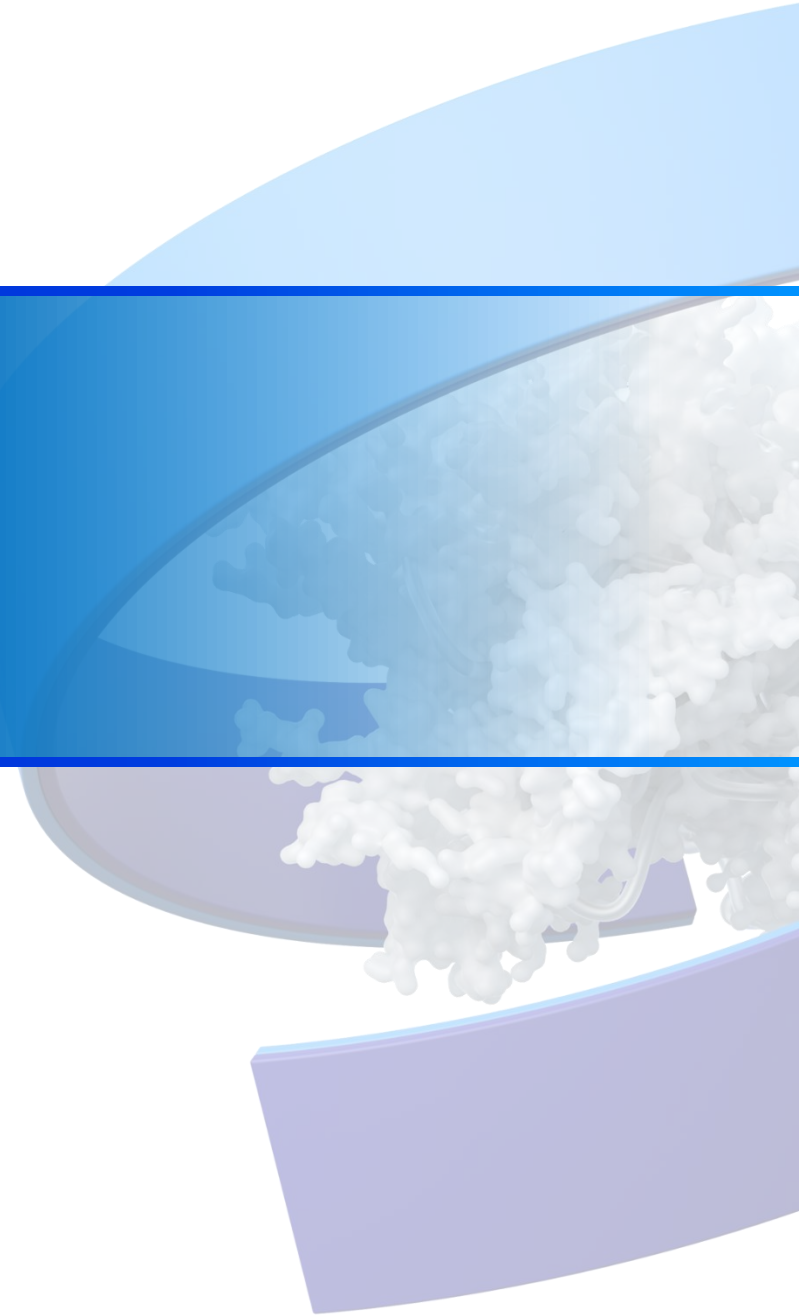




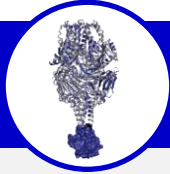
# RSVpreF Adult Clinical Development Update

Iona Munjal, MD

ACIP Meeting 26 June 2024



# RSVpreF Adult Clinical Development Program Updates



## ABRYSVO® (Respiratory Syncytial Virus Vaccine)

### Bivalent Stabilized Prefusion F

- Based on contemporary RSV A & RSV B strains



### Additional Clinical Trial Data

- ≥60 years (RENOIR trial) Season 2 analyses
- ≥18 years at High Risk for RSV (MONeT trial)
- Real-world effectiveness data

## Indication for ABRYSVO



### Maternal

Immunize pregnant women to prevent RSV-associated lower respiratory tract disease (LRTD) in infants from birth through 6 months of age



### Older Adult

Active immunization to prevent RSV-associated LRTD in adults ≥ 60 years of age

## Extending Adult Indication

### Application Submitted for FDA Review



Active immunization to prevent RSV-associated LRTD in adults 18-59 years of age


# RSVpreF Adult – Clinical Development Program

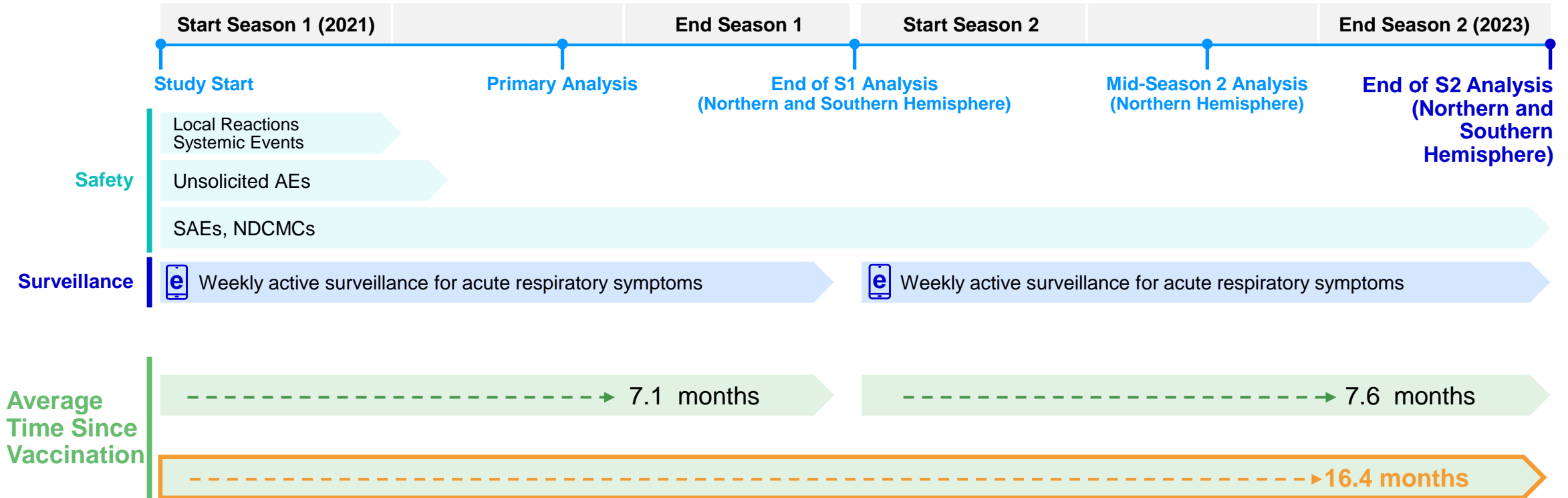
Updated Data on RENOIR, Real-World Evidence, and MONeT

Older Adults ≥ 60					Adults ≥ 18		
RENOIR	Adults ≥ 60		COVID COAD	FLU COAD	REAL-WORLD	MONeT	
			Adults ≥ 65	Adults ≥ 65	Adults ≥ 60	Adults 18–59	Adults ≥ 18
<ul style="list-style-type: none"> <li>• Efficacy through 2 seasons</li> </ul>	<ul style="list-style-type: none"> <li>• Revaccination Y1 and Y2</li> </ul>	<ul style="list-style-type: none"> <li>• Revaccination Y3 and Y4</li> </ul>	<ul style="list-style-type: none"> <li>• Non-inferiority demonstrated</li> </ul>	<ul style="list-style-type: none"> <li>• Non-inferiority demonstrated</li> </ul>	<ul style="list-style-type: none"> <li>• KPSC Observational Retrospective Case Control Study</li> </ul>	<ul style="list-style-type: none"> <li>• Adults 18-59 with chronic medical conditions</li> </ul>	<ul style="list-style-type: none"> <li>• Adults ≥ 18 with immuno-compromising conditions</li> </ul>
	Ongoing	Ongoing			Ongoing		Ongoing

# The RSV Vaccine Efficacy Study in Older Adults Immunized Against RSV Disease



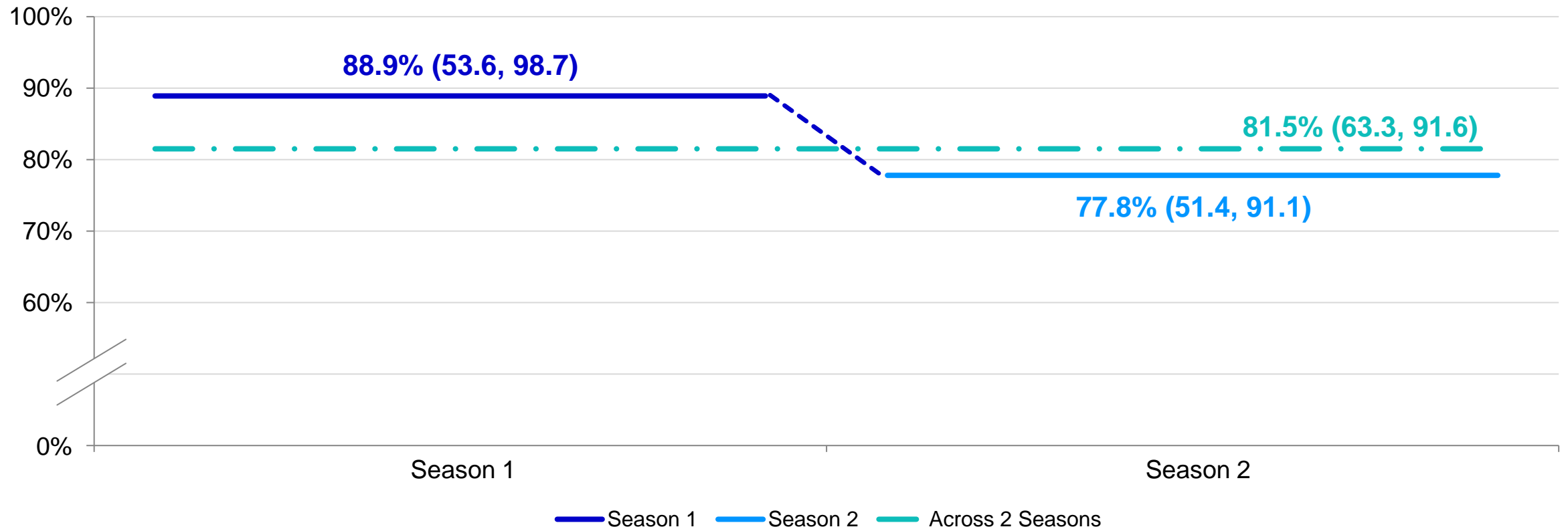
 38,863 participants / Adults ≥60 years



RSV, respiratory syncytial virus; RSVpreF, respiratory syncytial virus prefusion F subunit, AE, adverse event; NDCMC, newly diagnosed chronic medical condition; SAE, serious adverse event.

# RSVPreF Maintained High Efficacy in Season 2

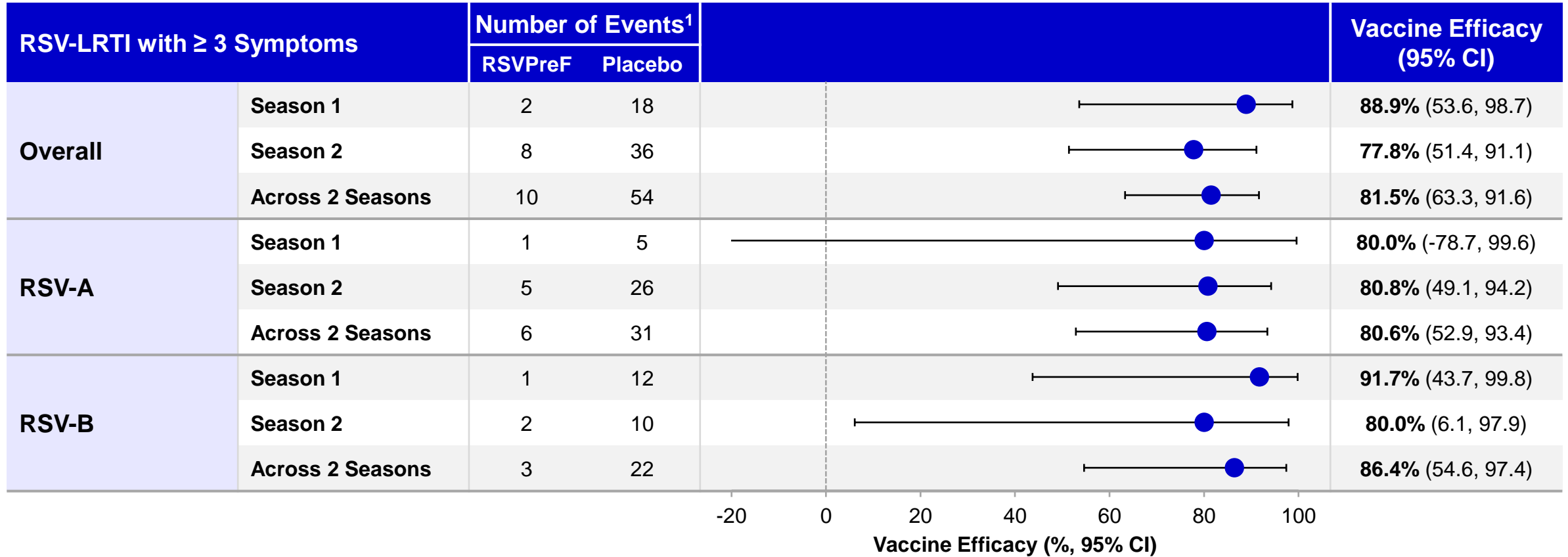
VE Against RSV-associated LRTD in Subjects with  $\geq 3$  New or Worsened Lower Respiratory Symptoms (95% CI)<sup>1,2</sup>



LRTD = lower respiratory tract disease

1. Eiras D. 2024 (May 17-22). ATS 2. Walsh EE, et al. *N. Engl J Med.* 2023;338:1465-1477.

# Consistent Efficacy was Observed Across RSV Overall and by Subgroups A and B



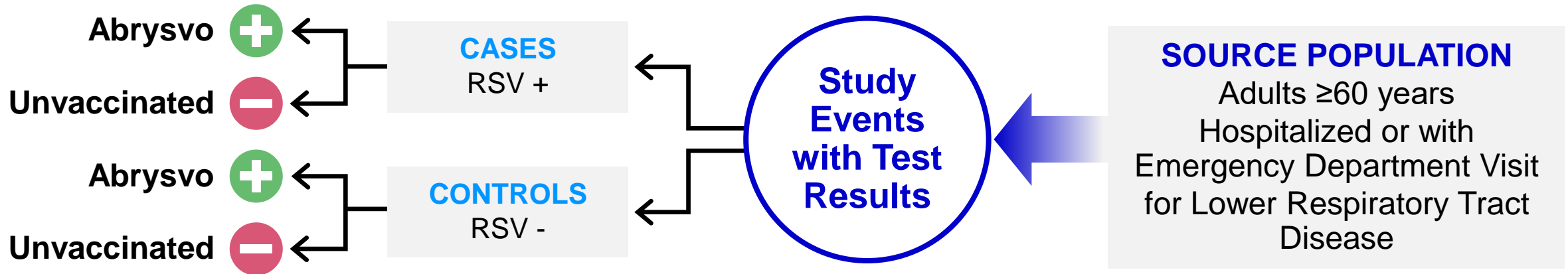
1. Represents LRTD (lower respiratory tract disease) events. One S1 case and one S2 case (both in the placebo group) and one S2 case in RSVPreF group were based on local testing without RSV subgroup. One S2 case in placebo group had both A and B subgroups;  
Notes: RSV, respiratory syncytial virus; VE, vaccine efficacy

# RSVpreF Adult – Clinical Development Program

Updated Data on RENOIR, Real-World Evidence, and MONeT

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RENOIR			COVID COAD	FLU COAD	REAL-WORLD	MONeT	
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	Ongoing	Ongoing			Ongoing		Ongoing

# Kaiser Permanente Southern California Real-World Data: Observational Retrospective Test Negative Design Case Control Vaccine Effectiveness Study



## Leveraging KPSC High-quality Real-World Data Platform

- Large healthcare network with high-risk population: Kaiser Permanente Southern California (KPSC)
- ↑ RSV testing by salvaging NP/nasal swabs collected for other respiratory pathogen testing
- VE against RSV-related LRTD hospitalization/ED visits calculated using multivariable logistic regression
  - Primary analysis controls: RSV-, hMPV-, influenza-, SARS-CoV-2-, and non-vaccine-preventable disease pathogen+
  - Sensitivity analysis with all RSV negative as controls



# Early Real-World Data Reinforces VE among Persons at Highest Risk of Severe RSV Disease: 89% -- Similar to Randomized Clinical Trial VE Results

## Vaccine Effectiveness against RSV-related LRTD hospitalization or ED visit

	Test Negative Controls <sup>a</sup> N (%)		Test Positive Cases N (%)		Crude VE (95%CI)	Adjusted VE <sup>b</sup> (95% CI)
	Unvaccinated, n (%)	Vaccinated, n (%)	Unvaccinated, n (%)	Vaccinated, n (%)		
Primary Analysis <sup>a</sup> (n=1336)	734 (96.6%)	26 (3.4%)	574 (99.7%)	2 <sup>c</sup> (0.3%)	90% (58–98)	<b>89%</b> <b>(52–97)</b>

## Results

- Study population description
  - 57% of study population was over 75 years of age
  - 93% ≥1 Charlson comorbidity
  - 14% immunocompromised
- Primary analysis VE= 89% (95% CI: 52–97) (Table)
  - Sensitivity Analysis (controls with any RSV negative) VE = 89% (95% CI: 54–97)
  - Study extension planned to provide Abrysvo VE for specific population subgroups (e.g., by age, high-risk conditions) and seasons 2, 3, and beyond

<sup>a</sup> Pre-specified primary analysis controls test negative for RSV, flu and SARS-CoV2 and test positive for a non-vaccine preventable disease in the primary analysis. A sensitivity analysis includes a broader control group definition which is all who test negative for RSV. <sup>b</sup> Adjusted for age, sex, encounter months, race/ethnicity, Charlson index, previous outpatient encounters, previous inpatient encounters, previous ED encounters, COPD, diabetes, renal disease, and peripheral vascular disease. <sup>c</sup> Patient 1: 93 years old, Charlson index of 6; Patient 2: 63 years old, Charlson index of 4.

# RSVpreF Adult – Clinical Development Program

Updated Data on RENOIR, Real-World Evidence, and MONEt

Older Adults ≥ 60					Adults ≥ 18		
RENOIR			COVID COAD	FLU COAD	REAL-WORLD	MONEt	
Adults ≥ 60			Adults ≥ 65	Adults ≥ 65	Adults ≥ 60	Adults 18–59	Adults ≥ 18
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	Ongoing	Ongoing			Ongoing		Ongoing

# Safety in Adults 18–59 Years Has Been Demonstrated in 7 Clinical Studies

Licensure in 18–59 Years of Age Will Be Based on Satisfactory Safety and Immunogenicity Compared to RSVPreF in Adults  $\geq$  60 Years

## Totality of Safety Data to Support Licensure in Adults $\geq$ 18 to 59 Years

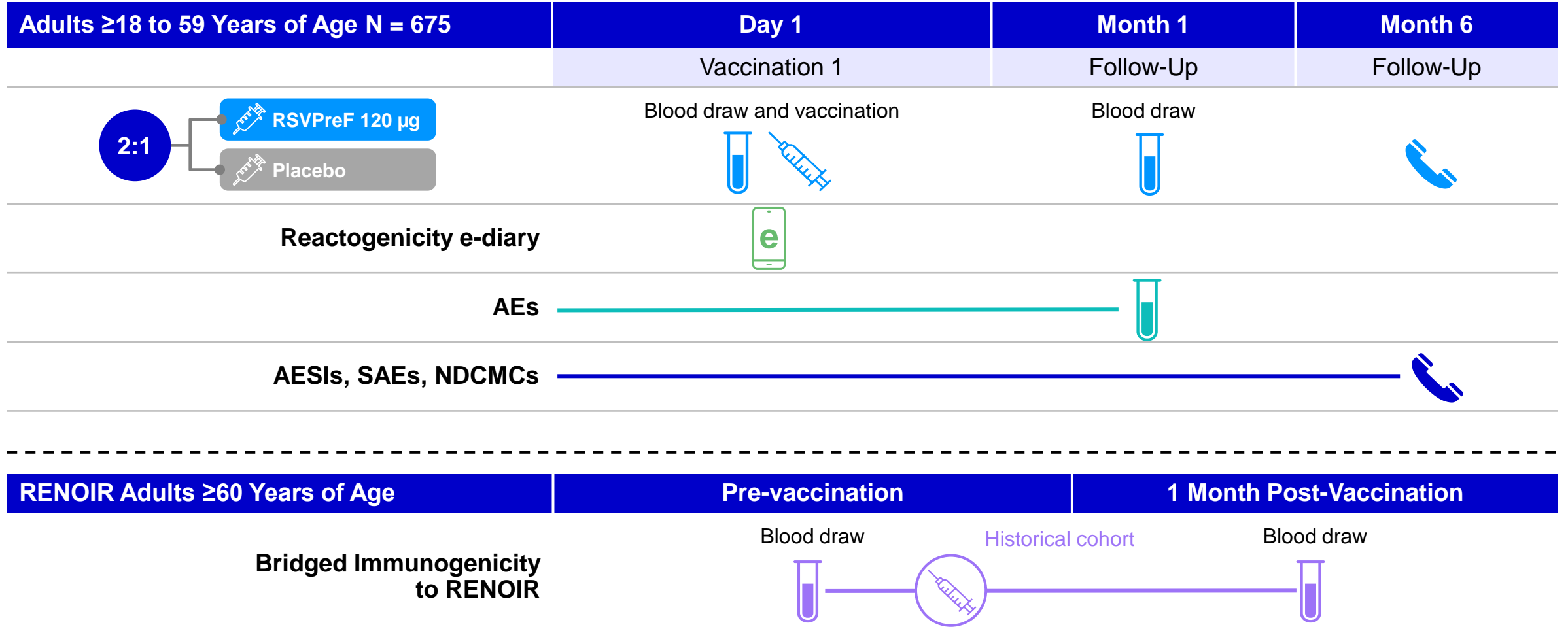
①	<b>Study 1001 (n=98):</b> Phase 1/2 Dose Ranging
②	<b>Human Challenge (n=35):</b> Safety and Efficacy of 120 $\mu$ g without Adjuvant
③	<b>Study 1014 (n=745):</b> Lot Consistency
④	<b>Study 1004 (n=282):</b> Non-pregnant Concomitant Tdap
⑤	<b>Study 1003 (n=115):</b> Pregnant Women, Safety, Early Efficacy
⑥	<b>Study 1008 (n=3689):</b> Pregnant Women, Safety, Pivotal Efficacy
⑦	<b>Study 1023 (n=453):</b> (MONEt) Immunogenicity & Safety



**>5,400 Adults Aged 18-59 Years of Age**

# RSVPreF in Adults $\geq 18$ to 59 Years of Age at High Risk of Severe RSV Disease

Phase 3 Study Design MONeT Substudy A (Chronic Conditions)



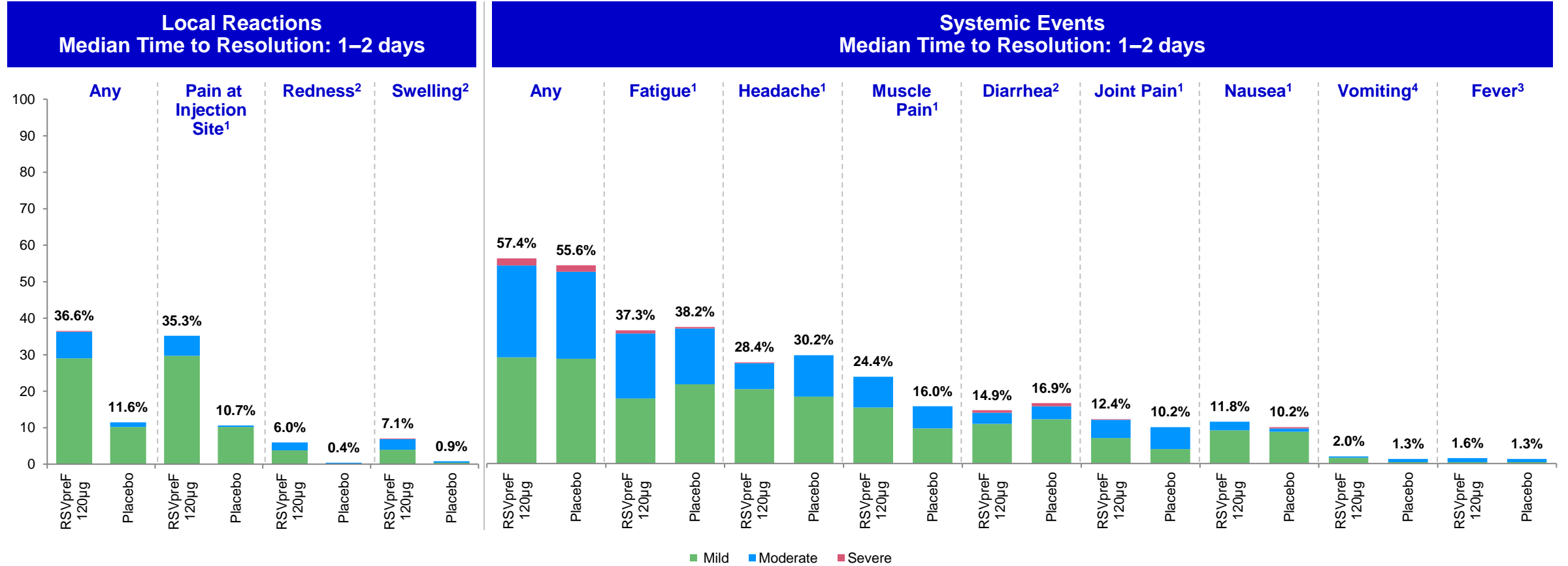
# Demographics Between Vaccine and Placebo Recipients

	<b>RSVPreF 120 µg (N = 453); n (%)</b>	<b>Placebo (N = 225); n (%)</b>	<b>Total (N = 678); n (%)</b>
<b>Sex</b>			
Male	193 (42.6)	73 (32.4)	266 (39.2)
Female	260 (57.4)	152 (67.6)	412 (60.8)
<b>Race</b>			
White	312 (68.9)	152 (67.6)	464 (68.4)
Black or African American	106 (23.4)	57 (25.3)	163 (24.0)
Asian	24 (5.3)	9 (4.0)	33 (4.9)
<b>Ethnicity</b>			
Hispanic/Latino	102 (22.5)	48 (21.3)	150 (22.1)
Non-Hispanic/non-Latino	348 (76.8)	175 (77.8)	523 (77.1)
<b>Age at Vaccination</b>			
18-49 Years	<b>240 (53.0)</b>	<b>113 (50.2)</b>	<b>353 (52.1)</b>
50-59 Years	<b>213 (47.0)</b>	<b>112 (49.8)</b>	<b>325 (47.9)</b>
Mean (SD)	46.8 (9.9)	46.4 (10.5)	46.7 (10.1)

	<b>RSVPreF 120 µg (N = 453); n (%)</b>	<b>Placebo (N = 225); n (%)</b>	<b>Total (N = 678); n (%)</b>
With At Least 1 Prespecified Medical Condition*	<b>453 (100.0)</b>	<b>223 (99.1)</b>	<b>676 (99.7)</b>
<b>Chronic Pulmonary Conditions</b>			
COPD	25 (5.5)	11 (4.9)	36 (5.3)
Asthma	198 (43.7)	88 (39.1)	286 (42.2)
<b>Cardiovascular Conditions</b>			
CHF	9 (2.0)	3 (1.3)	12 (1.8)
CAD	19 (4.2)	4 (1.8)	23 (3.4)
Diabetes	<b>189 (41.7)</b>	<b>101 (44.9)</b>	<b>290 (42.8)</b>
Other	<b>139 (30.7)</b>	<b>68 (30.2)</b>	<b>207 (30.5)</b>
<b>Liver Disease</b>			
Liver Disease	20 (4.4)	13 (5.8)	33 (4.9)
<b>Renal Disease</b>			
Renal Disease	17 (3.8)	4 (1.8)	21 (3.1)
<b>Neurologic Disease</b>			
Neurologic Disease	16 (3.5)	1 (0.4)	17 (2.5)
<b>Tobacco Use</b>			
Current Tobacco Use	78 (17.2)	39 (17.3)	117 (17.3)

\* Participants with multiple comorbidities are represented more than once

# Solicited Local/Systemic Reactions & Systemic Events Were Mild to Moderate and Resolved Quickly in Participants 18–59 Years



1. Severity definition: mild = no interference with daily activity; moderate = some interference with daily activity; severe = prevents daily activity

2. Severity definition: mild = >2-5 cm, moderate = >5-10 cm; severe = >10 cm

RSVPreF N = 451; placebo N = 225

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

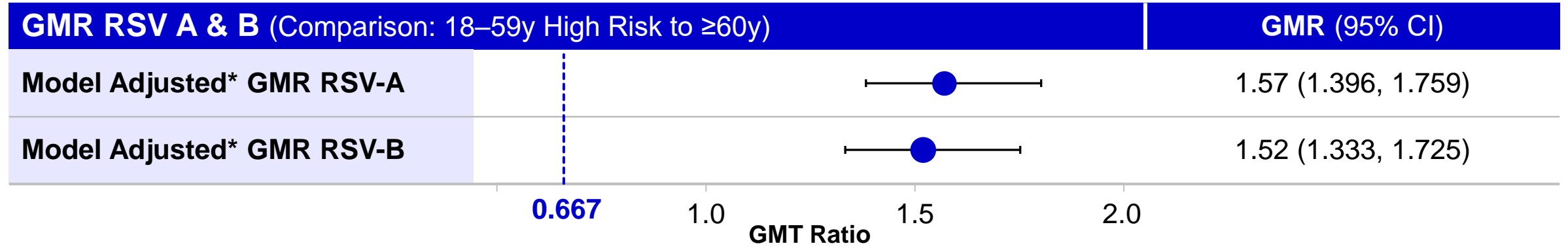
RSVPreF N = 451; Placebo N = 225

# Adverse Events Comparable Between Vaccine and Placebo Groups

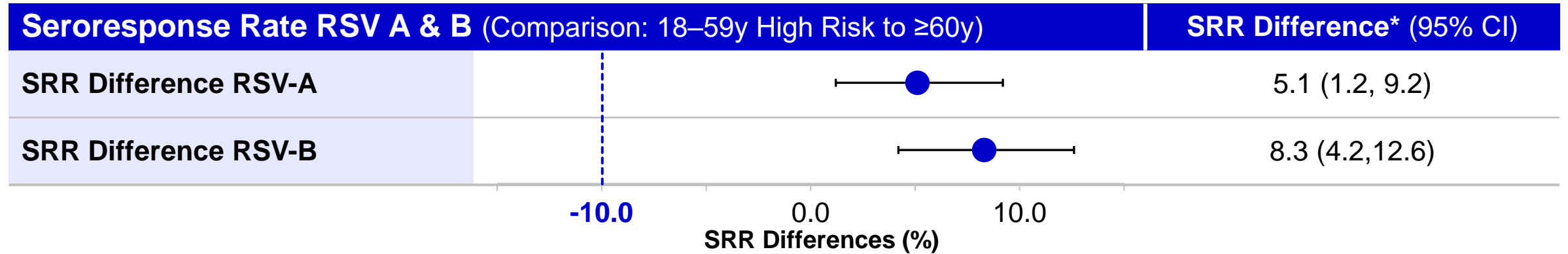
Adverse Event Category	RSVPreF 120 µg (N = 453); n (%)	Placebo (N = 225); n (%)
<b>From Vaccination Through 1-Month Follow-Up Visit</b>		
Any Event	31 (6.8)	17 (7.6)
Related*	1 (0.2)	0
Severe	1 (0.2)	4 (1.8)
<b>From Vaccination Throughout the Study</b>		
SAE	5 (1.1)	7 (3.1)
Related SAE	0	0
AE Leading to Withdrawal	1 (0.2)	1 (0.4)
AE Leading to Death	1 (0.2)	0
AE of Special Interest (includes GBS and atrial fibrillation)	0	0

\*Related event was urticaria Grade 1 on the day of vaccination that resolved without treatment or medical attention;  
Abbreviations: AE, adverse event; NDCMC, newly diagnosed chronic medical condition; SAE, serious adverse event.

# Non-Inferiority Met for All Four Co-Primary Endpoints



**Both Primary Endpoints Met Non-inferiority (CI LB >0.667)**



**Both Primary Endpoints Met Non-inferiority (CI LB > -10%)**

Abbreviations: GMR = geometric mean ratio; SRR=seroresponse rate

\*Analysis of covariance model used as per protocol with sex and baseline titer (in logarithm scale) adjusted



# Summary of Clinical Development Updates of RSVPreF in Adults

- ✓ RENOIR study has shown duration of protection is at least 2 years with high efficacy in season 2
- ✓ Preliminary real-world observational data supports RCT efficacy in older population, largely with comorbidities
- ✓ RSVpreF in adults 18–59 years of age (MONeT study) demonstrated robust RSV-A and RSV-B subgroup neutralizing responses that met NI to the RENOIR study, where safety and efficacy were demonstrated
- ✓ RSVPreF is currently under review by the FDA for use in adults 18-59 years of age

**RSVPreF Addresses a Significant Burden in Adults and Those With Chronic Conditions**