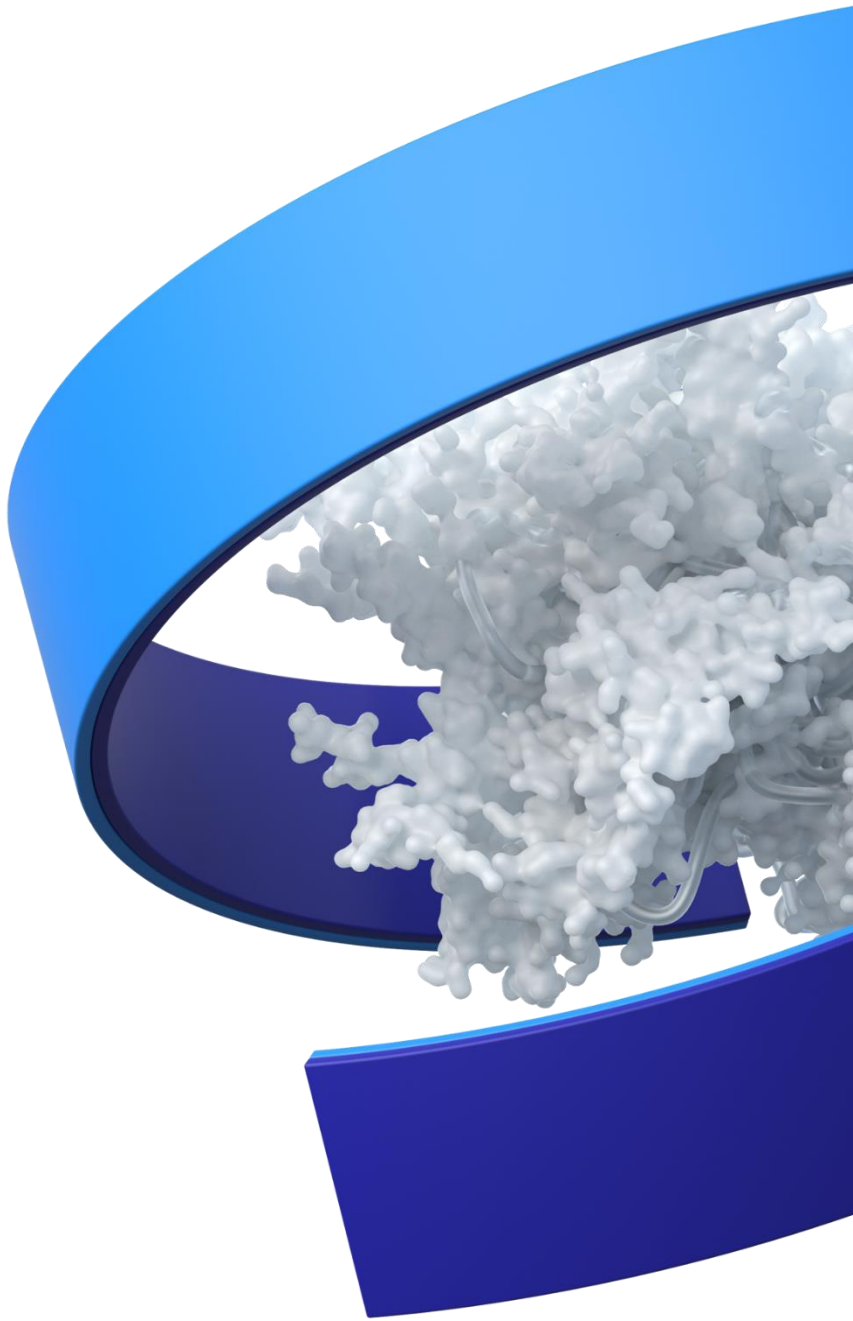
Safety and Efficacy of Bivalent RSV Prefusion F Vaccine in Vaccinated Mothers and their Infants

Iona Munjal, MD

Senior Director, Vaccine Research and Development



Bivalent RSV Prefusion F Vaccine

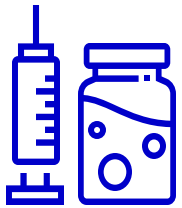
Proposed Indication:

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

Infants from birth through 6 months of age by active immunization of pregnant individuals

DOSE LEVEL

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



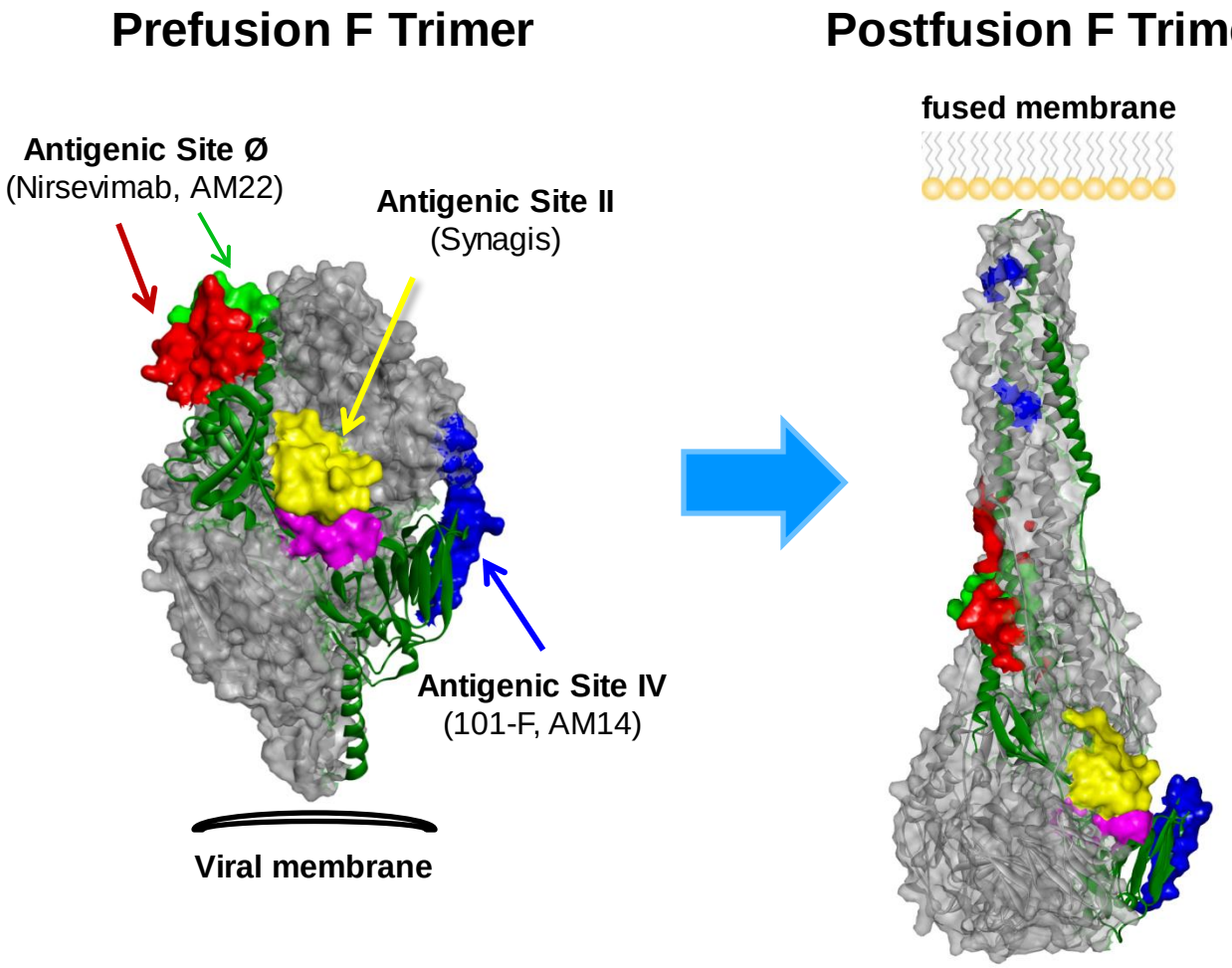
PRESENTATION

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

STORAGE

- **Refrigeration at 2°C to 8°C**

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

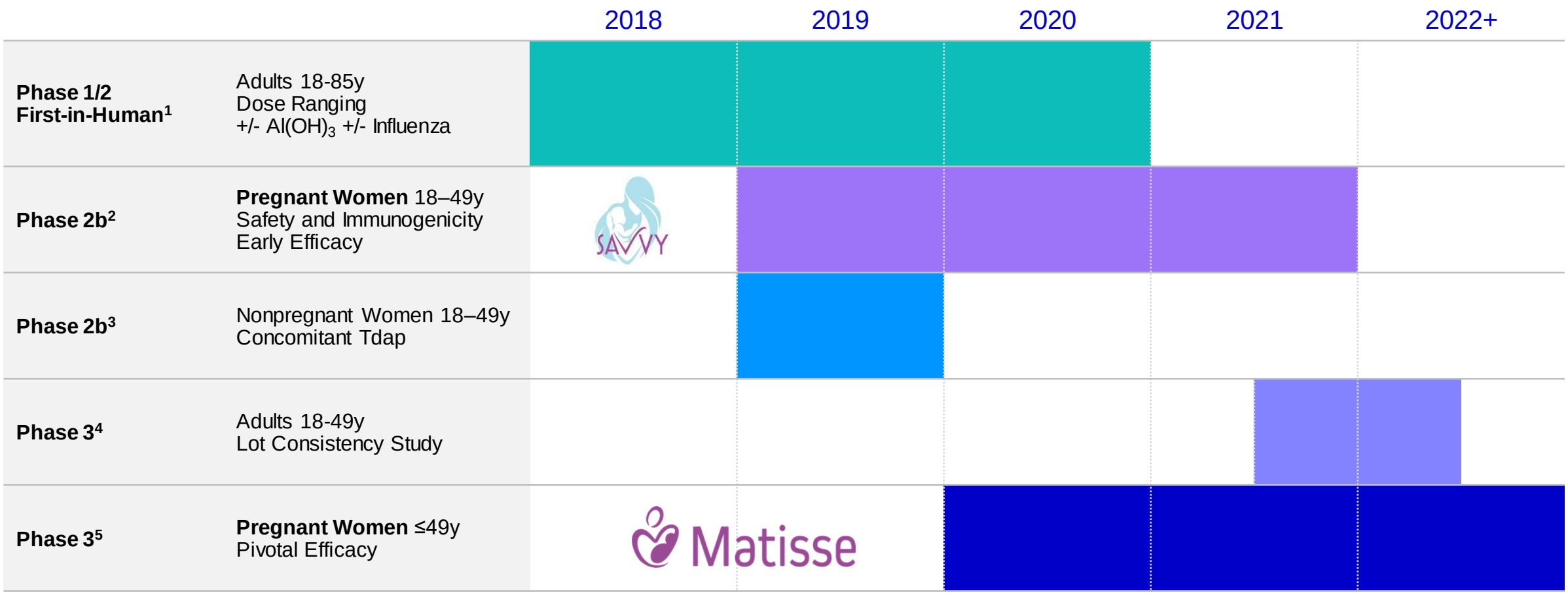


Only prefusion F can bind host cells for RSV to infect

Antibodies specific to the prefusion form are most effective at blocking virus infection

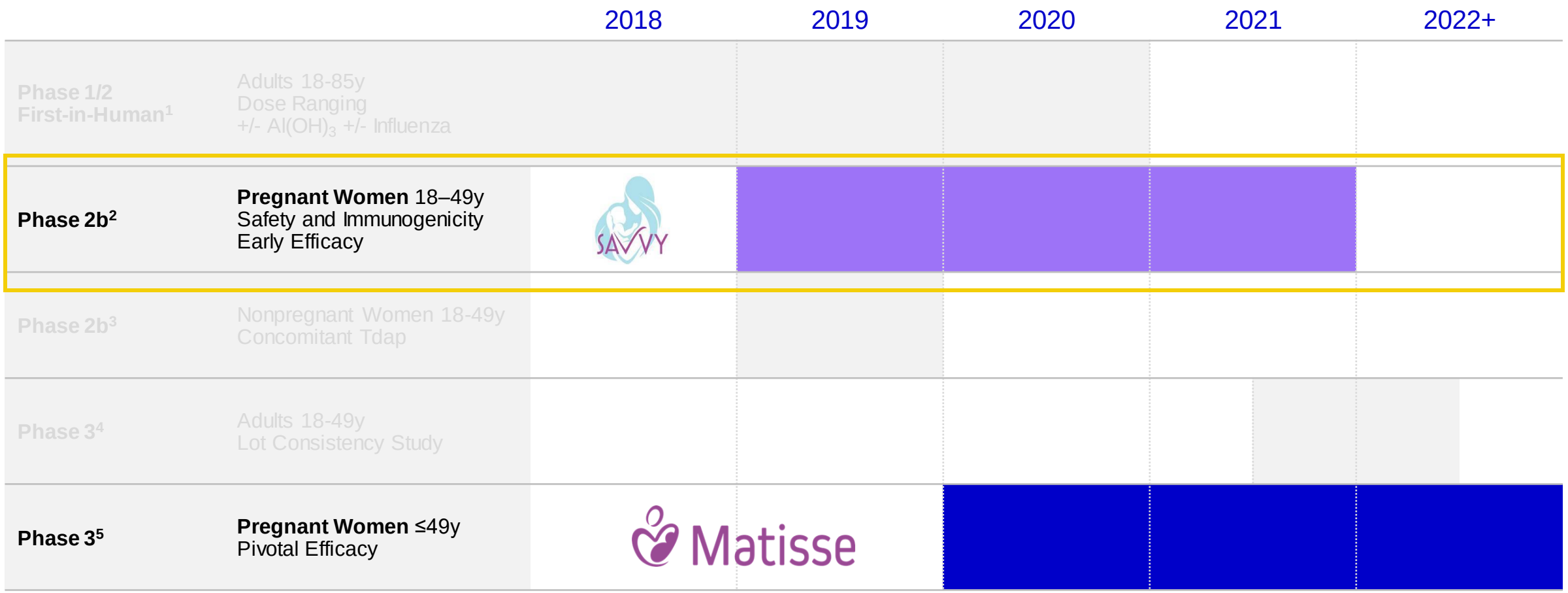
McLellan et al. *Science*, Nov 2013

Pfizer's RSVpreF Maternal Immunization Clinical Development Program



1. A Study to Describe the Safety and Immunogenicity of a RSV Vaccine in Healthy Adults. NCT03529773.
2. A Phase 2b Placebo-Controlled, Randomized Study of an RSV Vaccine in Pregnant Women. NCT04032093.
3. A Study of an RSV Vaccine When Given Together with Tdap in Healthy Nonpregnant Women Aged Between 18 to 49 Years. NCT04071158.
4. Clinical Lot Consistency for RSVpreF in a Population of Healthy Adults 18 to ≤49 Years of Age. NCT05096208.
5. A Trial to Evaluate the Efficacy and Safety of RSVpreF in Infants Born to Women Vaccinated During Pregnancy. NCT04424316.

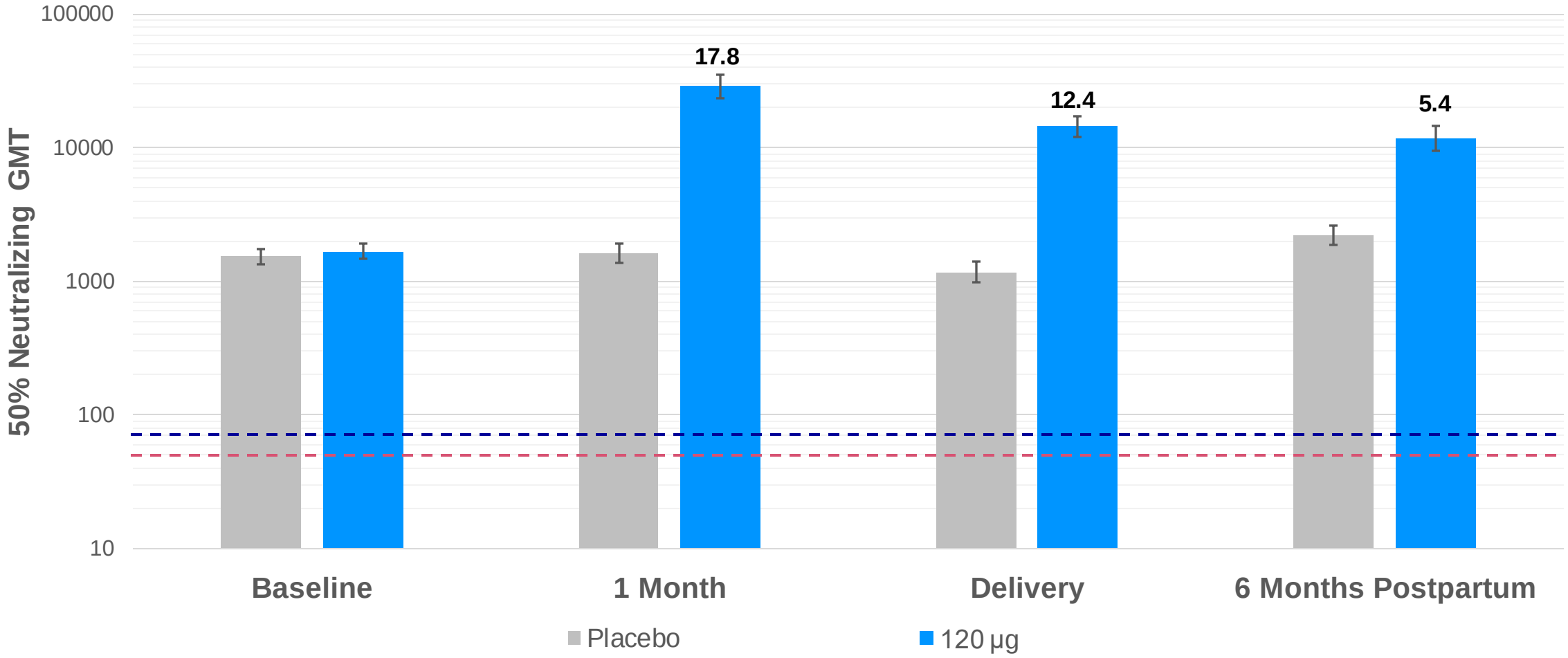
Pfizer's RSVpreF Maternal Immunization Clinical Development Program



1. A Study to Describe the Safety and Immunogenicity of a RSV Vaccine in Healthy Adults. NCT03529773.
2. A Phase 2b Placebo-Controlled, Randomized Study of an RSV Vaccine in Pregnant Women. NCT04032093.
3. A Study of an RSV Vaccine When Given Together with Tdap in Healthy Nonpregnant Women Aged Between 18 to 49 Years. NCT04071158.
4. Clinical Lot Consistency for RSVpreF in a Population of Healthy Adults 18 to ≤49 Years of Age. NCT05096208.
5. A Trial to Evaluate the Efficacy and Safety of RSVpreF in Infants Born to Women Vaccinated During Pregnancy. NCT04424316.

RSVpreF Elicits Maternal Neutralizing Titer with GMR >12 at Delivery*

Phase 2b Combined A/B 50% Neutralization Geometric Mean Titers & Geometric Mean Ratio vs. Placebo – in Maternal Participants at Baseline (24-36 weeks GA), 1M (if Delivery had not Occurred), Delivery and Postpartum; All Evaluable (N=116 participants)



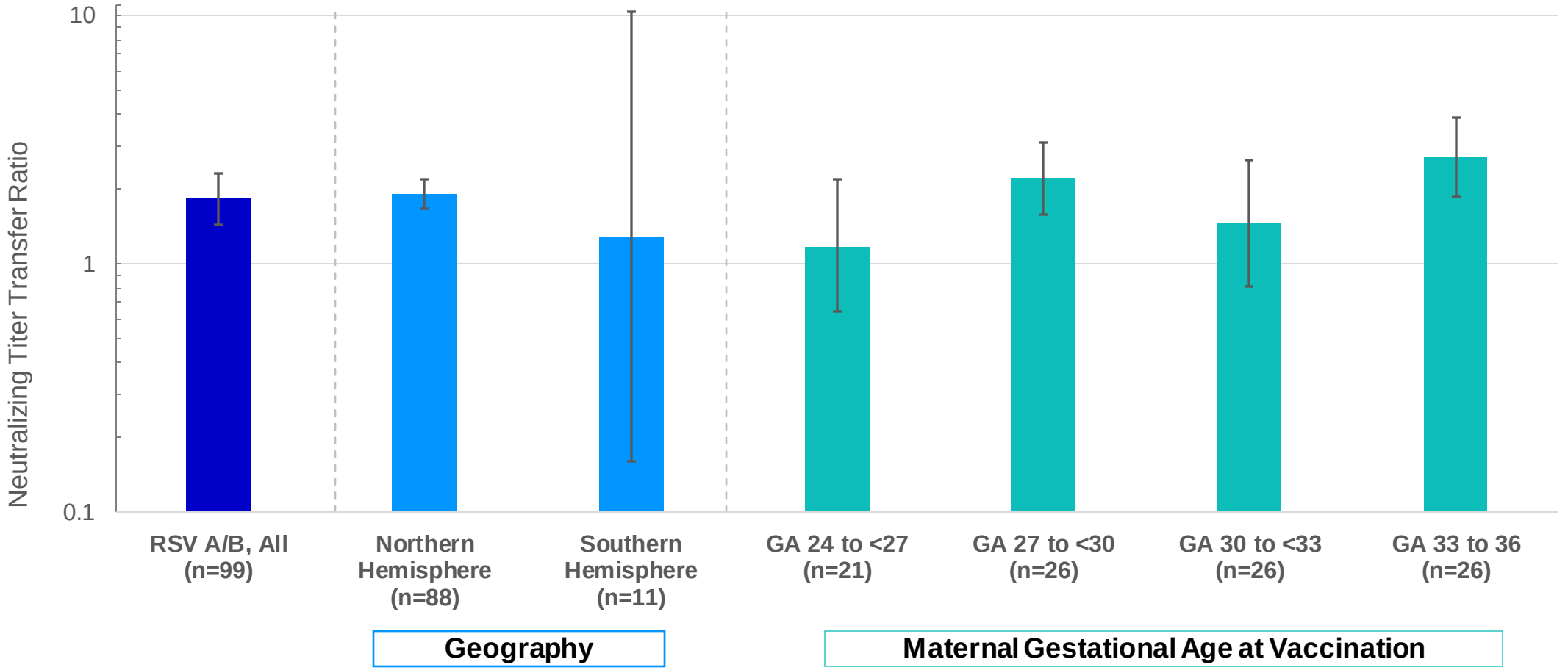
Lower Limit of Quantification (LLOQ), RSV A

LLOQ, RSV B

*Mean time from vaccination to delivery, 61.4 days

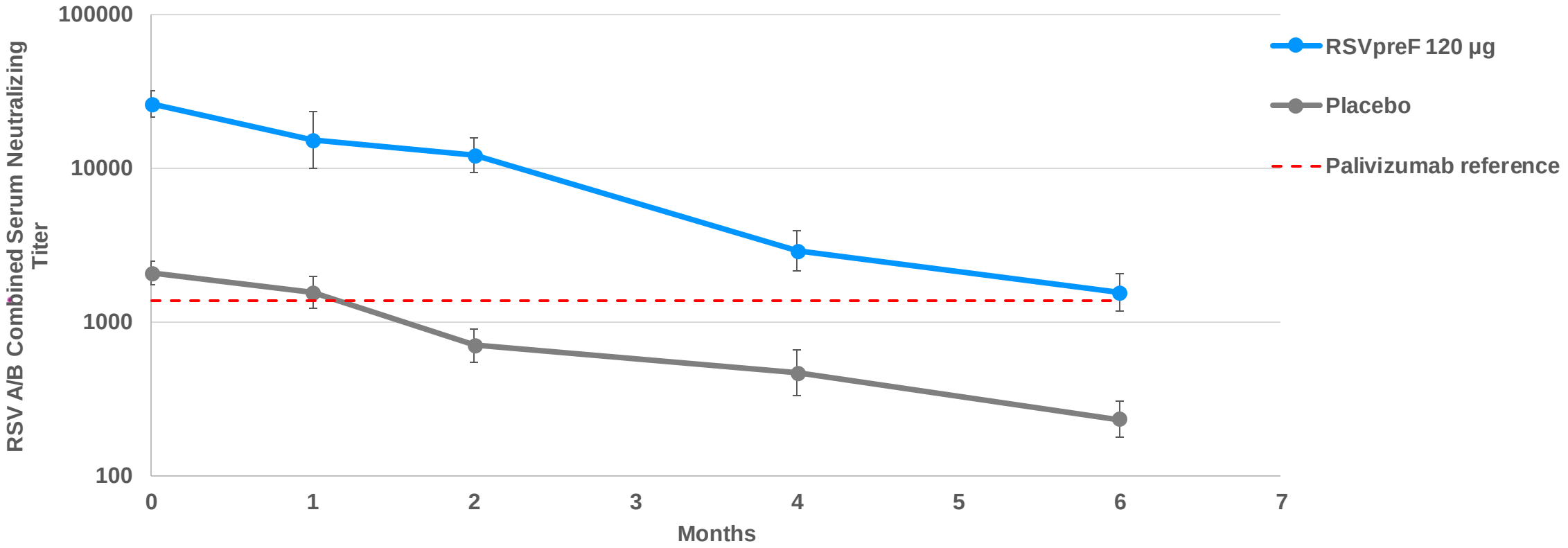
Transplacental Transfer Ratios >1 Overall and by Geography and Gestational Age

Combined RSV A/B 50% Neutralization Antibody Infant v. Maternal Ratio for Phase 3 selected dose Evaluable Population, RSVpreF Groups (N=99)



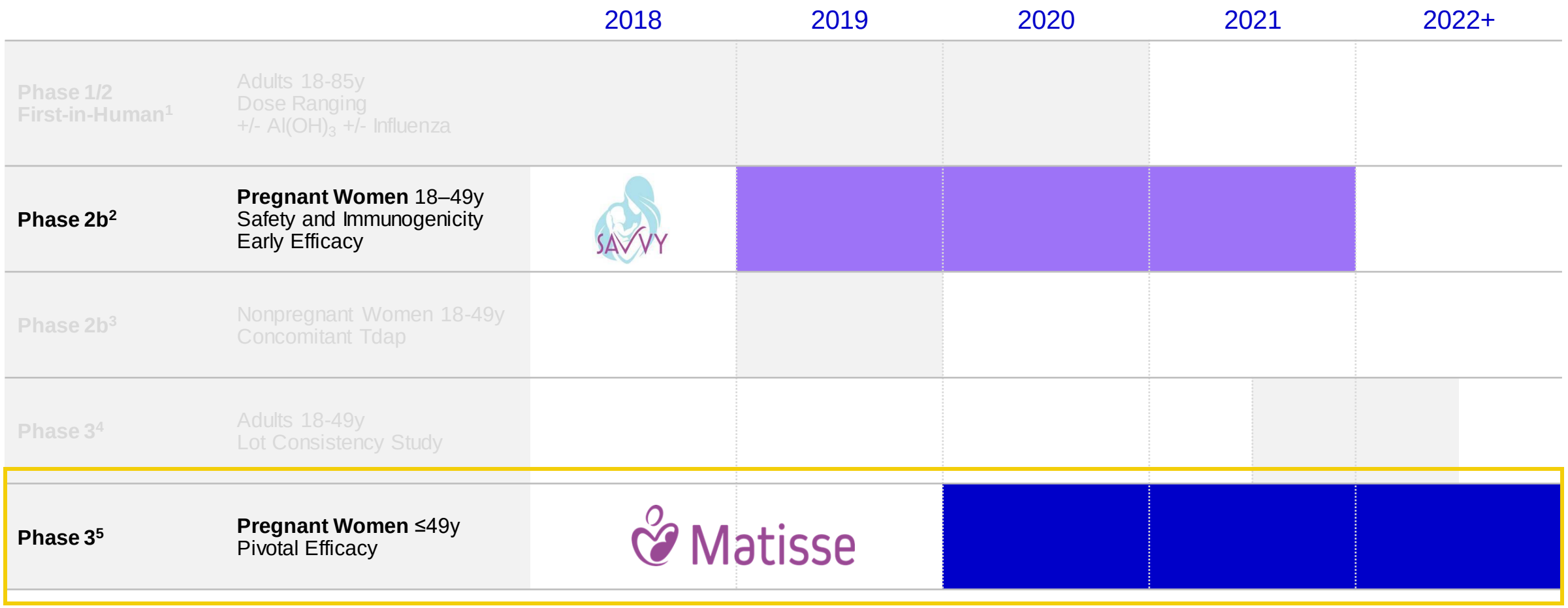
Infant Neutralizing Titers Remain High Through 6 Months

RSV A/B Combined 50% Geometric Mean Neutralizing Titers by Month in Infants born to Mothers Vaccinated at 24-36 weeks



Palivizumab reference line = 50% A/B neutralizing titer of a 100ug/mL palivizumab dose, demonstrated to be efficacious in preventing infant RSV-associated ICU admission (Forbes ML, Kumar VR, Yogev R, et al. Hum Vaccin Immunother 2014;10:2789-94.)

Pfizer's RSVpreF Maternal Immunization Clinical Development Program



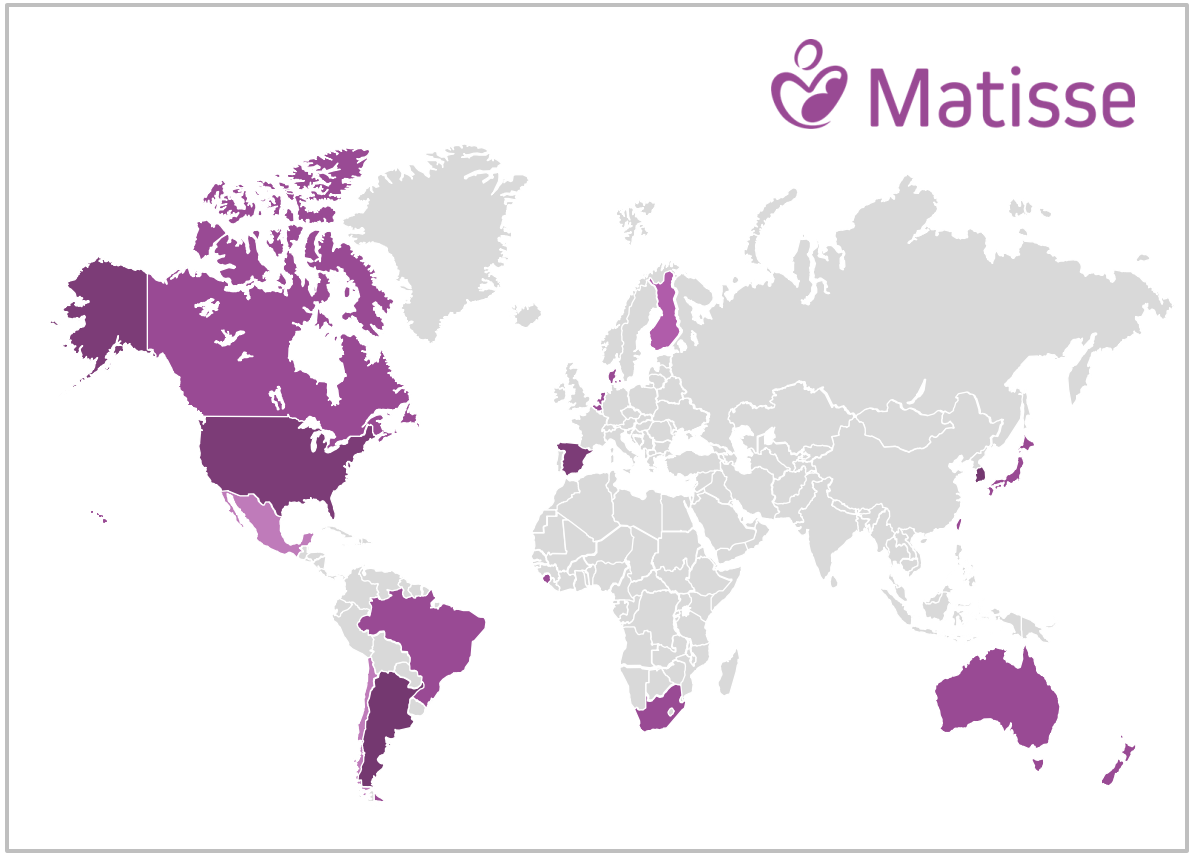
1. A Study to Describe the Safety and Immunogenicity of a RSV Vaccine in Healthy Adults. NCT03529773.
2. A Phase 2b Placebo-Controlled, Randomized Study of an RSV Vaccine in Pregnant Women. NCT04032093.
3. A Study of an RSV Vaccine When Given Together with Tdap in Healthy Nonpregnant Women Aged Between 18 to 49 Years. NCT04071158.
4. Clinical Lot Consistency for RSVpreF in a Population of Healthy Adults 18 to ≤49 Years of Age. NCT05096208.
5. A Trial to Evaluate the Efficacy and Safety of RSVpreF in Infants Born to Women Vaccinated During Pregnancy. NCT04424316.

MATISSE: A Phase 3 Trial to Evaluate the Efficacy and Safety of RSVpreF in Infants Born to Women Vaccinated During Pregnancy

7,392 Maternal Participants in 18 Countries
Randomized 1:1 RSVpreF 120µg or Placebo

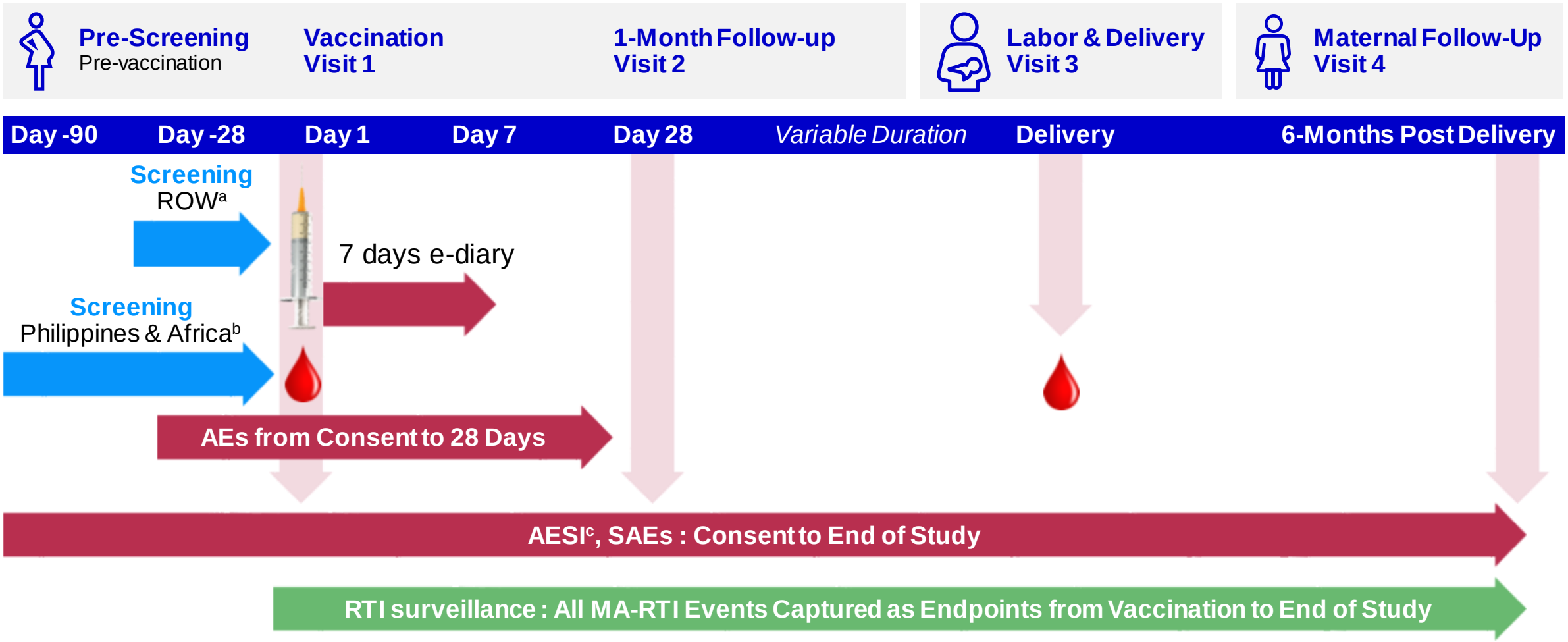
Pregnant persons ≤49 years between ≥24 and ≤36 weeks gestation

7,128 Infants enrolled



A Trial to Evaluate the Efficacy and Safety of RSVpreF in Infants Born to Women Vaccinated During Pregnancy. NCT04424316.

Maternal Immunogenicity & Safety Assessment Timeline



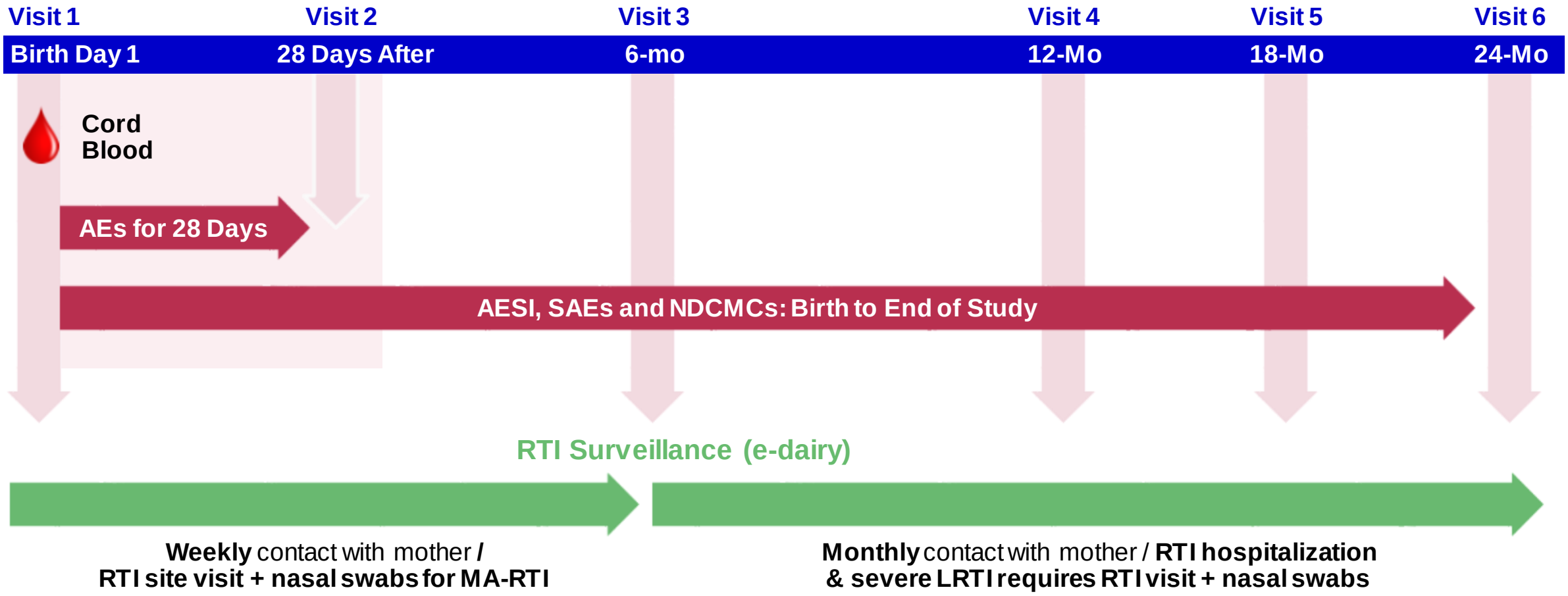
a. Screening bloods and fetal anomaly ultrasound (if not standard of care); ROW, Rest of World
b. Fetal dating and dating ultrasounds (if not standard of care).
c. AESI (AE of Special Interest including preterm delivery and asymptomatic SARS-CoV-2 test positive).

Infant Efficacy, Immunogenicity & Safety Assessment Timeline

Delivery & Infant RTI Surveillance Period*
*Starts 72 hours after delivery

12-Mo Follow-up for All Infants

24-mo Follow-up for Infants Born in Study-year 1



AESI (AE of Special Interest including preterm birth, low birth weight, developmental delay, and asymptomatic SARS-CoV-2 test positive)
SAE (Serious Adverse Event)
NDCMC (Newly Diagnosed Chronic Medical Condition)

Demographic Characteristics
(Maternal Safety Population)

	RSVpreF 120 µg (N[a]=3682); n (%)	Placebo (N[a]=3675); n (%)	Total (N[a]=7357); n (%)
Race			
White	2383 (64.7)	2365 (64.4)	4748 (64.5)
Black or African American	720 (19.6)	723 (19.7)	1443 (19.6)
Asian	454 (12.3)	464 (12.6)	918 (12.5)
American Indian or Alaskan Native	38 (1.0)	37 (1.0)	75 (1.0)
Native Hawaiian or Other Pacific Islander	9 (0.2)	12 (0.3)	21 (0.3)
Multiracial	30 (0.8)	21 (0.6)	51 (0.7)
Ethnicity			
Hispanic/Latino	1049 (28.5)	1075 (29.3)	2124 (28.9)

a. N = number of participants in the specified vaccine group. This value is the denominator for the percentage calculations.
b. n = Number of participants in the specified category.

Demographic Characteristics (continued 2/2)
(Maternal Safety Population)

	RSVpreF 120 µg (N[a]=3682); n (%)	Placebo (N[a]=3675); n (%)	Total (N[a]=7357); n (%)
Age at Vaccination (years)			
N	3682	3675	7357
Mean (SD)	29.1 (5.64)	29.0 (5.74)	29.0 (5.69)
Median (Range)	29.0 (16–45)	29.0 (14–47)	29.0 (14–47)
Gestational Age (GA) at Vaccination*			
≥24 weeks to <28 weeks	941 (25.6)	909 (24.7)	1850 (25.1)
≥28 weeks to <32 weeks	1085 (29.5)	1128 (30.7)	2213 (30.1)
≥32 weeks to ≤36 weeks	1653 (44.9)	1632 (44.4)	3285 (44.7)
>36 weeks	3 (<0.1)	6 (0.2)	9 (0.1)

*Average GA at vaccination = 30 weeks

Note: One participant is counted under ≥24 weeks to <28 weeks however actual age was 23 weeks 6 days.
a. N = number of participants in the specified vaccine group. This value is the denominator for the percentage calculations.
b. n = Number of participants in the specified category.

Demographic Characteristics
(Infant Safety Population)

	RSVpreF 120 µg (N[a]=3568); n (%)	Placebo (N[a]=3558); n (%)	Total (N[a]=7126); n (%)
Sex			
Male	1816 (50.9)	1793 (50.4)	3609 (50.6)
Female	1752 (49.1)	1765 (49.6)	3517 (49.4)
Race			
White	2294 (64.3)	2284 (64.2)	4578 (64.2)
Black or African American	687 (19.3)	688 (19.3)	1375 (19.3)
Asian	420 (11.8)	430 (12.1)	850 (11.9)
American Indian or Alaskan Native	42 (1.2)	36 (1.0)	78 (1.1)
Native Hawaiian or other Pacific Islander	13 (0.4)	11 (0.3)	24 (0.3)
Multiracial	65 (1.8)	59 (1.7)	124 (1.7)
Ethnicity			
Hispanic/Latino	1033 (29.0)	1039 (29.2)	2072 (29.1)

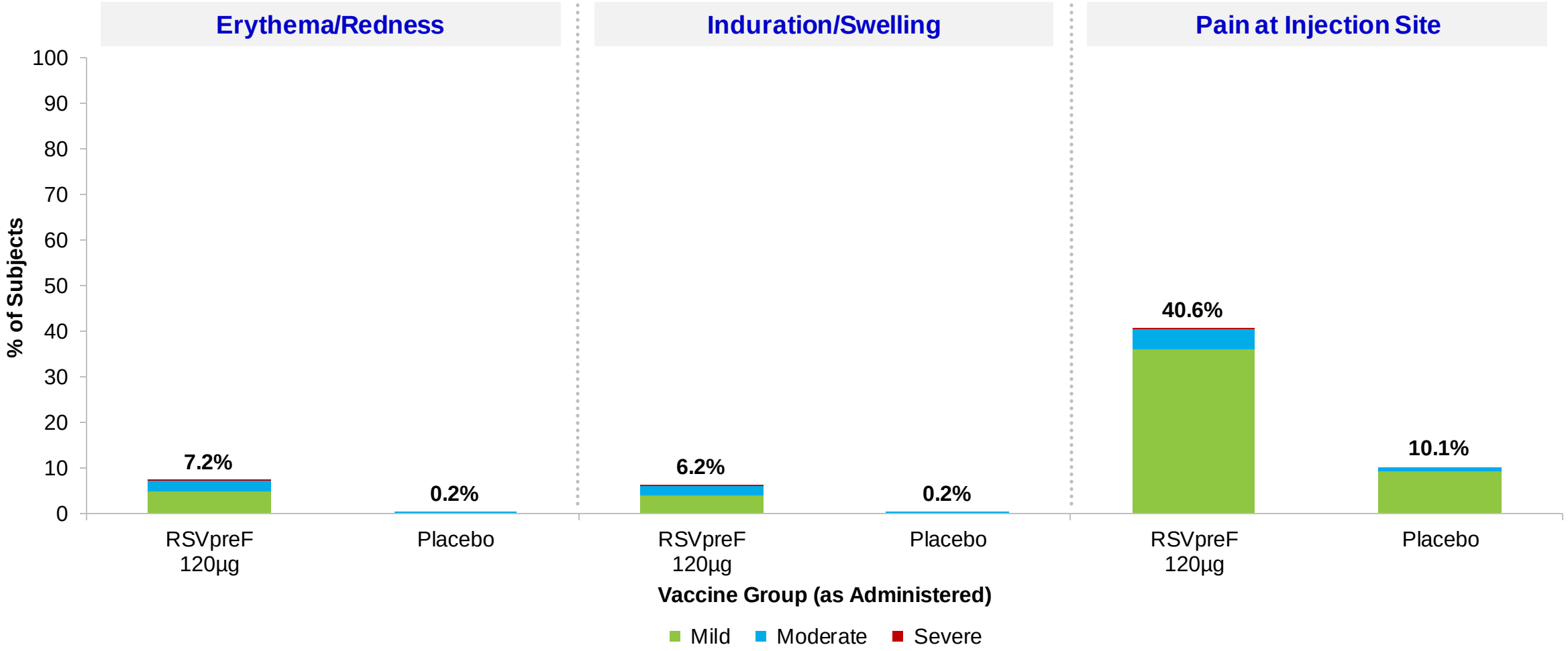
a. N = number of participants in the specified vaccine group. This value is the denominator for the percentage calculations.
b. n = Number of participants in the specified category.

Phase 3 Study Objectives

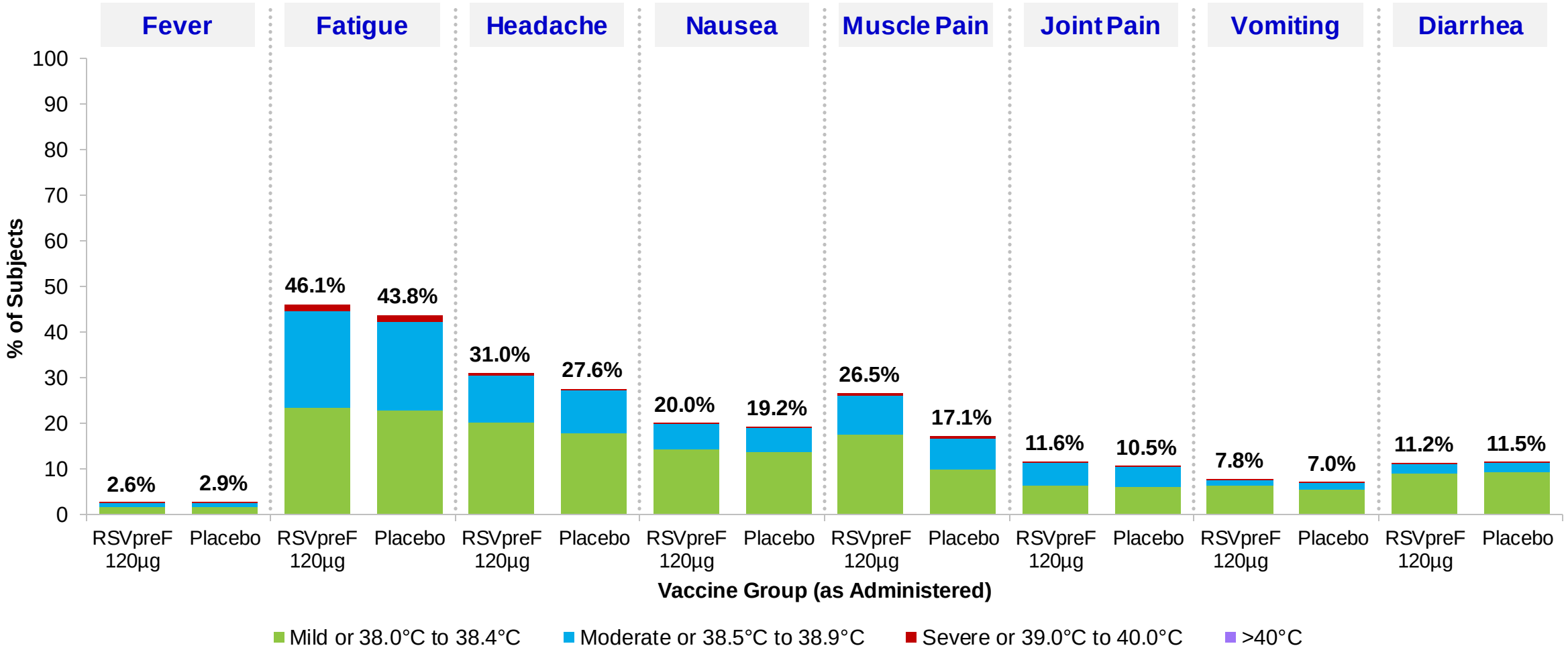
Safety		• Describe the safety profile of RSVpreF Local reactions and systemic events within 7 days post-vaccination AEs through 1-month post-vaccination (Maternal) AEs through 1-month after birth (Infant) AESIs, SAEs (Maternal and Infant) and NDCMCs (Infant) throughout study
Efficacy	**Primary**	• Prevention of RSV MA-LRTI within 180 days after birth • Prevention of RSV severe MA-LRTI within 180 days after birth
	Secondary	• Prevention of RSV MA-LRTIs within 360 days after birth • Prevention of RSV hospitalization within 360 days after birth • Prevention of MA-LRTIs due to any cause within 360 days after birth

AE, adverse event; AESI, adverse event of special interest; NDCMC, newly diagnosed chronic medical condition; SAE, serious adverse event; MA, medically attended; LRTI, lower respiratory tract illness; RSV, respiratory syncytial virus

Local Reactions, by Maximum Severity, within 7 Days After Vaccination Maternal Participants (n=7357)

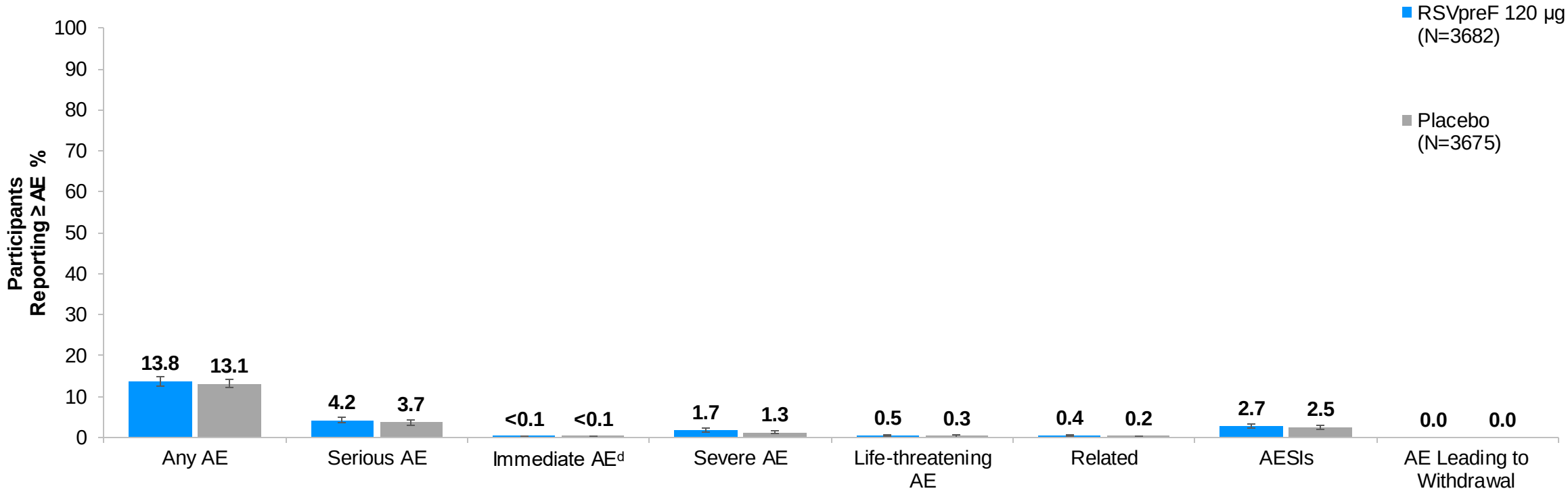


Systemic Events, by Maximum Severity, Within 7 Days After Vaccination Maternal Participants (n=7357)



Number (%) of Participants Reporting Adverse Events by Category Within 1 Month After Vaccination

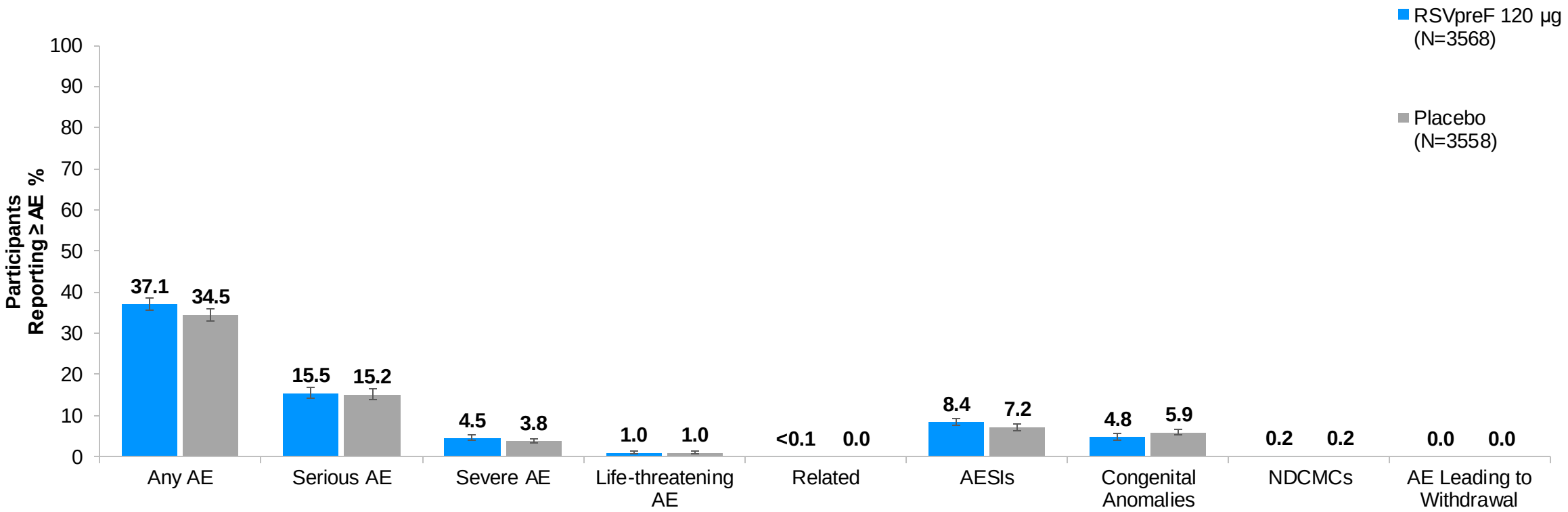
Maternal Participants[a,b,c]



Abbreviations: AESIs = adverse events of special interest; NDCMCs = newly diagnosed chronic medical conditions.
Notes: The severity of the event is in the determination of the investigator. Per statistical analysis plan, 1 month after birth or 1 month after vaccination reflects a 30-day period. However, as per protocol, non-serious adverse events were only solicited through 28 days after birth/vaccination. AESIs and SAEs were solicited throughout the study for maternal participants.
a. N = number of participants in the specified vaccine group. This value is the denominator for the percentage calculations. b. n = Number of participants reporting at least 1 occurrence of the specified adverse event. For "any event", n = number of participants reporting at least 1 occurrence of any adverse event. c. Exact 2-sided confidence interval (CI) calculated using the Clopper and Pearson method. d. An immediate AE is defined as any AE that occurred within the first 30 minutes after administration of the investigational product for maternal participants.

Number (%) of Participants Reporting Adverse Events by Category Within 1 Month After Birth

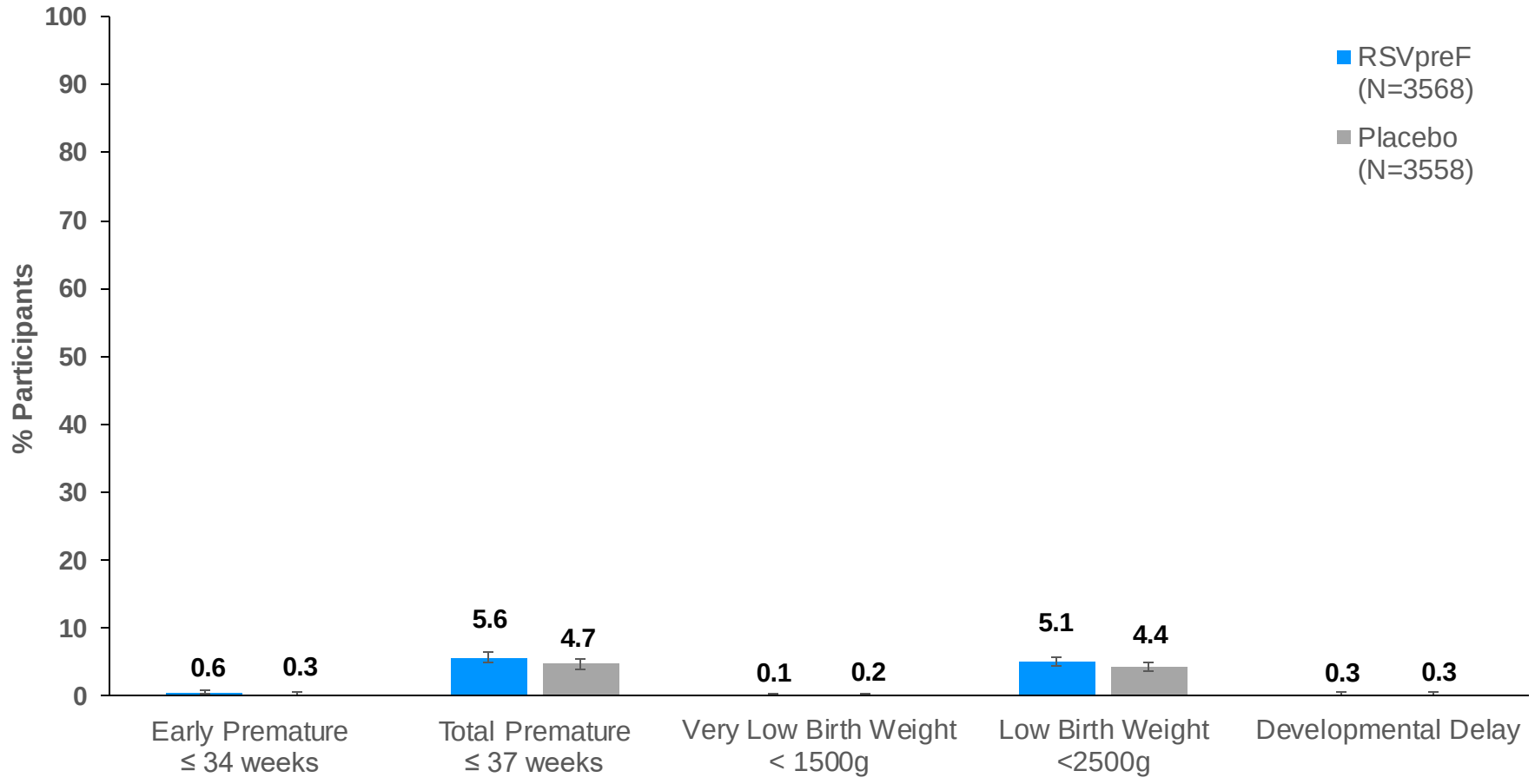
Infant Participants[a,b,c]



Abbreviations: AESIs = adverse events of special interest; NDCMCs = newly diagnosed chronic medical conditions.
Notes: The severity of the event is in the determination of the investigator. Per statistical analysis plan, 1 month after birth or 1 month after vaccination reflects a 30-day period. However, as per protocol, non-serious adverse events were only solicited through 28 days after birth/vaccination. AESIs and SAEs were solicited throughout the study for maternal participants.
a. N = number of participants in the specified vaccine group. This value is the denominator for the percentage calculations. b. n = Number of participants reporting at least 1 occurrence of the specified adverse event. For "any event", n = number of participants reporting at least 1 occurrence of any adverse event. c. Exact 2-sided confidence interval (CI) calculated using the Clopper and Pearson method. d. An immediate AE is defined as any AE that occurred within the first 30 minutes after administration of the investigational product for maternal participants.

Birth Outcomes and Developmental Delay – Infant Participants

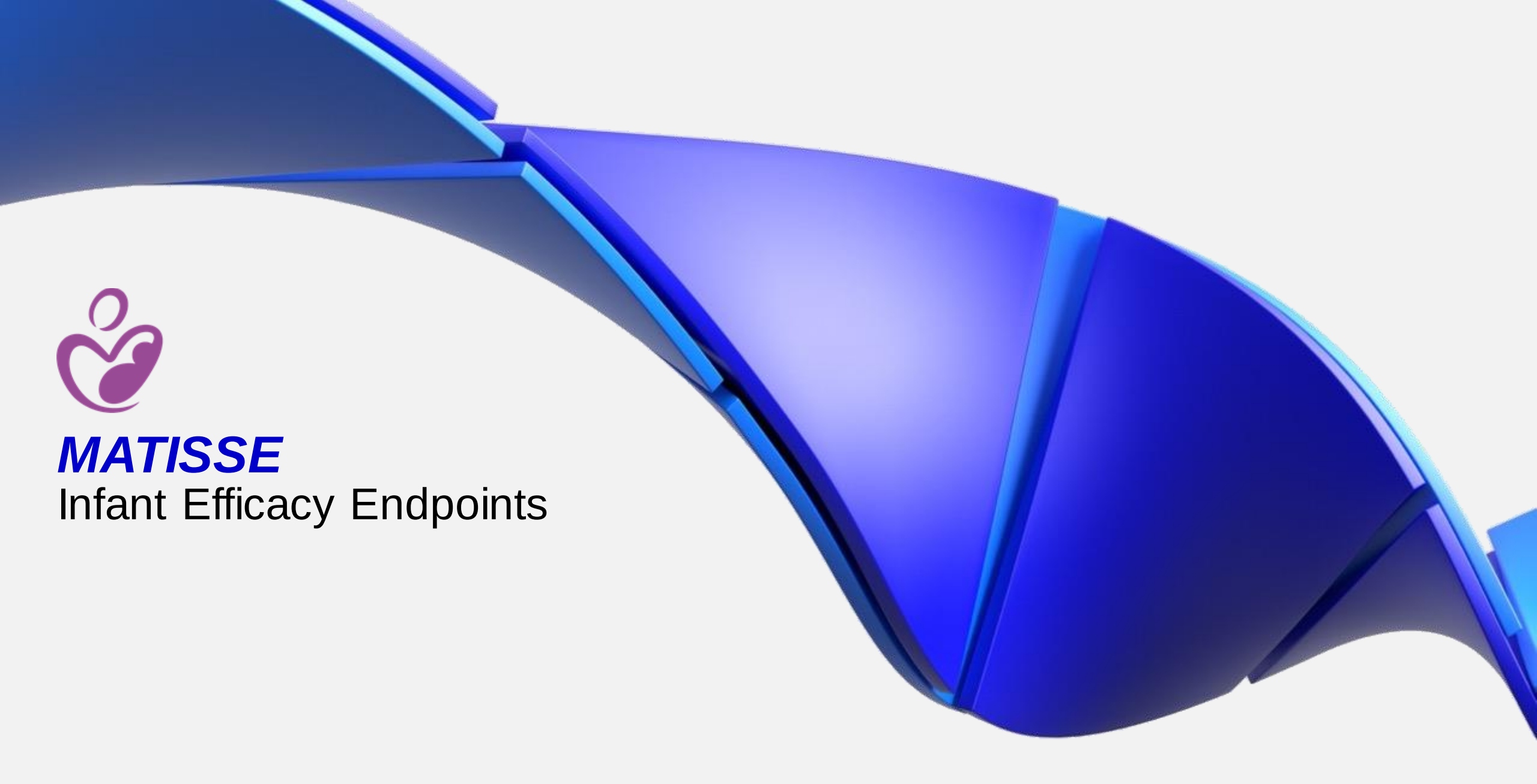
Infant Participants with Prematurity, Low Birth Weight, or Developmental Delay (Adverse Events of Special Interest)



Deaths and Fetal Losses Reported in the Trial (all unrelated)

	Event Type	RSVpreF 120 µg (N=3682)	Placebo (N=3675)
Maternal Death: n = 1			
• 1 in a maternal participant who received RSVpreF	Maternal Death	1 (<0.1%)	0
Fetal Demise: n = 18			
• 18 fetal demises in maternal participants who received Vaccine/Placebo	Fetal death or stillbirth	10 (0.3%)	8 (0.2%)

	Event Type	RSVpreF 120 µg (N=3568)	Placebo (N=3558)
Infant Death: n = 17			
• 16 due to various causes • 1 infant adjudicated "Acute Respiratory Illness due to RSV" (placebo group)	Infant Death	5 (0.1%)	12 (0.3%)



MATISSE

Infant Efficacy Endpoints

Phase 3 Efficacy Endpoints Defined

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

Primary Endpoints	Criteria
Medically attended RSV LRTI	Medically attended visit **and ≥1**: • tachypnea (RR ≥60 (<2 m [60 days]) or ≥50 (≥2 to 12 m) • peripheral capillary oxygen saturation (SpO2) measured in room air <95% • chest wall indrawing
Medically attended severe RSV LRTI	Medically attended visit **and ≥1**: • tachypnea (RR ≥70 (<2 m [60 days]) or ≥60 (≥2 to 12 m) • SpO2 measured in room air <93% • high-flow nasal cannula or mechanical ventilation • ICU admission for >4 hours; unresponsive/unconscious

Positive validated RT-PCR in central laboratory

Medically attended visit: Infant participant taken to or seen by a healthcare provider (e.g. outpatient or inpatient visit, emergency room, urgent care, or home visit)

LRTI: Lower respiratory tract illness; SpO2: peripheral capillary oxygen saturation

C3671008: https://clinicaltrials.gov/ct2/show/NCT04424316?term=C3671008&draw=2&rank=1

Primary Endpoints:

Vaccine Efficacy by Cumulative Days after Birth for Two Primary Endpoints

	Maternal Vaccine Group (as Randomized)		
RSV-Positive Severe MA-LRTI	RSVpreF 120 µg (N[a]=3495)	Placebo (N[a]=3480)	
Time Interval	**Number of Cases (%)**	**Number of Cases (%)**	**Vaccine Efficacy[b] (%) (CI*)**
90 Days after birth	6 (0.2)	33 (0.9)	81.8 (40.6, 96.3)
120 Days after birth	12 (0.3)	46 (1.3)	73.9 (45.6, 88.8)
150 Days after birth	16 (0.5)	55 (1.6)	70.9 (44.5, 85.9)
180 Days after birth	19 (0.5)	62 (1.8)	69.4 (44.3, 84.1)
RSV-Positive MA-LRTI			
Time Interval	**Number of Cases (%)**	**Number of Cases (%)**	**Vaccine Efficacy[b] (%) (CI*)**
90 Days after birth	24 (0.7)	56 (1.6)	57.1 (14.7, 79.8)
120 Days after birth	35 (1.0)	81 (2.3)	56.8 (31.2, 73.5)
150 Days after birth	47 (1.3)	99 (2.8)	52.5 (28.7, 68.9)
180 Days after birth	57 (1.6)	117 (3.4)	51.3 (29.4, 66.8)

*99.5% CI for 90 days, 97.58% CI for 120/150/180 days. CI LB >20% for all time points.

Abbreviations: RSV = respiratory syncytial virus. a. N = number of participants (at risk) in the specified group. These values are used as the denominators for the percentage calculations. b. Vaccine efficacy was calculated as 1-(P/[1-P]), where P is the number of cases in the RSVpreF group divided by the total number of cases. The confidence interval was adjusted using Bonferroni procedure and accounting for the primary endpoints results.

Secondary Endpoint: RSV-Positive MA-LRTIs within 360 Days After Birth

RSV-Positive MA-LRTIs Occurring Within 360 Days After Birth Met Statistical Criteria for Success (CI LB>0%)

	Maternal Vaccine Group (as Randomized)		
	RSVpreF 120 µg (N[a]=3495)	Placebo (N[a]=3480)	
Time Interval	**Number of Cases (%)**	**Number of Cases (%)**	**Vaccine Efficacy[b] (%) (99.17% CI)**
210 Days after birth	70 (2.0)	127 (3.6)	44.9 (17.9, 63.5)
240 Days after birth	76 (2.2)	133 (3.8)	42.9 (16.1, 61.6)
270 Days after birth	82 (2.3)	137 (3.9)	40.1 (13.0, 59.2)
360 Days after birth	92 (2.6)	156 (4.5)	41.0 (16.2, 58.9)

Abbreviations: MA-LRTI = medically attended lower respiratory tract illness; RSV = respiratory syncytial virus.
a. N = number of participants (at risk) in the specified group. These values are used as the denominators for the percentage calculations.
b. Vaccine efficacy was calculated as 1-(P/[1-P]), where P is the number of cases in the RSVpreF group divided by the total number of cases. The confidence interval was adjusted using Bonferroni procedure and accounting for the primary endpoints results.

Secondary Endpoint: Hospitalizations Due to RSV within 360 Days After Birth

Hospitalizations Due to RSV through 180 days Met Statistical Criteria for Success (CI LB>0%)

	Maternal Vaccine Group (as Randomized)		
	RSVpreF 120 µg (N[a]=3495)	Placebo (N[a]=3480)	
Time Interval	**Number of Cases (%)**	**Number of Cases (%)**	**Vaccine Efficacy[b] (%) (99.17% CI)**
90 Days after birth	10 (0.3)	31 (0.9)	67.7 (15.9, 89.5)
180 Days after birth	19 (0.5)	44 (1.3)	56.8 (10.1, 80.7)
360 Days after birth	38 (1.1)	57 (1.6)	33.3 (-17.6, 62.9)

Abbreviations: EAC = endpoint adjudication committee; RSV = respiratory syncytial virus.
a. N = number of participants (at risk) in the specified group. These values are used as the denominators for the percentage calculations.
b. Vaccine efficacy was calculated as 1-(P/[1-P]), where P is the number of cases in the RSVpreF group divided by the total number of cases. The confidence interval was adjusted using Bonferroni procedure and accounting for the primary endpoints results.

Exploratory Endpoint: RSV-Positive MA-RTIs (EAC confirmed) within 180 Days After Birth

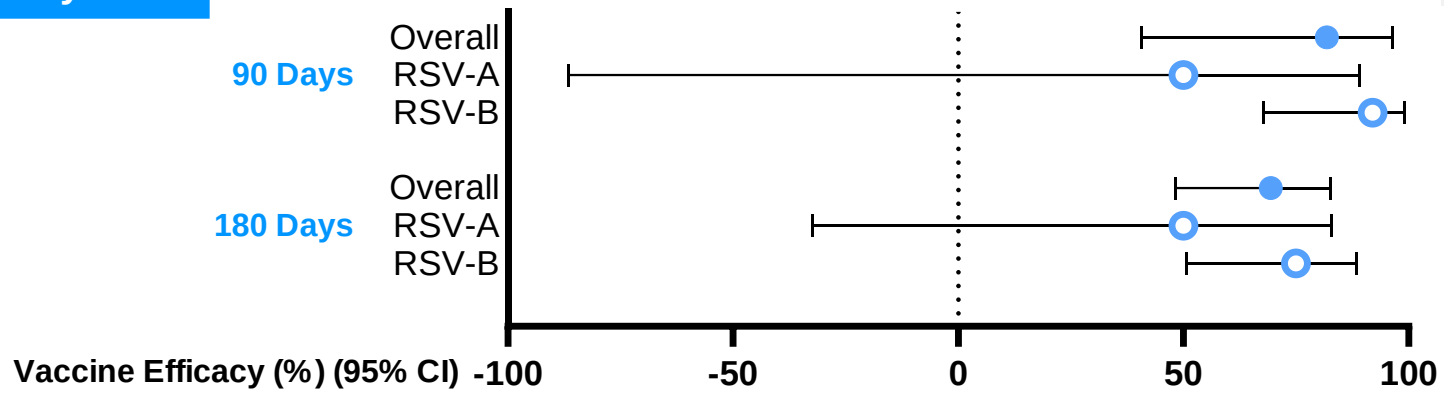
RSV-Positive MA-RTIs through 180 Days After Birth

	Maternal Vaccine Group (as Randomized)		
	RSVpreF 120 µg (N[a]=3495)	Placebo (N[a]=3480)	
Time Interval	**Number of Cases (%)**	**Number of Cases (%)**	**Vaccine Efficacy[b] (%) (95% CI)**
90 Days after birth	67 (1.9)	110 (3.2)	39.1 (16.7, 55.7)
180 Days after birth	157 (4.5)	253 (7.3)	37.9 (24.0, 49.5)

Abbreviations: EAC = endpoint adjudication committee; MA-RTI = medically attended respiratory tract illness; RSV = respiratory syncytial virus.
a. N = number of participants (at risk) in the specified group. These values are used as the denominators for the percentage calculations.
b. Vaccine efficacy was calculated as 1-(P/[1-P]), where P is the number of cases in the RSVpreF group divided by the total number of cases.

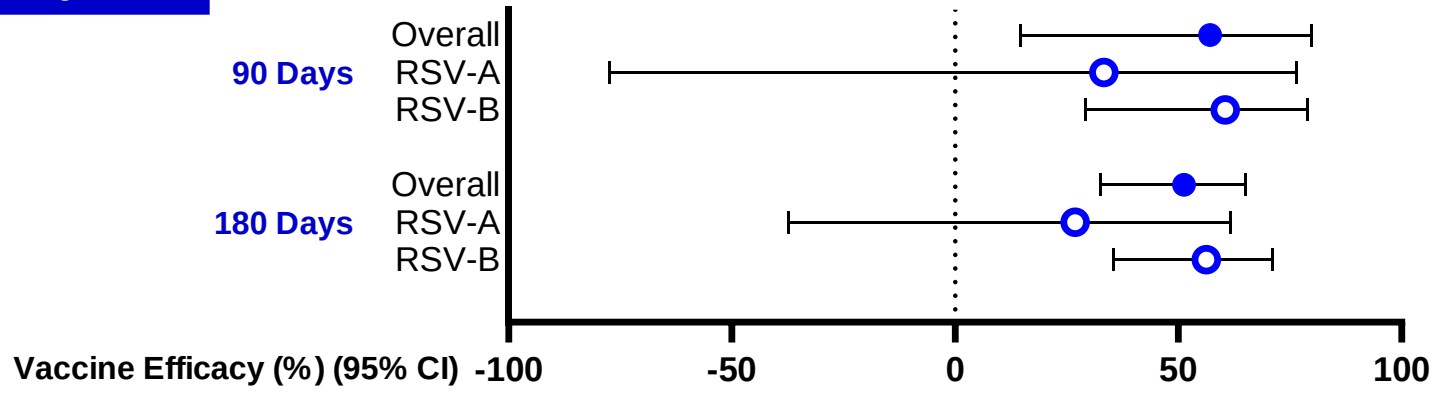
Consistent efficacy Was Observed Across RSV Subgroup A and B*

RSV Severe MA-LRTI 90, 180 Days



	Case Split (RSVpreF/Placebo)	VE
90 Days Overall	6:33	81.8%
90 Days RSV-A	4:8	50.0%
90 Days RSV-B	2:25	92.0%
180 Days Overall	19:62	69.4%
180 Days RSV-A	7:14	50.0%
180 Days RSV-B	11:44	75.0%

RSV MA-LRTI 90, 180 Days



	Case Split (RSVpreF/Placebo)	VE
90 Days Overall	24:56	57.1%
90 Days RSV-A	8:12	33.3%
90 Days RSV-B	17:43	60.5%
180 Days Overall	57:117	51.3%
180 Days RSV-A	19:26	26.9%
180 Days RSV-B	38:87	56.3%

* Exploratory Endpoint – no prespecified criterion for RSV A and B

RSVpreF Efficacious Against Severe Infant MA-LRTI in Phase 3 with a Favorable Safety Profile

Primary Endpoint: Severe MA-LRTI

Time Period	Vaccine Efficacy
First 90 days of life*	**81.8%** (CI: 40.6%, 96.3%)
Six-month follow-up*	**69.4%** (CI: 44.3%, 84.1%)

Primary Endpoint: MA-LRTI

Time Period	Vaccine Efficacy
First 90 days of life*	**57.1%** (CI: 14.7%, 79.8%)
Six-month follow-up*	**51.3%** (CI: 29.4%, 66.8%)

*Confidence intervals are 99.5% CI at 90 days and 97.58% CI at later intervals.

RSVpreF investigational vaccine was well-tolerated with a favorable benefit-risk profile for the maternal populations and their newborns.

*RSV = Respiratory Syncytial Virus; IA: Interim Analysis; MATISSE: **MAT**ernal **I**mmunization **S**tudy for **S**afety and **E**fficacy; MA-LRTI: Medically Attended Lower Respiratory Tract Illness; CI: Confidence Interval; DMC: Data Monitoring Committee; BLA: Biologics License Application; FDA: Food and Drug Administration*

Source: Pfizer Press release, Oct 31, 2022

Thanks to

- The participants and their families
- The study investigators, nurses, coordinators, and laboratory personnel
- Pfizer essential colleagues and our vendors