20-valent Pneumococcal Conjugate Vaccine (PCV20) Phase 3 in Adults

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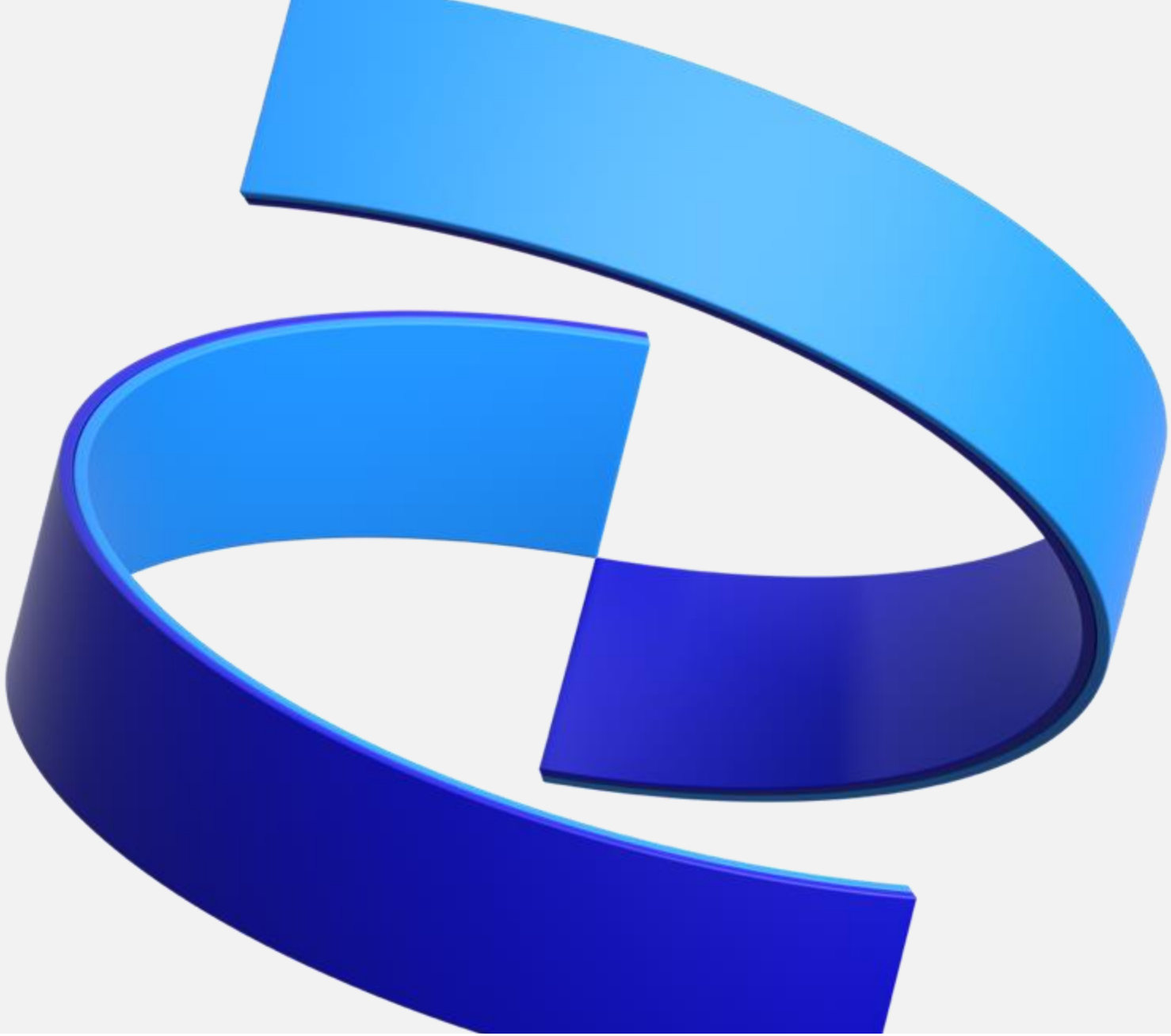


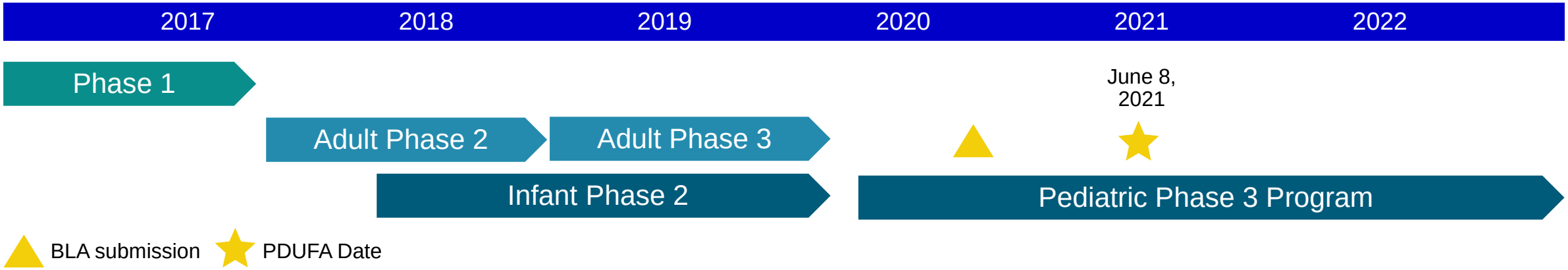
Background of PCV20

PCV20 is PCV13 with 7 Additional Polysaccharide Conjugates

- PCV20 contains PCV13 components + 7 additional serotypes to broaden disease coverage for IPD and pneumonia in adults
- The 7 additional conjugates were modelled on the PCV13 Pfizer platform

Licensure and Proposed Indications

- Licensure based on acceptable safety and immunogenicity vs PCV13 (13 matched serotypes) and PPSV23 (7 additional serotypes)
- Seeking same indications as PCV13
- FDA granted Breakthrough Designation for PCV20
  - Recognition of the benefit of conjugate technology in long term protection and importance for prevention of pneumococcal pneumonia



Phase 3 PCV20 Adult Clinical Development Program

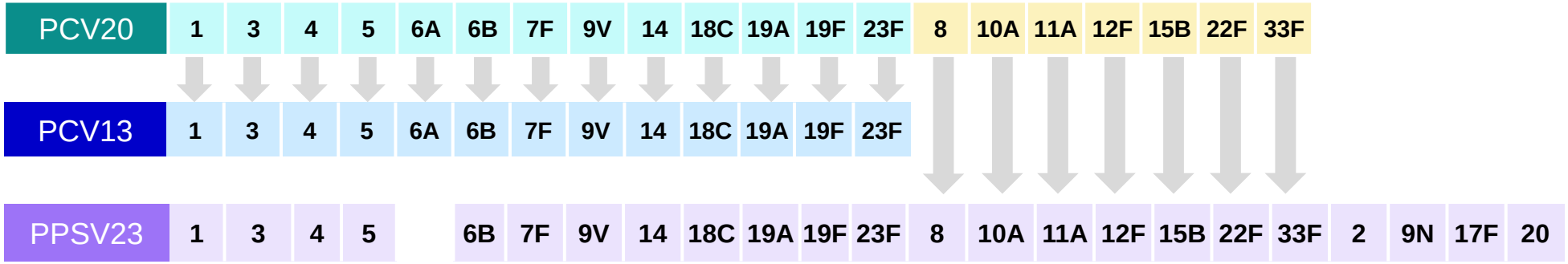
Three Phase 3 Safety and Immunogenicity Studies Modelled on PCV13 Adult Program

Populations Studied	• >4000 adult recipients (over 1000 individuals ≥65 years of age) • Individuals with stable chronic medical conditions • Individuals with prior pneumococcal vaccination • No individuals with immunocompromising conditions
Immunogenicity Analysis	• Comparison of PCV20 to PCV13 and PPSV23 in ≥60 years of age • Bridge to 18–59 years of age • PCV20 in ≥65 years of age with prior PPSV23, PCV13, or both
Ongoing	• Concomitant use with Fluad® Quad in ≥65 years of age

Immunologic Comparisons Form the Basis to Infer Efficacy/Effectiveness of PCV20 for Adults

- OPA correlates with vaccine activity, but no specific level predicts protection
- Primary measure of immune response = OPA GMTs measured 1 month after vaccination
- Statistical noninferiority (NI) for all 20 serotypes analyzed
- Failure of a serotype to meet NI does not directly translate into lower protection → need to consider totality of data

Pivotal Phase 3 Comparison



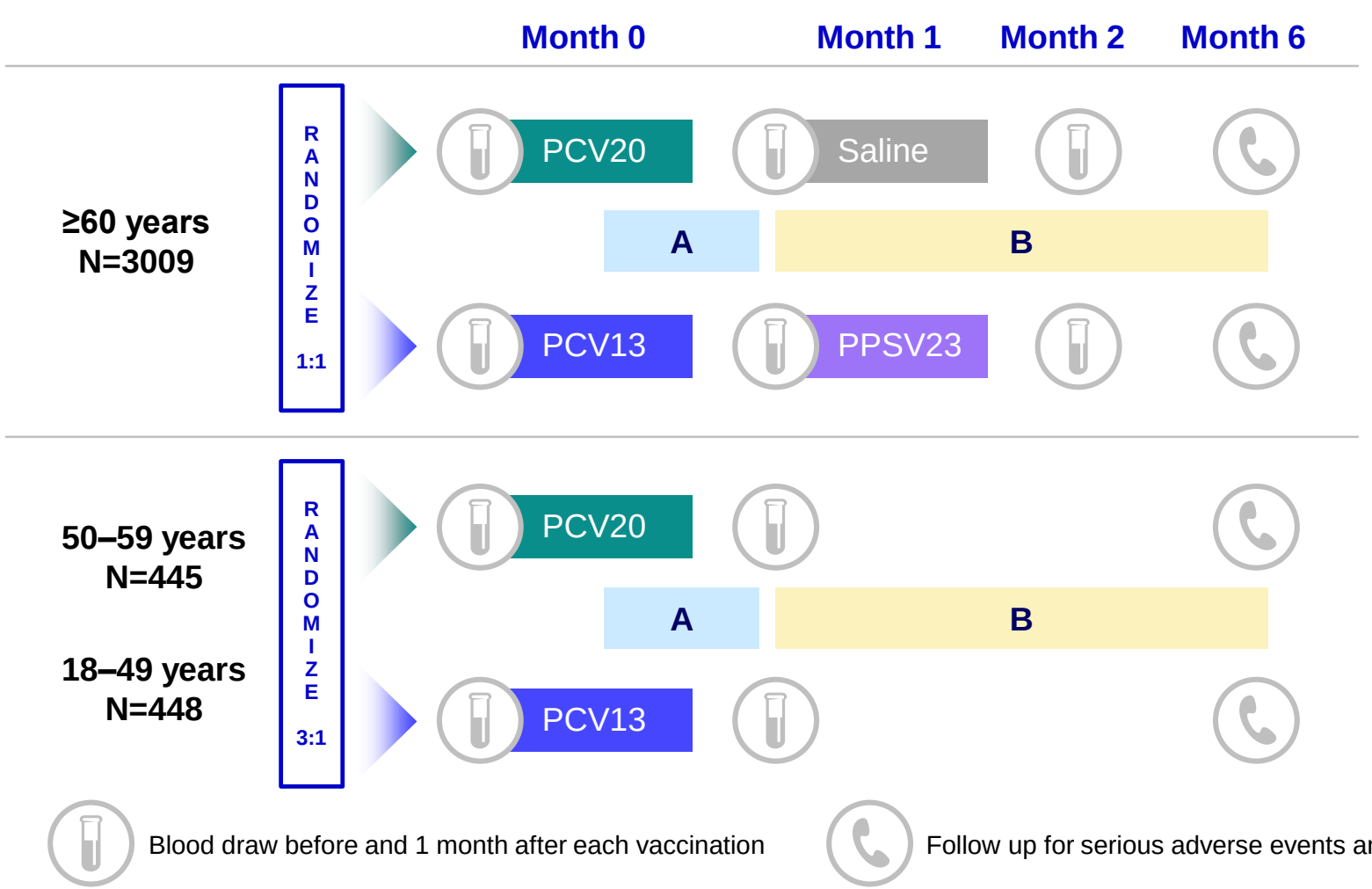
OPA: opsonophagocytic activity; GMT: geometric mean titers

Summary of the Phase 3 Studies Conducted to Evaluate Safety and Immunogenicity

Study / Population	Cohorts, Groups and Number Randomized	Key Objectives
Pivotal Comparison Study (B7471007) (USA, Sweden) ≥18 years of age, naïve to pneumococcal vaccine N = 3902 (2184 PCV20)	**≥60 years of age**: • PCV20/saline, n = 1514 or PCV13/PPSV23, n = 1495 **50 through 59 years of age:** • PCV20, n = 334 or PCV13, n =111 **18 through 49 years of age:** • PCV20, n = 336 or PCV13, n = 112	• Safety of PCV20 • Compare PCV20 immunogenicity to PCV13 (13 matched serotypes) in ≥60 years of age • Compare PCV20 immunogenicity to PPSV23 (7 additional serotypes) in ≥60 years of age • Bridge PCV20 immunogenicity in adults 18–49 and 50–59 years of age to adults 60-64 years of age
Study in Pneumococcal Vaccine-Experienced Adults (B7471006) (USA, Sweden) ≥65 years of age, prior pneumococcal vaccination N = 875 (626 PCV20)	**PPSV23 1-5 year prior:** • PCV20, n = 253 or PCV13, n = 122 **PCV13 ≥6 months prior:** • PCV20, n = 248 or PPSV23, n = 127 **PCV13/PPSV23 ≥1 year prior:** • PCV20, n = 125	• Safety of PCV20 • Describe PCV20 immunogenicity in adults ≥65 years of age with prior pneumococcal vaccination (PCV20 recipients only)
Lot Consistency Study (B7471008) (USA) 18–49 years of age, naïve to pneumococcal vaccine N = 1710 (1465 PCV20)	**PCV20 Lot 1, Lot 2, and Lot 3** • n = 486-490/lot **PCV13:** • n = 245	• Safety of PCV20 • Compare immunogenicity of 3 different lots of PCV20

Design and Safety Assessments of PCV20 in the Pivotal Study

Phase 3, Randomized, Double-blind, Multicentre (B7471007) Study (NCT03760146)



Safety Assessments

A

Prompted local reactions at the injection site within 10 days after vaccination

Prompted systemic events within 7 days after vaccination

Adverse events (AEs) 1 month after vaccination

B

Serious AEs (SAEs) collected for 6 months after PCV20

Newly diagnosed chronic medical conditions (NDCMCs) collected for 6 months after PCV20

Blood draw before and 1 month after each vaccination

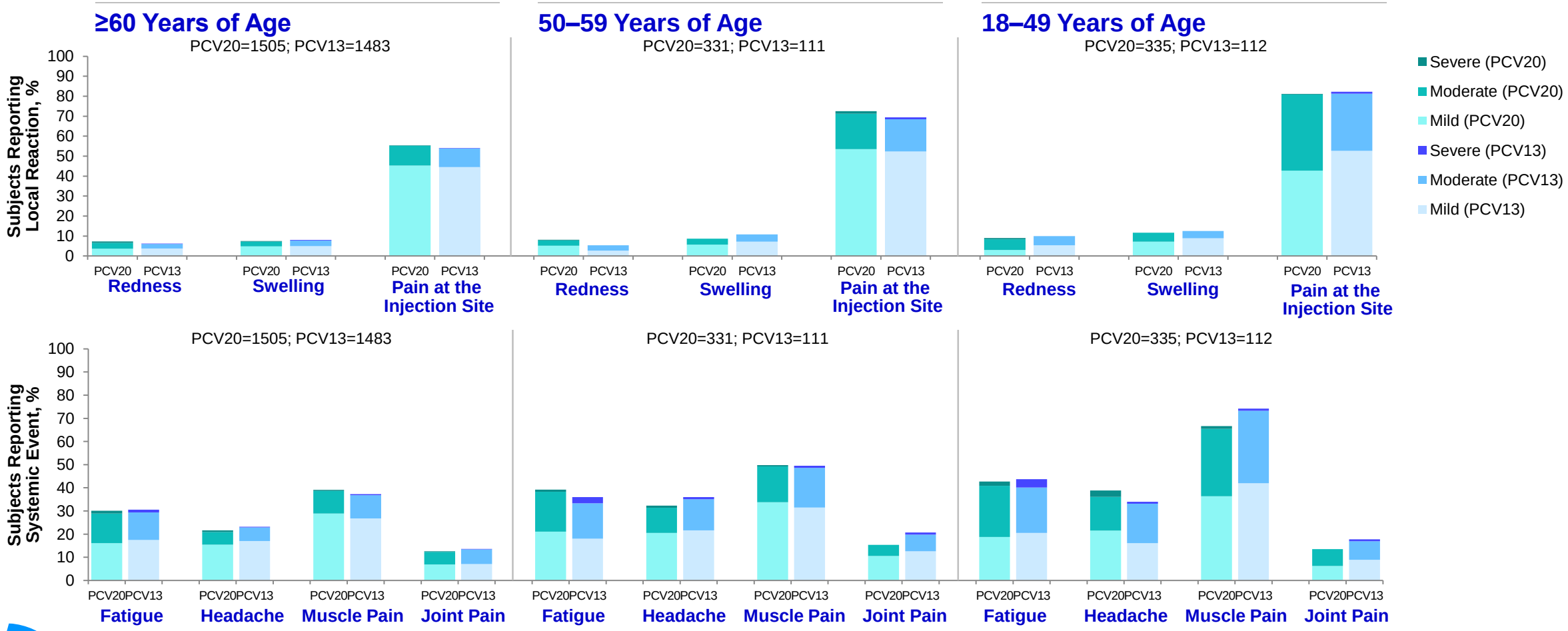
Follow up for serious adverse events and newly diagnosed chronic medical conditions after PCV20

Demographics Were Similar Between Vaccine Groups in the Pivotal Study

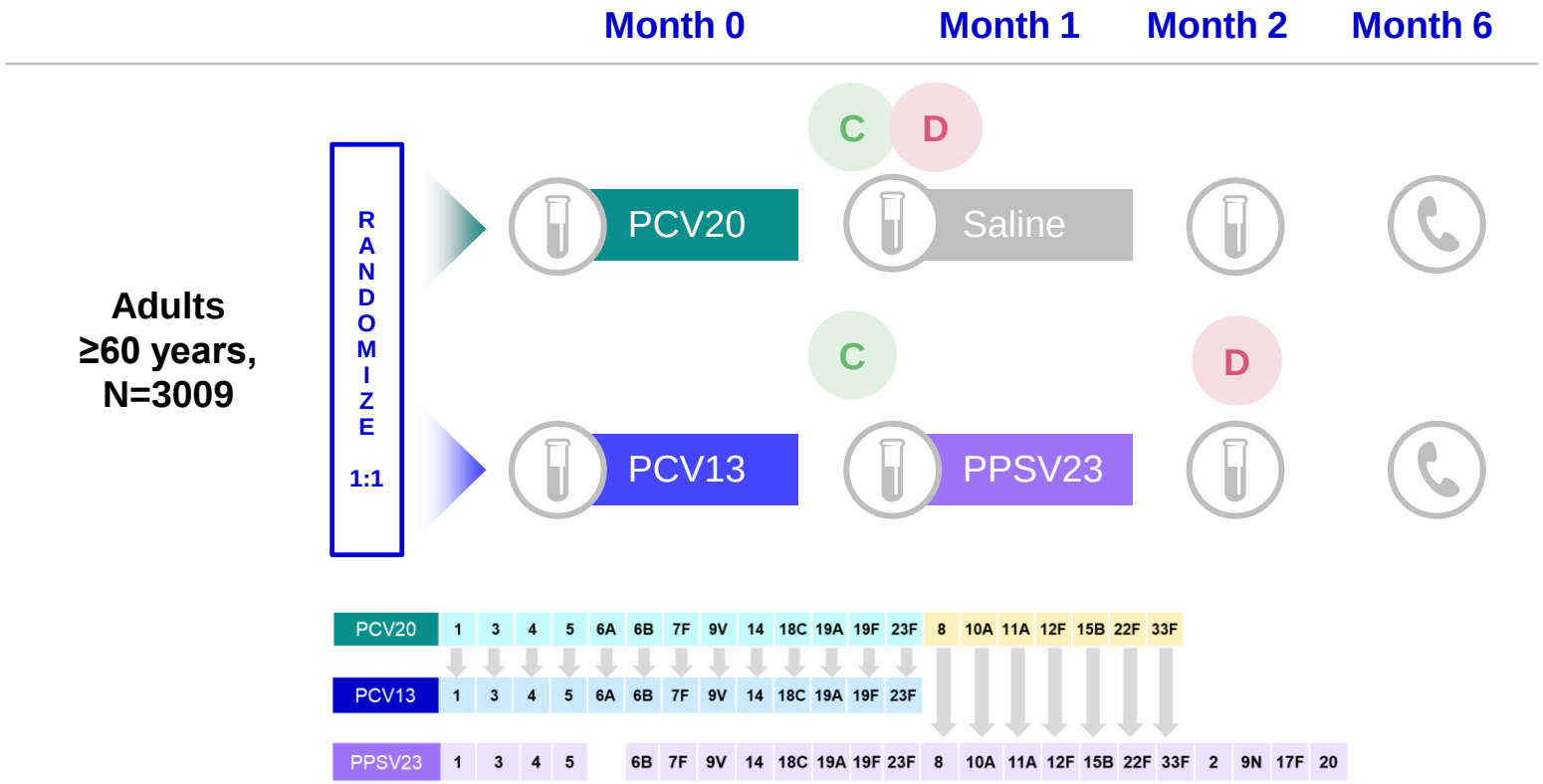
	≥60 Years of Age		50–59 Years of Age		18–49 Years of Age	
	PCV20/Saline	PCV13/PPSV23	PCV20	PCV13	PCV20	PCV13
Randomized, n (%)	1514 (100)	1495 (100)	334 (100)	111 (100)	336 (100)	112 (100)
Completed study, n (%)	1418 (93.7)	1417 (94.8)	323 (96.7)	109 (98.2)	319 (94.9)	104 (92.9)
Select Demographics						
Male, n (%)	610 (40.5)	611 (41.0)	139 (41.6)	42 (37.8)	121 (36.1)	35 (31.1)
White, n (%)	1295 (85.9)	1237 (83.0)	278 (83.2)	90 (81.1)	274 (81.8)	101 (90.2)
Black /African Amer, n (%)	177 (11.7)	212 (14.2)	35 (10.5)	15 (13.5)	34 (10.1)	7 (6.3)
Mean Age in Years ± SD	64.6±4.8	64.6±4.8	54.9±2.8	55.0±3.1	34.0±8.8	33.9±8.0
60 to 64 Years	996 (65.8)	992 (66.4)				
≥65 Years	518 (34.2)	503 (33.6)				
Risk Factors, n (%)						
1 or more Risk Factor	465 (32.4)	516 (36.3)	104 (32.4)	32 (29.6)	79 (24.9)	31 (29.2)
Chronic Cardiovascular Disease	71 (4.9)	109 (7.7)	12 (3.7)	3 (2.8)	3 (0.9)	0
Chronic Liver Disease	5 (0.3)	7 (0.5)	2 (0.6)	0	0	0
Chronic Pulmonary Disease	130 (9.1)	117 (8.2)	22 (6.9)	5 (4.6)	30 (9.5)	10 (9.4)
Diabetes Mellitus	209 (14.6)	243 (17.1)	1 (0.3)	1 (0.9)	9 (2.8)	3 (2.8)
Current Smoker	163 (11.4)	179 (12.6)	50 (15.6)	16 (14.8)	46 (14.5)	19 (17.9)

Safety Profile of PCV20 was Similar to PCV13 in the Pivotal Study

- Most reported local reactions, systemic events were mild or moderate
- Adverse events and serious adverse events were similar between groups
- No serious adverse events were considered related to vaccine



Immunogenicity Comparison of PCV20 to PCV13 and PPSV23 in the Pivotal Study in Adults ≥60 years



C **Immunogenicity Assessments for 13 Matched Serotypes**
Noninferiority comparison of PCV20 to PCV13 at 1 month after vaccination

D **Immunogenicity Assessments for 7 Additional Serotypes**
Noninferiority comparison of PCV20 to PPSV23 at 1 month after vaccination

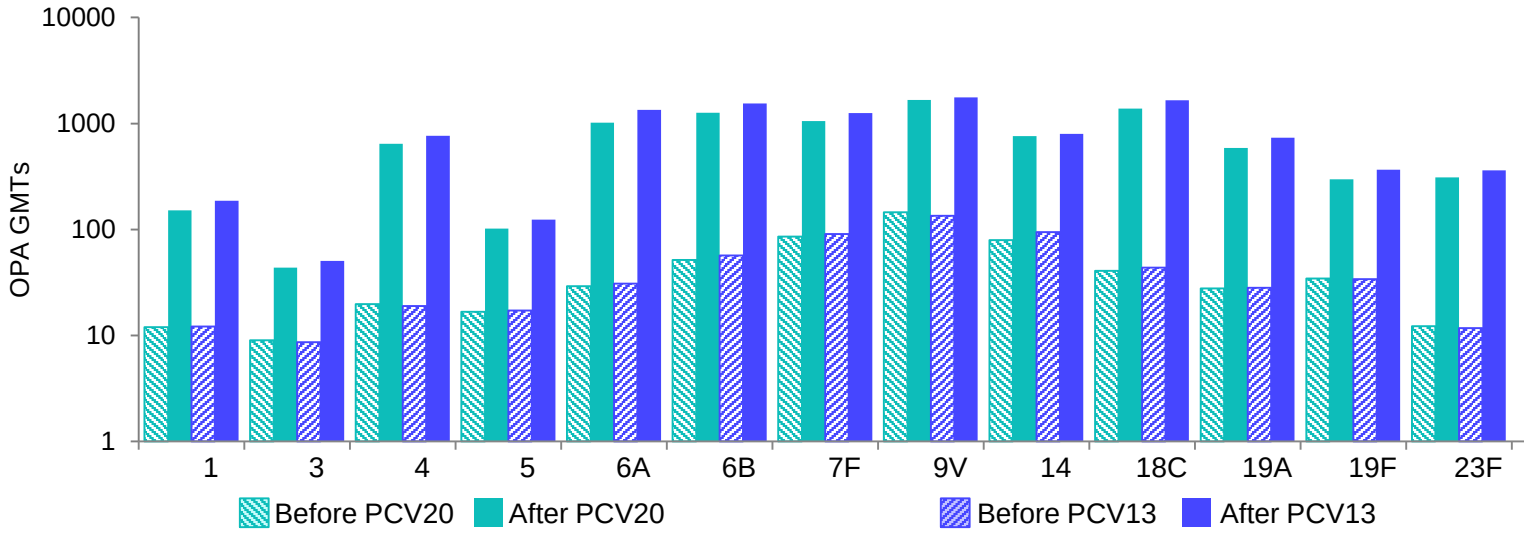
Blood draw before and 1 month after each vaccination

Follow up for serious adverse events and newly diagnosed chronic medical conditions after PCV20

PCV20 Induced Robust Immune Responses to All 20 Serotypes in Adults ≥60 years of Age

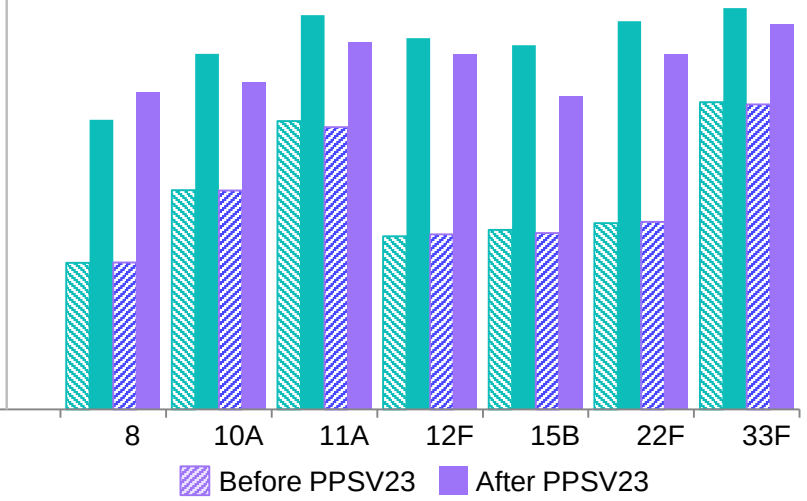
PCV20 and PCV13

PCV20 met NI criteria (lower 95% CI of OPA GMT ratio >0.5) for all 13 matched serotypes



PCV20 and PPSV23

Serotype 8 narrowly missed NI criteria (lower 95% CI of 0.49)

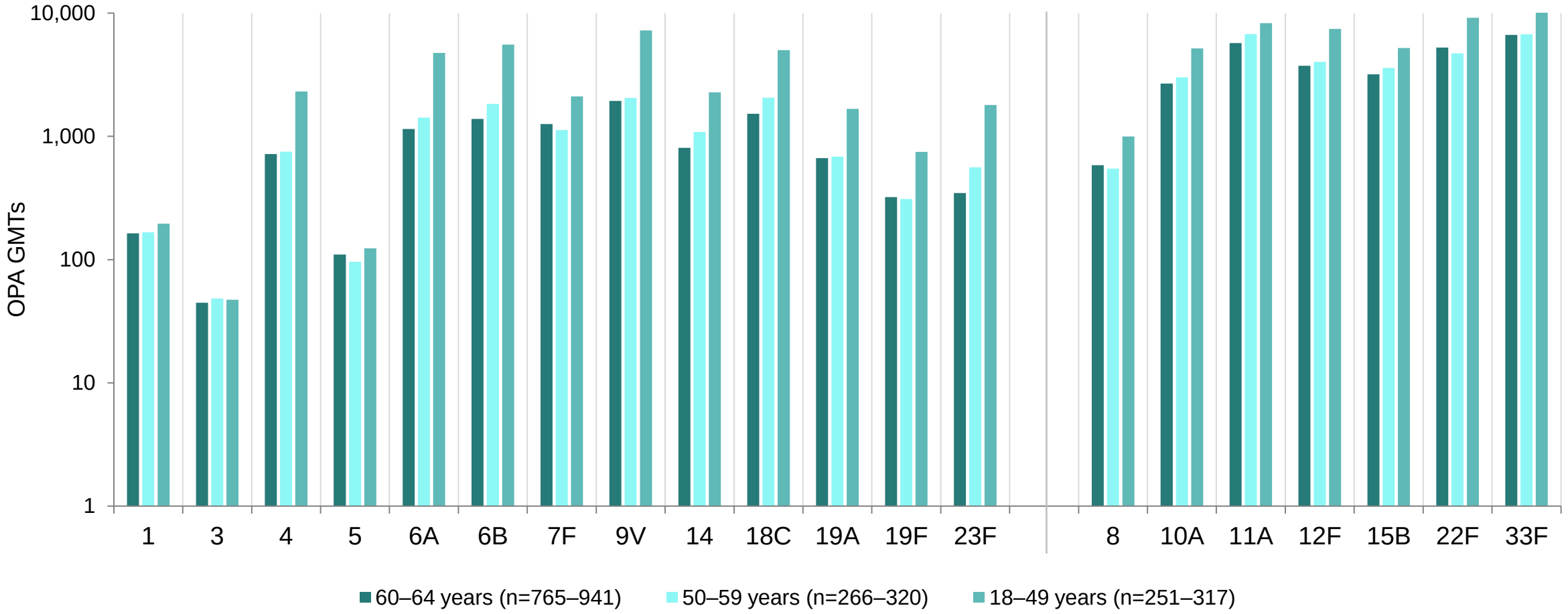


After PCV20, 77.8% of participants had ≥4-fold rises to serotype 8 – within range of 13 vaccine serotypes after PCV13 (54%–84%)

% w ≥4-fold Rise

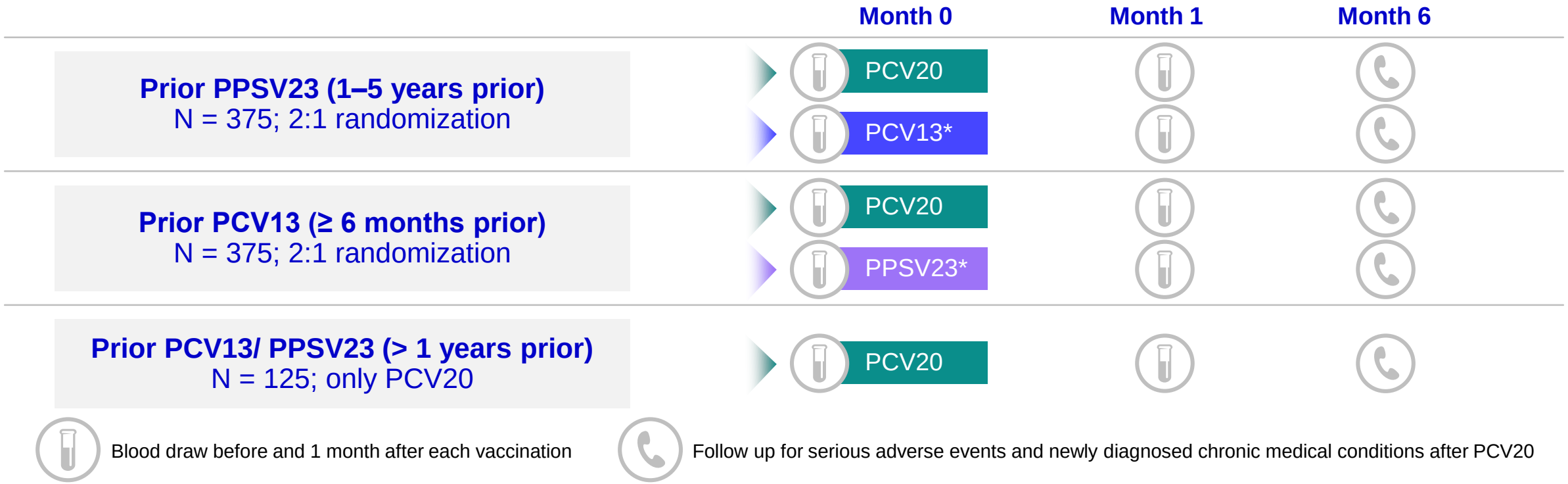
PCV20	8	PCV13	1	3	4	5	6A	6B	7F	9V	14	18C	19A	19F	23F
	77.8		74.8	61.7	79.6	60.6	84	77.6	72.3	69.3	54	79.6	77.5	66.9	74.4

PCV20 Immune Responses in Adults 50–59 or 18–49 Years of Age Met NI to Adults 60–64 Years of Age



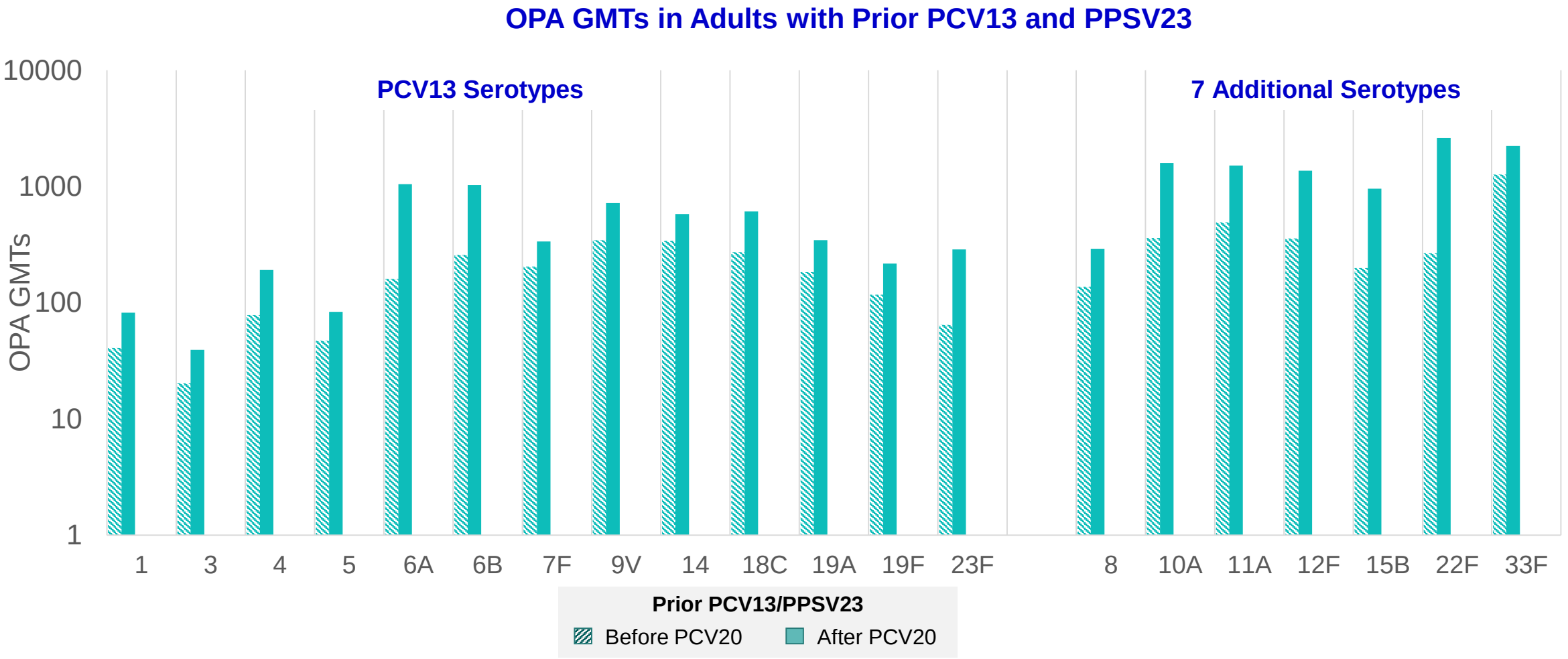
Study of PCV20 in Adults ≥65 Years of Age with Prior Pneumococcal Vaccination as Part of Routine Care

- Open-label, descriptive study conducted in US and Sweden
- Of note, Sweden only contributed to the group with prior PPSV23
- Study population meant to reflect current immunization status of existing US population ≥65 year of age



*PCV13 and PPSV23 were controls for safety assessments only. Immunogenicity measured in PCV20 group only.

PCV20 Elicited Immune Responses to the PCV13 and Additional 7 Serotypes in Adults ≥65 Years of Age with Prior Pneumococcal Vaccination



- The tolerability and safety after vaccination with PCV20 were similar regardless of prior pneumococcal vaccine

Summary of PCV20

- PCV20 contains PCV13 components + 7 additional serotypes to broaden disease coverage for IPD and pneumonia in adults
- FDA granted Breakthrough Designation for PCV20 recognizing the benefit of conjugate technology in long term protection and importance for prevention of pneumonia
- PCV20 is well tolerated and has a safety profile similar to PCV13 regardless of prior pneumococcal vaccination, and across subgroups of age, sex, and race
- PCV20 is immunogenic across all ages, including in those with chronic medical conditions and regardless of prior pneumococcal vaccination
- PCV20 offers a potentially simplified and impactful approach to the prevention of pneumococcal disease in adults, particularly pneumonia
- PCV20 is currently under review by the FDA for the prevention of IPD and pneumonia in adult 18 years of age and older with target action date of June 8, 2021

Back Up