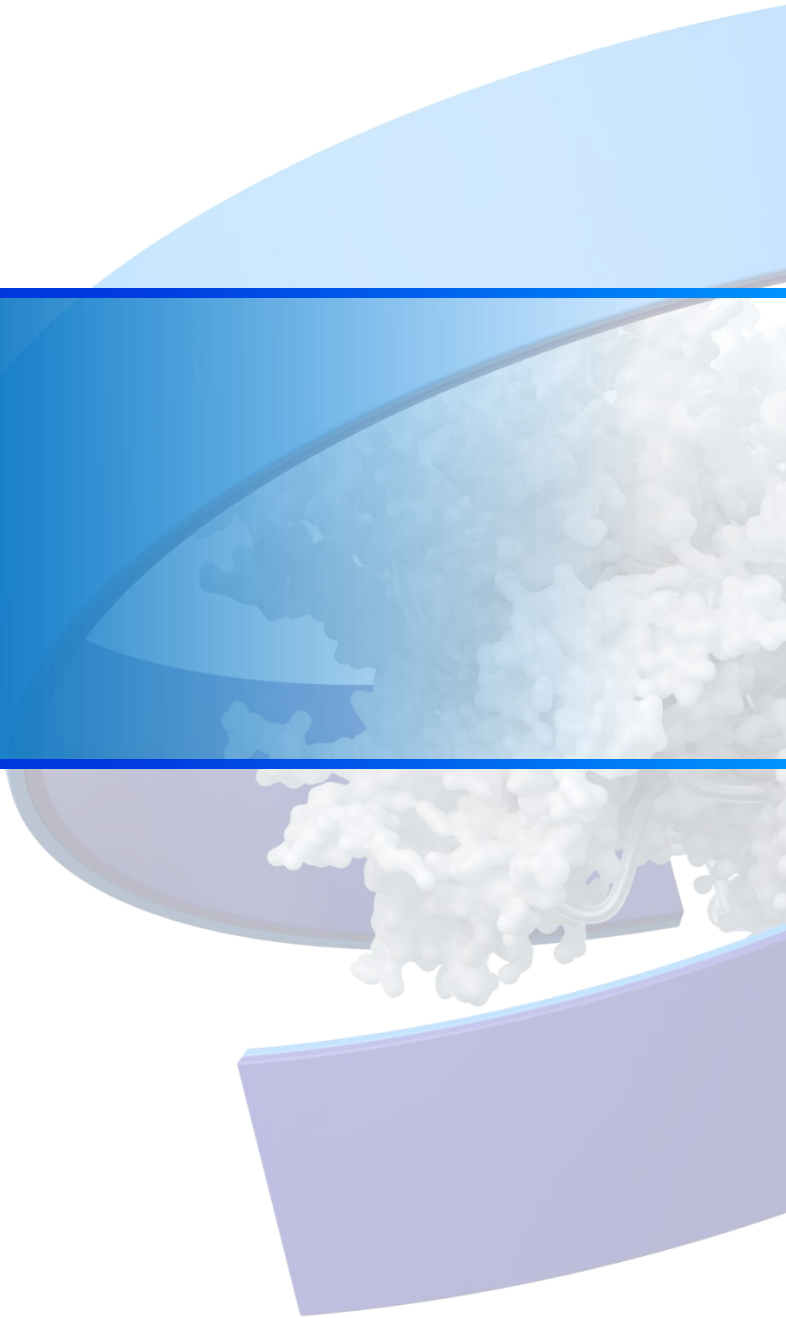
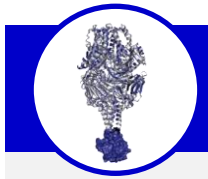
RSVpreF Adult Clinical Development Update



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

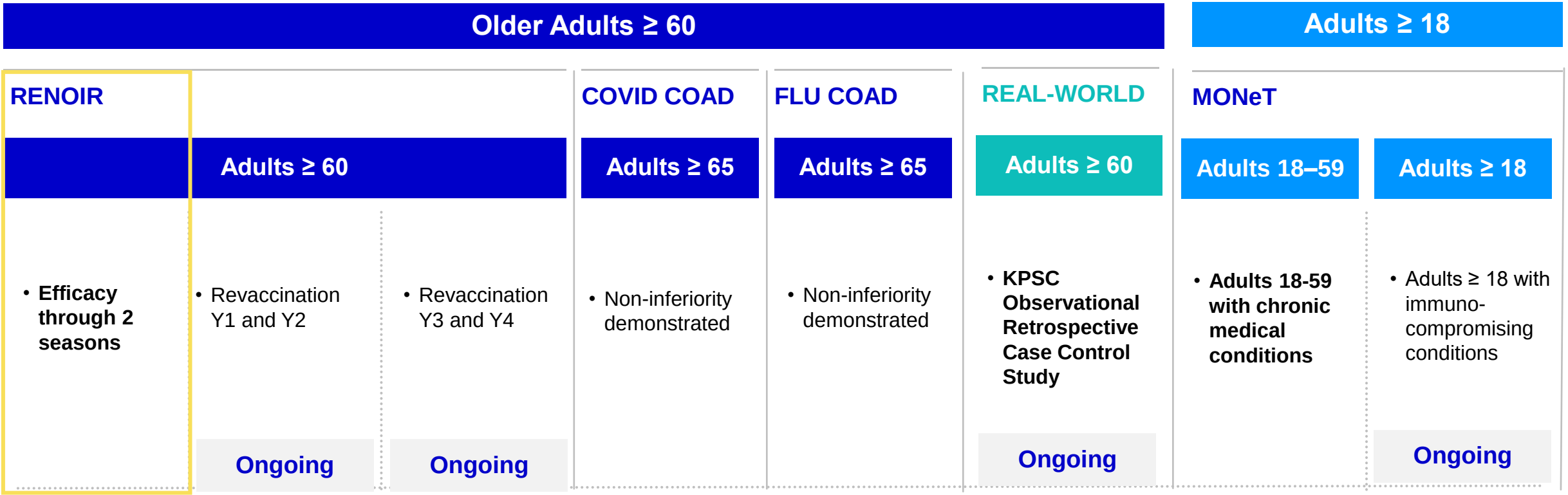
Extending Adult Indication

Application Submitted for FDA Review

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

RSVpreF Adult – Clinical Development Program

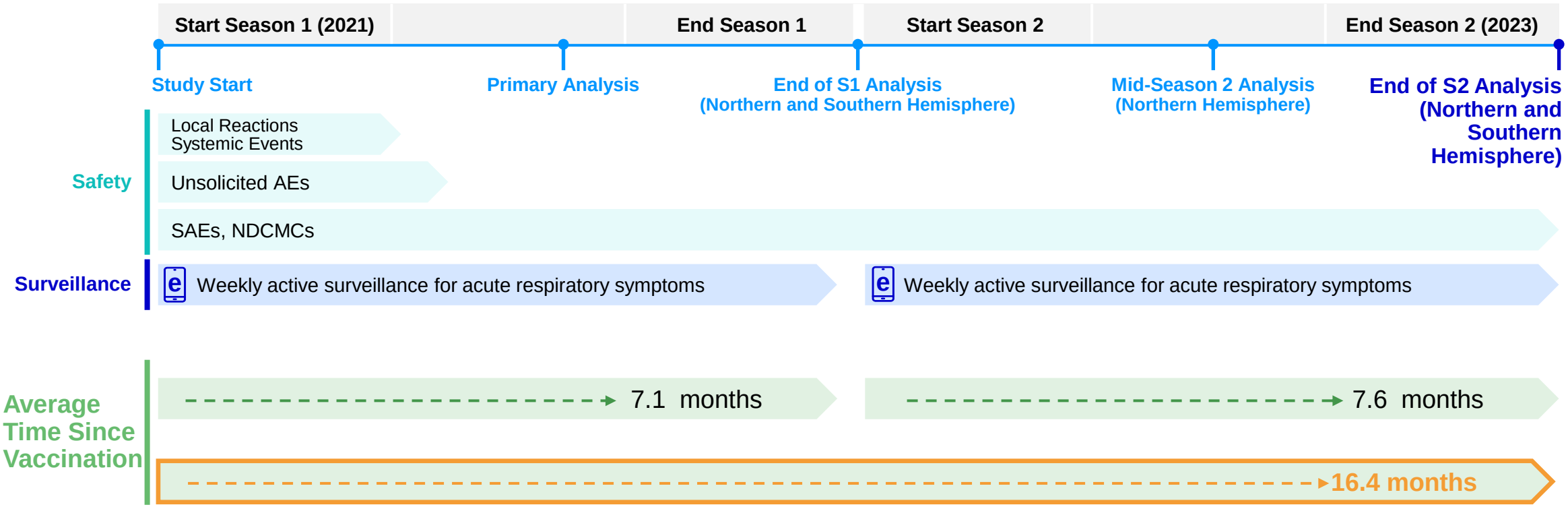
Updated Data on RENOIR, Real-World Evidence, and MONeT



KPSC, Kaiser Permanente Southern California

The RSV Vaccine Efficacy Study iN Older Adults Immunized Against RSV Disease

38,863 participants / Adults **≥60 years**

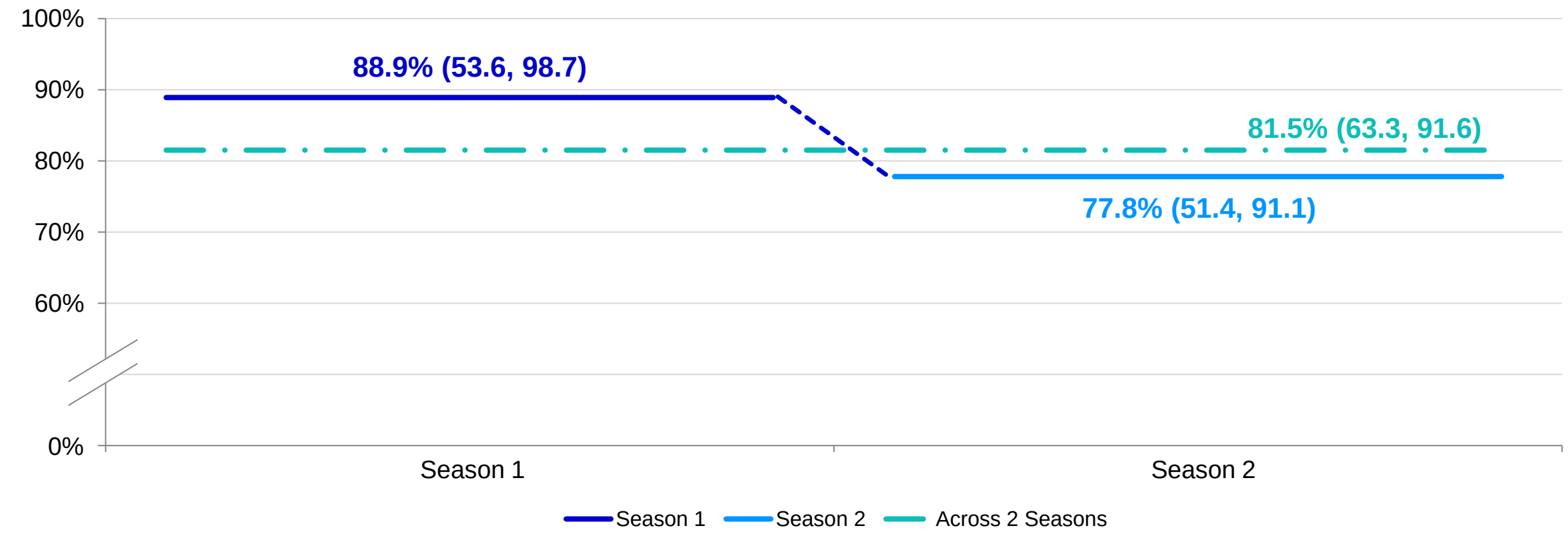


RSV, respiratory syncytial virus; RSVpreF, respiratory syncytial virus prefusion F subunit, AE, adverse event; NDCMC, newly diagnosed chronic medical condition; SAE, serious adverse event.

Primary endpoint:
RSV-LRTD with ≥3 symptoms

RSVPreF Maintained High Efficacy in Season 2

VE Against RSV-associated LRTD in Subjects with ≥3 New or Worsened Lower Respiratory Symptoms (95% CI)[1,2]

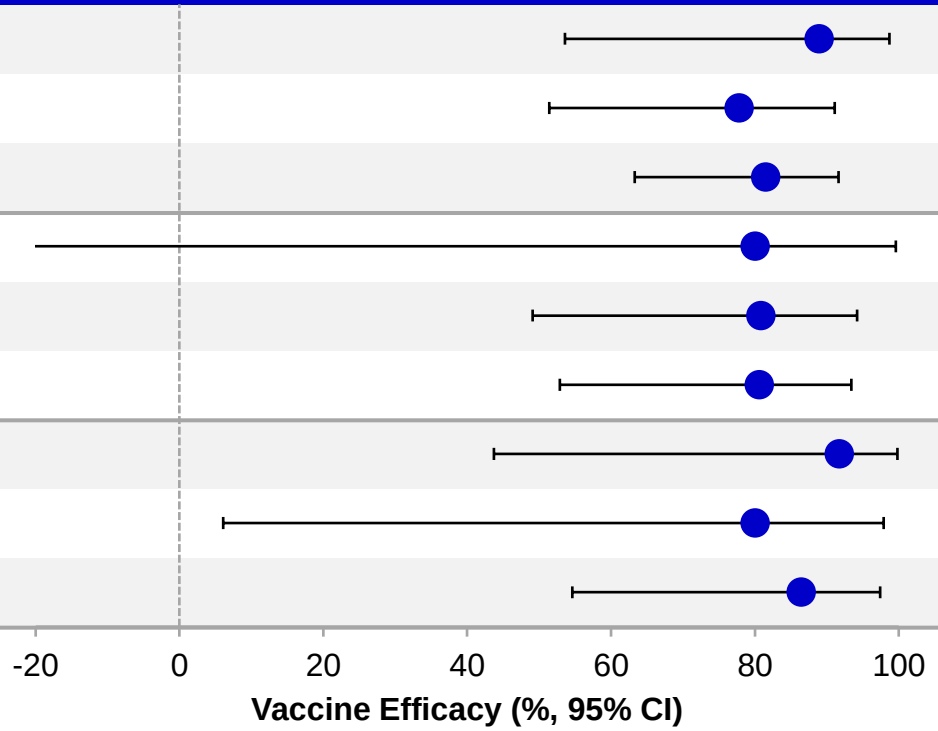


LRTD = lower respiratory tract disease

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**

RSV-LRTI with ≥ 3 Symptoms		Number of Events[1]		Vaccine Efficacy (95% CI)
		RSVPreF	Placebo	
Overall	**Season 1**	2	18	**88.9%** (53.6, 98.7)
	Season 2	8	36	**77.8%** (51.4, 91.1)
	Across 2 Seasons	10	54	**81.5%** (63.3, 91.6)
RSV-A	**Season 1**	1	5	**80.0%** (-78.7, 99.6)
	Season 2	5	26	**80.8%** (49.1, 94.2)
	Across 2 Seasons	6	31	**80.6%** (52.9, 93.4)
RSV-B	**Season 1**	1	12	**91.7%** (43.7, 99.8)
	Season 2	2	10	**80.0%** (6.1, 97.9)
	Across 2 Seasons	3	22	**86.4%** (54.6, 97.4)

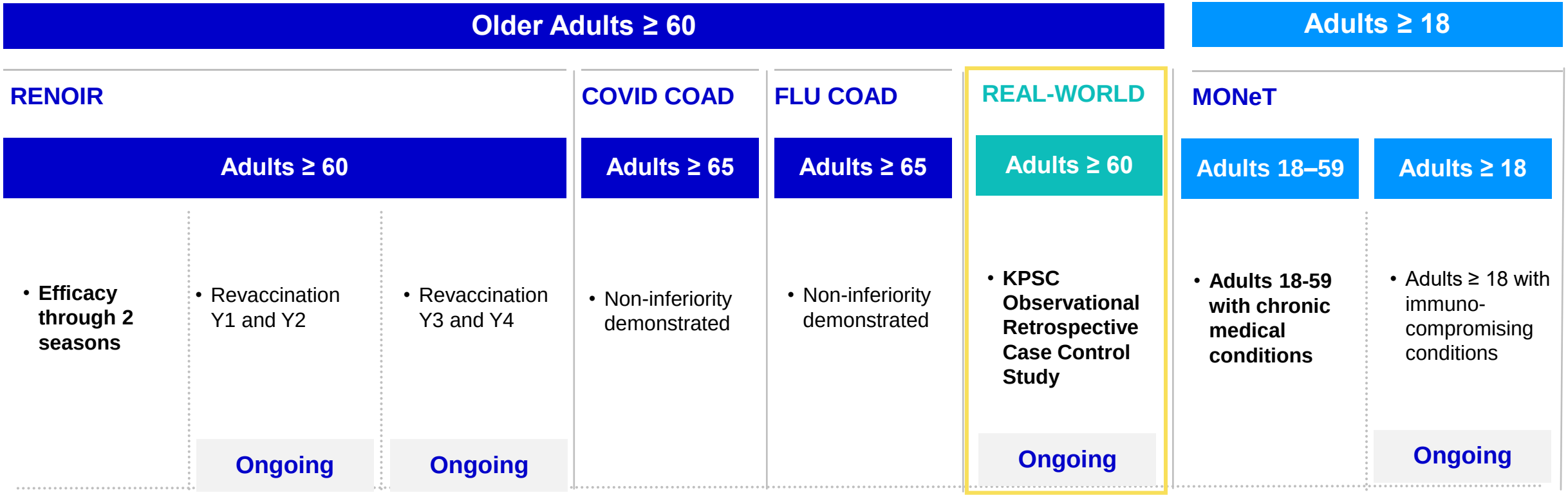


1. Represents LRTD (lower respiratory tract disease) events. One S1 case and one S2 case (both in the placebo group) and one S2 case in RSVPreF group were based on local testing without RSV subgroup. One S2 case in placebo group had both A and B subgroups;

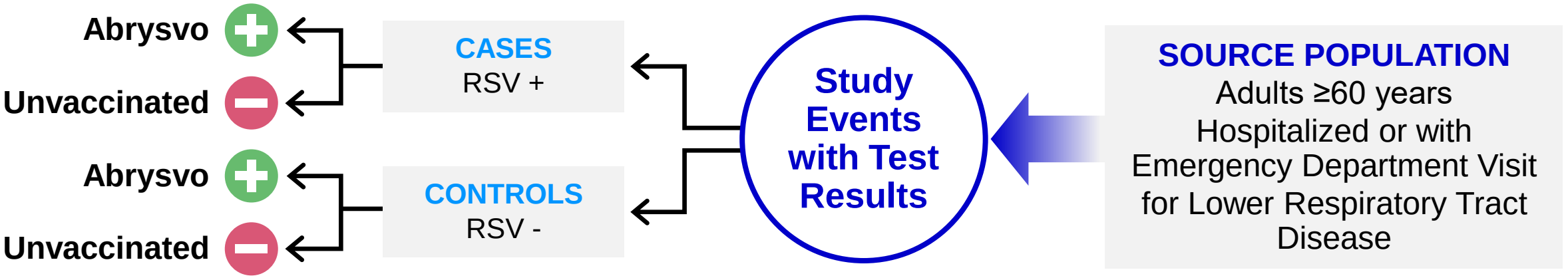
Notes: RSV, respiratory syncytial virus; VE, vaccine efficacy

RSVpreF Adult – Clinical Development Program

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



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

Figure adapted from: Fukushima et al (2017) Basic principles of test-negative design in evaluating influenza vaccine effectiveness
ARI, acute respiratory illness; ED, emergency department; hMPV, human metapneumovirus; LRTD , lower respiratory tract disease; NP, nasopharyngeal; RSV, respiratory syncytial virus; VE, vaccine efficacy; VPD, vaccine preventable disease

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

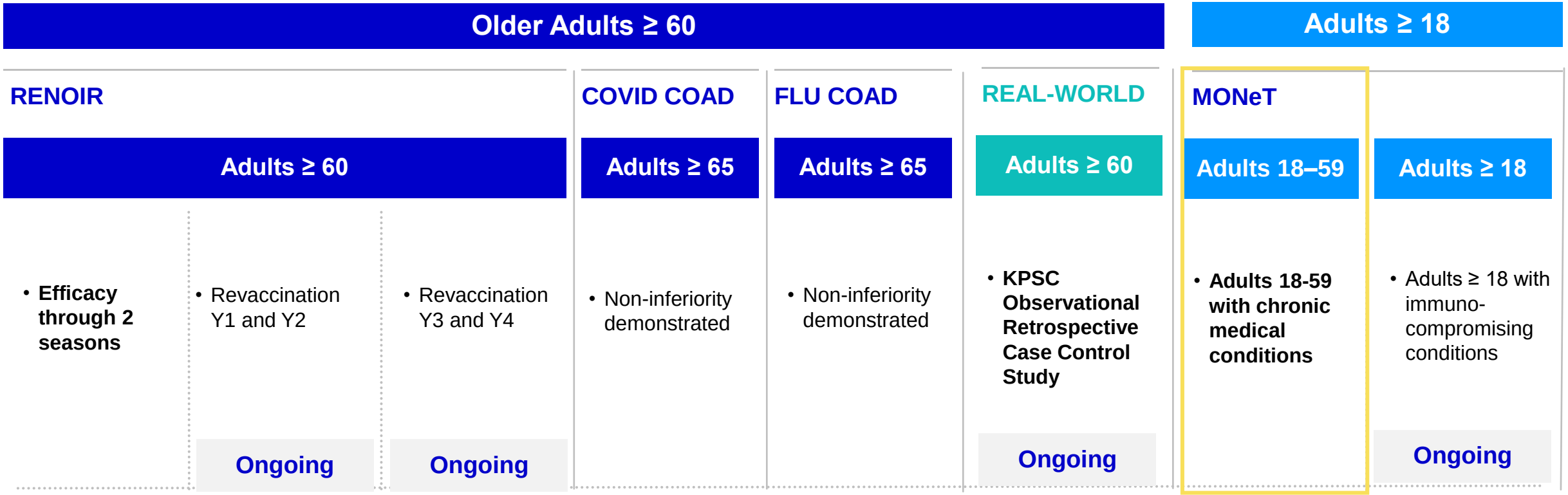
Results

- 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

[a] 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. [b] 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. [c] 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



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 ≥ 60 Years

Totality of Safety Data to Support Licensure in Adults ≥18 to 59 Years	
1	**Study 1001 (n=98):** Phase 1/2 Dose Ranging
2	**Human Challenge (n=35):** Safety and Efficacy of 120µg without Adjuvant
3	**Study 1014 (n=745):** Lot Consistency
4	**Study 1004 (n=282):** Non-pregnant Concomitant Tdap
5	**Study 1003 (n=115):** Pregnant Women, Safety, Early Efficacy
6	**Study 1008 (n=3689):** Pregnant Women, Safety, Pivotal Efficacy
7	**Study 1023 (n=453):** (MONeT) Immunogenicity & Safety

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

RSVPreF in Adults ≥18 to 59 Years of Age at High Risk of Severe RSV Disease

Phase 3 Study Design MONeT Substudy A (Chronic Conditions)

Adults ≥18 to 59 Years of Age N = 675	Day 1	Month 1	Month 6
	Vaccination 1	Follow-Up	Follow-Up
2:1 RSVPreF 120 µg / Placebo	Blood draw and vaccination	Blood draw	
Reactogenicity e-diary	e		
AEs			
AESIs, SAEs, NDCMCs			

RENOIR Adults ≥60 Years of Age	Pre-vaccination	1 Month Post-Vaccination
Bridged Immunogenicity to RENOIR	Blood draw — Historical cohort	Blood draw

1. Clinicaltrials.gov NCT05842967 2. Pfizer Data on File

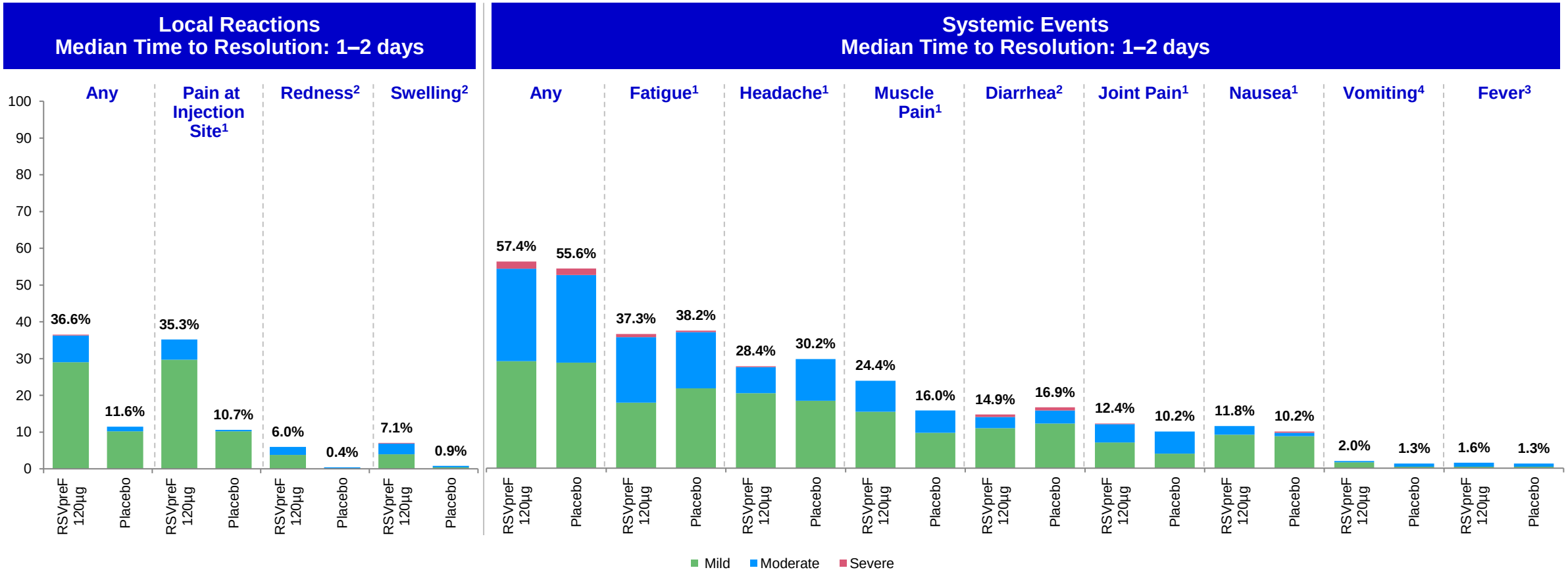
Demographics Between Vaccine and Placebo Recipients

	RSVPreF 120 µg (N = 453); n (%)	Placebo (N = 225); n (%)	Total (N = 678); n (%)
Sex			
Male	193 (42.6)	73 (32.4)	266 (39.2)
Female	260 (57.4)	152 (67.6)	412 (60.8)
Race			
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)
Ethnicity			
Hispanic/Latino	102 (22.5)	48 (21.3)	150 (22.1)
Non-Hispanic/non-Latino	348 (76.8)	175 (77.8)	523 (77.1)
Age at Vaccination			
18-49 Years	**240 (53.0)**	**113 (50.2)**	**353 (52.1)**
50-59 Years	**213 (47.0)**	**112 (49.8)**	**325 (47.9)**
Mean (SD)	46.8 (9.9)	46.4 (10.5)	46.7 (10.1)

	RSVPreF 120 µg (N = 453); n (%)	Placebo (N = 225); n (%)	Total (N = 678); n (%)
With At Least 1 Prespecified Medical Condition*	**453 (100.0)**	**223 (99.1)**	**676 (99.7)**
Chronic Pulmonary Conditions	**239 (52.8)**	**116 (51.6)**	**355 (52.4)**
COPD	25 (5.5)	11 (4.9)	36 (5.3)
Asthma	198 (43.7)	88 (39.1)	286 (42.2)
Cardiovascular Conditions	**38 (8.4)**	**16 (7.1)**	**54 (8.0)**
CHF	9 (2.0)	3 (1.3)	12 (1.8)
CAD	19 (4.2)	4 (1.8)	23 (3.4)
Diabetes	**189 (41.7)**	**101 (44.9)**	**290 (42.8)**
Other	**139 (30.7)**	**68 (30.2)**	**207 (30.5)**
Liver Disease	20 (4.4)	13 (5.8)	33 (4.9)
Renal Disease	17 (3.8)	4 (1.8)	21 (3.1)
Neurologic Disease	16 (3.5)	1 (0.4)	17 (2.5)
Tobacco Use			
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

1. Clinicaltrials.gov NCT05842967 2. Pfizer Data on File

Adverse Events Comparable Between Vaccine and Placebo Groups

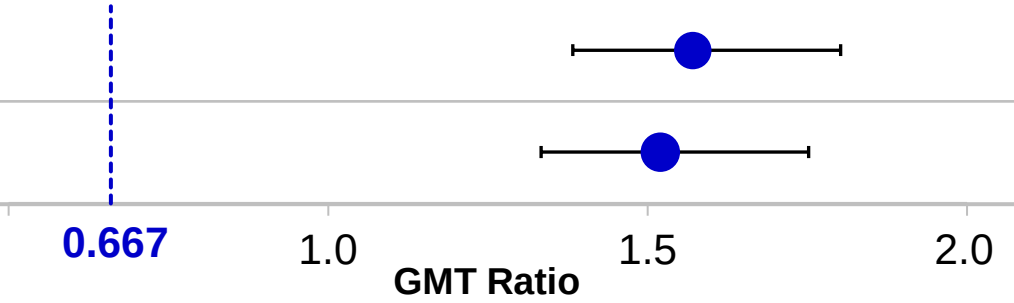
Adverse Event Category	RSVPreF 120 µg (N = 453); n (%)	Placebo (N = 225); n (%)
From Vaccination Through 1-Month Follow-Up Visit		
Any Event	31 (6.8)	17 (7.6)
Related*	1 (0.2)	0
Severe	1 (0.2)	4 (1.8)
From Vaccination Throughout the Study		
SAE	5 (1.1)	7 (3.1)
Related SAE	0	0
AE Leading to Withdrawal	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.

1. Clinicaltrials.gov NCT05842967 2. Pfizer Data on File

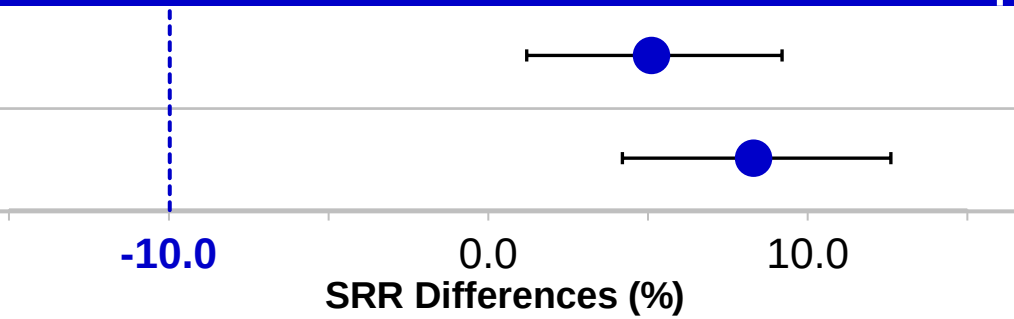
Non-Inferiority Met for All Four Co-Primary Endpoints

GMR RSV A & B (Comparison: 18–59y High Risk to ≥60y)	**GMR** (95% CI)
Model Adjusted* GMR RSV-A	1.57 (1.396, 1.759)
Model Adjusted* GMR RSV-B	1.52 (1.333, 1.725)



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

Seroresponse Rate RSV A & B (Comparison: 18–59y High Risk to ≥60y)	**SRR Difference*** (95% CI)
SRR Difference RSV-A	5.1 (1.2, 9.2)
SRR Difference RSV-B	8.3 (4.2,12.6)



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

1. Clinicaltrials.gov NCT05842967 2. Pfizer Data on File

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