INVENTING FOR LIFE

# Pneumococcal Polysaccharide 15-Valent Conjugate Vaccine (V114, VAXNEUVANCE):

# Pediatric Clinical Development Program

## Advisory Committee on Immunization Practices

February 24, 2022

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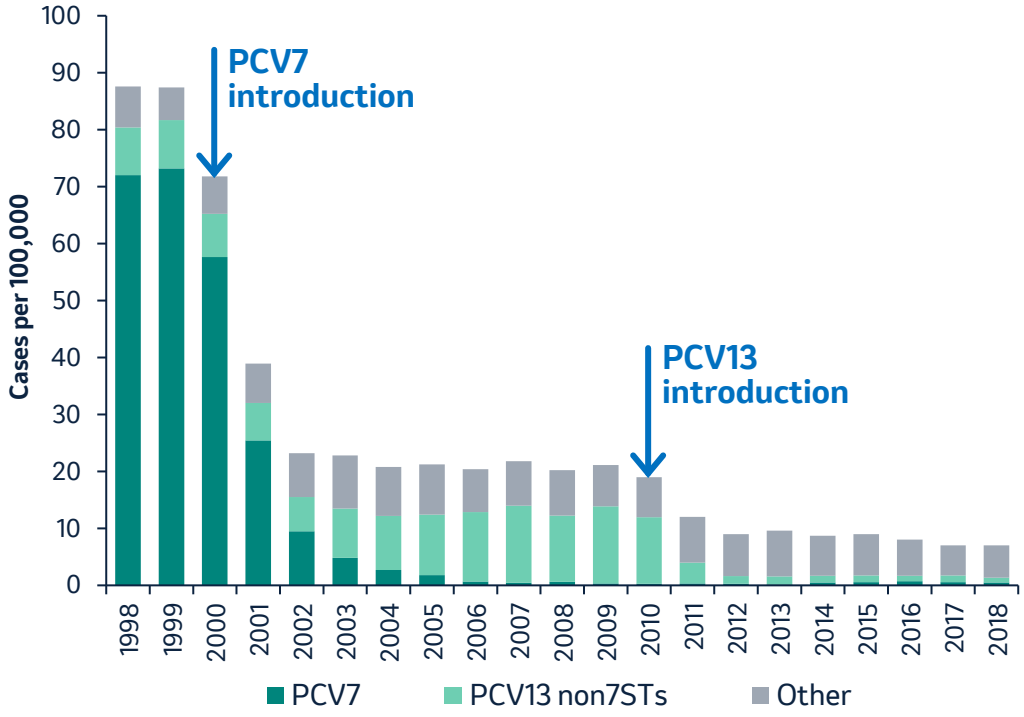
# Presentation Topics

- Rationale for the development of V114
- Overview of the Pediatric Clinical Development Program
- Immunogenicity Results
- Safety Results
- Supportive studies
- Conclusions
- Q&A

# In the post-PCV era, serotypes 3, 22F, and 33F are leading causes of IPD in children <5 years of age in the US

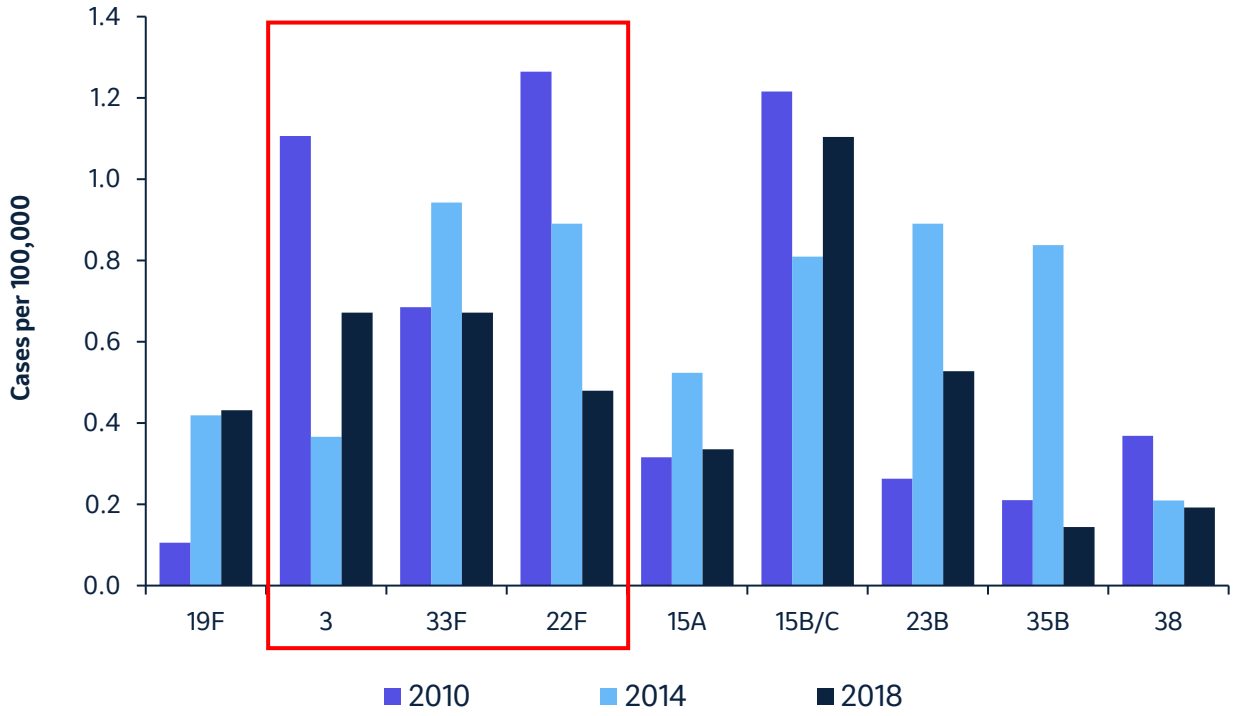
## IPD incidence by vaccine-types, children <5 Years




US CDC ABC Surveillance Network, 1998-2017

## Key serotypes causing IPD in US children <5 years of age

**Top serotypes 2010-2018 (excluding ST19A)**




Epidemiology of IPD following 18 years of PCV use in the US; Pilishvili et al, CDC

# Rationale for development of Merck 15-valent PCV (V114)

- Increase availability of pneumococcal conjugate vaccines (PCVs) worldwide given the value of multiple suppliers in strengthening **global supply**
- Develop single vaccine formulation for adult and pediatric indication to:
  - Maintain robust immune responses to serotypes included in currently available PCVs
  - Extend serotype coverage to key non-vaccine serotypes
  - Improve immunogenicity for serotype 3
  - Demonstrate that safety profile is comparable to licensed PCVs

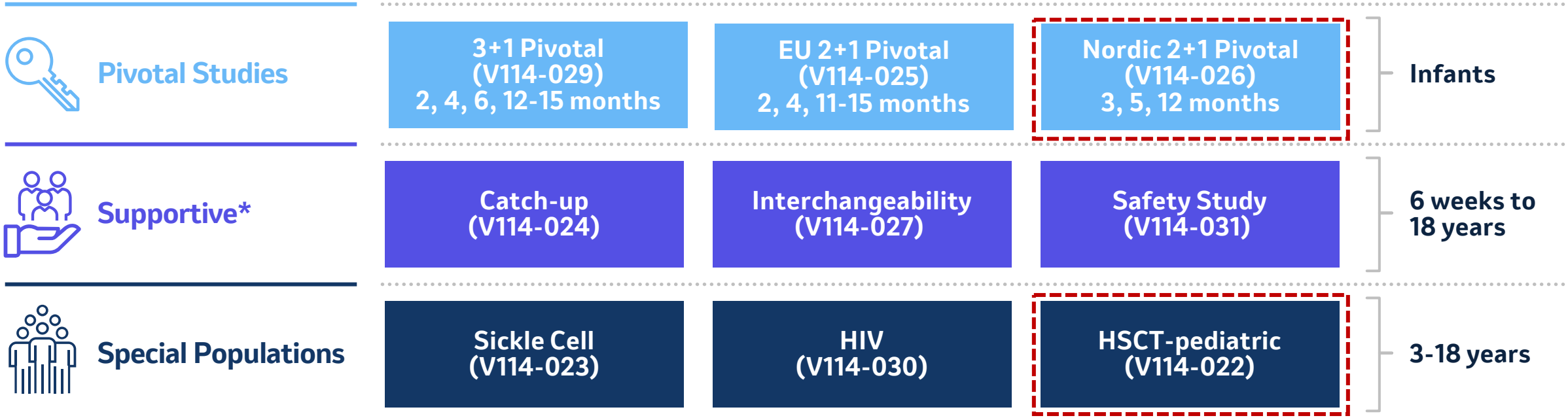
**Clinical Program designed to evaluate V114 in populations with an *unmet medical need* for pneumococcal disease prevention**


**V114 adult US licensure, 16-July-2021**
**Pediatric US submission PDUFA, 1-April-2022**

# Clinical studies of the V114 Phase-3 Pediatric Program

## Common Elements

- Multi-center, randomized, double blind studies
- Total Phase 3 pediatric study population: ~8,500 participants, with ~5,300 receiving V114
- Infant preterm population (V114-027, V114-029, V114-031): ~290 participants, with ~140 receiving V114.




Studies ongoing

HIV = Human Immunodeficiency Virus; HSCT = hematopoietic stem cell transplant

# Immunogenicity & safety endpoints in the V114 Pediatric Program

## Safety endpoints

- Solicited **injection-site** AEs: erythema, swelling, induration, pain (**Days 1–14**)
- Solicited **systemic** AEs (**Days 1–14**):
  - Infants: irritability, drowsiness, appetite lost, and hives or welts
  - Children: myalgia, arthralgia, headache, fatigue, and hives or welts/urticaria
- Maximum body **temperature** measurements (**Days 1–7**)
- Any other injection-site or systemic AEs (**Days 1–14**)
- **Serious** adverse events (up to **6 months** following V114)

**Adverse events (AEs) and postvaccination temperature measurements collected directly from participants via a Vaccination Report Card**

## Immunogenicity endpoints

- Serotype-specific **IgG response rates** ( ≥0.35 µg/mL)
- Serotype-specific **IgG** Geometric Mean Concentrations (**GMC**)
- Serotype-specific opsonophagocytic activity (**OPA**) Geometric Mean Titers (**GMT**)
- Reverse Cumulative Distribution Curves (**RCDC**)
- For **infants**, measured 30 days post-primary series, immediately prior to the toddler dose, and 30 days following the toddler dose
- For **children**, measured at baseline and 30 days following last dose

**Immunogenicity was evaluated via a validated pneumococcal electrochemiluminescence** (bridged to WHO ELISA) **and multiplex OPA assays**

# *V114-029*

## *Pivotal Ph-3 study evaluating 3+1 dosing regimen*

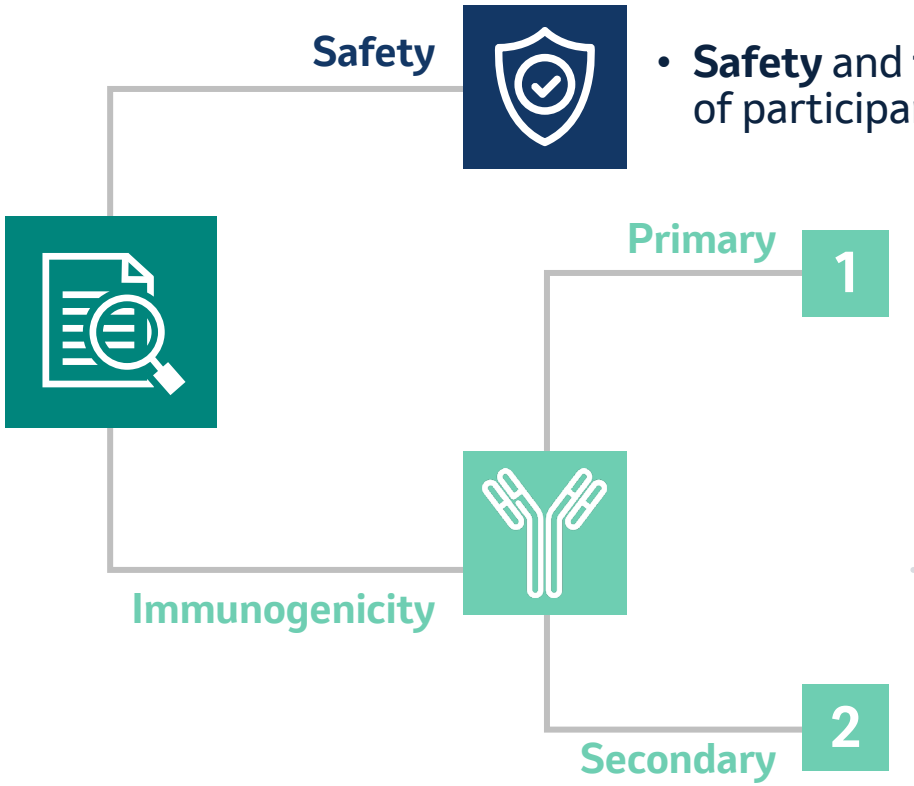
# Study design

| Visit | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|
| Age | ~2 months | ~4 months | ~6 months | 1 month after Dose 3 | ~12–15 months | 1 month after Dose 4 |
| Vaccination | V114 or PCV13<br>Additional pediatric vaccines | V114 or PCV13<br>Additional pediatric vaccines | V114 or PCV13<br>Additional pediatric vaccines | | V114 or PCV13<br>Additional pediatric vaccines | |
| Blood drawn for immunogenicity assessment | | | | ✓ | ✓ | ✓ |
| Safety Assessment | eVRC | | | | | |
| | SAEs (Day 1 through end of study) | | | | | |

**Randomization** 1 : 1 (V114 : PCV13)

**Total N Randomized** N = 1720

# Study objectives



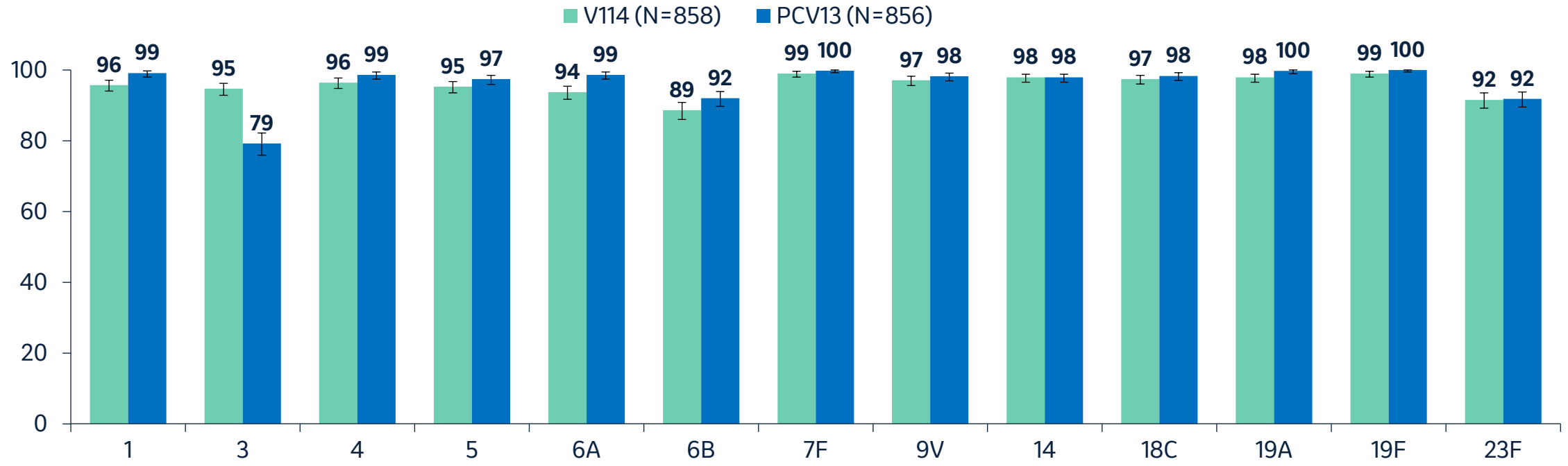

- **Safety** and **tolerability** of V114 with respect to the proportion of participants with adverse events (AEs)

- **Noninferiority:** IgG **response rates** at 30 days following **Dose 3**
- **Noninferiority:** **IgG GMC** at 30 days following **Dose 3 and Dose 4**

- **Descriptive:** **OPA GMT and response rates** at 30 days following **Dose 3** *(20% of study population with sufficient blood volume for both IgG and OPA tests)*
- **Noninferiority:** Antigen-specific response rates to the **co-administered routine childhood vaccines**
- **Superiority:** Responses (IgG GMC and response rates) of unique serotypes (**22F and 33F**) and shared **ST3** at **PD3** and **PD4**

# PD3: V114 is **noninferior** to PCV13 for all 13 **shared** serotypes based on the proportion of **responders** (IgG ≥0.35 µg/mL)

## Observed response (%)



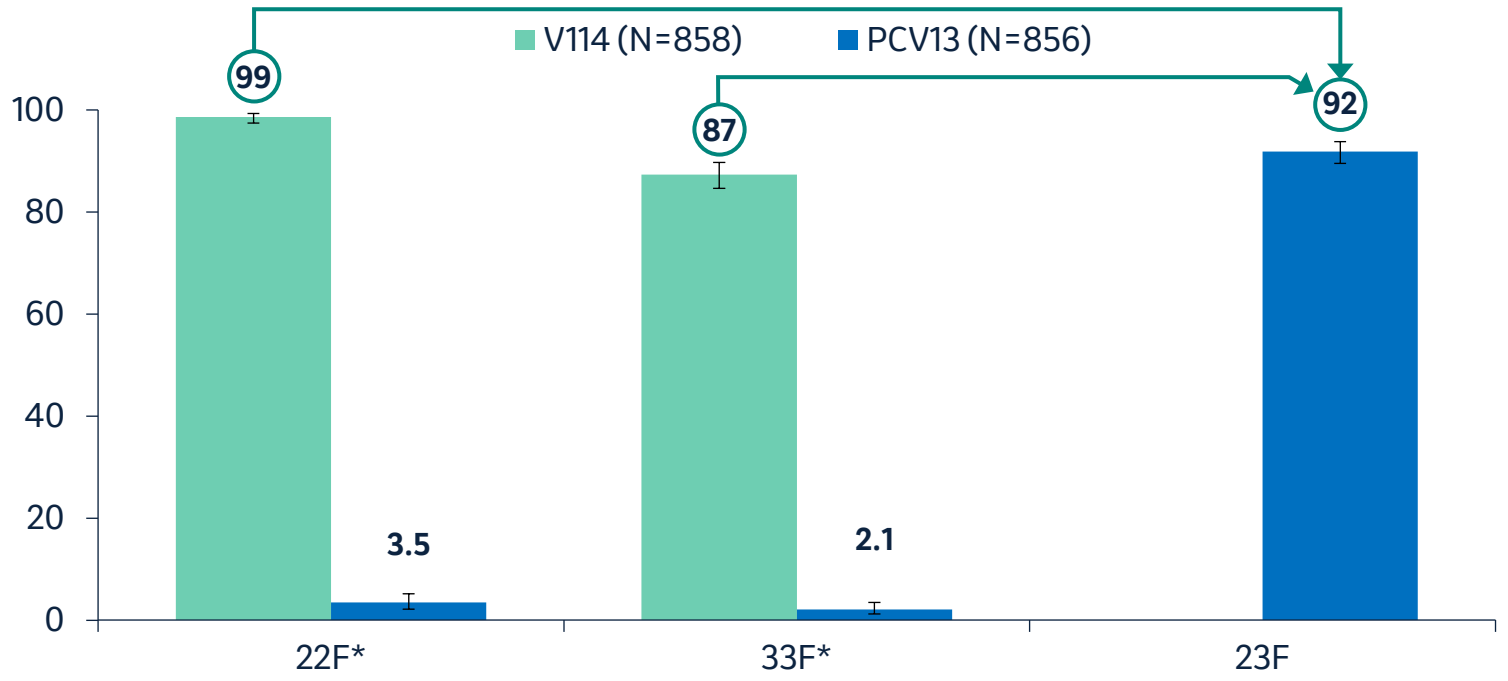

| | 1 | 3 | 4 | 5 | 6A | 6B | 7F | 9V | 14 | 18C | 19A | 19F | 23F |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Percentage point difference (V114-PCV13) | −3.4 (**−5.2**, −1.8) | 15.6 (**12.1**, 19.2) | -2.2 (**-4.0**, -0.6) | -2.1 (**-4.2**, -0.2) | -4.9 (**-7.1**, -3.0) | -3.4 (**-6.6**, -0.3) | -0.8 (**-1.9**, -0.1) | -1.0 (**-2.8**, 0.6) | -0.0 (**-1.6**, 1.6) | -0.9 (**-2.6**, 0.7) | -1.8 (**-3.2**, -0.8) | -1.0 (**-2.1**, -0.4) | -0.3 (**-3.2**, 2.7) |
| P-value (1-sided) | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 |

**Noninferiority requires the lower bound of the 2-sided 95% CI for the difference in response rates (V114 – PCV13) to be >-10 percentage points (1-sided p-value <0.025).**

Error bars indicate 95% CIs; CI=confidence interval, IgG=immunoglobulin G

# PD3: V114 is **noninferior** to PCV13 for the 2 serotypes **unique** to V114 based on the proportion of **responders** (IgG ≥0.35 µg/mL)

Observed response (%)




| | | |
|---|---|---|
| **Percentage point difference (V114-PCV13)†** | 6.7 (**4.6**, 9.2) | -4.5 (**-7.8**, -1.3) |
| **P-value (1-sided)** | <0.001 | <0.001 |

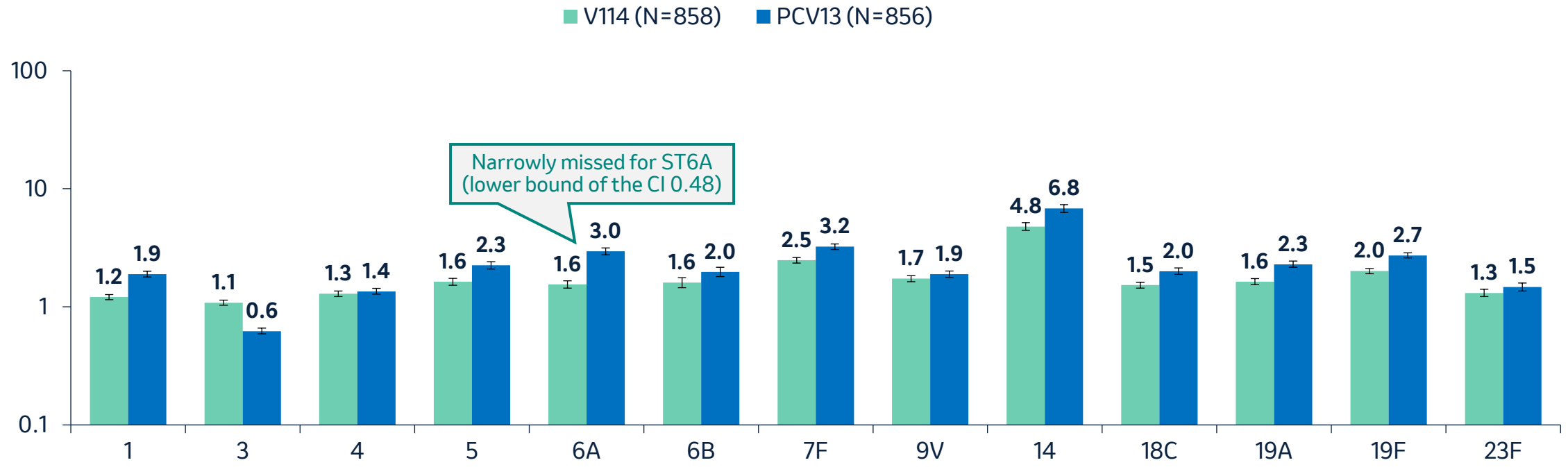
†Difference for unique serotypes compared with lowest observed response rate in PCV13 excluding serotype 3 (serotype 23F)

**Noninferiority requires the lower bound of the 2-sided 95% CI for the difference in response rates (V114 – PCV13) to be >-10 percentage points (1-sided p-value <0.025).**

Error bars indicate 95% CIs; CI=confidence interval; IgG=immunoglobulin G; *Serotypes not included in PCV13

# PD3: V114 is **noninferior** to PCV13 for 12/13 **shared** serotypes based on **IgG GMC** ratio

## IgG GMC (95% CI)



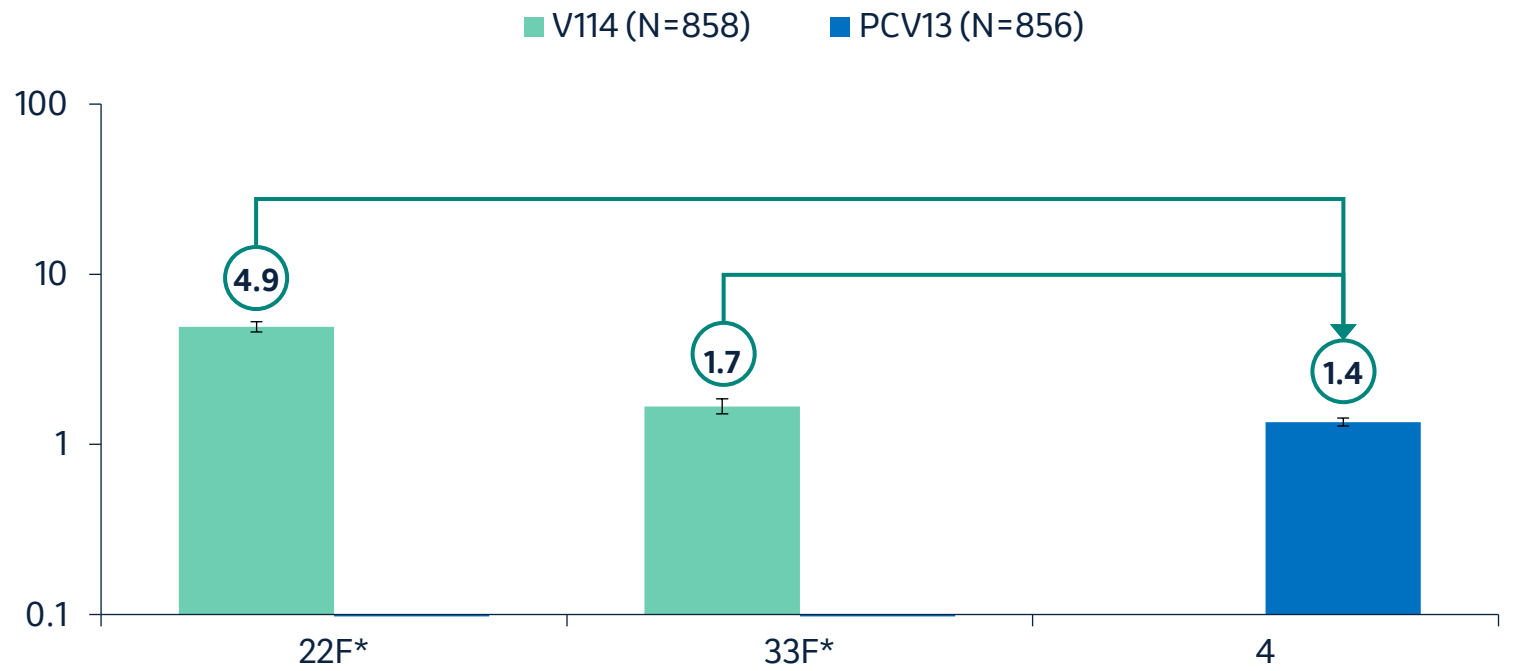

| | 1 | 3 | 4 | 5 | 6A | 6B | 7F | 9V | 14 | 18C | 19A | 19F | 23F |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| GMC ratio (V114/PCV13) | 0.64 (**0.59**, 0.69) | 1.73 (**1.61**, 1.87) | 0.95 (**0.88**, 1.03) | 0.72 (**0.66**, 0.80) | 0.52 (**0.48**, 0.58) | 0.81 (**0.71**, 0.93) | 0.77 (**0.71**, 0.83) | 0.91 (**0.84**, 1.00) | 0.70 (**0.63**, 0.78) | 0.76 (**0.70**, 0.83) | 0.71 (**0.65**, 0.77) | 0.74 (**0.69**, 0.79) | 0.89 (**0.80**, 0.99) |
| P-value (1-sided) | <0.001 | <0.001 | <0.001 | <0.001 | 0.167 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 |

**Noninferiority requires the lower bound of the 2-sided 95% CI for IgG GMC ratio (V114/PCV13) to be >0.5 (1-sided p-value <0.025).**

Error bars indicate 95% CIs; CI=confidence interval; GMC = geometric mean concentration (µg/mL); IgG=immunoglobulin G

# PD3: V114 is **noninferior** to PCV13 for the 2 serotypes **unique** to V114 based on **IgG GMC** ratio

## IgG GMC (95% CI)




| | 22F* | 33F* |
|---|---|---|
| GMC ratio (V114/PCV13)† | 3.64 (**3.33**, 3.98) | 1.24 (**1.10**, 1.39) |
| P-value (1-sided) | <0.001 | <0.001 |

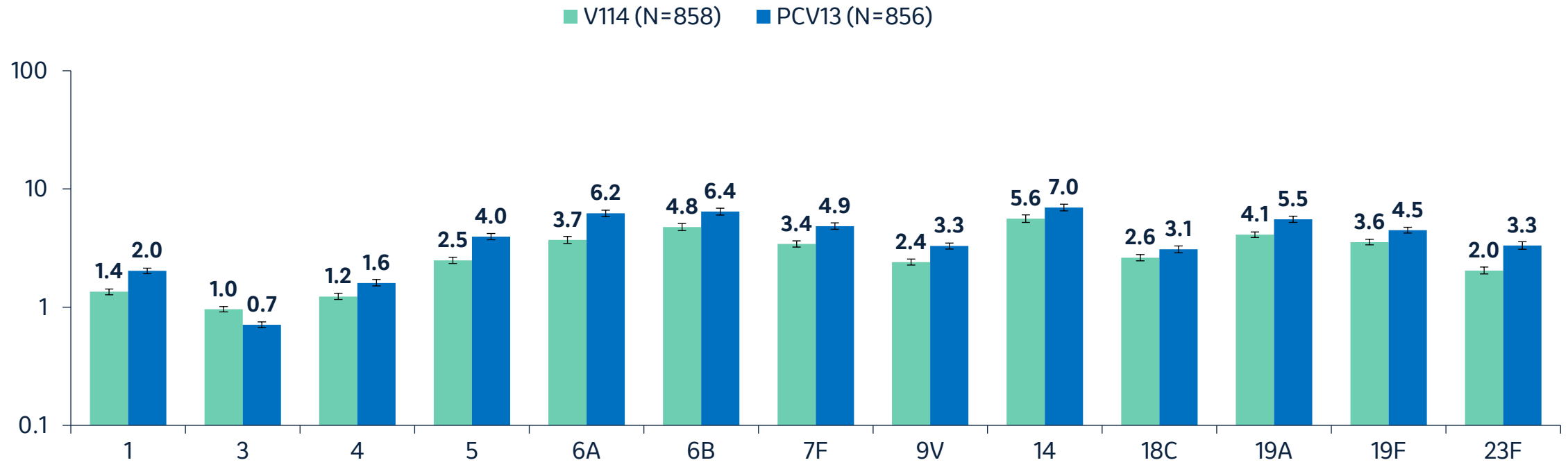
†Ratio compared with lowest observed IgG GMC in PCV13 excluding serotype 3 (serotype 4)

**Noninferiority requires the lower bound of the 2-sided 95% CI for IgG GMC ratio (V114/PCV13) to be >0.5 (1-sided p-value <0.025).**

Error bars indicate 95% CIs; CI=confidence interval; GMC = geometric mean concentration (µg/mL); IgG=immunoglobulin G; *Serotypes not included in PCV13

# PD4: V114 is **noninferior** to PCV13 for all 13 **shared** serotypes based on **IgG GMC** ratio

## IgG GMC (95% CI)



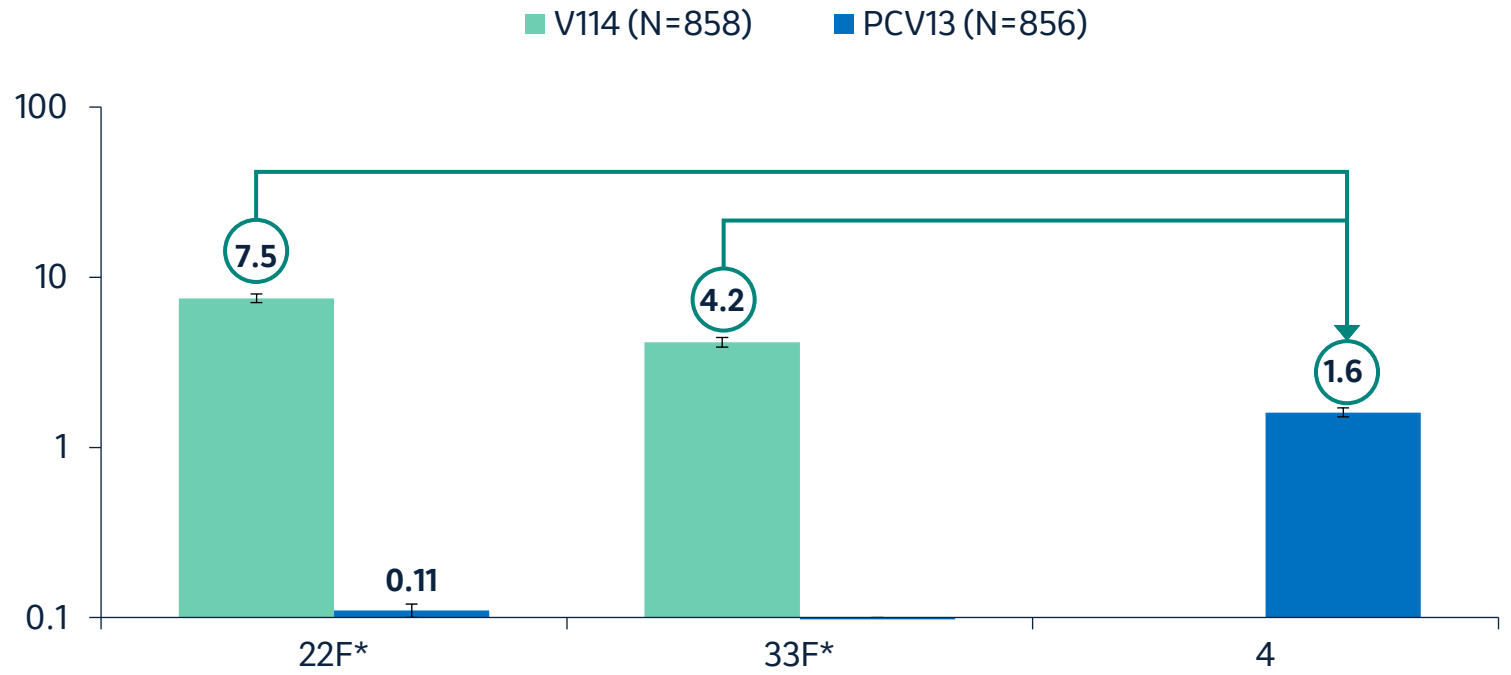

| | 1 | 3 | 4 | 5 | 6A | 6B | 7F | 9V | 14 | 18C | 19A | 19F | 23F |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| GMC ratio (V114/PCV13) | 0.66 (**0.62**, 0.72) | 1.35 (**1.25**, 1.46) | 0.77 (**0.71**, 0.84) | 0.63 (**0.58**, 0.69) | 0.60 (**0.54**, 0.65) | 0.74 (**0.67**, 0.81) | 0.70 (**0.65**, 0.77) | 0.73 (**0.67**, 0.80) | 0.81 (**0.73**, 0.89) | 0.85 (**0.78**, 0.93) | 0.74 (**0.68**, 0.80) | 0.79 (**0.74**, 0.86) | 0.61 (**0.56**, 0.68) |
| P-value (1-sided) | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 | <0.001 |

**Noninferiority requires the lower bound of the 2-sided 95% CI for IgG GMC ratio (V114/PCV13) to be >0.5 (1-sided p-value <0.025).**

Error bars indicate 95% CIs; CI=confidence interval; GMC = geometric mean concentration (µg/mL); IgG=immunoglobulin G

# PD4: V114 is noninferior to PCV13 for the 2 serotypes unique to V114 based on IgG GMC ratio

## IgG GMC (95% CI)




| | 22F* | 33F* |
|---|---|---|
| GMC ratio (V114/PCV13)† | 4.69 (**4.30**, 5.11) | 2.59 (**2.36**, 2.83) |
| P-value (1-sided) | <0.001 | <0.001 |

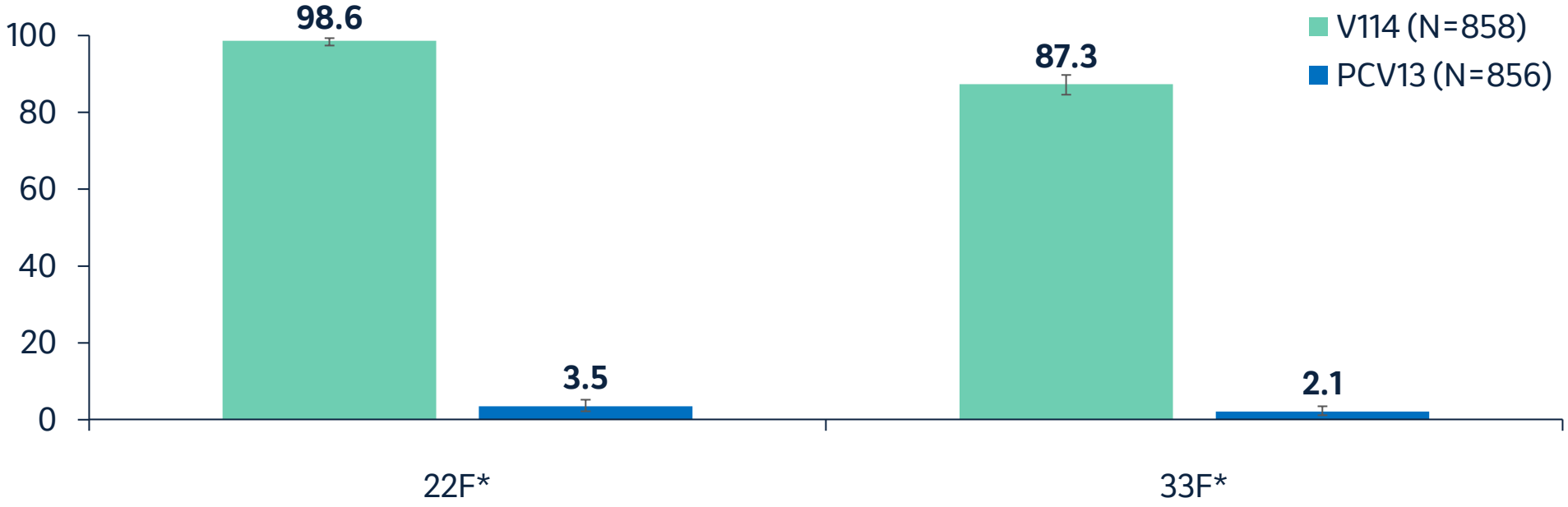
†Ratio compared with lowest observed IgG GMC in PCV13 excluding serotype 3 (serotype 4)

**Noninferiority requires the lower bound of the 2-sided 95% CI for IgG GMC ratio (V114/PCV13) to be >0.5 (1-sided p-value <0.025).**

Error bars indicate 95% CIs; CI=confidence interval; GMC = geometric mean concentration (µg/mL); IgG=immunoglobulin G; *Serotypes not included in PCV13

# PD3: V114 is **superior** to PCV13 for the 2 serotypes **unique** to V114 based on the proportion of **responders** (IgG ≥0.35 µg/mL)

Observed response (%)




| | 22F* | 33F* |
|---|---|---|
| **Percentage point difference (V114-PCV13)†** | 95.1 (**93.1**, 96.5) | 85.2 (**82.3**, 87.7) |
| **P-value (1-sided)** | <0.001 | <0.001 |

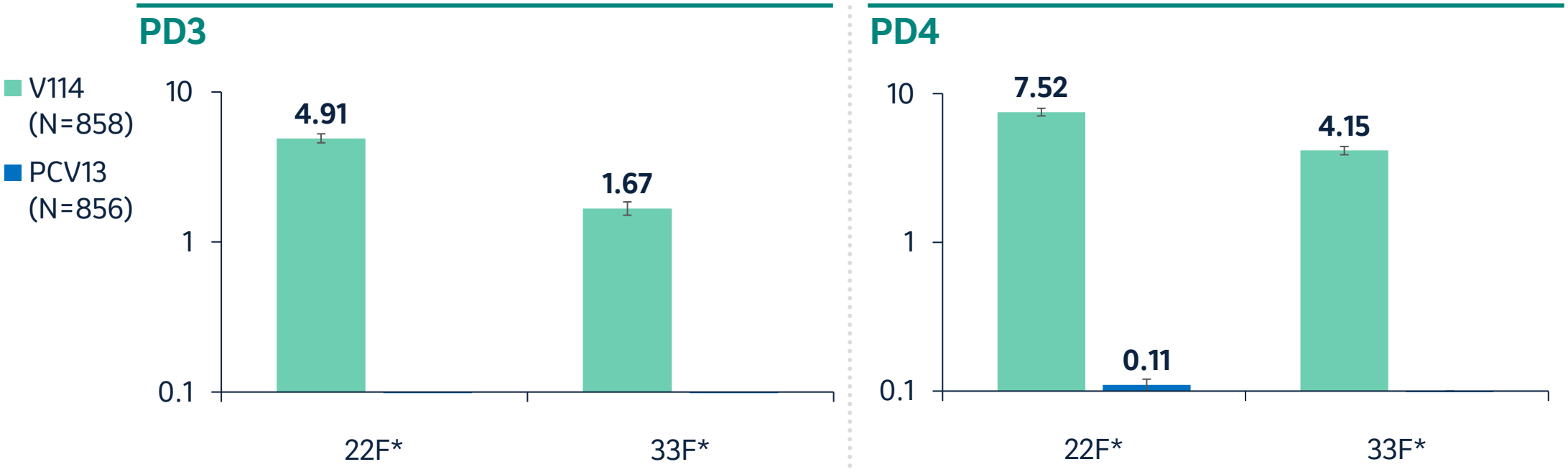
†Estimate (95% CI)

**A conclusion of superiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the difference in response rates (V114 - PCV13) being >10 percentage points for each serotype (1-sided p-value <0.025).**

Error bars indicate 95% CIs; CI=confidence interval; IgG=immunoglobulin G; *Serotypes not included in PCV13

# PD3&4: V114 is **superior** to PCV13 for the 2 serotypes **unique** to V114 as assessed by **IgG GMC** ratio

IgG GMC (95% CI)



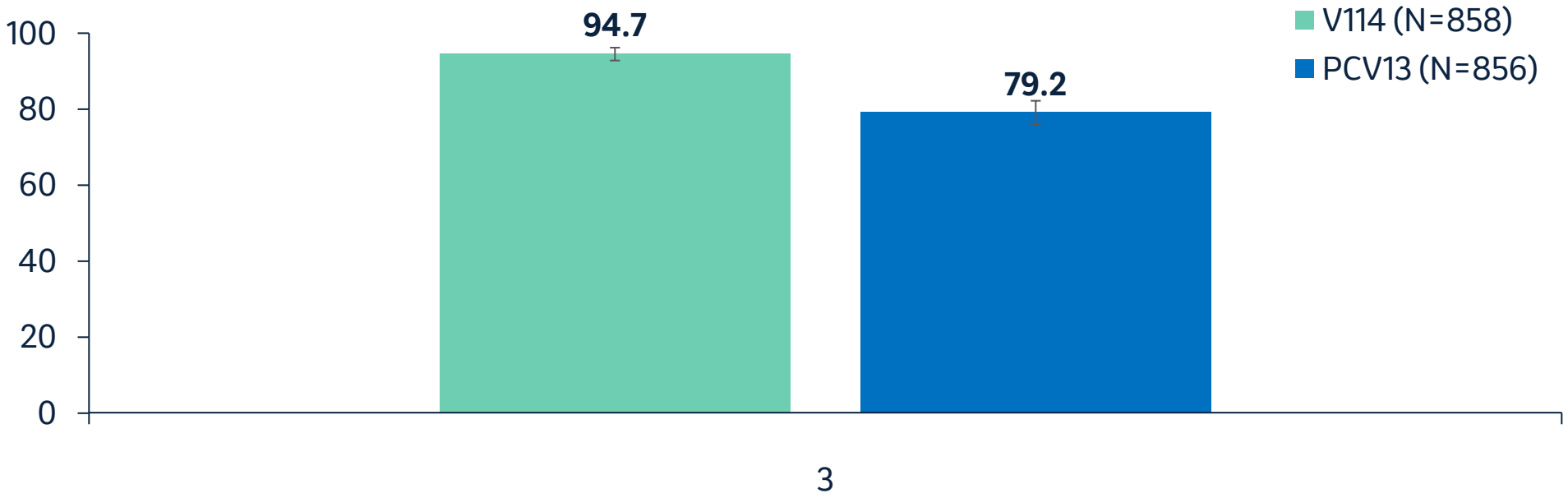

| | PD3 | | PD4 | | |
|---|---|---|---|---|---|
| **GMC ratio (V114/PCV13)†** | 92.03 (**83.47**, 101.47) | 29.50 (**26.16**, 33.26) | 68.80 (**63.10**, 75.02) | 44.91 (**41.04**, 49.14) | †Estimate (95% CI) |
| **P-value (1-sided)** | <0.001 | <0.001 | <0.001 | <0.001 | |

**A conclusion of superiority of V114 to PCV13 is based on the lower bound of the 2-sided 95% CI for the GMC ratio (V114/PCV13) being >2.0 (1-sided p-value <0.025).**

Error bars indicate 95% CIs; CI=confidence interval; GMC=geometric mean concentration (µg/mL); IgG=immunoglobulin G; *Serotypes not included in PCV13

# PD3: V114 is **superior** to PCV13 for the shared **ST3** as assessed by the proportion of **responders** (IgG ≥0.35 µg/mL)

Observed response (%)




| | 3 |
|---|---|
| **Percentage point difference (V114-PCV13)†** | 15.6 (**12.1**, 19.2) |
| **P-value (1-sided)** | <0.001 |

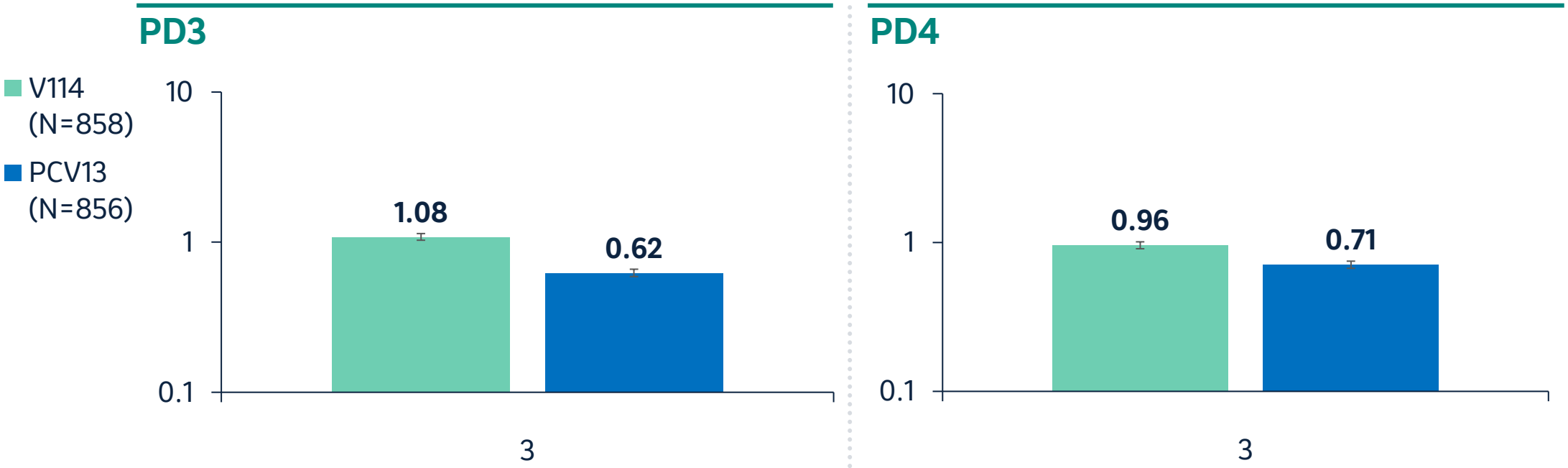
†Estimate (95% CI)

**A conclusion of superiority of V114 to PCV13is based on the lower bound of the 2-sided 95% CI for the difference in response rates (V114 - PCV13) being >0 percentage points (1-sided p-value <0.025).**

Error bars indicate 95% CIs; CI=confidence interval; IgG=immunoglobulin G.

# PD3&4: V114 is **superior** to PCV13 for the shared **ST3** as assessed by **IgG GMC** ratio

## IgG GMC (95% CI)




| | PD3 | PD4 |
|---|---|---|
| GMC ratio (V114/PCV13)† | 1.73 (**1.61**, 1.87) | 1.35 (**1.25**, 1.46) |
| P-value (1-sided) | <0.001 | <0.001 |

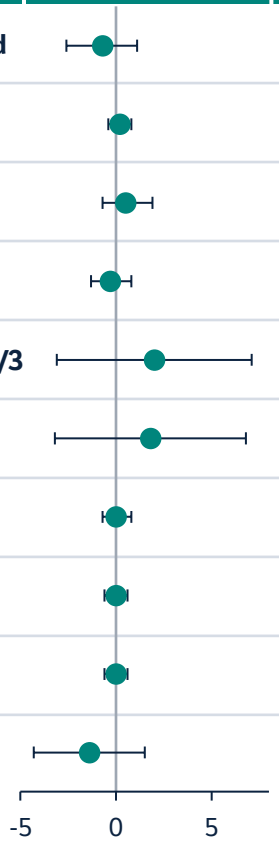
†Estimate (95% CI)

**A conclusion of superiority of V114 to PCV13is based on the lower bound of the 2-sided 95% CI for the IgG GMC ratio (V114/PCV13) being >1.2 (1-sided p-value <0.025).**

Error bars indicate 95% CIs; CI=confidence interval; GMC=geometric mean concentration (µg/mL); IgG=immunoglobulin G.

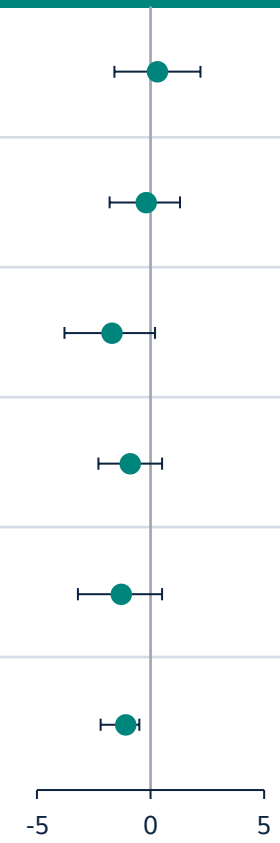
# Noninferiority met for V114 concomitant use with **Pentacel, VAQTA, MMRII, HIBERIX, VARIVAX**

| Antigen | Endpoint | V114 n | V114 % | PCV13 n | PCV13 % | Diff (95% CI) |
|---|---|---|---|---|---|---|
| Diphtheria toxoid | % ≥ 0.1 I U/mL | 703 | 96.9 | 666 | 97.6 | -0.7 (-2.6, 1.1) |
| Tetanus toxoid | % ≥ 0.1 I U/mL | 703 | 100.0 | 666 | 99.8 | 0.2 (-0.4, 0.8) |
| Pertussis – PT | % ≥ 5 EU/mL | 703 | 99.0 | 666 | 98.5 | 0.5 (-0.7, 1.9) |
| Pertussis – FHA | % ≥ 5 EU/mL | 703 | 99.1 | 666 | 99.4 | -0.3 (-1.3, 0.8) |
| Pertussis – FIM 2/3 | % ≥ 20 EU/mL | 703 | 63.7 | 666 | 61.7 | 2.0 (-3.1, 7.1) |
| Pertussis – PRN | % ≥ 5 EU/mL | 703 | 63.7 | 666 | 65.5 | 1.8 (-3.2, 6.8) |
| Poliovirus 1 | % with Nab ≥ 1.8 dilution | 662 | 99.8 | 619 | 99.8 | 0.0 (-0.7, 0.8) |
| Poliovirus 2 | % with Nab ≥ 1.8 dilution | 648 | 100.0 | 614 | 100.0 | 0.0 (-0.6, 0.6) |
| Poliovirus 3 | % with Nab ≥ 1.8 dilution | 650 | 100.0 | 607 | 100.0 | 0.0 (-0.6, 0.6) |
| Hib-PRP | % ≥ 0.15 µg/mL | 648 | 92.1 | 615 | 93.5 | -1.4 (-4.3, 1.5) |




**Percentage Point Difference (V114-PCV13)**

| Antigen | Endpoint | V114 n | V114 % | PCV13 n | PCV13 % | Diff (95% CI) |
|---|---|---|---|---|---|---|
| Hepatitis A | % ≥ 10 mIU/mL | 649 | 97.4 | 626 | 97.1 | 0.3 (-1.6, 2.2) |
| Measles | % ≥255 mIU/mL | 670 | 98.1 | 648 | 98.3 | -0.2 (-1.8, 1.3) |
| Mumps | % ≥ 10 mumps Ab units/mL | 670 | 95.8 | 648 | 97.5 | -1.7, (-3.8, 0.2) |
| Rubella | % ≥ 10 I U/mL | 670 | 98.1 | 648 | 98.9 | -0.9 (-2.3, 0.5) |
| VZV | % ≥ 5 gpELISA units/mL | 715 | 96.4 | 685 | 97.7 | -1.3 (-3.2, 0.5) |
| Hib-PRP | % ≥ 0.15 µg/mL | 650 | 98.9 | 626 | 100.0 | -1.1 (-2.2, -0.5) |



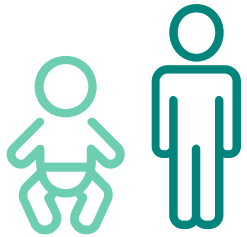

**Percentage Point Difference (V114-PCV13)**

# Outcomes of primary & secondary hypotheses

| | Hypothesis # | Endpoint | Outcome |
|---|---|---|---|
| **Primary Objectives** | 1 | Response rates **PD3** (13 shared serotypes) | ✓ |
| | 2 | Response rates **PD3** (2 unique serotypes) | ✓ |
| | 3 | IgG GMC **PD3** (13 shared serotypes) | **12/13 serotypes** |
| | 4 | IgG GMC **PD3** (2 unique serotypes) | ✓ |
| | 5 | IgG GMC **PD4** (13 shared serotypes) | ✓ |
| | 6 | IgG GMC **PD4** (2 unique serotypes) | ✓ |
| **Secondary Objectives: Concomitant use with pediatric vaccines** | 7 | Pentacel **PD3** (DTaP, Hib, IPV) | ✓ |
| | 8 | VAQTA **PD4** (hepatitis A) | ✓ |
| | 9 | MMRII **PD4** (measles, mumps, rubella) | ✓ |
| | 10 | VARIVAX **PD4** (varicella) | ✓ |
| | 11 | HIBERIX **PD4** (Hib) | ✓ |
| **Secondary Objectives: Superiority hypotheses** | 12 | Response rates ST22F and ST33F **PD3** | ✓ |
| | 13 | IgG GMC ST22F and ST33F **PD3** | ✓ |
| | 14 | IgG GMC ST22F and ST33F **PD4** | ✓ |
| | 15 | Response rate ST3 **PD3** | ✓ |
| | 16 | IgG GMC ST3 **PD3** | ✓ |
| | 17 | IgG GMC ST3 **PD4** | ✓ |

# Safety Database

# V114 Pediatric safety database



## Populations analyzed (7 clinical trials)

## ~7,200 participants (6 weeks to 17 years of age), of whom ~4,800 received V114

- **Healthy Infants** (~6,100 participants 6 to 12 weeks of age, of whom ~4,300 received V114)
  - ISS* population (pooled data from V114-027, V114-029, and V114-031)
    - Included a subgroup analysis in ~290 **preterm infants** (born <37 weeks gestation), of whom ~140 received V114
  - Proof of concept Phase 2 study (V114-008)
- Children (7 months–17 years of age) who are **delayed in receiving PCV** (V114-024)
- Children (5–17 years of age) with **sickle cell disease** (V114-023)
- Children (6–17 years of age) living with **HIV** (V114-030)

*Safety data following administration of PCV were pooled across 3 Phase-3 studies based on similarities in study population and study design. For V114-027, only participants who were randomized to the complete dosing schedule of Prevnar 13™ (Group 1) or V114 (Group 5) are included in the ISS.

# Baseline characteristics are generally comparable between groups

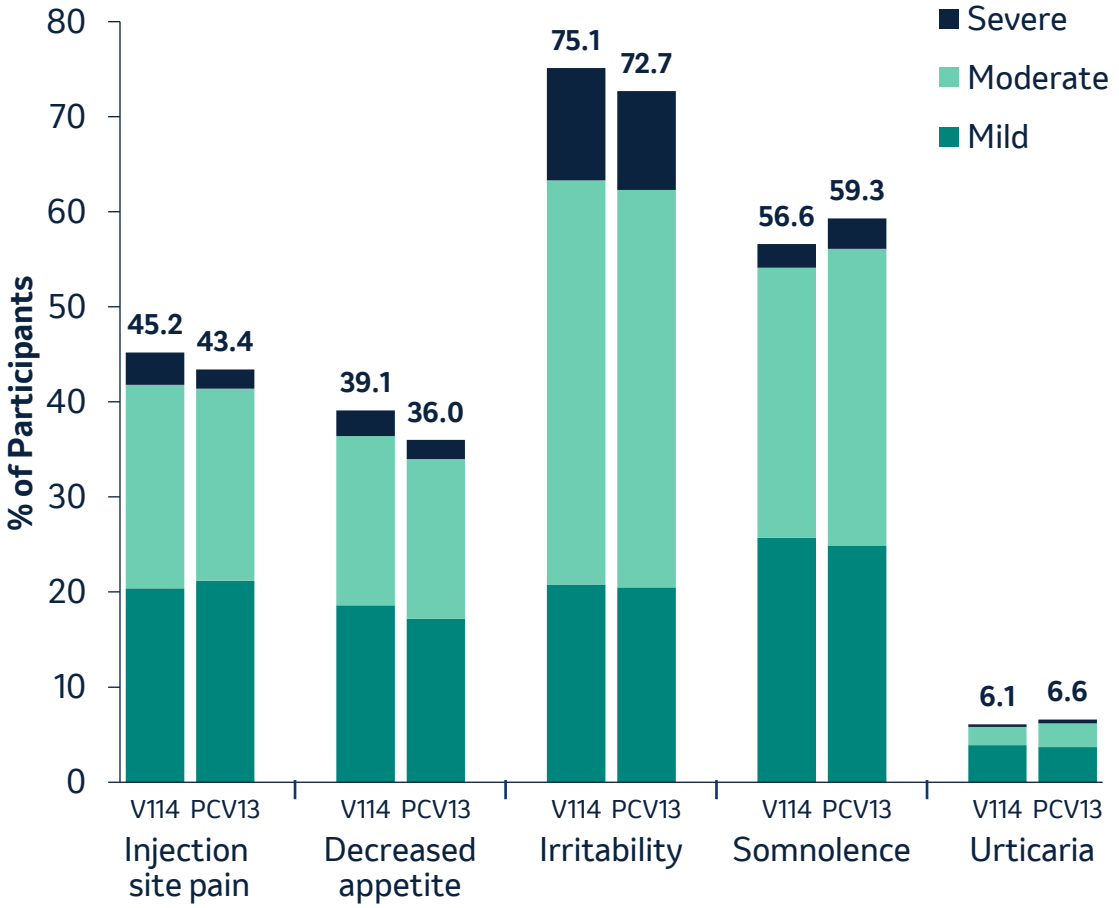
| | V114 | | PCV13 | | Total | |
|---|---|---|---|---|---|---|
| | N=3,004 | n (%) | N=1,471 | n (%) | N=4,475 | n (%) |
| **Gender** | | | | | | |
| Male | 1,575 | (52.4) | 742 | (50.4) | 2,317 | (51.8) |
| Female | 1,429 | (47.6) | 729 | (49.6) | 2,158 | (48.2) |
| **Age (weeks)** | | | | | | |
| Mean | 8.6 | | 8.5 | | 8.6 | |
| SD | 1.4 | | 1.3 | | 1.4 | |
| Median | 9.0 | | 9.0 | | 9.0 | |
| Range | 6 to 12 | | 6 to 12 | | 6 to 12 | |

| | V114 | | PCV13 | | Total | |
|---|---|---|---|---|---|---|
| | N=3,004 | n (%) | N=1,471 | n (%) | N=4,475 | n (%) |
| **Race** | | | | | | |
| American Indian or Alaska Native | 70 | (2.3) | 34 | (2.3) | 104 | (2.3) |
| Asian | 989 | (32.9) | 414 | (28.1) | 1,403 | (31.4) |
| Black or African American | 115 | (3.8) | 80 | (5.4) | 195 | (4.4) |
| Multiple | 280 | (9.3) | 130 | (8.8) | 410 | (9.2) |
| Native Hawaiian or Other Pacific Islander | 9 | (0.3) | 5 | (0.3) | 14 | (0.3) |
| White | 1,538 | (51.2) | 808 | (54.9) | 2,346 | (52.4) |
| **Ethnicity** | | | | | | |
| Hispanic Or Latino | 542 | (18.0) | 310 | (21.1) | 852 | (19.0) |
| **Gestational Age (Weeks)** | | | | | | |
| <37 | 142 | (4.7) | 144 | (9.8) | 286 | (6.4) |
| ≥37 | 2,862 | (95.3) | 1,327 | (90.2) | 4,189 | (93.6) |

SD=standard deviation

# The safety profile of V114 is generally comparable to PCV13

| Summary of AEs | V114 N=3,002 n (%) | PCV13 N=1,467 n (%) |
|---|---|---|
| **≥1 AE** | 2,808 (93.5) | 1,362 (92.8) |
| Injection-site AEs | 2,074 (69.1) | 989 (67.4) |
| Systemic AEs | 2,730 (90.9) | 1,320 (90.0) |
| **Vaccine-related AEs** | 2,674 (89.1) | 1,268 (86.4) |
| Injection-site AEs | 2,071 (69.0) | 987 (67.3) |
| Systemic AEs | 2,411 (80.3) | 1,106 (75.4) |
| **Serious AEs** | 301 (10.0) | 147 (10.0) |
| Serious vaccine-related AEs | 2 (0.1) | 0 (0.0) |
| **Who died** | 2 (0.1) | 2 (0.1) |
| **Who discontinued vaccine due to an AE** | 0 (0.0) | 0 (0.0) |




AE = adverse event. Vaccine-related AEs were those determined by the investigator to be related to the vaccine. Reported adverse events include nonserious adverse events that occurred within 14 days of any vaccination and serious adverse events that occurred after dose 1 through completion of study participation.

Injection site pain, decreased appetite, irritability, somnolence, and urticaria were solicited from Day 1 through Day 14 following each dose.

# Maximum temperatures, by the Brighton Collaboration cut points, are comparable between the groups

| | Infant Series | | | | | | | | Toddler Dose | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Dose 1 | | Dose 2 | | Dose 3 | | Dose 4 | | | | | |
| | V114 (N = 3002) | | PCV13 (N = 1467) | | V114 (N = 2939) | | PCV13 (N = 1414) | | V114 (N = 2894) | | PCV13 (N = 1374) | | V114 (N = 2803) | | PCV13 (N = 1312) | |
| | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) | n | (%) |
| **Patients in population** | 3002 | | 1467 | | 2939 | | 1414 | | 2894 | | 1374 | | 2803 | | 1312 | |
| Without temperature data (Day 1 through Day 7) | 7 | (0.2) | 9 | (0.6) | 37 | (1.3) | 20 | (1.4) | 29 | (1.0) | 30 | (2.2) | 31 | (1.1) | 25 | (1.9) |
| With temperature data (Day 1 through Day 7) | 2995 | (99.8) | 1458 | (99.4) | 2902 | (98.7) | 1394 | (98.6) | 2865 | (99.0) | 1344 | (97.8) | 2772 | (98.9) | 1287 | (98.1) |
| **Maximum temperature (rectal or rectal equivalent)** | | | | | | | | | | | | | | | | |
| <100.4°F | 1639 | (54.7) | 808 | (55.4) | 1656 | (57.1) | 761 | (54.6) | 1724 | (60.2) | 798 | (59.4) | 1742 | (62.8) | 822 | (63.9) |
| ≥100.4°F and <101.3°F | 998 | (33.3) | 475 | (32.6) | 844 | (29.1) | 434 | (31.1) | 753 | (26.3) | 379 | (28.2) | 694 | (25.0) | 331 | (25.7) |
| ≥101.3°F and <102.2°F | 300 | (10.0) | 138 | (9.5) | 305 | (10.5) | 131 | (9.4) | 273 | (9.5) | 123 | (9.2) | 230 | (8.3) | 93 | (7.2) |
| ≥102.2°F and <103.1°F | 41 | (1.4) | 28 | (1.9) | 65 | (2.2) | 53 | (3.8) | 72 | (2.5) | 28 | (2.1) | 61 | (2.2) | 23 | (1.8) |
| ≥103.1°F and <104.0°F | 13 | (0.4) | 9 | (0.6) | 26 | (0.9) | 11 | (0.8) | 28 | (1.0) | 13 | (1.0) | 26 | (0.9) | 15 | (1.2) |
| ≥104.0°F and <104.9°F | 3 | (0.1) | 0 | (0.0) | 3 | (0.1) | 3 | (0.2) | 11 | (0.4) | 1 | (0.1) | 10 | (0.4) | 3 | (0.2) |
| ≥104.9°F and <105.8°F | 1 | (0.0) | 0 | (0.0) | 0 | (0.0) | 0 | (0.0) | 4 | (0.1) | 0 | (0.0) | 4 | (0.1) | 0 | (0.0) |
| ≥105.8°F | 0 | (0.0) | 0 | (0.0) | 3 | (0.1) | 1 | (0.1) | 0 | (0.0) | 2 | (0.1) | 5 | (0.2) | 0 | (0.0) |

# Supportive clinical studies and populations

*V114-27 (Interchangeability)*
*V114-24 (Catch-up)*
*V114-23 (Sickle Cell Disease)*
*V114-30 (HIV)*
*V114-027/029/031 (Preterm infants)*

# Conclusions

## Safety

Vaccination with V114 is well tolerated with a safety profile that is generally comparable to PCV13, in:

- **healthy children,** 7 months through 17 years of age, receiving **catch-up** vaccination (P024)
- children with **SCD**, 5-17 years of age, receiving 1 dose of PCV (P023)
- **heathy infants** receiving **mixed dosing,** PCV13-V114 (P027)
- children living with **HIV**, 6-17 years of age, receiving 1 dose of PCV followed by PPSV23 (P030)
- **Preterm infants** (P027/029/031)

## Immunogenicity

V114 is immunogenic in all studied populations:

- V114 induces **IgG** responses for all 15 serotypes that are **comparable** for the shared serotypes and **higher** for 2 serotypes unique to V114 as compared with PCV13
  - Responses to **ST3** were consistently higher in the V114 group
- V114 is associated with an increase in **functional antibodies** for all 15 serotypes
- **Mixed dosing** elicit comparable responses for the shared serotypes, and higher responses for the unique serotypes in recipients of **at least 1 dose** of V114 as compared with PCV13 regimen
- Immune response is maintained when V114 is followed by **PPSV23** 8 weeks later
- The pattern of immune responses in **preterm infants** is consistent with that observed in the overall healthy infant population

# Conclusions

# Conclusions of the V114 pediatric clinical development program

**In children with an unmet medical need for pneumococcal disease prevention:**

- V114 is **well tolerated** with a safety profile that is consistent with licensed PCVs
- V114 induces **robust immune responses** to **13 serotypes shared** with PCV13 without significant loss of immunogenicity
- V114 is **superior** to PCV13 for **shared serotype 3**, the single most frequent serotype causing residual disease
- V114 is **superior** to PCV13 for **serotypes 22F and 33F,** which are of high Public Health importance

**Therefore, V114 has the potential to significantly address the burden of remaining pneumococcal disease due to vaccine-types (including serotype 3) and leading non-vaccine types (serotypes 22F, 33F) in children.**

INVENTING FOR LIFE

# Thank You.

# Questions & discussion