



V116: An Investigational Adult Specific Pneumococcal Conjugate Vaccine

Key Results from the Phase 3 Clinical Development Program

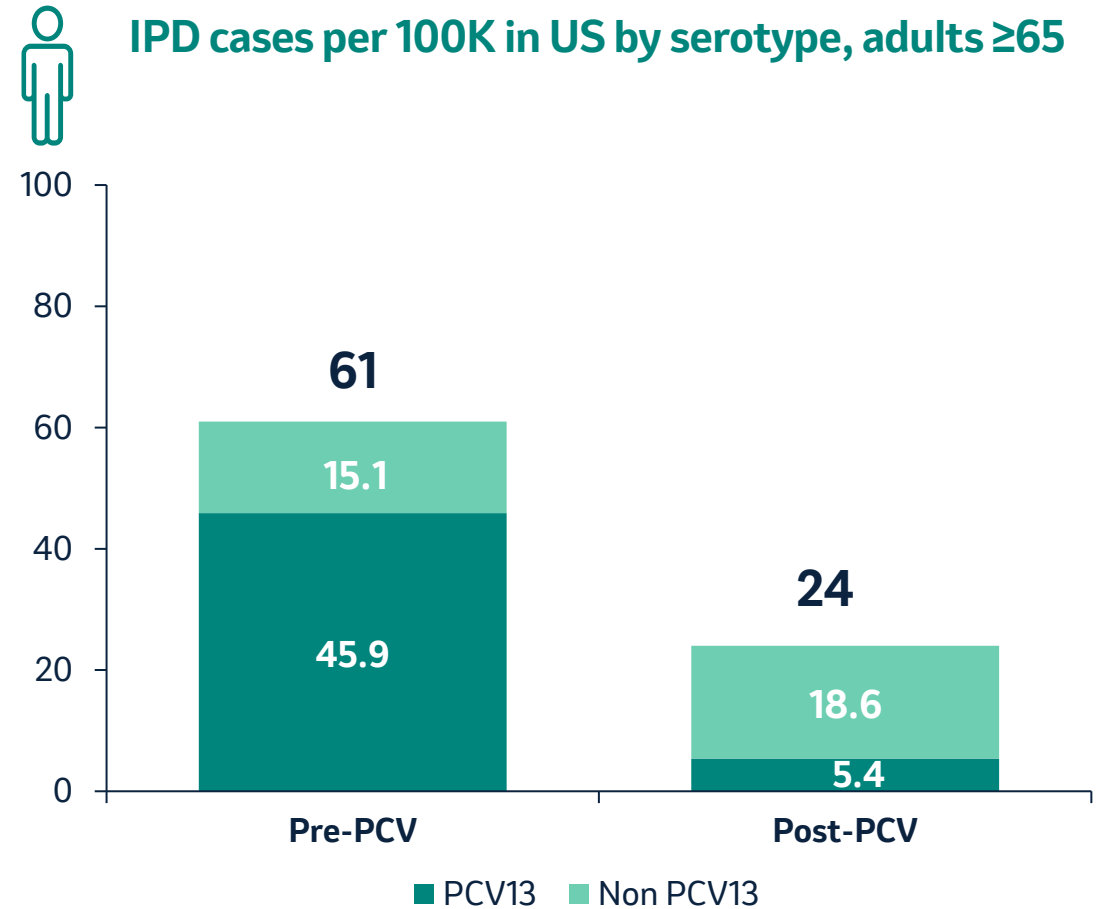
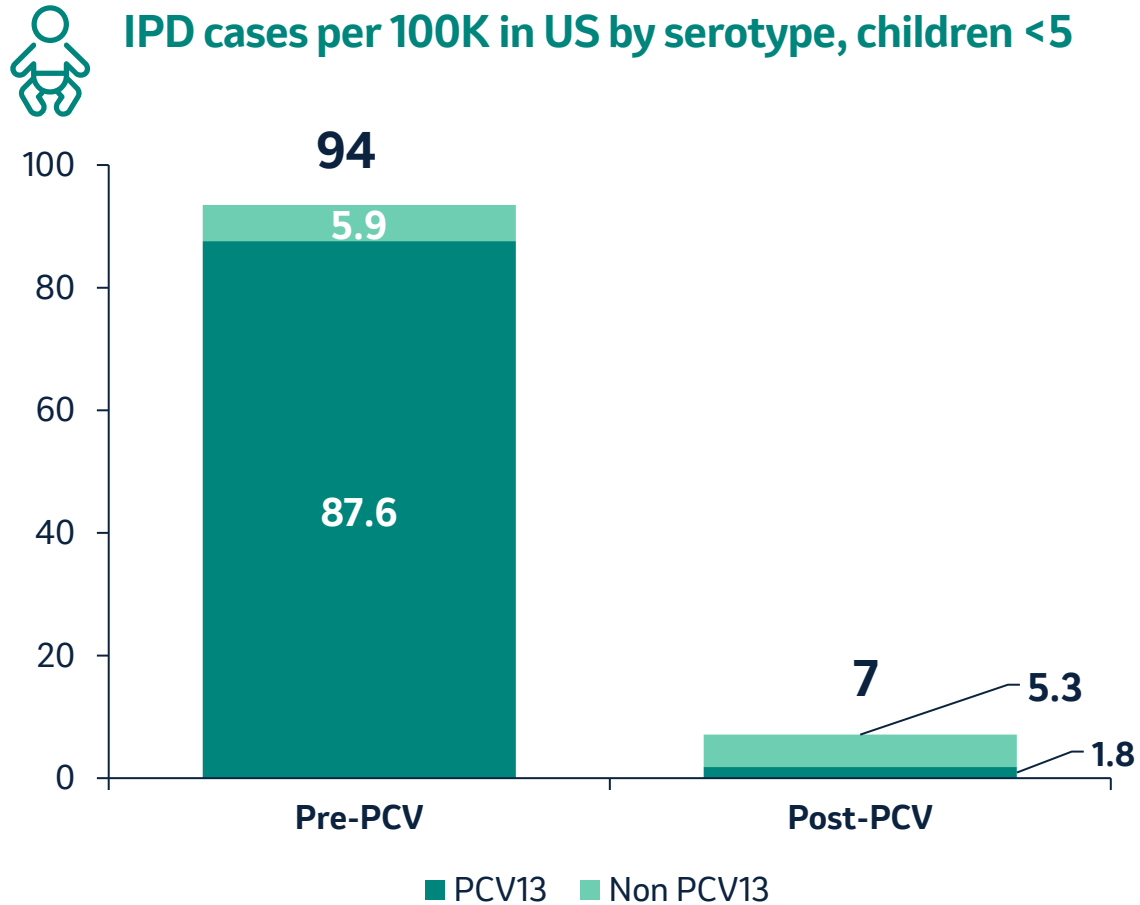
ACIP Meeting, 29-Feb-2024

Heather Platt, M.D., on behalf of the V116 team
Distinguished Scientist, Global Clinical Development
Merck Research Laboratories
Merck & Company, Inc.

Presentation

- ◆ Rationale for Development of V116
- ◆ Overview of V116 Adult Clinical Development Program
- ◆ Immunogenicity Results
 - Vaccine naïve adults ≥ 18 years of age
 - Vaccine experienced adults ≥ 50 years of age
- ◆ Integrated Summary of Safety
 - Vaccine naïve and vaccine experienced adults ≥ 18 years of age
- ◆ Supportive Studies
 - V116 in individuals living with HIV
 - V116 administered with concomitant influenza vaccine
 - V116 lot consistency
- ◆ Conclusions
- ◆ Questions

The introduction of PCVs has significantly decreased disease incidence in children and changed epidemiology of IPD in adults in the US



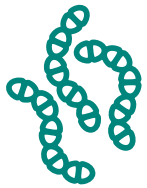
*Centers for Disease Control and Prevention, IPD serotype data 2019, as compiled from data provided through Active Bacterial Core surveillance (ABCs).

Rationale for Development of V116



Indirect protection through pediatric vaccination

PCV use in infants has significantly decreased the burden of disease in adults through **indirect protection**.



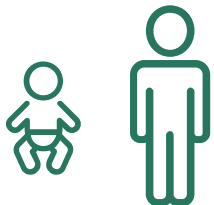
Unmet medical need in adults

The burden of disease in adults remains high; IPD due to **non-vaccine serotypes** has increased in adults.



Population-specific vaccination

V116 being developed as a **population-specific vaccine** to prevent invasive disease and pneumonia in adults.

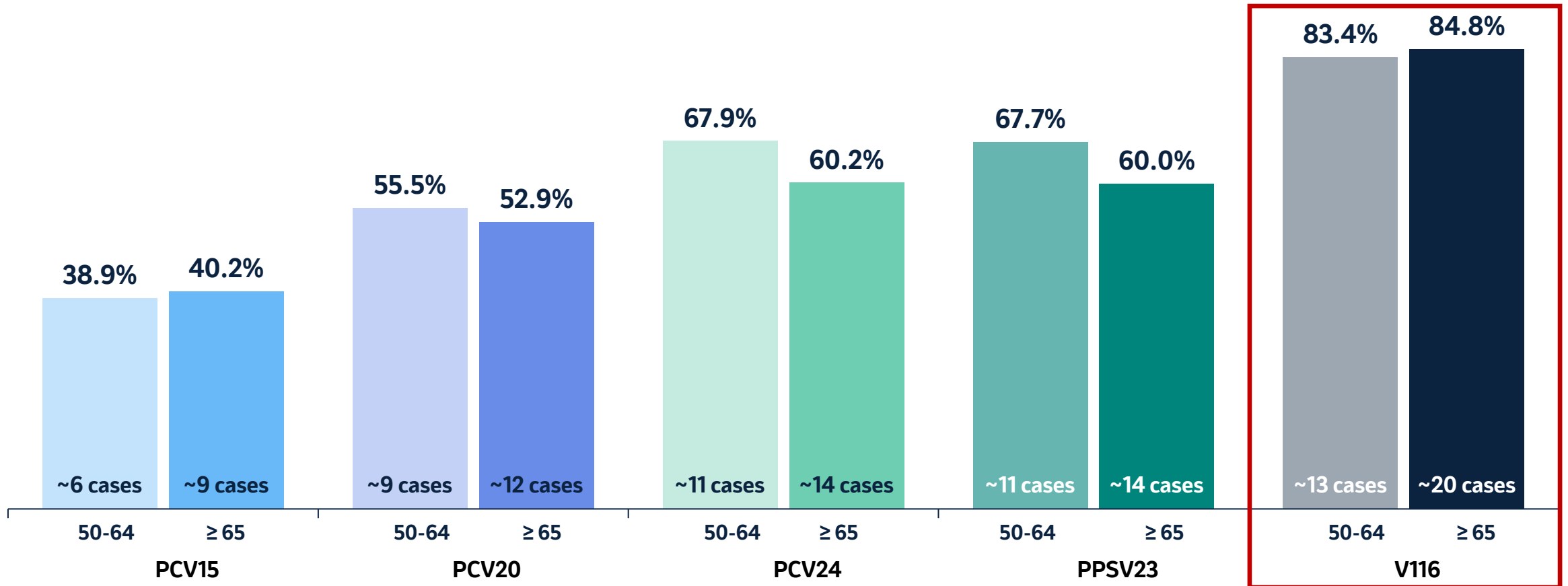


Complementary to pediatric PCVs

V116 is designed to **complement PCV pediatric immunization** programs.

In adults 50–64 and ≥65 years of age, serotypes in V116 are responsible for the majority of residual IPD in adults

IPD coverage (% of serotypes and cases per 100,000) in US Adults 50–64 and ≥65 years of age, 2019



V116 Phase 3 Clinical Development Program

V116 Clinical Development Program focused on enrolling participants at risk for pneumococcal disease

V116-P004
Clinical Lot Consistency
(n=2040)

18 - 49 years old

V116-P003
Pivotal
(n=2600)

≥ 18 years old

V116-P005
Concomitant Flu
(n=1000)

≥ 50 years old

V116-P006
Vaccine Experienced
(n=700)

V116-007
High Risk (HIV)
(n=300)

≥ 18 years old

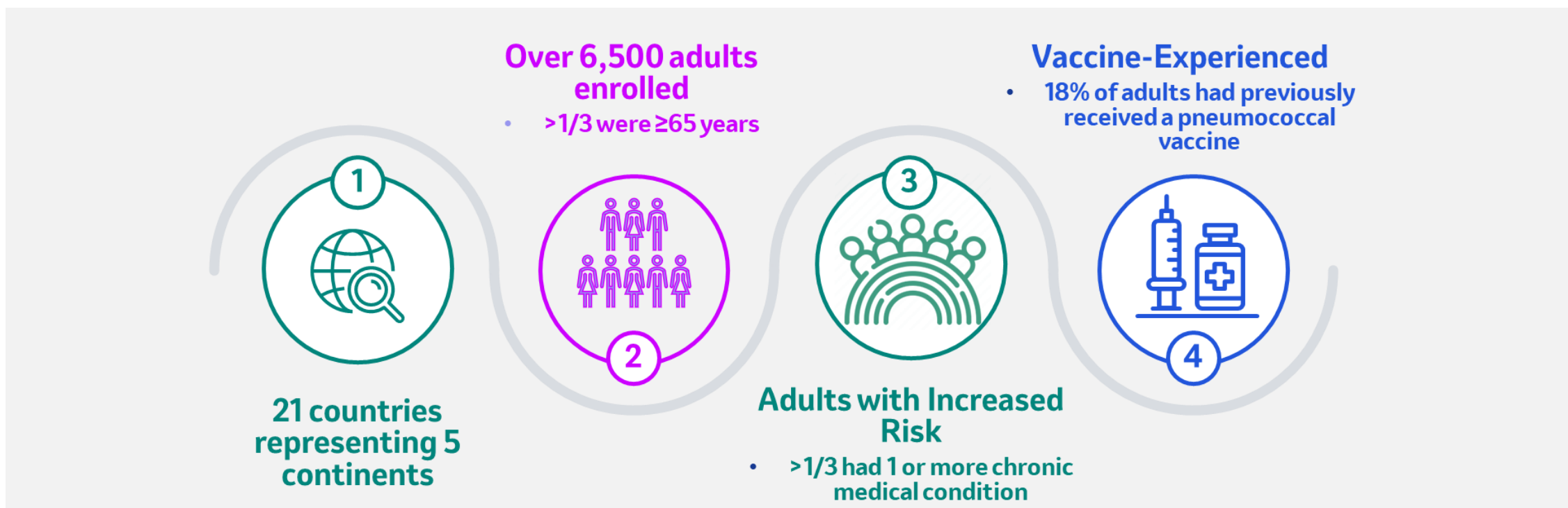
V116-008
At-Risk Adults
(n=900)

18 - 64 years old

V116-013
Pediatric with Increased Risk
(n=820)

≥ 2 - <18 years old

4 Studies in the V116 BLA submission represent a broad, diverse patient population



Immunogenicity & Safety Endpoints in the V116 Program



Immunogenicity Endpoints

OPA responses supported primary objectives:

- Serotype specific OPA Geometric Mean Titers (GMTs)
- Proportion of participants with ≥ 4 -fold rise in OPA responses from baseline to Day 30 postvaccination

OPA and IgG responses supported secondary objectives:

- Serotype specific IgG Geometric Mean Concentrations (GMCs)
- Proportion of participants with ≥ 4 -fold rise in IgG responses from baseline to Day 30 postvaccination
- Geometric Mean Fold Rise (GMFR) of OPA and IgG responses
- Reverse Cumulative Distribution Curves (RCDCs) for OPA and IgG responses

Immune responses were assessed in validated multiplex opsonophagocytic (OPA) and electrochemiluminescence (ECL IgG) assays



Safety Endpoints

Primary Safety Endpoints:

- Solicited injection site events Day 1-5 postvaccination: erythema, swelling, injection-site pain
- Solicited systemic events Days 1-5 postvaccination: headache, myalgia, fatigue
- Serious vaccine-related events Day 1 through the duration of participation in the study

Additional Safety Endpoints:

- Unsolicited AEs, Vaccine related AEs, Any SAE
- Maximum temperature Day 1-5 postvaccination

Participants reported adverse events on an electronic vaccine report card.

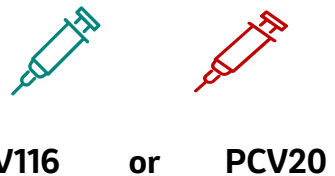
V116-003

A Phase 3, Randomized, Double-blind, Active Comparator-controlled Clinical Study to Evaluate the Safety, Tolerability, and Immunogenicity of V116 in Pneumococcal Vaccine-naïve Adults

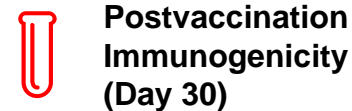
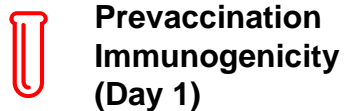
V116-003 Study Design

Cohort 1 (≥50 years of age)
 N=2362 Participants
 randomized 1:1, V116 to PCV20
 (Stratified by age: 50-64, 65-74, 75-84, ≥85)

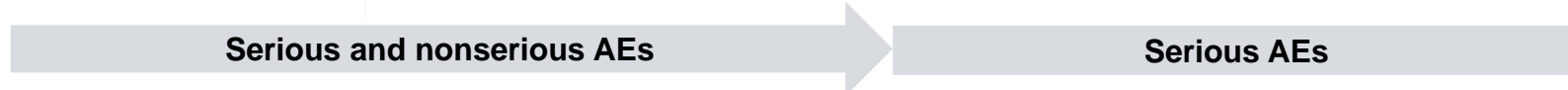
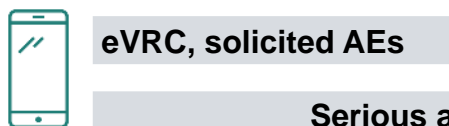
Cohort 2 (18-49 years of age)
 N=301 Participants
 randomized 2:1, V116 to PCV20



Immunogenicity assessment



Safety assessment



V116-003: Primary study objectives

Primary immunogenicity

In adults ≥ 50 years:

- Demonstrate that V116 is **noninferior** to PCV20 for 10 common serotypes
 - Lower bound of the 2-sided 95% CI of the OPA GMT ratio (V116/PCV20) to be **>0.5**
- Demonstrate that V116 is **superior** to PCV20 for 11 unique serotypes
 - Lower bound of the 2-sided 95% CI of the OPA GMT ratio (V116/PCV20) to be **>2.0**
 - 2-sided 95% CI of the differences (V116 - PCV20) between the proportions of participants with a ≥ 4 -fold rise to be **>10%**

In adults 18–49 years:

- Demonstrate V116 **immunobridges** to adults 50-64 years of age for 21 serotypes in V116
 - Lower bound of the 2-sided 95% CI of the OPA GMT ratio (V116 18-49/V116 50-64 years) to be **>0.5**

Primary safety

- To evaluate the safety and tolerability of V116 as assessed by the proportion of participants with adverse events (AEs)
 - **Solicited injection site** events Day 1–5 postvaccination: erythema, swelling, injection-site pain
 - **Solicited systemic events** Days 1–5 postvaccination: headache, myalgia, fatigue
 - **Serious vaccine-related events** Day 1 through the duration of participation in the study

V116-003 Baseline Characteristics

In each cohort, baseline characteristics were balanced between the treatment groups

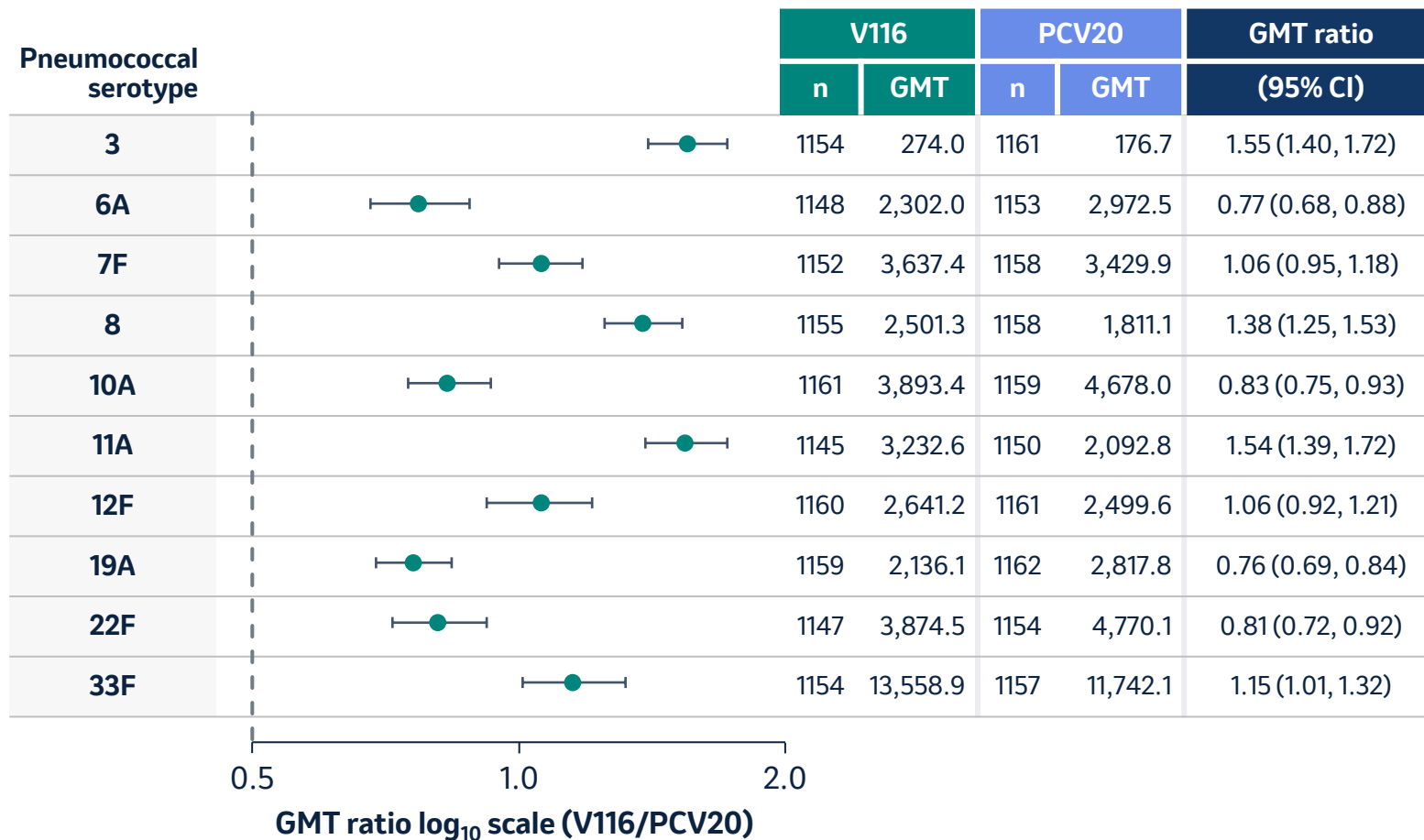
	Cohort 1 (Age ≥50 years)		Cohort 2 (Ages 18-49 years)	
	V116, N=1179	PCV20, N=1177	V116, N=200	PCV20, N=100
Sex				
Female	687 (58.3)	670 (56.9)	137 (68.5)	64 (64.0)
Age (yr)				
Median (min to max)	65 (50-91)	65 (50-97)	36 (18-49)	34 (18-49)
18-49, n (%)	0 (0)	0 (0)	200 (100)	100 (100)
50 to 64, n (%)	589 (50.0)	587 (49.9)	0 (0)	0 (0)
65 to 74, n (%)	464 (39.4)	464 (39.4)	0 (0)	0 (0)
75-84, n (%)	112 (9.5)	113 (9.6)	0 (0)	0 (0)
≥ 85, n (%)	14 (1.2)	13 (1.1)	0 (0)	0 (0)
Race				
Asian	148 (12.6)	168 (14.3)	38 (19.0)	15 (15.0)
Black or African American	116 (9.8)	115 (9.8)	13 (6.5)	14 (14.0)
Multiple	26 (2.2)	30 (2.5)	9 (4.5)	6 (6.0)
White	867 (73.5)	844 (71.7)	139 (69.5)	62 (62.0)
Other	21 (1.8)	19 (1.6)	1 (0.5)	3 (3.0)
Ethnicity				
Hispanic or Latino	259 (22.0)	242 (20.6)	58 (29.0)	24 (24.0)
Pneumococcal Risk Factors				
1 Risk Factor	347 (29.4)	328 (27.9)	45 (22.5)	18 (18.0)
2 or More Risk Factors	100 (8.5)	81 (6.9)	3 (1.5)	1 (1.0)

V116-003 Cohort 1: ≥50 years of age
V116 is noninferior to PCV20 for the 10 common serotypes

Primary immunogenicity objective

- V116 is noninferior to PCV20 for the 10 common serotypes.
- The lower bounds of the two-sided 95% confidence intervals (CIs) are greater than 0.5 for all 10 common serotypes.

Postvaccination OPA GMT Ratios for **Common Serotypes**

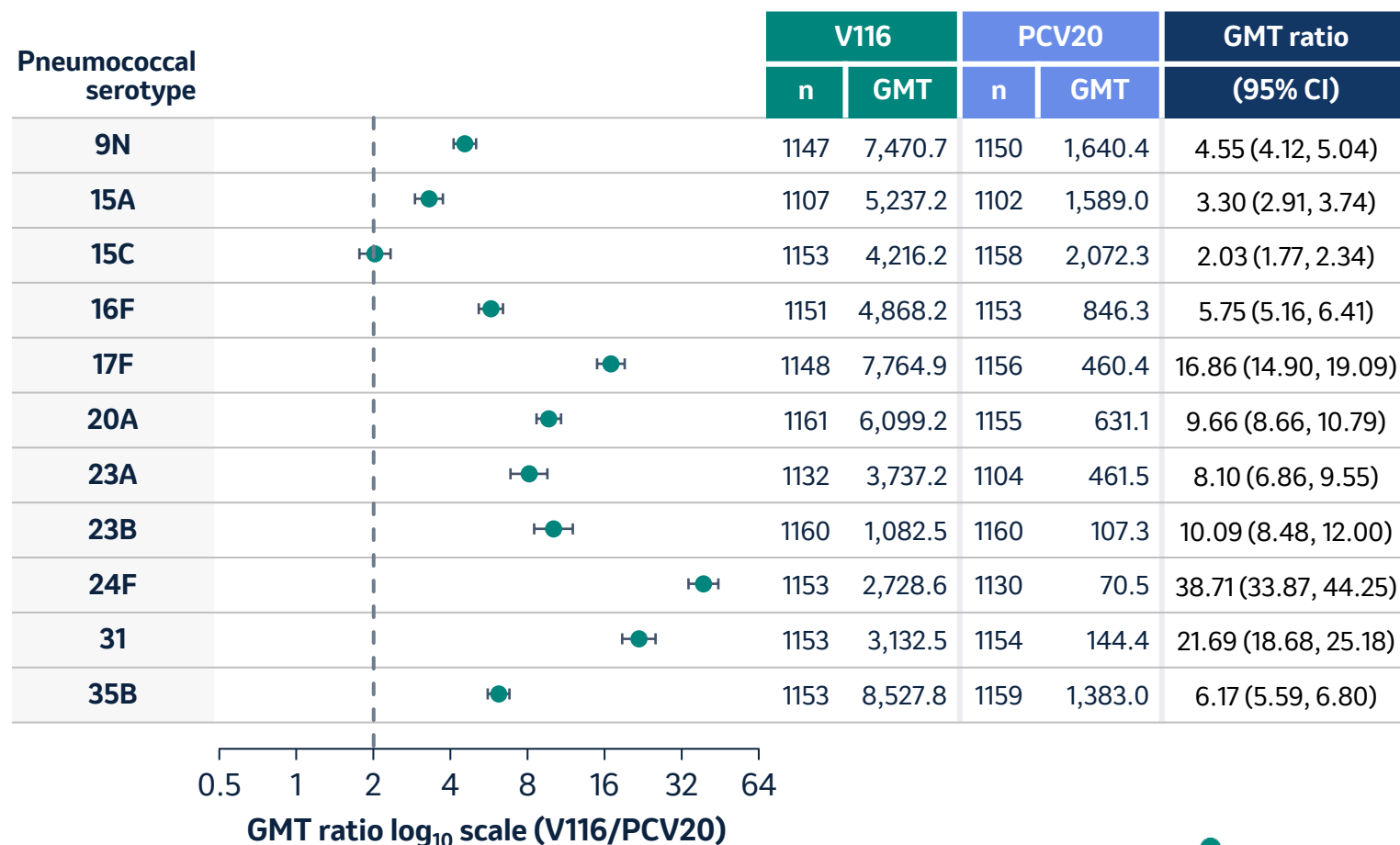


V116-003 Cohort 1: ≥50 years of age
V116 is superior to PCV20 for 10 of 11 unique serotypes

Primary immunogenicity objective

- V116 is superior to PCV20 for 10 of 11 unique serotypes in V116.
- The lower bounds of the two-sided 95% CIs are >2.0 for 10 of 11 unique serotypes in V116.
- For serotype 15C, the lower bound of the 95% CI is 1.77.

Postvaccination OPA GMT Ratios for **Unique Serotypes**



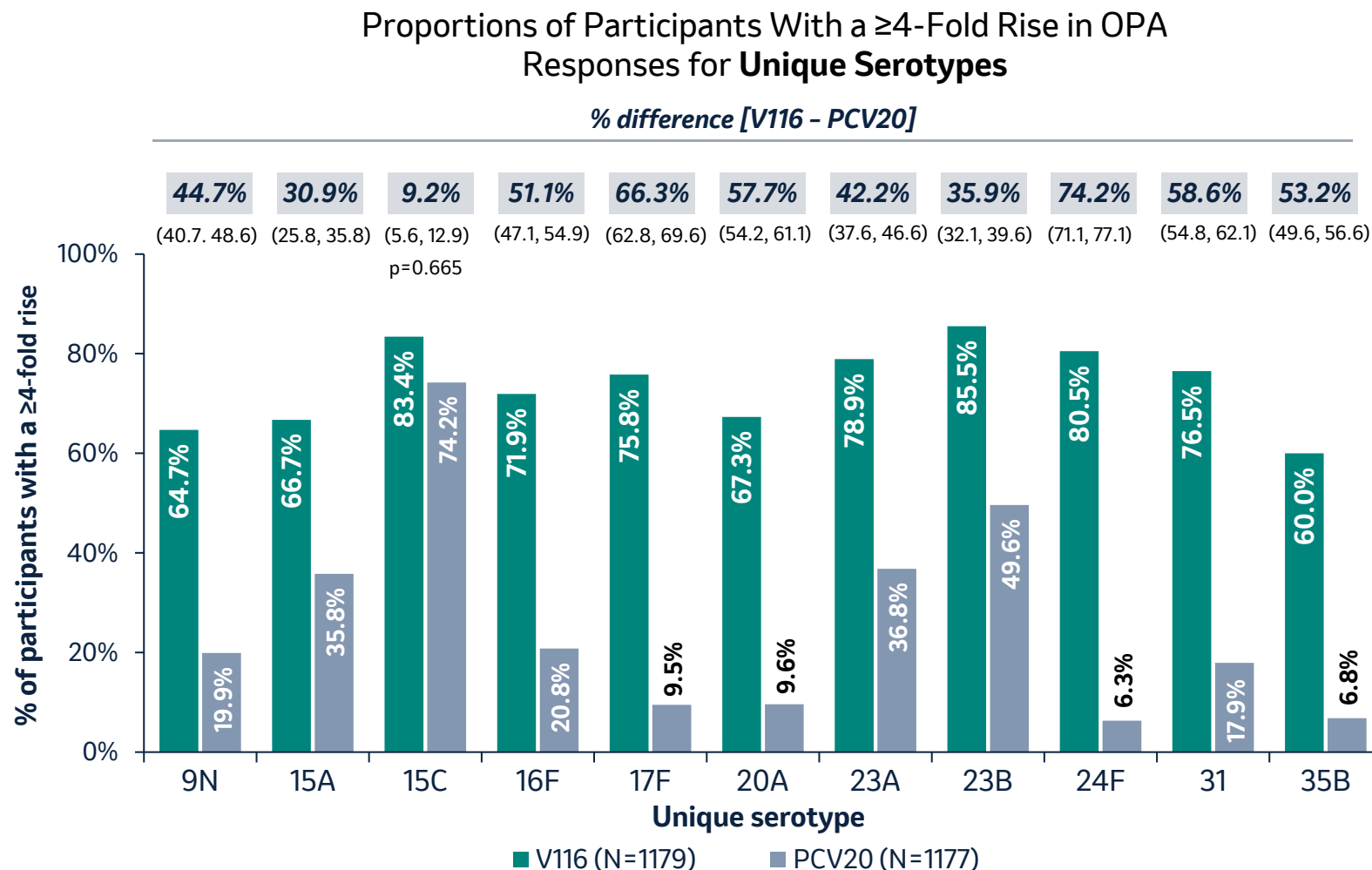
Superiority criteria met if the lower bound of the 95% CI is >2.0

V116-003 Cohort 1: ≥50 years of age

V116 is superior to PCV20 for 10 of 11 unique serotypes

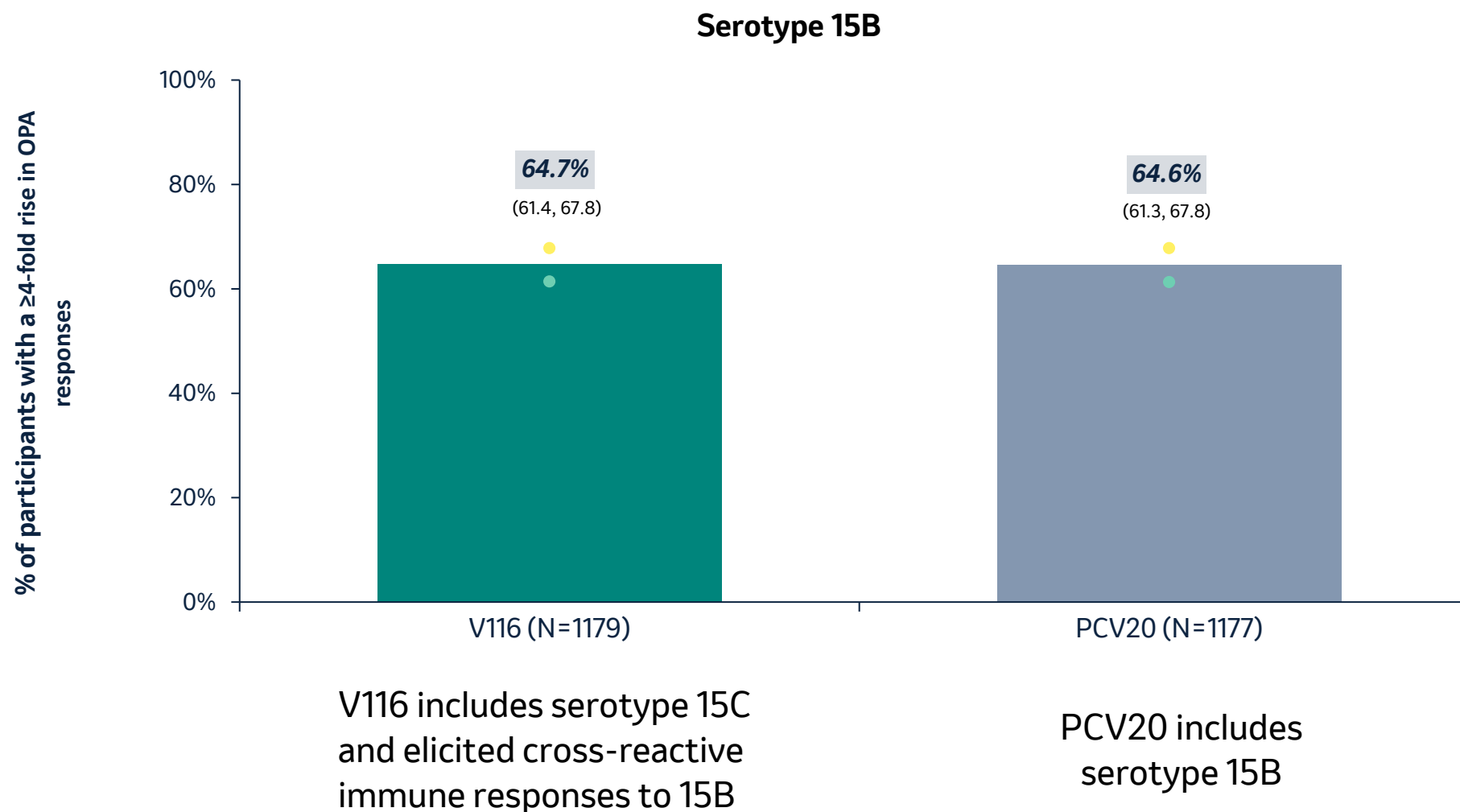
Primary immunogenicity objective

- V116 is superior to PCV20 for 10 of 11 unique serotypes in V116.
- The lower bounds of the 2-sided 95% CIs are > 10 percentage points for 10 of 11 serotypes.



V116-003 Cohort 1: ≥ 50 years of age

V116 elicits robust cross reactive antibody responses to serotype 15B

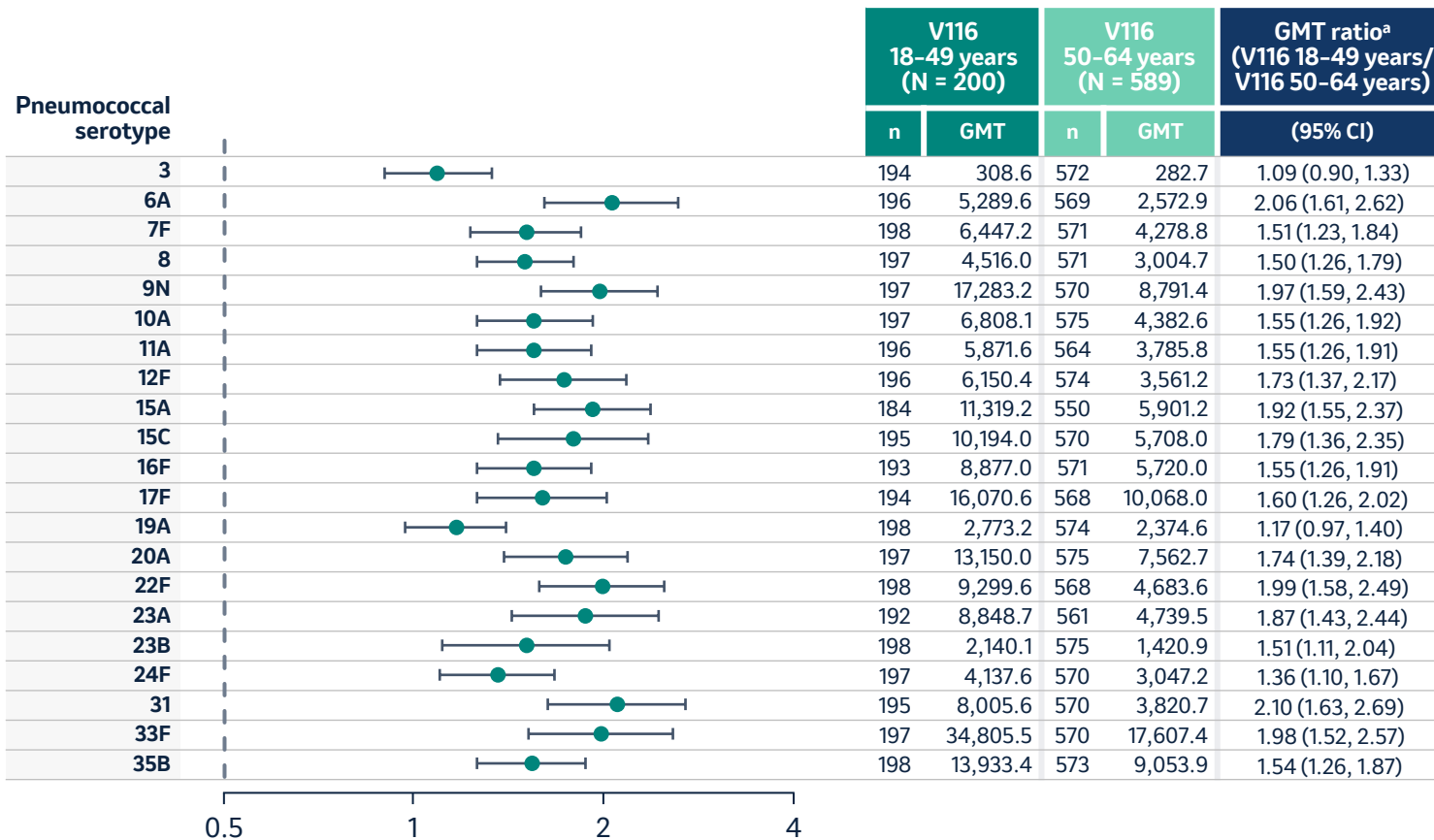


V116-003: Cohort 2: 18-49 years of age

V116 immunobridges to participants 50-64 years of age for all 21 serotypes

Primary immunogenicity objective

- V116 in participants 18 to 49 years of age immunobridges to V116 in participants 50 to 64 years of age for the 21 serotypes in V116.
- The lower bound of the two-sided 95% CIs is >0.5 for all 21 serotypes in V116.

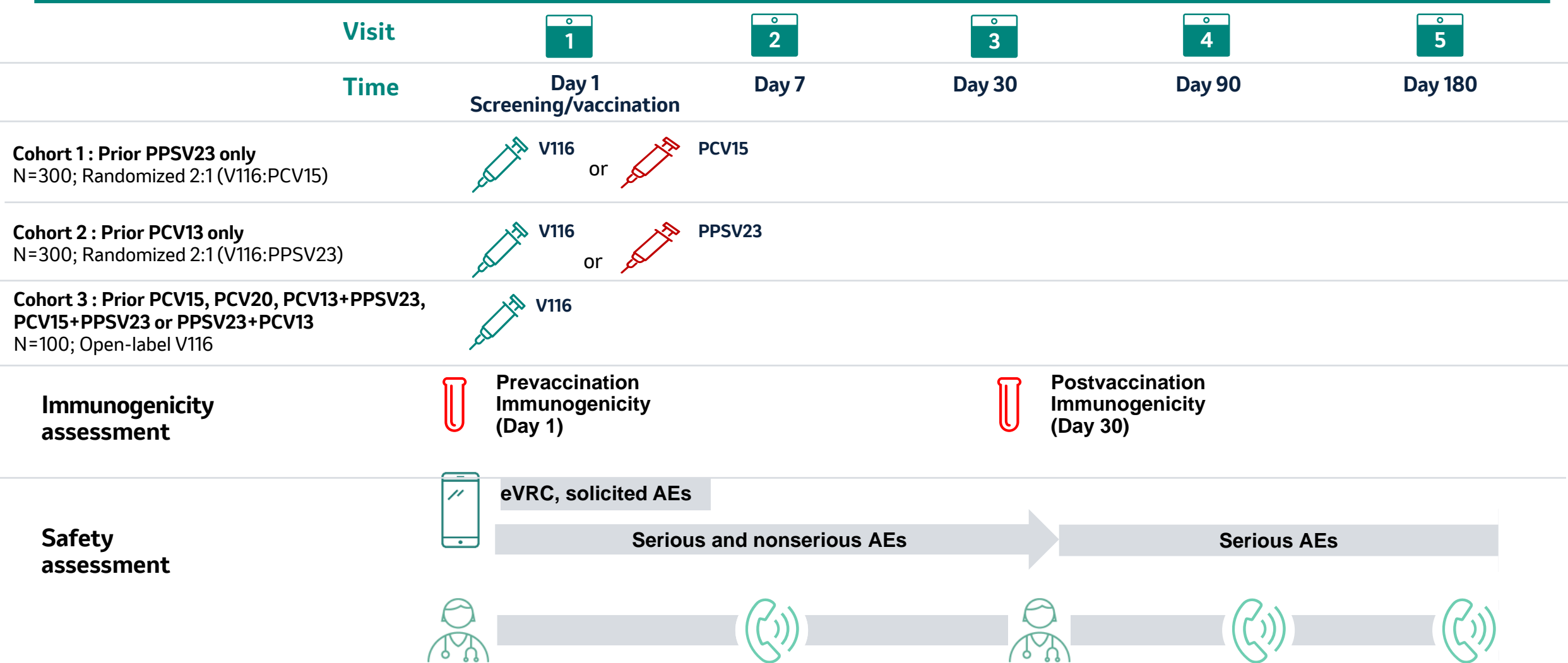


GMT ratio log₁₀ scale (V116 18-49/V116 50-64)

V116-006

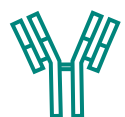
V116-006: A Phase 3 Clinical Study to Evaluate the Safety, Tolerability, and Immunogenicity of V116 in Pneumococcal Vaccine-Experienced Adults 50 Years of Age or Older

V116-006 Study Design



Participants used an electronic Vaccine Report Card (eVRC) to report solicited AEs Days 1-5 postvaccination and other AEs through Day 30 postvaccination

V116-006 Primary study objectives



Primary immunogenicity

In adults ≥ 50 years:

To evaluate the serotype-specific opsonophagocytic activity (OPA) geometric mean titers (GMTs) at 30 days postvaccination for all serotypes included in V116



Primary safety

- To evaluate the safety and tolerability of V116 as assessed by the proportion of participants with adverse events (AEs)
 - **Solicited injection site** events Day 1–5 postvaccination: erythema, swelling, injection-site pain
 - **Solicited systemic events** Days 1–5 postvaccination: headache, myalgia, fatigue
 - **Serious vaccine-related events** Day 1 through the duration of participation in the study

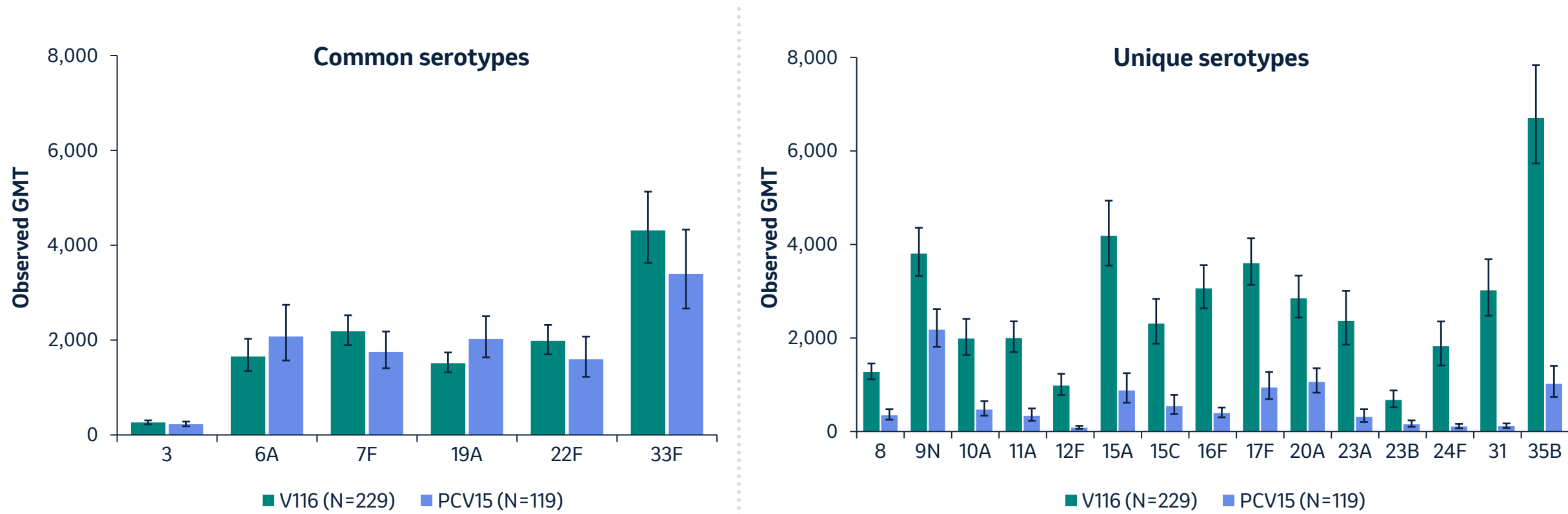
V116-006 Participant Characteristics

Enrollment is balanced in each cohort and reflects the pneumococcal vaccination history

	Cohort 1 (prior PPSV23)		Cohort 2 (prior PCV13)		Cohort 3
	V116 N=229	PCV15 N=119	V116 N=174	PPSV23 N=85	V116 N=105
Sex					
Male	112 (48.9)	59 (49.6)	74 (42.5)	36 (42.4)	50 (47.6)
Female	117 (51.1)	60 (50.4)	100 (57.5)	49 (57.6)	55 (52.4)
Age (yr)					
50 to 64	48 (21.0)	25 (21.0)	80 (46.0)	39 (45.9)	17 (16.2)
≥65	181 (79.0)	94 (79.0)	94 (54.0)	46 (54.1)	88 (83.8)
Mean ± SD	68.7 ± 7.5	69.0 ± 7.1	65.5 ± 7.8	65.4 ± 6.6	71.0 ± 7.6
Median (range)	69.0 (50 to 86)	69.0 (51 to 88)	66.0 (50 to 83)	65.0 (51 to 81)	71.0 (53 to 91)
Race					
Asian	96 (41.9)	47 (39.5)	55 (31.6)	25 (29.4)	13 (12.4)
Black or African American	6 (2.6)	3 (2.5)	3 (1.7)	1 (1.2)	6 (5.7)
Multiple	2 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.0)
White	125 (54.6)	69 (58.0)	116 (66.7)	59 (69.4)	85 (81.0)
Ethnicity					
Hispanic or Latino	21 (9.2)	17 (14.3)	34 (19.5)	16 (18.8)	14 (13.3)
Time since last pneumococcal vaccination					
1 to 4 years	108 (47.2)	54 (45.4)	135 (77.6)	66 (77.6)	78 (74.3)
5 to 9 years	85 (37.1)	45 (37.8)	33 (19.0)	18 (21.2)	27 (25.7)
≥10 years	36 (15.7)	20 (16.8)	6 (3.4)	1 (1.2)	0 (0.0)

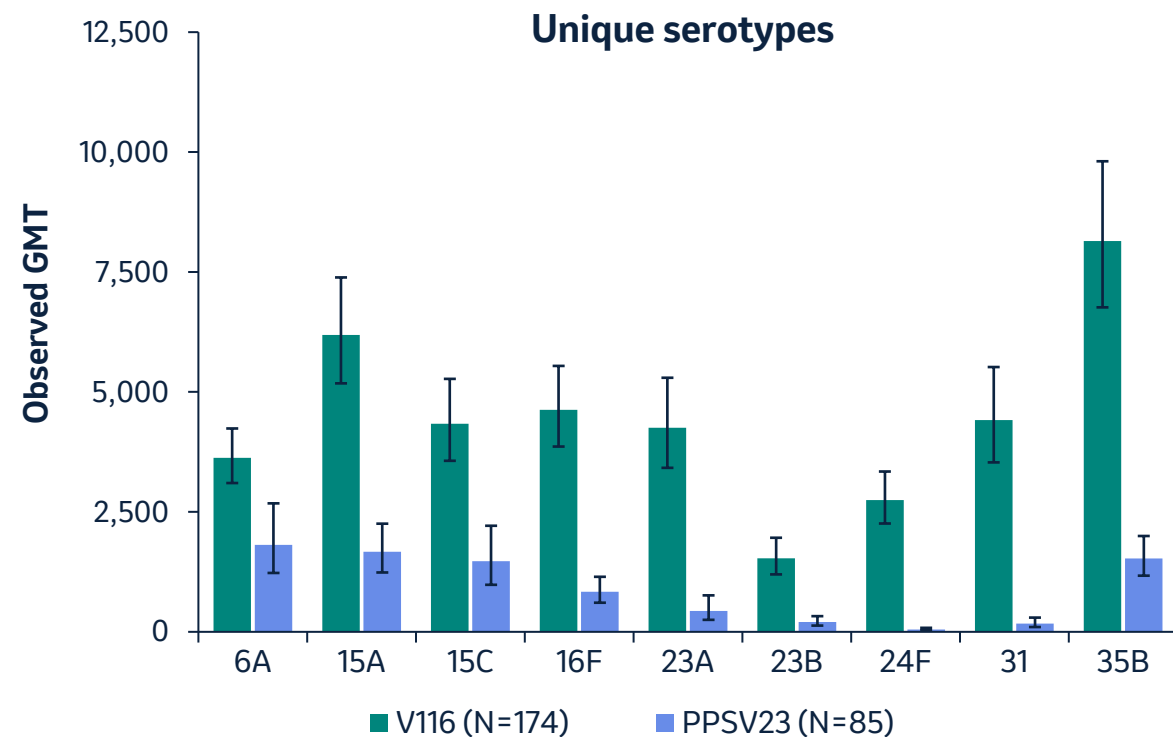
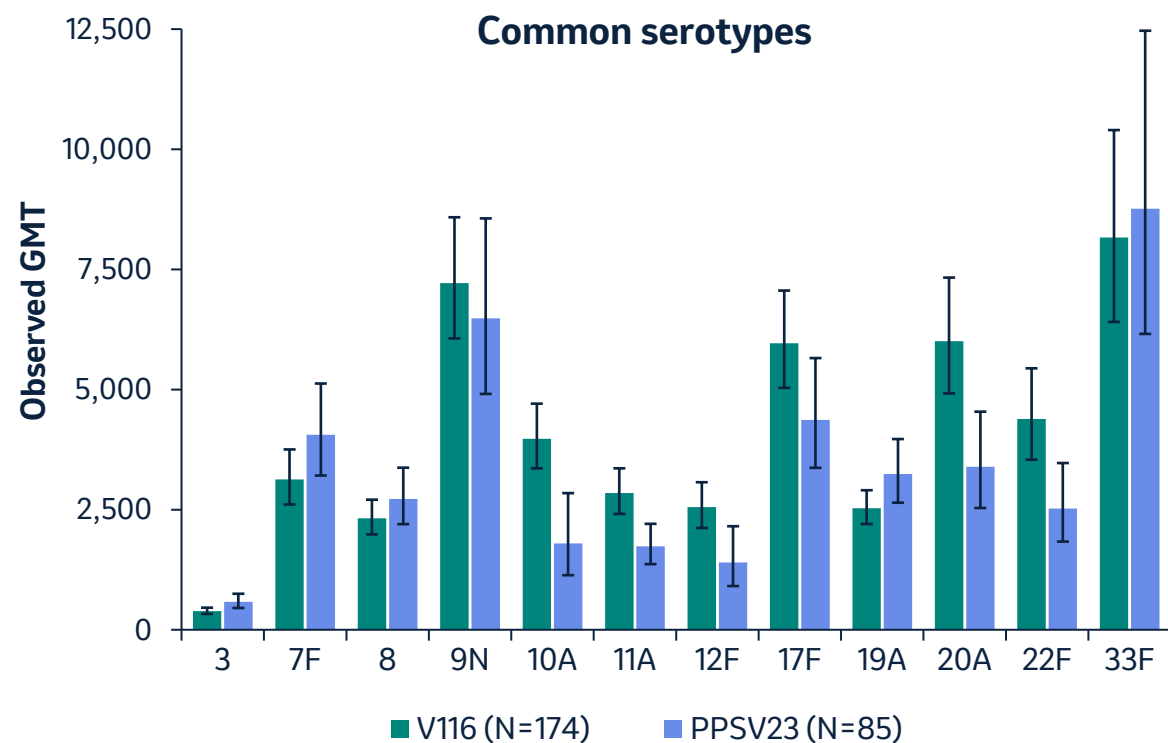
V116-006 Cohort 1: ≥ 50 years of age who previously received PPSV23

V116 elicits comparable immune responses to PCV15; higher immune responses for serotypes unique to V116

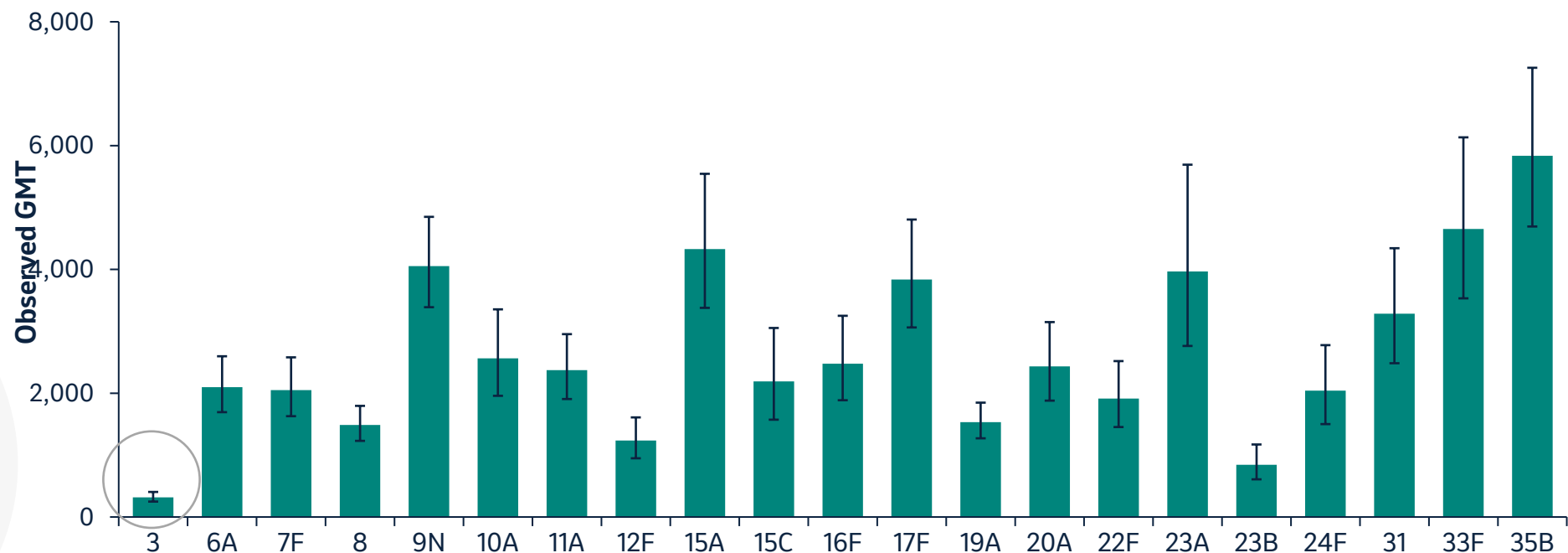
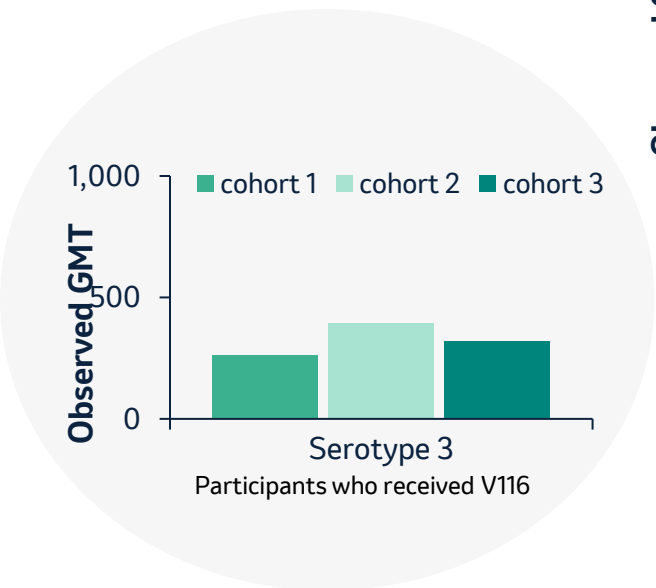


V116-006 Cohort 2: ≥ 50 years of age who previously received PCV13

V116 elicits comparable immune responses to PPSV23; higher immune responses for serotypes unique to V116



V116-006 Cohort 3: ≥50 years of age who previously received other pneumococcal vaccine(s)*
V116 is immunogenic in individuals who previously received a pneumococcal vaccine



*Prior PCV13+PPSV23 [n=45], PCV15+PPSV23 [n=5], PPSV23+PCV13 [n=54], PCV15 [n=1], or PCV20 [n=0]

Integrated Summary of Safety

Integrated Analysis of Safety in the
Phase 3 Clinical Development Program

V116 is well tolerated in adults ≥ 18 years of age with a safety profile comparable to currently licensed pneumococcal vaccines

Adverse Event Summary (V116-003, V116-004, V116-005 ^a , V116-006)	V116 (N=4,020)		Control ^b (N=2,018)	
	n	(%)	n	(%)
With adverse events (Day 1 – 30)	2695	(67.0)	1386	(68.7)
With vaccine-related adverse events (Day 1-30) ^c	2555	(63.3)	1297	(64.3)
Solicited	2516	(62.6)	1279	(63.4)
Unsolicited	313	(7.8)	123	(6.1)
with SAEs (Day 1 - Day 30)	14	(0.3)	7	(0.3)
with vaccine-related SAEs (Day 1 - Day 30)	2	(0.0)	0	(0.0)
with SAEs within 30 minutes postvaccination	1	(0.0)	0	(0.0)
Who died ^d	6	(0.1)	3	(0.1)
with vaccine-related deaths ^c	0	(0.0)	0	(0.0)

^a Only participants from V116-005 vaccinated with V116 in the sequential group are included in the V116 group.

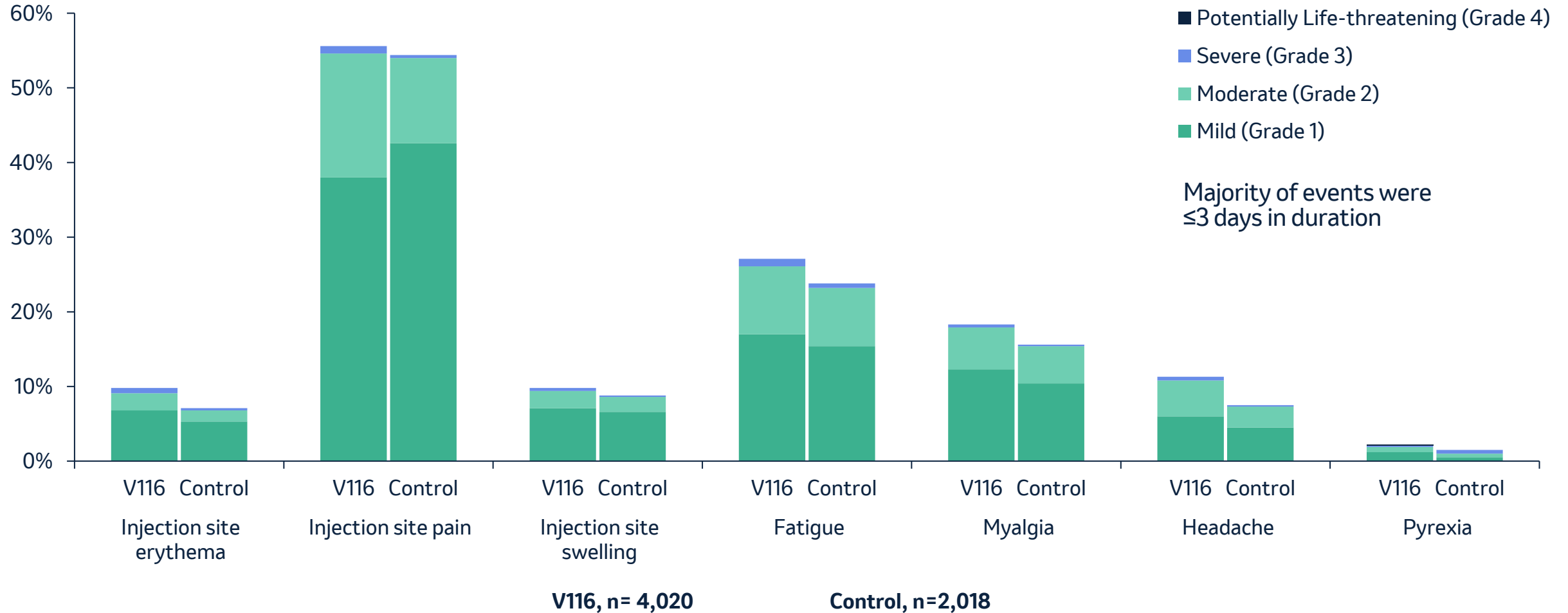
^b Control group includes participants vaccinated with PCV15, PCV20, or PPSV23

^c As determined by the investigator; all injection site adverse events are assessed as vaccine-related

^d 6 deaths in the V116 group in the Integrated Safety Summary; 7 deaths in the V116 group across the Phase 3 studies when the concomitant group from P005 is included.

Frequency and intensity of solicited adverse events were comparable in V116 and control groups

Solicited adverse events by intensity (%)



Solicited events include erythema, injection site pain, injection site swelling, fatigue, headache, and myalgia were solicited from Day 1 through Day 5 postvaccination. Pyrexia was defined as temperature ≥ 100.4 °F (38.0 C) solicited from Day 1 through Day 5 postvaccination.

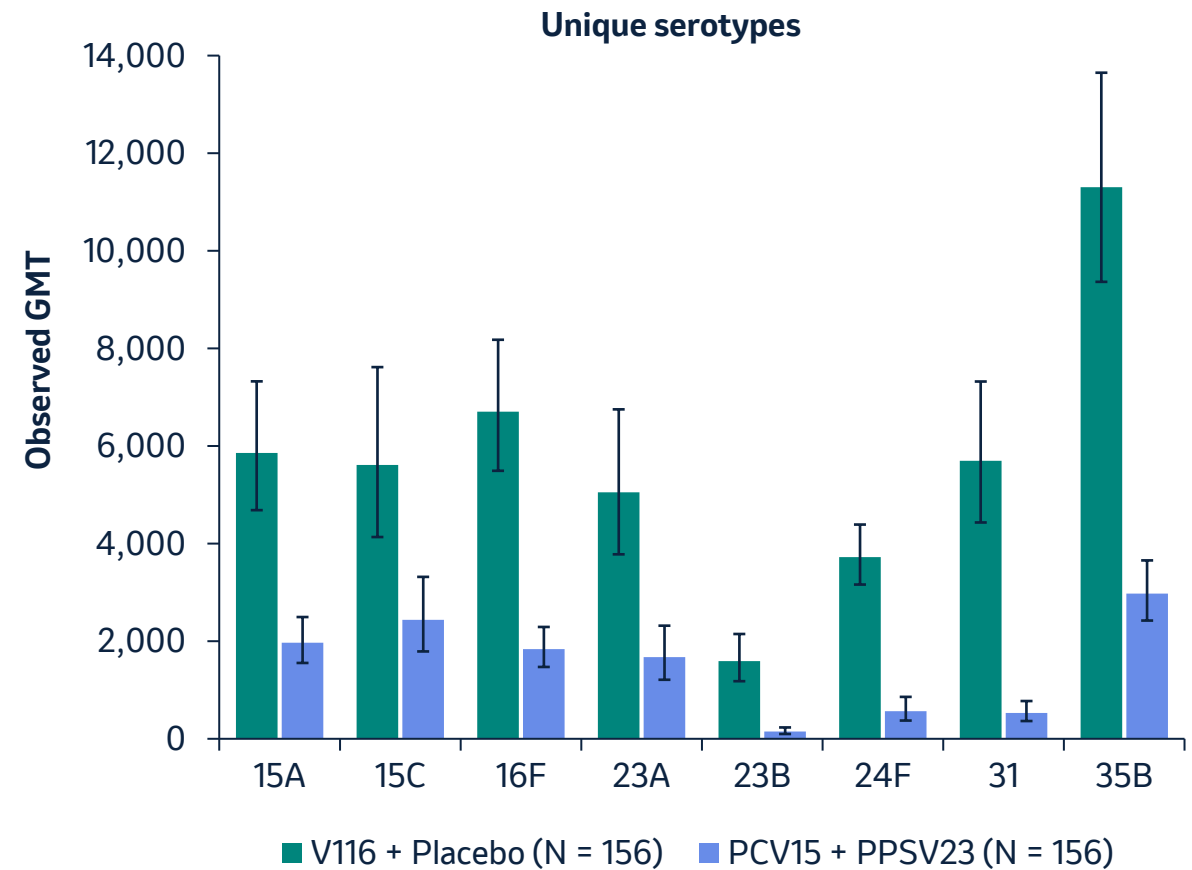
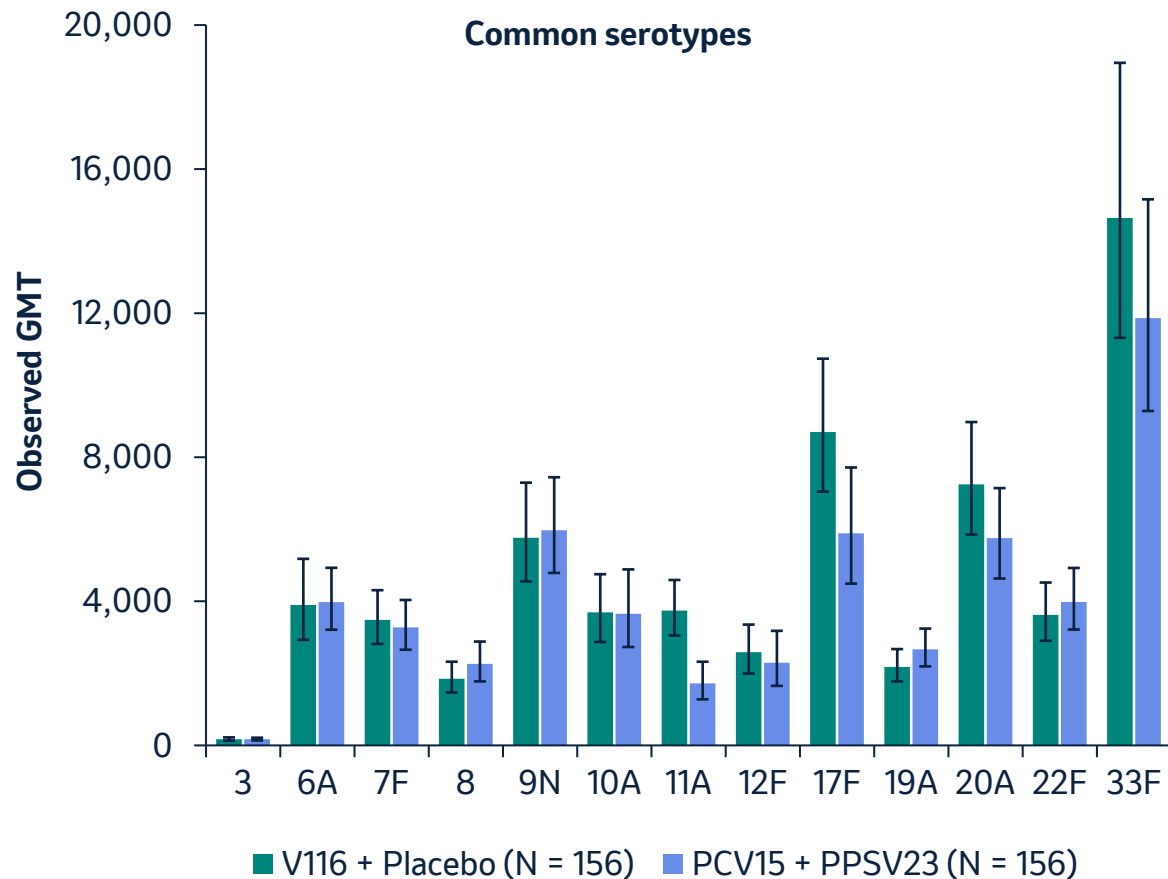
Phase 3 Supportive Studies

V116-007: V116 in Adults Living with HIV

V116-005: V116 with Concomitant Quadrivalent Influenza Vaccine (QIV)

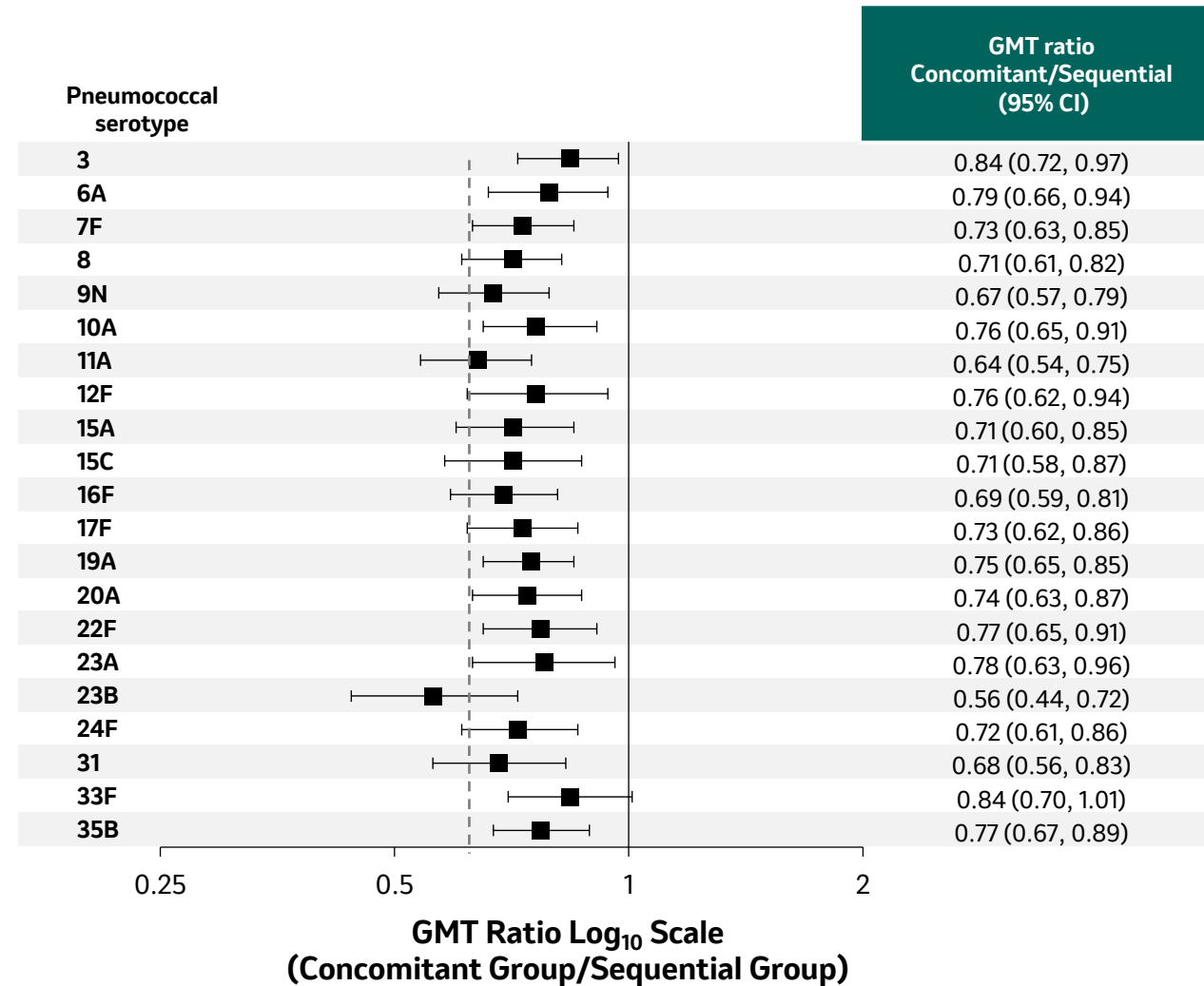
V116-004: V116 Lot Consistency

V116-007: In adults living with HIV, V116 elicits comparable immune responses to PCV15+PPSV23, & higher immune responses for unique serotypes

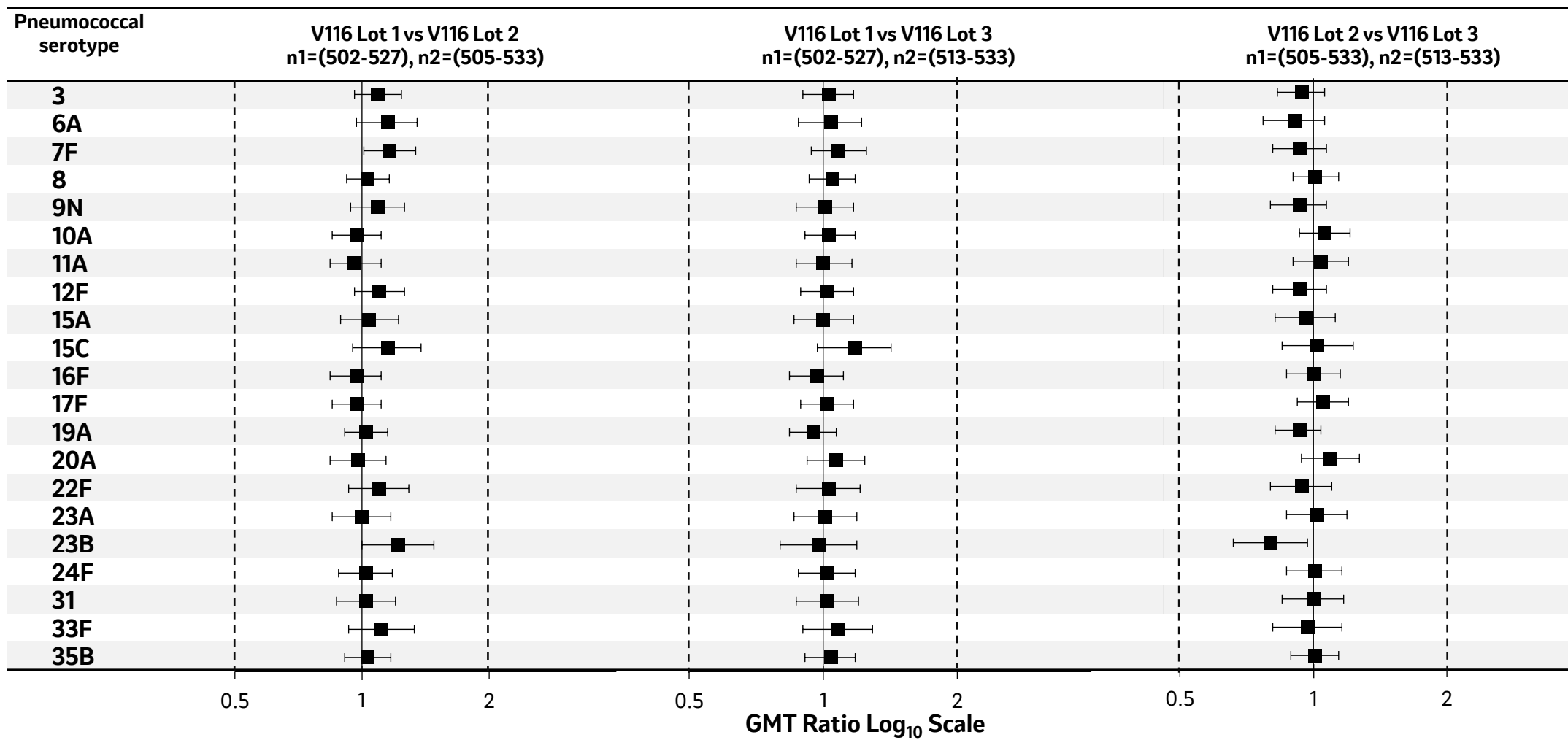


V116-005: V116 elicits robust immune responses when administered concomitantly with influenza vaccine

- V116 administered concomitantly with influenza vaccine is noninferior to V116 administered sequentially with influenza vaccine for 20 of 21 serotypes
- QIV administered concomitantly is noninferior to QIV administered sequentially for 3 of 4 strains



V116-004: V116 Immune responses were equivalent across 3 manufacturing lots



Note: dashed lines indicate the margins for the equivalence test

Phase 3 Summary & Conclusions

V116 Phase 3 Clinical Development Summary



In adults ≥ 18 years of age, who are pneumococcal vaccine-naïve and vaccine experienced, with and without risk conditions:

- V116 elicits **robust immune responses** to all 21 serotypes contained in the vaccine
- V116 is **noninferior to PCV20** for all common serotypes and **superior to PCV20** for 10 of 11 serotypes unique to V116 in pneumococcal vaccine-naïve adults ≥ 50 years of age.
- V116 is immunogenic in pneumococcal **vaccine experienced adults**, regardless of the prior vaccine received
- V116 is immunogenic when administered concomitantly with inactivated **influenza vaccine**.
- V116 is **well-tolerated** with a safety profile generally comparable to currently licensed pneumococcal vaccines.

V116 is the first adult specific PCV with the potential for broad public health impact through the prevention of invasive disease and pneumonia due to *S. pneumoniae*.

Thank you



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