Phase 1/2, First-in-Human Study of the Safety, Tolerability, and Immunogenicity of an RSV Prefusion F-Based Subunit Vaccine Candidate

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on behalf of the C3671001 study team

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Disclosures:
Beate Schmoele-Thoma; Kena A Swanson; Agnieszka Zareba; David Cooper; William C Gruber; Kathrin U Jansen; David Radley; Alejandra Gurtman; Daniel A Scott; and Philip R Dormitzer are employed by Pfizer and own stock in the company.
Ann R Falsey is an unpaid consultant for Pfizer, Medimmune, Moderna, Sanofi Pasteur, and Merck Sharpe & Dohme and has received research funding from Pfizer, Gilead, Janssen, and BioFire Diagnostics and a personal honorarium from Medavera.
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Important Features of Pfizer's RSVpreF Vaccine Candidate

Prefusion F

VACCINE ANTIGEN

- Stabilized prefusion F with rigorously monitored conformation
- Sequence based on contemporary strains
- Elicits 50-fold higher NAb titers than postfusion F in non-human primates
- Does not enhance respiratory pathology in cotton rats

INDICATIONS

- **Maternal**
  - Immunize pregnant women to prevent RSV-associated lower respiratory tract illness (LRTI) in infants
  - Aim to protect infants from birth to 4-6 months of age
- **Older adult**
  - Prevent RSV-associated moderate to severe LRTI in adults ≥ 60 years of age
  - Anticipate annual immunization, concomitant with flu vaccine

FIH Study Design

A PHASE 1/2, PLACEBO-CONTROLLED, RANDOMIZED, OBSERVER-BLIND, DOSE-FINDING, FIRST-IN-HUMAN STUDY TO DESCRIBE THE SAFETY, TOLERABILITY, AND IMMUNOGENICITY OF A RESPIRATORY SYNCYTIAL VIRUS (RSV) VACCINE IN HEALTHY ADULTS

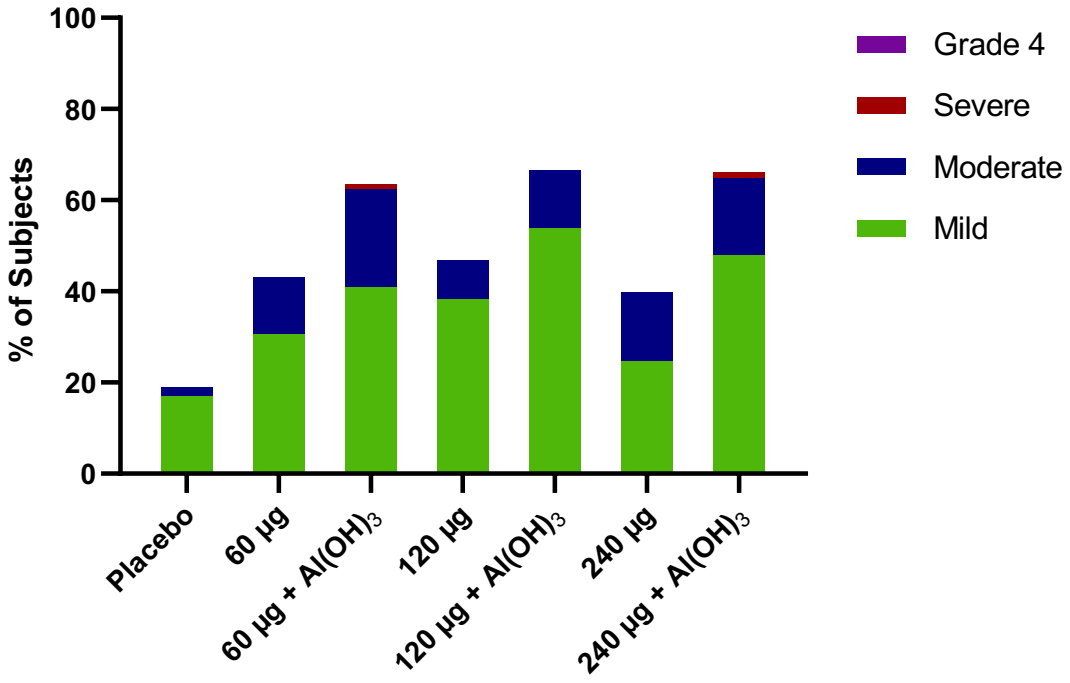
Sentinel cohort				
Dose / Formulation / Regimen	Visit 1	18-49 Yrs of Age	50-85 Yrs of Age	Total
60 µg	RSV	12	12	24
	RSV + Al(OH)$_3$	12	12	24
	Placebo	4	4	8
	Total	**28**	**28**	**56**
120 µg	RSV	12	12	24
	RSV + Al(OH)$_3$	12	12	24
	Placebo	4	4	8
	Total	**28**	**28**	**56**
240 µg	RSV	12	12	24
	RSV + Al(OH)$_3$	12	12	24
	Placebo	4	4	8
	Total	**28**	**28**	**56**
	Total Sentinel	**84**	**84**	**168**

Expanded cohort					
Dose / Formulation / Regimen	Visit 1	Visit 2	18-49 Yrs of Age	65-85 Yrs of Age	Total
60 µg	RSV Flu Vaccine	Placebo	39	39	78
	RSV Placebo	Flu Vaccine	39	39	78
	RSV +Al(OH)$_3$ Flu Vaccine	Placebo	39	39	78
	RSV +Al(OH)$_3$ Placebo	Flu Vaccine	39	39	78
120 µg	RSV Flu Vaccine	Placebo	39	39	78
	RSV Placebo	Flu Vaccine	39	39	78
	RSV +Al(OH)$_3$ Flu Vaccine	Placebo	39	39	78
	RSV +Al(OH)$_3$ Placebo	Flu Vaccine	39	39	78
240 µg	RSV Flu Vaccine	Placebo	39	39	78
	RSV Placebo	Flu Vaccine	39	39	78
	RSV +Al(OH)$_3$ Flu Vaccine	Placebo	39	39	78
	RSV +Al(OH)$_3$ Placebo	Flu Vaccine	39	39	78
	Placebo Placebo	Flu Vaccine	39	39	78
	Total Expanded		**507**	**507**	**1014**
	Total study size Sentinel + Expanded		**591**	**591**	**1182**

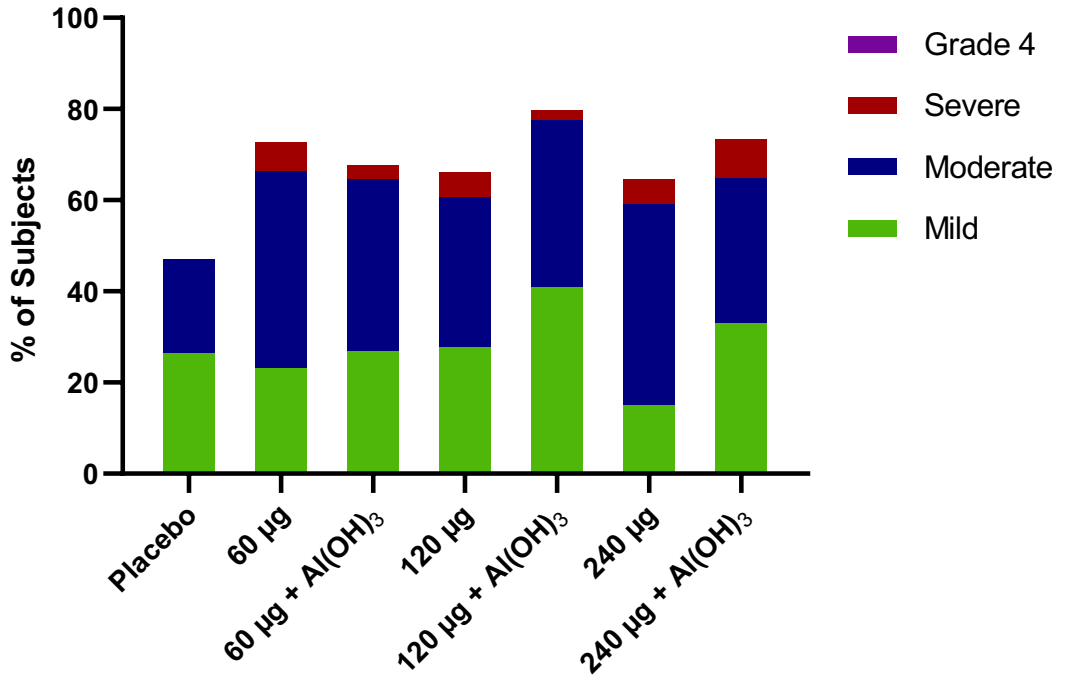
- Sentinel cohort initiated April 2018
- Expanded cohort initiated October 2018
- Immunogenicity assessments for Expanded cohort: 1, 2, 3, 6, 12 mo
- Expanded cohort reached 12 mo time point October 2019
- Study is on-going

Local Reactions and Systemic Events Within 14 Days After Vaccination

Local reactions



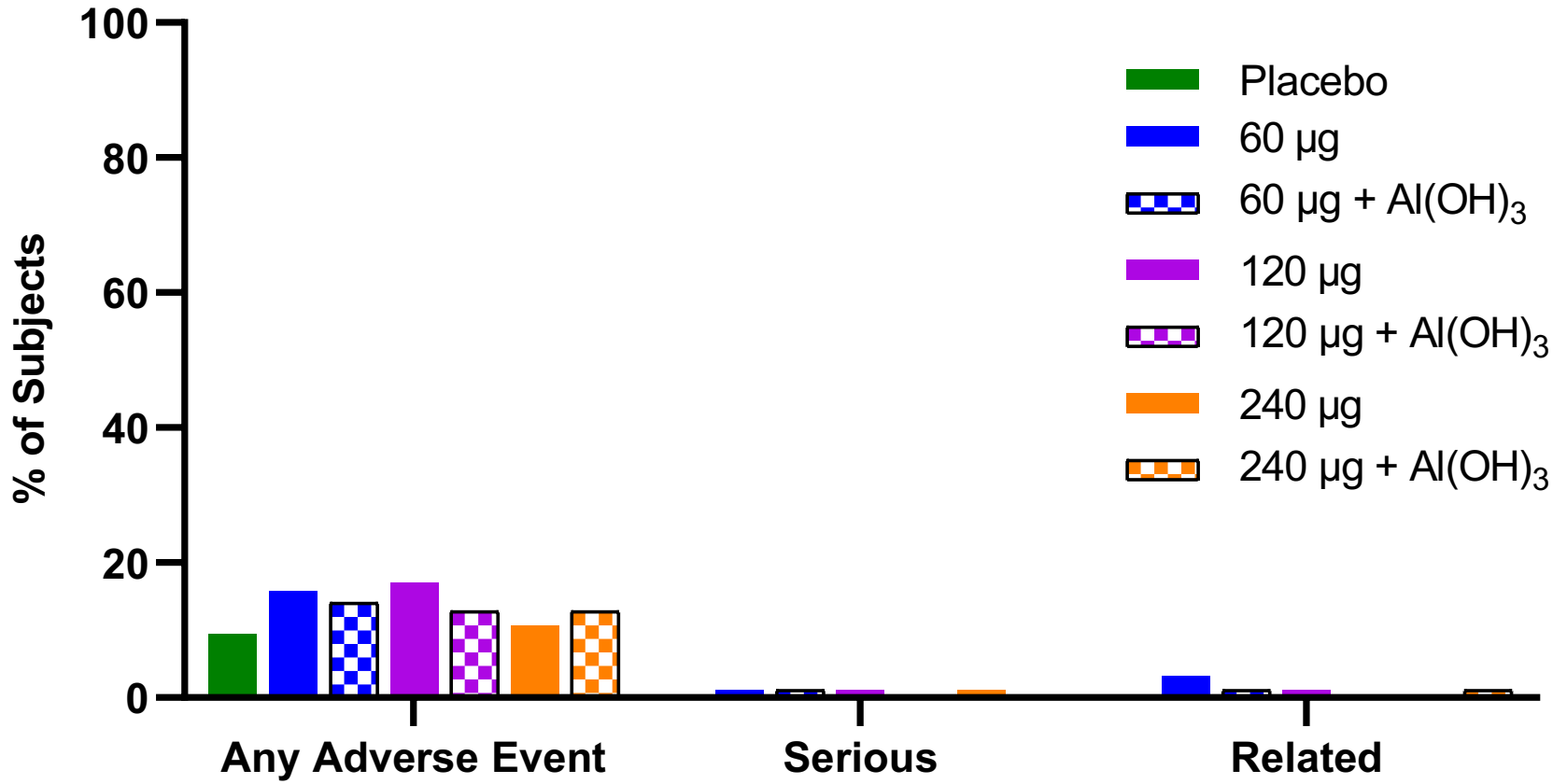
Systemic events



Most frequent: pain at the injection site, headache, muscle pain, and fatigue/tiredness.

Combined Sentinel and Expanded cohorts 18 to 49 years of age

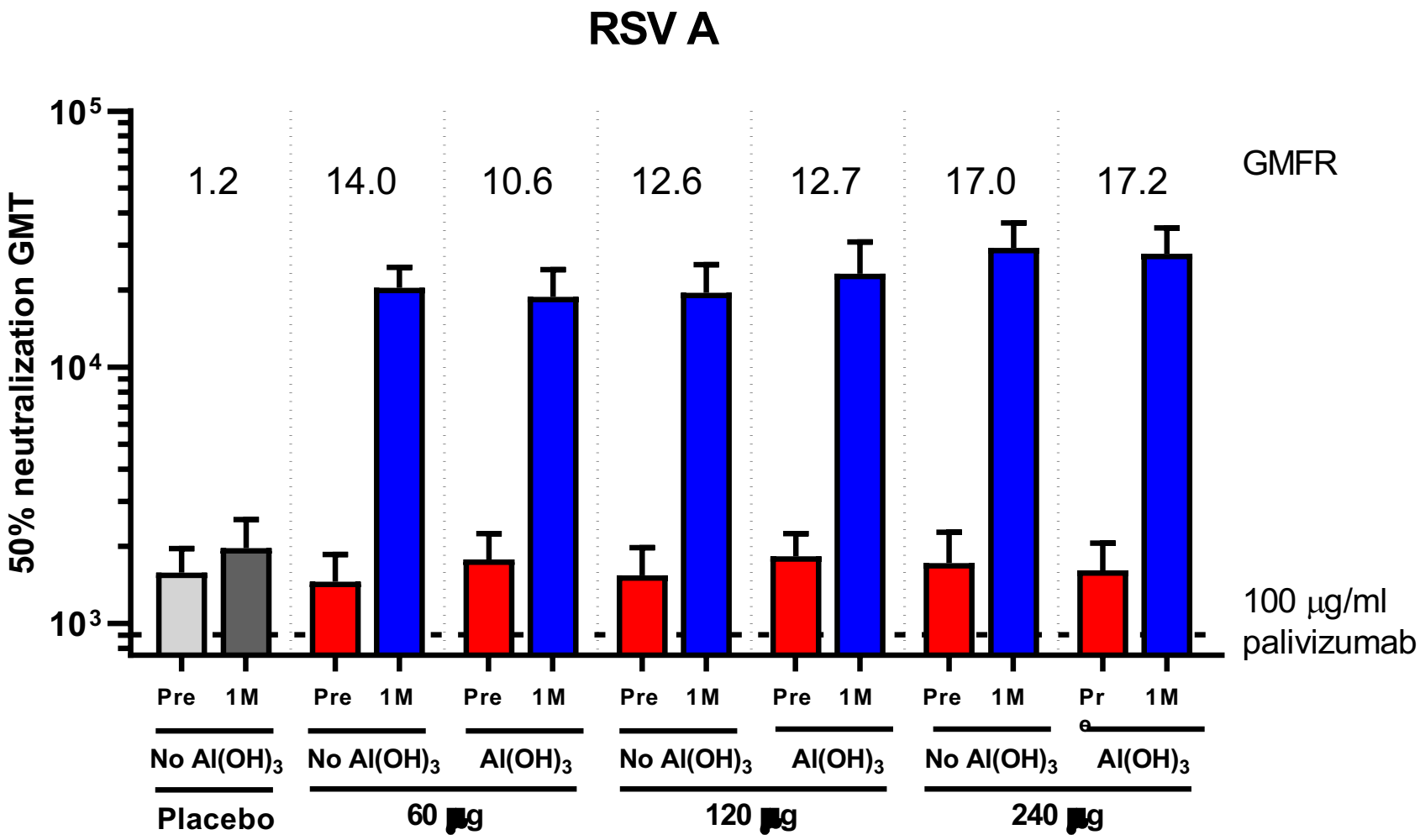
Adverse Events Within 1 Month After Vaccination



5 non-vaccine-related SAEs (0.6%), 12 vaccine-related events (1%)

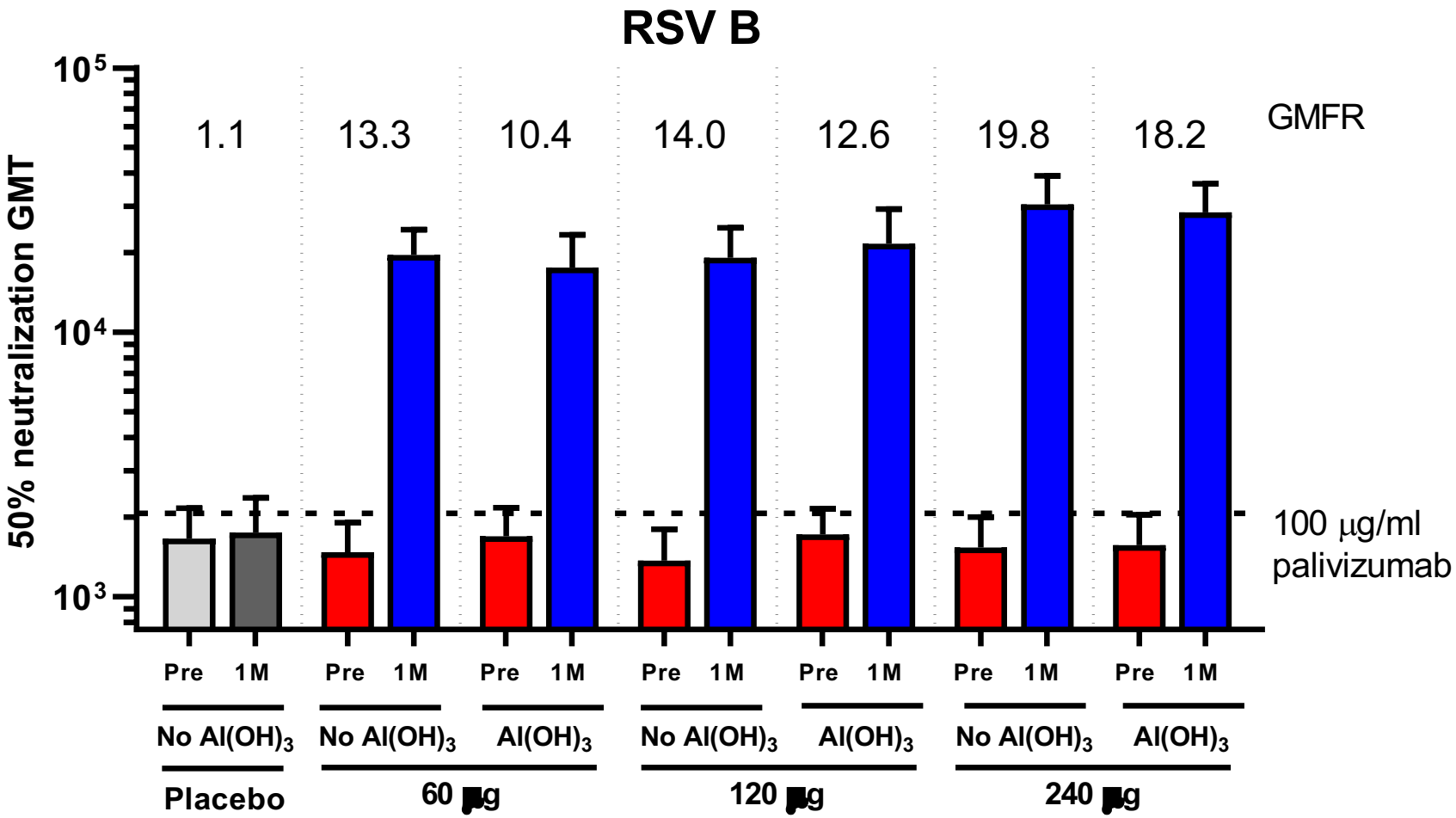
Combined Sentinel and Expanded cohorts 18 to 49 years of age

RSV A 50% Neutralizing GMTs and GMFRs



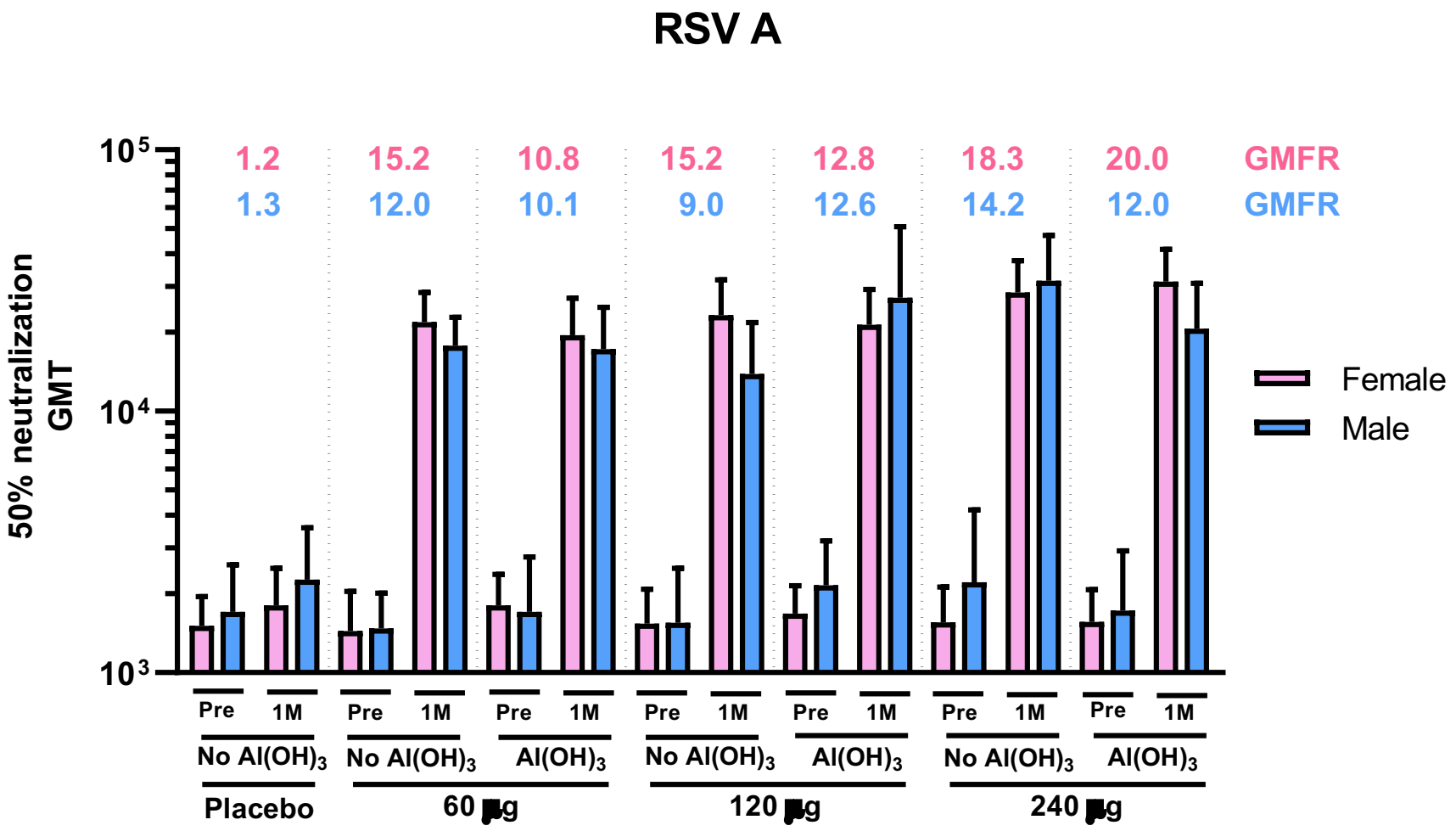
Combined Sentinel and Expanded cohorts 18 to 49 years of age, without flu vaccine

RSV B 50% Neutralizing GMTs and GMFRs



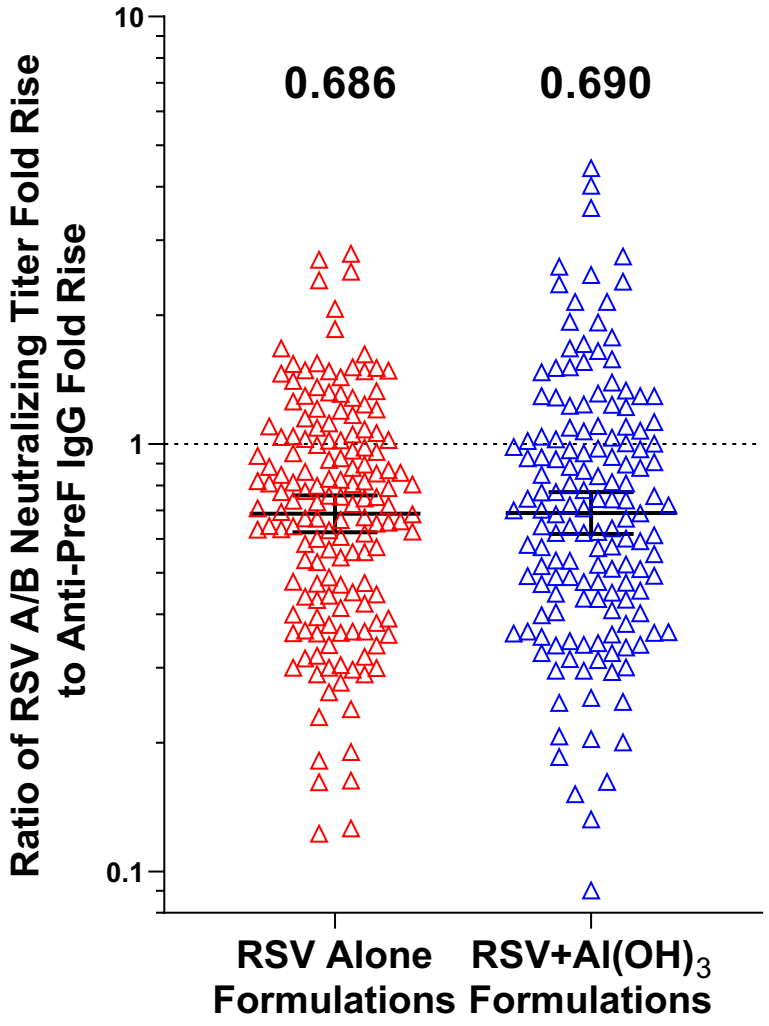
Combined Sentinel and Expanded cohorts 18 to 49 years of age, without flu vaccine

RSV A 50% Neutralizing GMTs and GMFRs by Gender



Combined Sentinel and Expanded cohorts 18 to 49 years of age

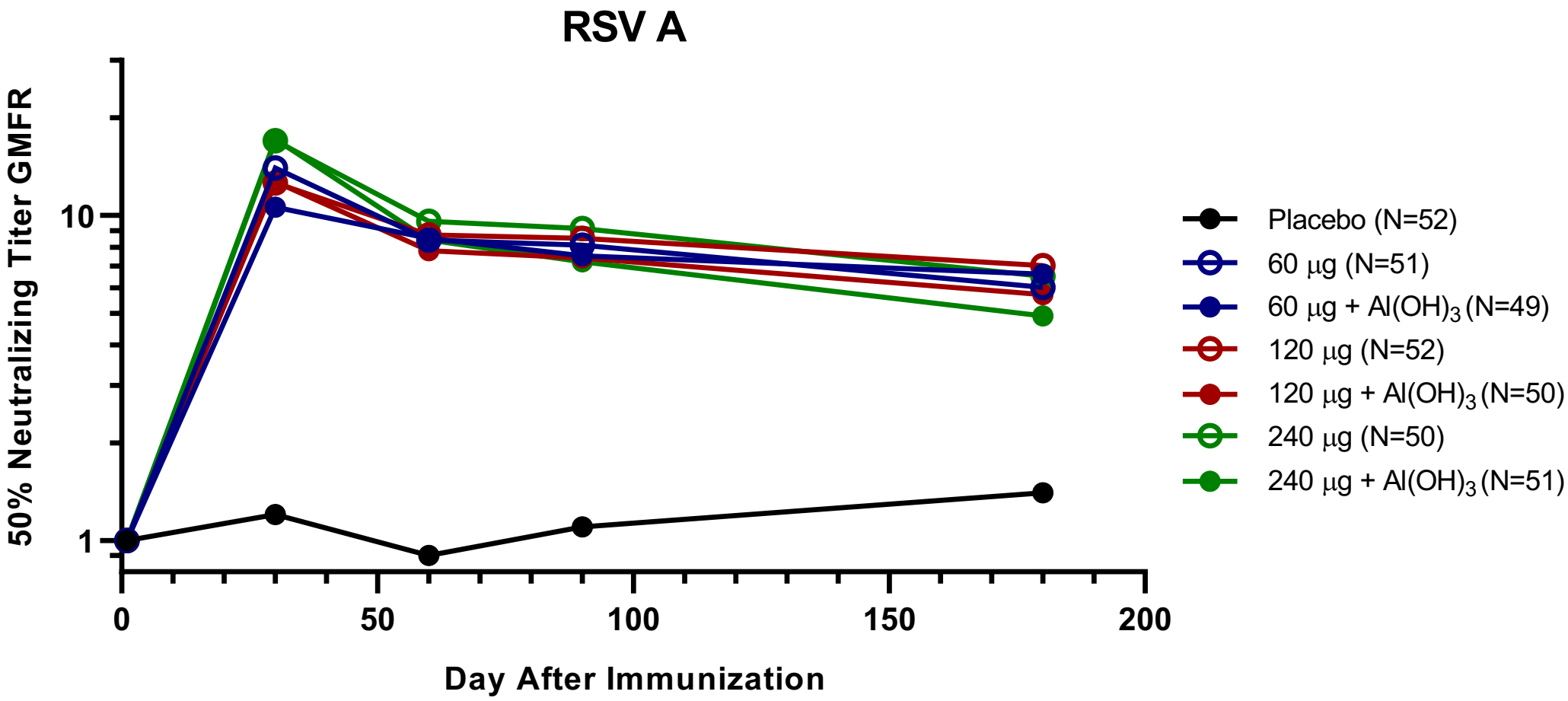
Ratio RSV A/B Neutralizing Titer Fold Rise to Anti-Prefusion F IgG Fold Rise



Geometric Mean Ratios

Data from 18-49 year old vaccine recipients in the combined sentinel and expanded cohorts, all dose levels combined
Error bars indicate Geometric Mean Ratio and 95% CI

Kinetics up to 6 Months After Vaccination for RSV A Neutralizing Antibody GMFRs



Combined Sentinel and Expanded cohorts 18 to 49 years of age

NEXT

A PHASE 2b, RANDOMIZED, PLACEBO-CONTROLLED, OBSERVER-BLINDED TRIAL TO EVALUATE THE SAFETY, TOLERABILITY, AND IMMUNOGENICITY OF A RESPIRATORY SYNCYTIAL VIRUS (RSV) VACCINE IN PREGNANT WOMEN 18 THROUGH 49 YEARS OF AGE AND THEIR INFANTS

- ❑ Up to 650 pregnant women and their infants
- ❑ Doses/formulations tested: 120 µg or 240 µg [each ± $Al(OH)_3$] or placebo
- ❑ Started August 2019

SAVVY
RSV Vaccine Clinical Research