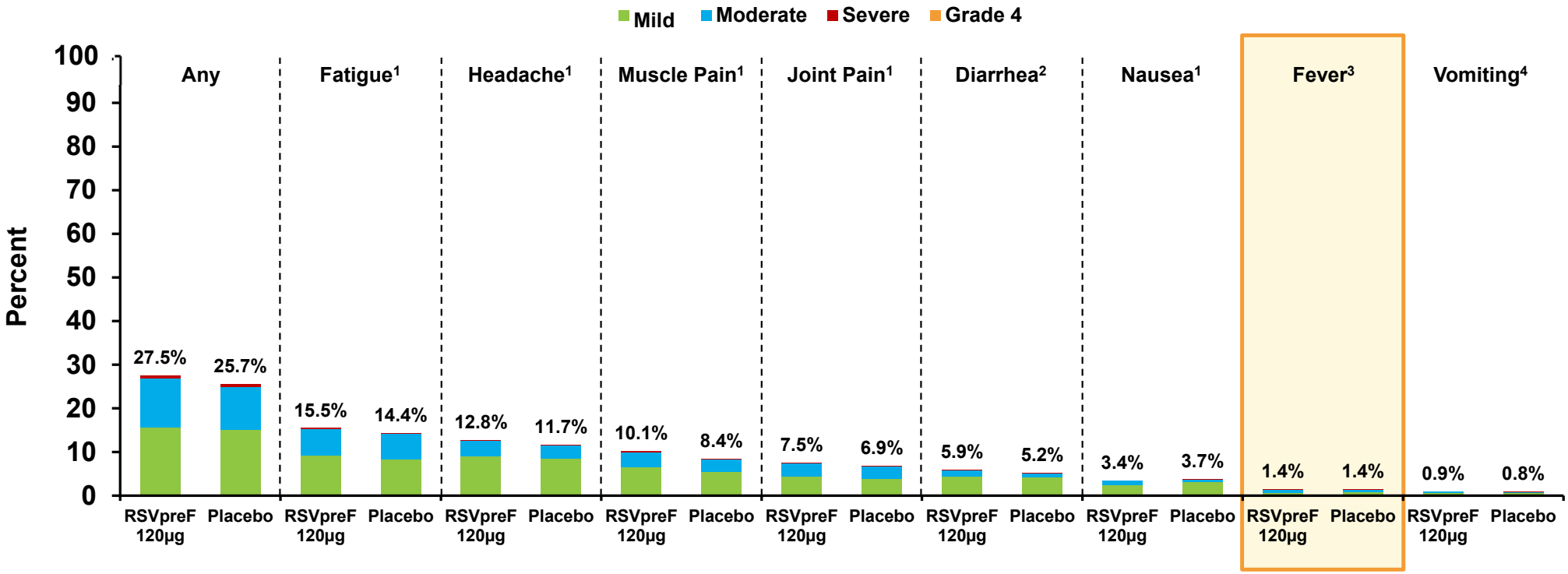
Systemic Events, by Maximum Severity, Within 7 Days After Vaccination



1. Severity definition: mild = no interference with daily activity; moderate = some interference with daily activity; severe = prevents daily activity
2. Severity definition: mild = 2-3 loose stools in 24h; moderate = 4-5 loose stools in 24h; severe = 6 or more loose stools in 24h
3. Severity definition: mild 38.0°C-38.4 °C; moderate >38.4°C-38.9 °C; severe >38.9°C-40.0 °C; grade 4 >40.0 °C
4. Severity definition: mild = 1-2 time(s) in 24h; moderate = >2 times in 24h; severe = requires intravenous hydration

RSVpreF N = 3619-3621: Placebo N = 3532-3539

Systemic Events, by Maximum Severity, Within 7 Days After Vaccination



1. Severity definition: mild = no interference with daily activity; moderate = some interference with daily activity; severe = prevents daily activity
2. Severity definition: mild = 2-3 loose stools in 24h; moderate = 4-5 loose stools in 24h; severe = 6 or more loose stools in 24h
3. Severity definition: mild 38.0°C-38.4 °C; moderate >38.4°C-38.9 °C; severe >38.9°C-40.0 °C; grade 4 >40.0 °C
4. Severity definition: mild = 1-2 time(s) in 24h; moderate = >2 times in 24h; severe = requires intravenous hydration

RSVpreF N = 3619-3621: Placebo N = 3532-3539

Adverse Events, by Category, from Vaccination through 1-Month Follow Up Visit and Through Data Cutoff (14Jul2022): Safety Population

Adverse Event Category	RSVpreF 120 µg N 17,215		Placebo N 17,069	
	n (%)	(95% CI)	n (%)	(95% CI)
From Vaccination through 1-Month Follow-Up Visit				
Any Event	**1,537 (8.9)**	**(8.5, 9.4)**	**1,451 (8.5)**	**(8.1, 8.9)**
Related	**230 (1.3)**	**(1.2, 1.5)**	**159 (0.9)**	**(0.8, 1.1)**
Immediate AE[1]	**35 (0.2)**	**(0.1, 0.3)**	**31 (0.2)**	**(0.1, 0.3)**
Severe	**65 (0.4)**	**(0.3, 0.5)**	**51 (0.3)**	**(0.2, 0.4)**
Life-threatening	**24 (0.1)**	**(0.1, 0.2)**	**19 (0.1)**	**(0.1, 0.2)**
From Vaccination through 14Jul2022				
NDCMC	301 (1.7)	(1.6, 2.0)	313 (1.8)	(1.6, 2.0)
SAE	396 (2.3)	(2.1, 2.5)	387 (2.3)	(2.0, 2.5)
Related SAE	3 (<0.1)	(0.0, 0.1)	0	(0.0, 0.0)
AE leading to withdrawal	10 (<0.1)	(0.0, 0.1)	6 (<0.1)	(0.0, 0.1)
AE leading to death	52 (0.3)	(0.2, 0.4)	49 (0.3)	(0.2, 0.4)

Any reactogenicity reported as adverse events (from either reactogenicity subset or non-reactogenicity subset) during the specified time period are included in this table.
1. Immediate AE refers to an AE reported in the 30-minute post-vaccination observation period.
AE, adverse event; NDCMC, newly diagnosed chronic medical condition; SAE, serious adverse event.

Adverse Events, by Category, from Vaccination through 1-Month Follow Up Visit and Through Data Cutoff (14Jul2022): Safety Population

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Serious Adverse Events Assessed as Related by the Investigator n = 3 (<0.1%)

- Hypersensitivity (allergic reaction)
- Miller Fisher Syndrome
- Guillain-Barre Syndrome

Guillain Barré and Miller Fisher Cases – Brighton Collaboration Diagnostic Assessment

Age	Gender	Country	Latency	Neurological Examination	CSF	Electrophysiological Studies	Comments	Administered Drug Diagnosis BC Level
66	Female	Japan	9 days	Bilateral ophthalmoparesis, Reflexes not tested	Not performed	Not performed	Retrospective diagnosis Plausible time to onset Sore throat infection preceding MF	RSVpreF Miller Fisher BC Level 4
66	Male	USA	8 days	Consistent with GBS	Consistent with GBS	Consistent with GBS	Plausible time to onset preceded by myocardial infarction	RSVpreF GBS BC Level 1

Two other cases of GBS were reported as unrelated after the data lock point:
One in the RSV pre-F group 8 months after vaccination and preceeded by infection, and
One in the Placebo group 14 months after vaccination preceeded by worsening of diverticulitis

Serious Adverse Events (SAEs) from Vaccination through Data Cutoff (14Jul2022): Safety Population

	RSVpreF 120 µg N=17,215		Placebo N=17,069	
	n (%)	(95% CI)	n (%)	(95% CI)
Participants with Any SAE	396 (2.3)	(2.1, 2.5)	387 (2.3)	(2.0, 2.5)
System Organ Class[1]				
Cardiac disorders	81 (0.5)	(0.4, 0.6)	84 (0.5)	(0.4, 0.6)
Infections and infestations	78 (0.5)	(0.4, 0.6)	61 (0.4)	(0.3, 0.5)
Neoplasms benign, malignant and unspecified[2]	56 (0.3)	(0.2, 0.4)	54 (0.3)	(0.2, 0.4)
Nervous system disorders	49 (0.3)	(0.2, 0.4)	50 (0.3)	(0.2, 0.4)

1. System Organ Class categories listed are those with >0.2% participants in either the vaccine or placebo group reporting an SAE in that category.
2. Including cysts and polyps.

Safety Conclusions

- **RSVpreF was safe and well tolerated**
- **Local and systemic events were mostly mild to moderate and short lived**
- **AE profile did not suggest any safety concerns for RSVpreF vaccination in adults 60 years of age and older**

Efficacy

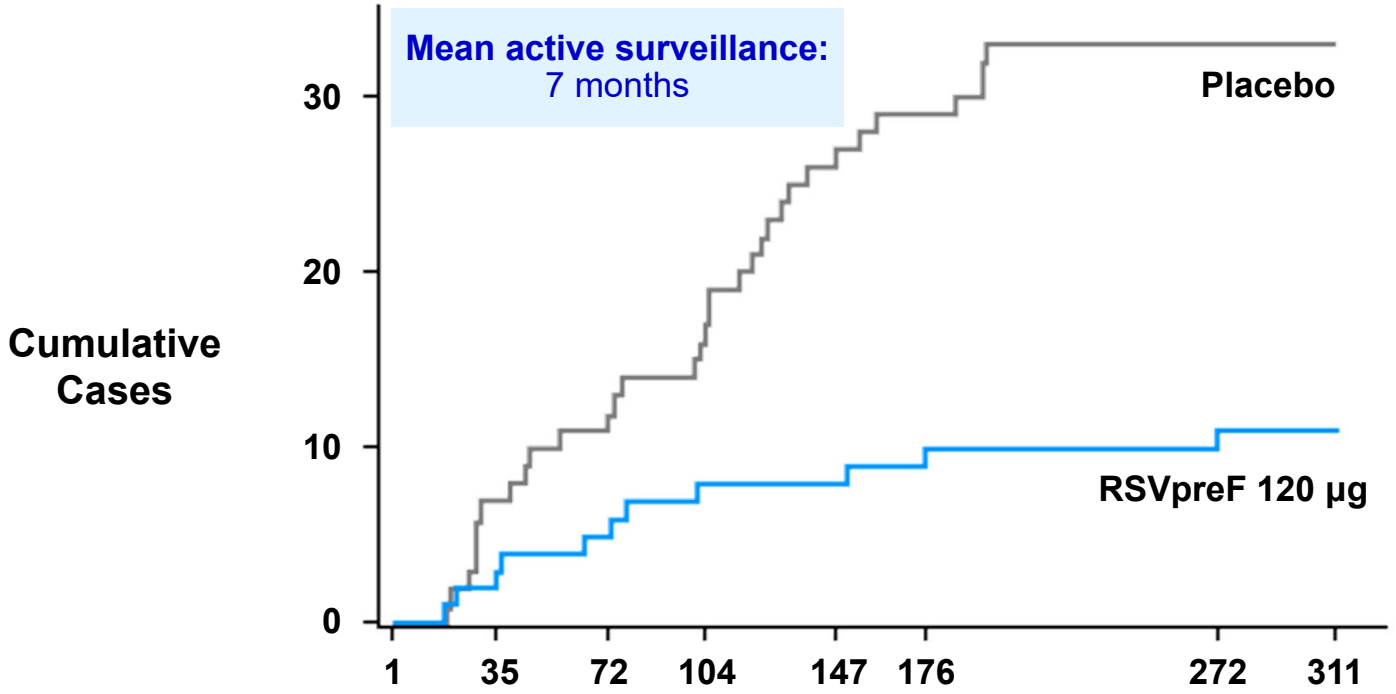
RSVpreF was Highly Efficacious Against LRTI-RSV During the First Season

	Total cases	Case Split RSVpreF/Placebo	VE	96.66% CI[1]
≥2 LRTI-RSV	44	11/33	66.7%	(28.8%, 85.8%)
≥3 LRTI-RSV	16	2/14	85.7%	(32.0%, 98.7%)

Both primary efficacy endpoints met licensure criteria

CI, confidence interval; LRTI-RSV, lower respiratory tract illness due to respiratory syncytial virus; VE, vaccine efficacy
1. CI obtained using the conditional exact test based on the binomial distribution of P, adjusted by Pocock error spending for interim analysis (alpha = 3.34%)

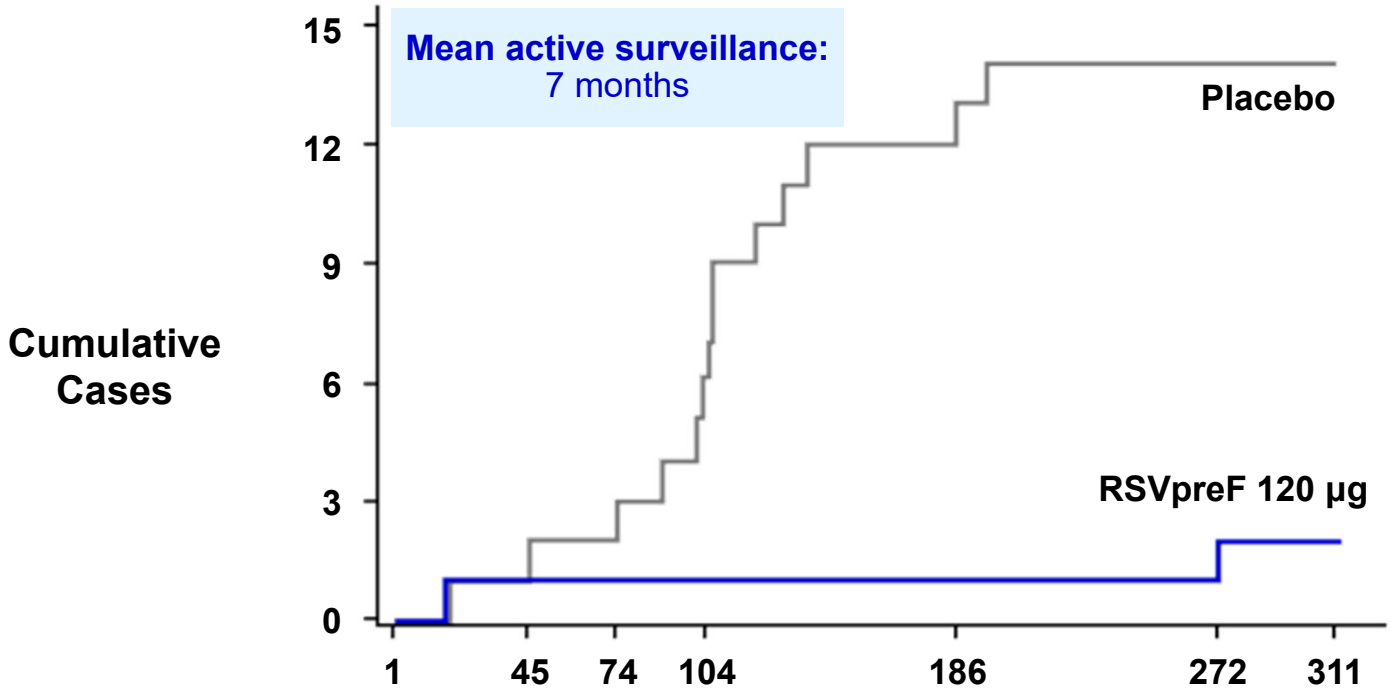
RSVpreF Efficacy Against LRTI-RSV with ≥2 Symptoms



Cumulative Events								
RSVpreF	0	3	5	8	8	10	11	11
Placebo	0	7	12	17	27	29	33	33

LRTI-RSV, lower respiratory tract illness due to respiratory syncytial virus

RSVpreF Efficacy Against LRTI-RSV with ≥3 Symptoms



Cumulative Events							
RSVpreF	0	1	1	1	1	2	2
Placebo	0	2	3	7	13	14	14

LRTI-RSV, lower respiratory tract illness due to respiratory syncytial virus

Clinical Characterization of LRTI-RSV with ≥2 and ≥3 Symptoms

LRTI Symptoms	% Among ≥2 LRTI-RSV Episodes (N=45)		% Among ≥3 LRTI-RSV Episodes (N=16)	
	n	%	n	%
Cough	44	97.8	15	93.8
Sputum production	38	84.4	13	81.3
Wheezing	17	37.8	15	93.8
Shortness of breath	13	28.9	11	68.8
Tachypnea	5	11.1	5	31.3

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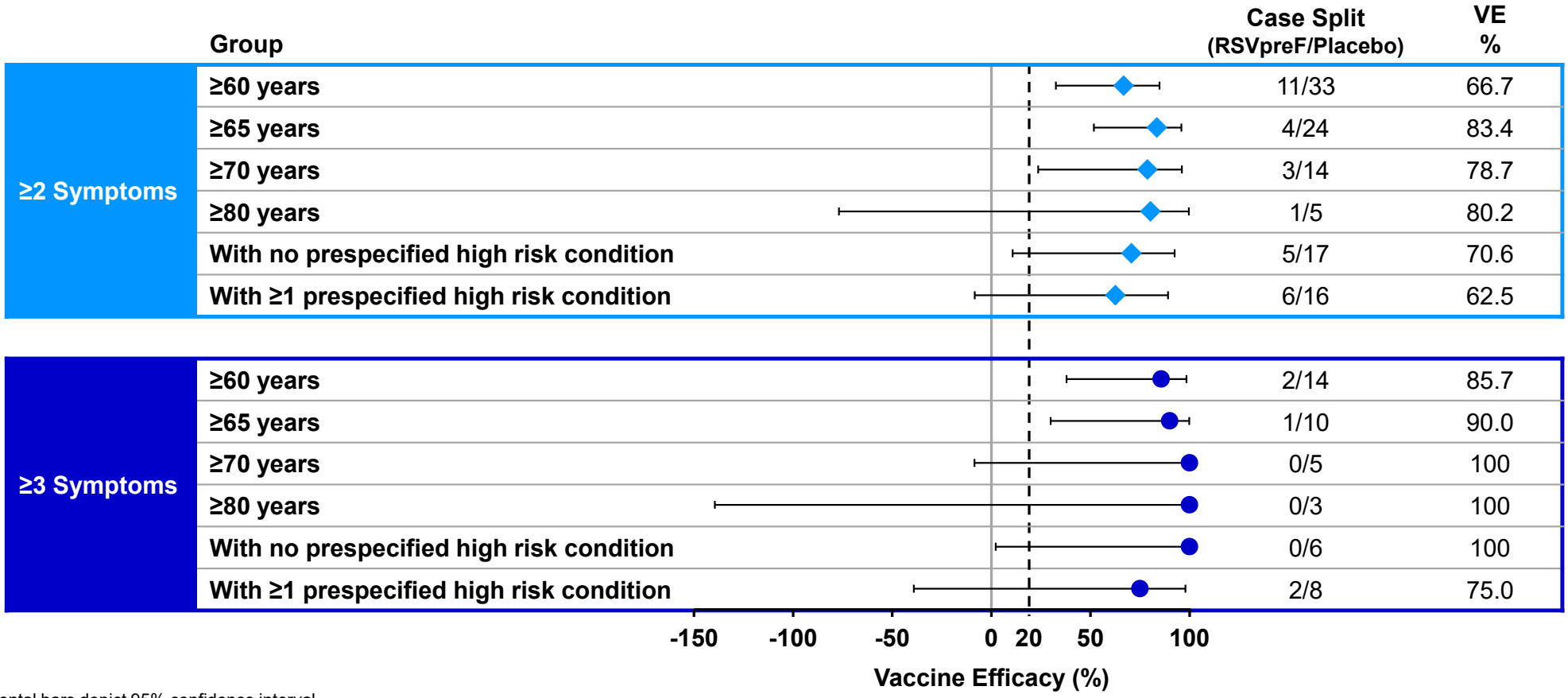
	44	97.8	15	93.8
Sputum production	38	84.4	13	81.3
Wheezing	17	37.8	15	93.8
Shortness of breath	13	28.9	11	68.8
Tachypnea	5	11.1	5	31.3

- **LRTIs with ≥3 respiratory symptoms included:**
  - 4 cases of pneumonia or bronchopneumonia,
  - 2 hospitalizations
  - 4 cases of bronchitis all requiring corticosteroids treatment

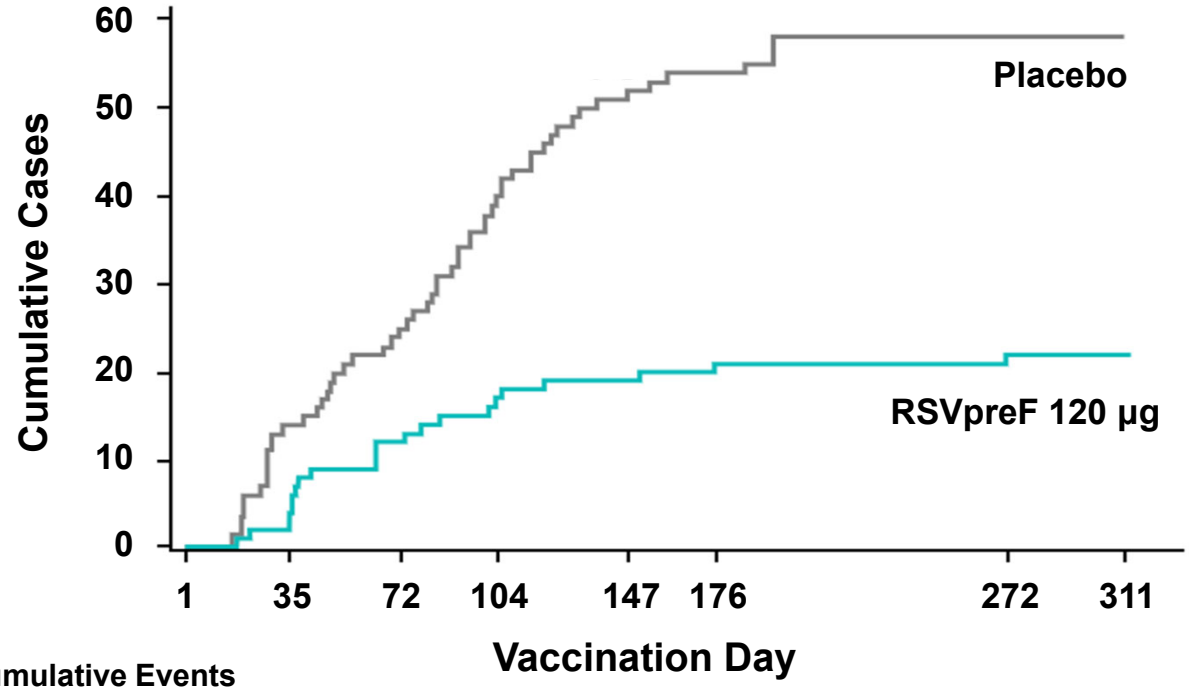
Consistent Efficacy was Observed Across Population Subgroup Analyses



Horizontal bars depict 95% confidence interval
VE, vaccine efficacy

RSVpreF Efficacy Against ARI-RSV

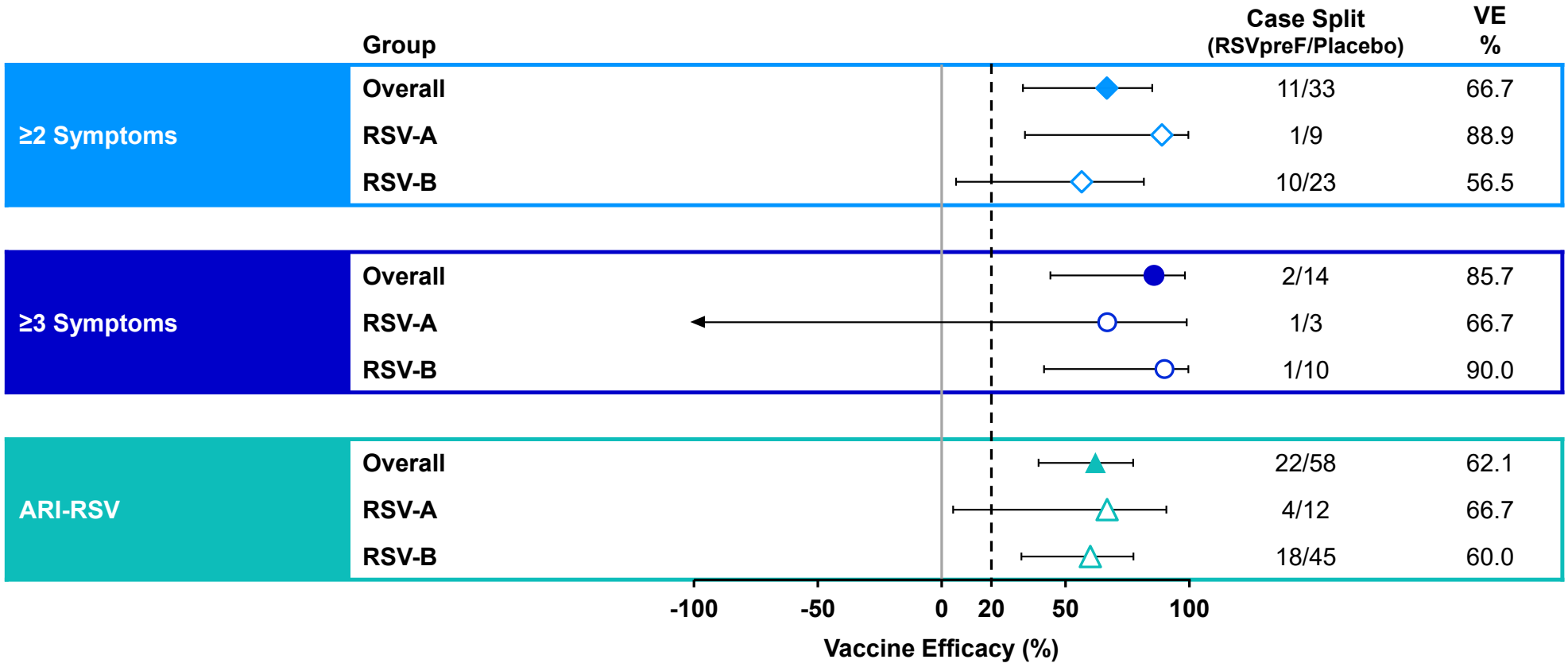
Total cases ARI-RSV	Case split RSVpreF/Placebo
80	22/58
VE	**95% CI**
62.1%	(37.1%, 77.9%)



Cumulative Events								
RSVpreF	0	4	12	17	19	21	22	22
Placebo	0	14	25	40	52	54	58	58

CI, confidence interval; ARI-RSV, acute respiratory illness due to respiratory syncytial virus; VE, vaccine efficacy.

Consistent Efficacy was Observed Across RSV Subgroup A and B



1. 95% CI for ARI-RSV and 96.66% CI for LRTI-RSV; 2. One case in placebo group was based on local test without RSV subgroup
ARI, acute respiratory illness; LRTI, lower respiratory tract illness; RSV, respiratory syncytial virus; VE, vaccine efficacy.

Medically Attended ARI-RSV and LRTI-RSV

Visits initiated by a participant because of medical need

- ER visit
- Urgent care visit
- Home healthcare services
- Primary care physician office visit
- Pulmonologist or specialist office visit
- Telehealth contact
- Hospitalization

Medically Attended LRTI-RSV or ARI-RSV Starting 14 Days After Vaccination, Evaluable Efficacy Population

Endpoint	RSVpreF N=16306 Cases – n (%) IR/1000 PY	Placebo N=16308 Cases – n (%) IR/1000 PY	VE[a], % (95% CI)
Medically attended LRTI-RSV with ≥2 symptoms	7 (0.04) 0.76	20 (0.12) 2.17	65.1 (14.0, 87.5)
Medically attended LRTI-RSV with ≥3 symptoms	2 (0.01) 0.22	10 (0.06) 1.09	80.0 (6.3, 97.9)
Medically attended ARI-RSV	8 (0.05) 0.87	26 (0.16) 2.82	69.3 (30.1, 88.0)

a. VE adjusted for follow-up time is calculated as 1-(hP/[1-P]), where P is the number of RSVpreF cases divided by the total number of cases and h is the ratio of total follow-up time in the placebo group to the total follow-up time in the RSVpreF group. Nominal 95% CI is obtained using the conditional exact test based on the binomial distribution of P adjusted person-time follow-up.

Depending on Level of Vaccine Uptake Among Older Adults, RSVpreF has the Potential* to Annually Prevent:

26,000 to 100,000
emergency room visits

34,000 to 136,000
hospitalizations

211,000 to 845,000
ARI-RSV-related outpatient visits

* Estimations based on 25% to 100% vaccine uptake; RENOIR vaccine efficacy estimates applied to annual US case projections estimates among person 65 years and older from McLaughlin JM et al. Rates of Medically Attended RSV Among US Adults: A Systematic Review and Meta-analysis. Open Forum Infect Dis. 2022 Jun 17;9(7):ofac300.

Efficacy Conclusions

- **RSVpreF was highly efficacious in reducing RSV-associated LRTI in adults 60 years and older**
- **RSVpreF was efficacious in reducing RSV-associated ARI in adults 60 years and older**

Pharmacovigilance & Surveillance

Pharmacovigilance

Proactive Risk Mitigation

- Labeling
- Educational materials
- Post-marketing safety studies

Pharmacovigilance

- **Detect unexpected safety events rapidly**
- Spontaneous report collection
- Post marketing study to further assess GBS/immune mediated demyelinating conditions
- Active follow-up
- Frequent signal detection and evaluation

Benefit Risk

Risks

PIVOTAL STUDY

17,215 Adult Participants ≥60 Years
Single dose of RSVpreF 120 µg

RISKS	
Safety Risks	No important identified safety risks detected
Local Reactions/ Systemic Events	Generally mild to moderate
Adverse Events	Similar between RSVpreF and placebo groups
Deaths	Not considered vaccine-related
Tolerance	Well tolerated in adults ≥60 years of age

Risk/Benefit

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BENEFITS		
Efficacious in preventing LRTI-RSV with:	**≥2 symptoms: 66.7%**	**≥3 symptoms: 85.7%**
Efficacy against first episode ARI-RSV:	**62.1%**	

RSVpreF in Adults 60 Years and Over: Conclusions

Safety

- **RSVpreF was safe and well tolerated**
- **Overall safety profile is favorable**

Efficacy

- **The pivotal Phase 3 study provides robust evidence that RSVpreF was**
  - Highly efficacious in reducing RSV-associated LRTI
  - Efficacious in reducing RSV-associated ARI

Benefit Risk

- **The benefit-to-risk ratio is highly favorable and supports the proposed indication**

Proposed Indication

Prevention of acute respiratory disease and lower respiratory tract disease caused by respiratory syncytial virus (RSV) in individuals 60 years of age and older by active immunization.

Acknowledgements