

VAX-31 OPUS-1 Pivotal Phase 3 Adult Trial: Topline Results



October 5, 2026

VAXCYTE
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Vaxcyte Leadership Team on Today's Call

Strong Track Record in Vaccines and Biopharma



GRANT PICKERING, MBA
Chief Executive Officer, Director
& Co-Founder



ANDREW GUGGENHIME, MBA
President & Chief Financial Officer



JIM WASSIL, MS, MBA
Executive VP, Chief Operating
Officer & Chief Scientific Officer



LUIS JODAR, PhD
Chief Medical Officer



MIKE MULLETTE, MBA
Chief Commercial Officer



Forward-Looking Statements

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. These statements include, but are not limited to, statements related to the potential benefits of Vaxcyte's carrier-sparing platform and vaccine candidates, including breadth of coverage and the ability to deliver potentially better immune responses, best-in-class vaccines and the improvement upon the standard-of-care; demand for Vaxcyte's vaccine candidates; the design, timing of initiation, progress and expected results of Vaxcyte's preclinical studies, clinical trials and research and development plans; the ability of Vaxcyte's cell-free platform to deliver the broadest-spectrum PCVs that provide protection against both currently circulating and historically prevalent strains; expectations with regard to serotype cross-reactivity; the standards for review and licensure of vaccines and regulators accepting Vaxcyte's study as designed; the ability of Vaxcyte to commercialize its PCV candidates and to meet the PCV franchise market demand for commercial markets; the growth and expansion of the pneumococcal vaccine market, and the potential to address the need for broader-spectrum of coverage in such market; the market opportunity for Vaxcyte's vaccines; Vaxcyte's expectations regarding the potential benefits, spectrum coverage, clinical or regulatory pathways, adoption speed and immunogenicity of its vaccine candidates and other statements that are not historical fact. The words "anticipate," "believe," "continue," "could," "designed," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "should," "target," "will," "would" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

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Agenda

INTRODUCTION AND RESULTS OVERVIEW

OPUS-1 STUDY AND TOPLINE RESULTS

Trial Design, Disposition and Demographics

Tolerability and Safety Data

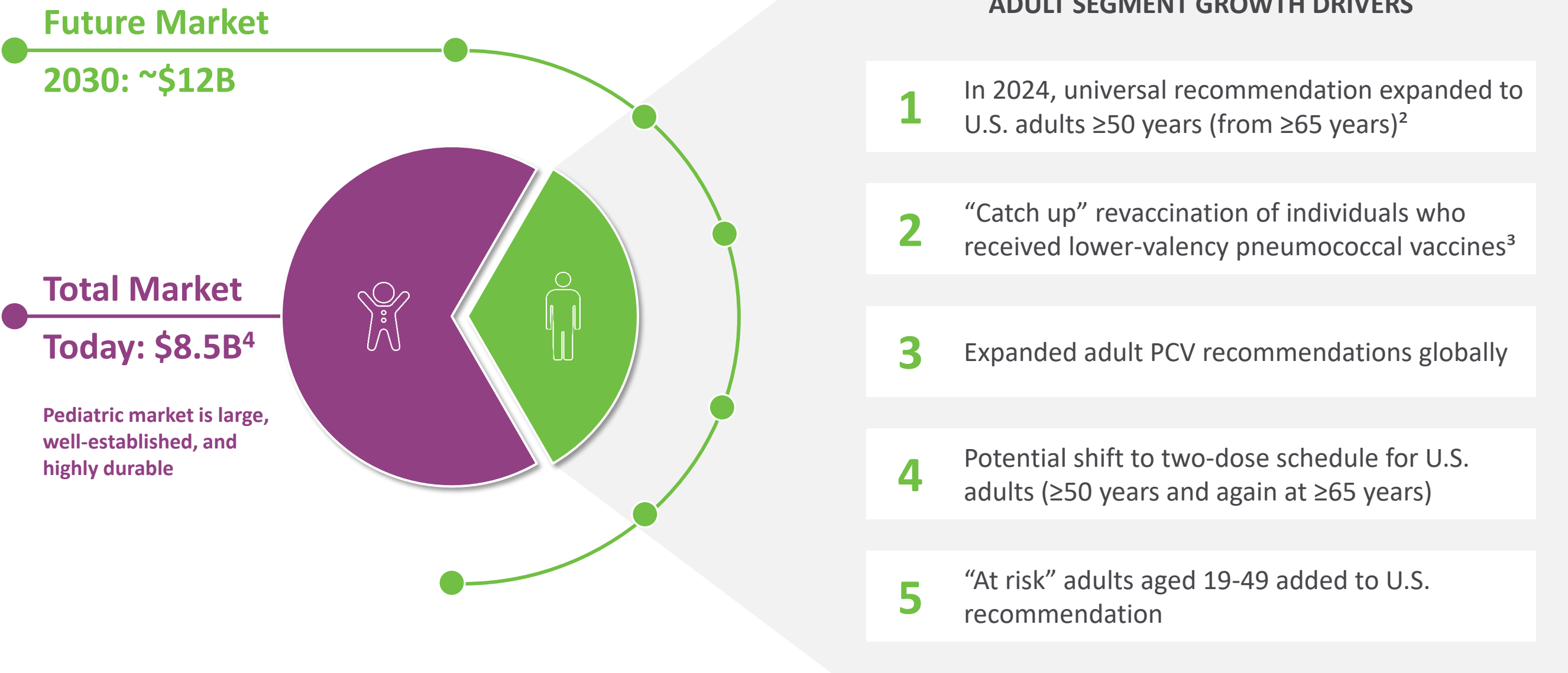
Immunogenicity in Adults Aged ≥ 50 Years and 18-49 Years

VAX-31 PROGRAM NEXT STEPS

Introduction and Results Overview

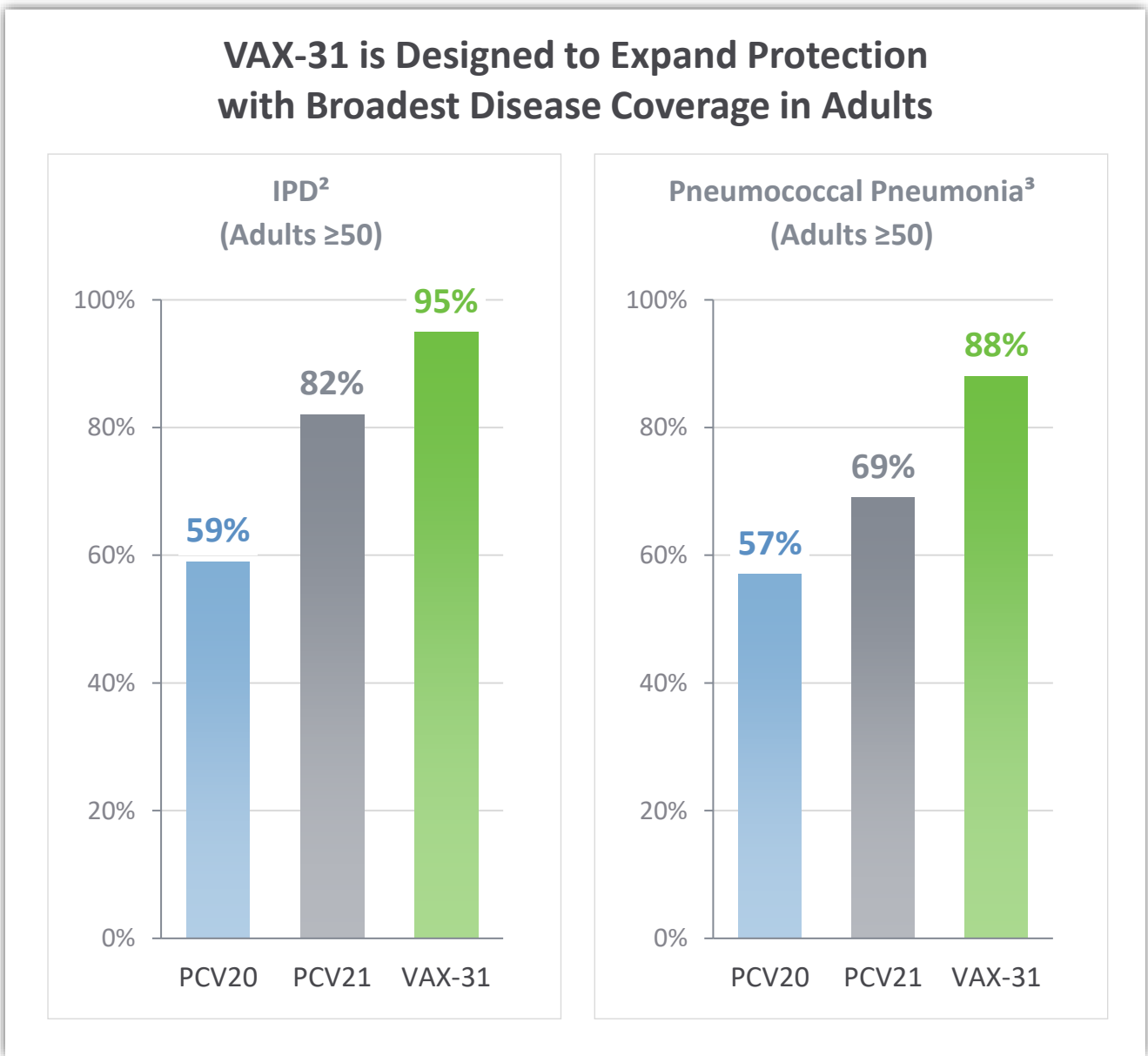
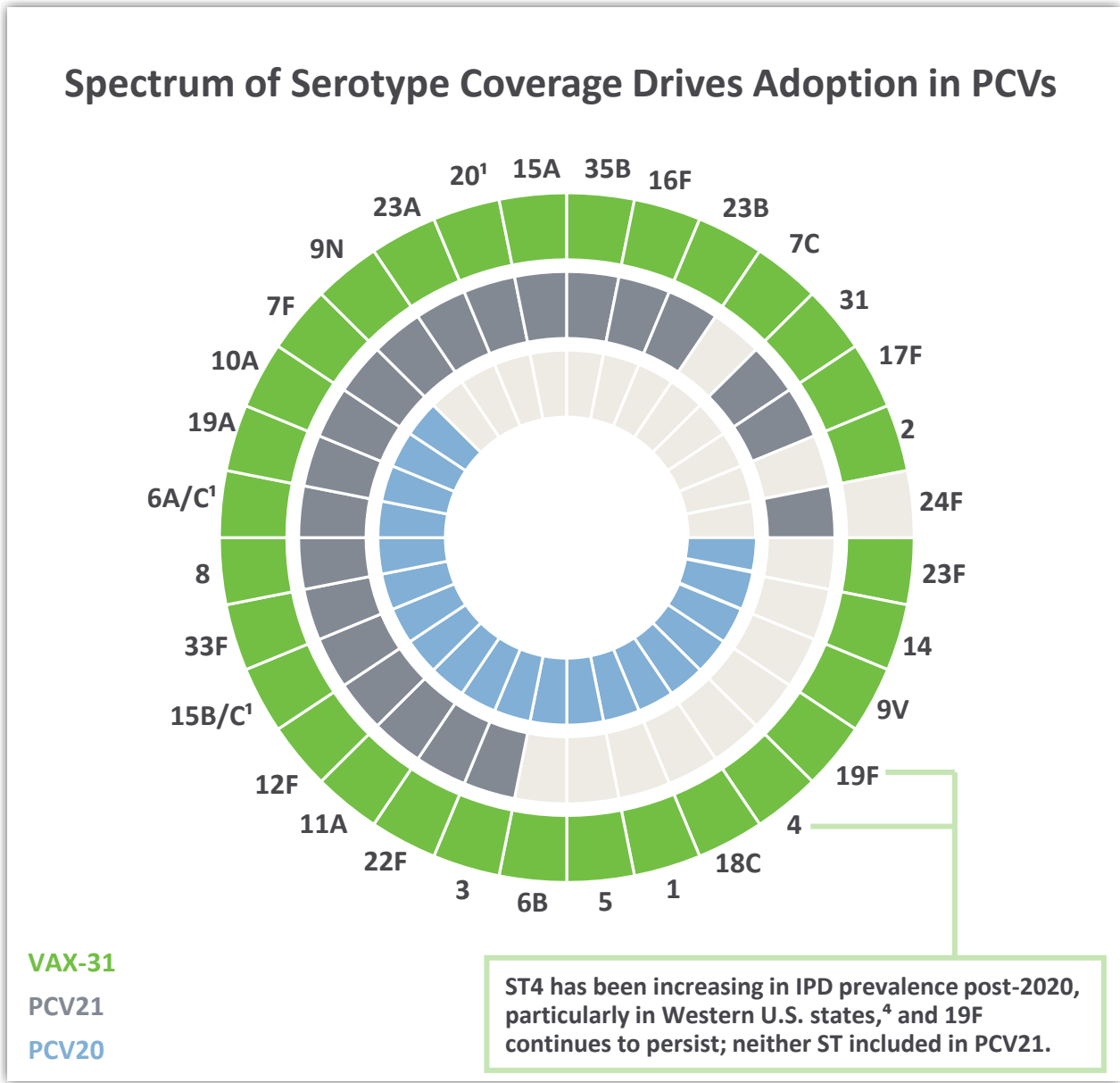
Pneumococcal Vaccine Market is Large, Durable and Poised for Significant Growth

Combined \$8.5B Market Expected to Grow to ~\$12B by 2030¹ Driven Primarily by Adult Market Expansion



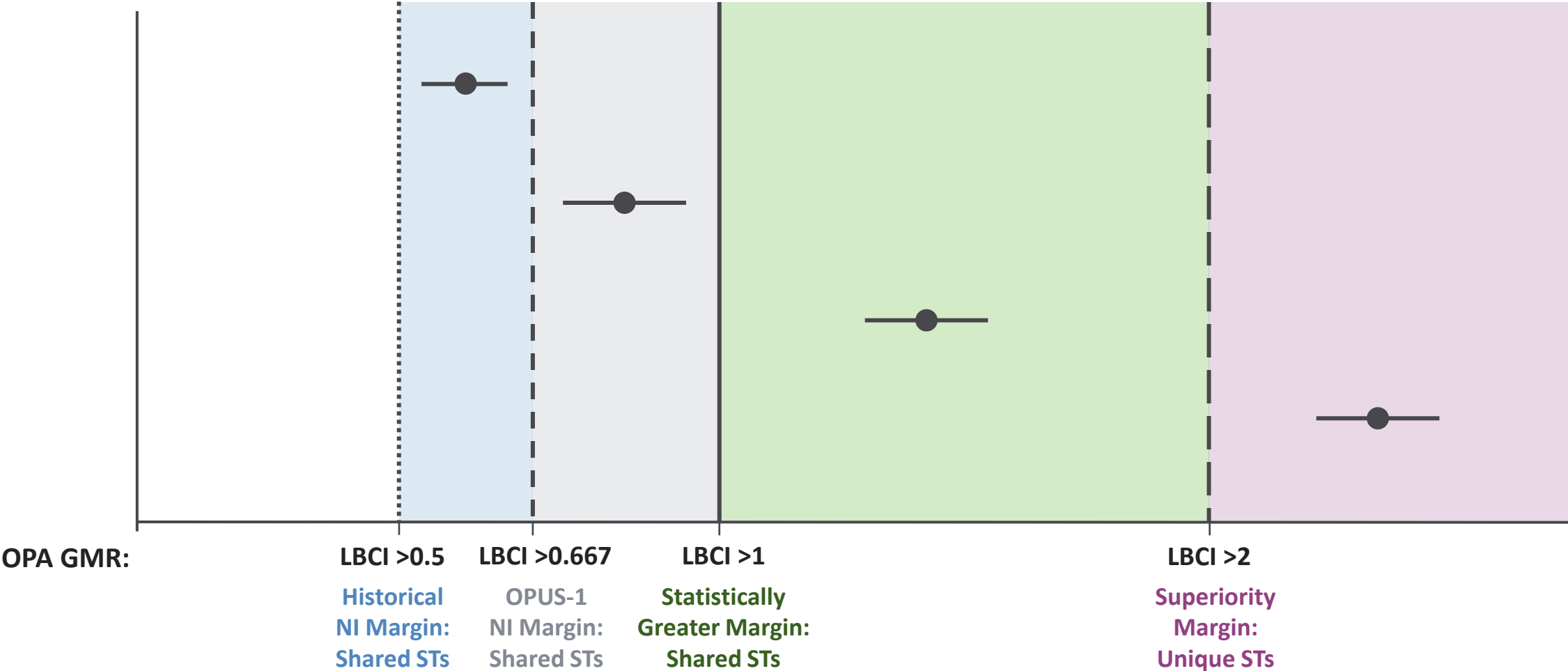
VAX-31 is Designed to Offer Comprehensive Coverage to Address Current Gaps

Broadening of Serotype and Disease Coverage Would Eliminate Tradeoffs Required by Current SoC



OPUS-1 Inaugurates a More Stringent >0.667 Noninferiority Standard, Setting a New Bar for Adult PCV Clinical Studies

Immune Response Standards for OPA GMRs



OPUS-1 Phase 3 Study: Statistical Framework to Define Success

Co-Primary Immunogenicity Objectives (Adults ≥50):

CO-PRIMARY ENDPOINT GROUP 1 11 serotypes shared by all 3 vaccines	CO-PRIMARY ENDPOINT GROUP 2 9 serotypes shared with PCV20 only	CO-PRIMARY ENDPOINT GROUP 3 8 serotypes shared with PCV21 only	CO-PRIMARY ENDPOINT GROUP 4 3 unique serotypes and cross-reactive 20B
Noninferiority vs PCV20 and/or PCV21 (OPA GMR: LBCI >0.667) ¹	Noninferiority vs PCV20 (OPA GMR: LBCI >0.667)	Noninferiority vs PCV21 (OPA GMR: LBCI >0.667)	Superiority vs PCV20 and/or PCV21 (OPA GMR: LBCI >2.0) ¹

Primary Immunobridging Objective (Adults 18-49):

If the above co-primary criteria are met: noninferiority of VAX-31 in adults aged 18-49 vs adults aged 50-64; all 32 comparisons² must meet OPA GMR NI at the LBCI >0.667.

Primary Safety Objective (Adults ≥18):

Evaluate **safety and tolerability of VAX-31** administered to adults aged 18-49 and ≥50.

Prespecified Individual Noninferiority Comparisons (Adults ≥50):

Evaluated **prespecified individual OPA GMR noninferiority comparisons of VAX-31 vs PCV20 or PCV21** in adults aged ≥50, among other immunogenicity evaluations, to provide additional data for regulators and recommending bodies.

OPUS-1 Phase 3 Topline Results:

VAX-31 Met All Primary Immunogenicity Endpoints and Safety Objectives

Co-Primary Immunogenicity Objectives (Adults ≥50):

CO-PRIMARY ENDPOINT GROUP 1 11 serotypes shared by all 3 vaccines	CO-PRIMARY ENDPOINT GROUP 2 9 serotypes shared with PCV20 only	CO-PRIMARY ENDPOINT GROUP 3 8 serotypes shared with PCV21 only	CO-PRIMARY ENDPOINT GROUP 4 3 unique serotypes and cross-reactive 20B
<u>11 of 11</u> met noninferiority (OPA GMR: LBCI >0.667) ¹	<u>9 of 9</u> met noninferiority (OPA GMR: LBCI >0.667)	<u>8 of 8</u> met noninferiority (OPA GMR: LBCI >0.667)	<u>4 of 4</u> met superiority (OPA GMR: LBCI >2.0) ¹

Primary Immunobridging Objective (Adults 18-49):

<u>32 of 32</u> comparisons met noninferiority (OPA GMR LBCI >0.667) ²
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Primary Safety Objective (Adults ≥18):

VAX-31 was well tolerated, with a safety profile similar to PCV20 and PCV21 across all ages studied
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Prespecified Individual Noninferiority Comparisons (Adults ≥50):

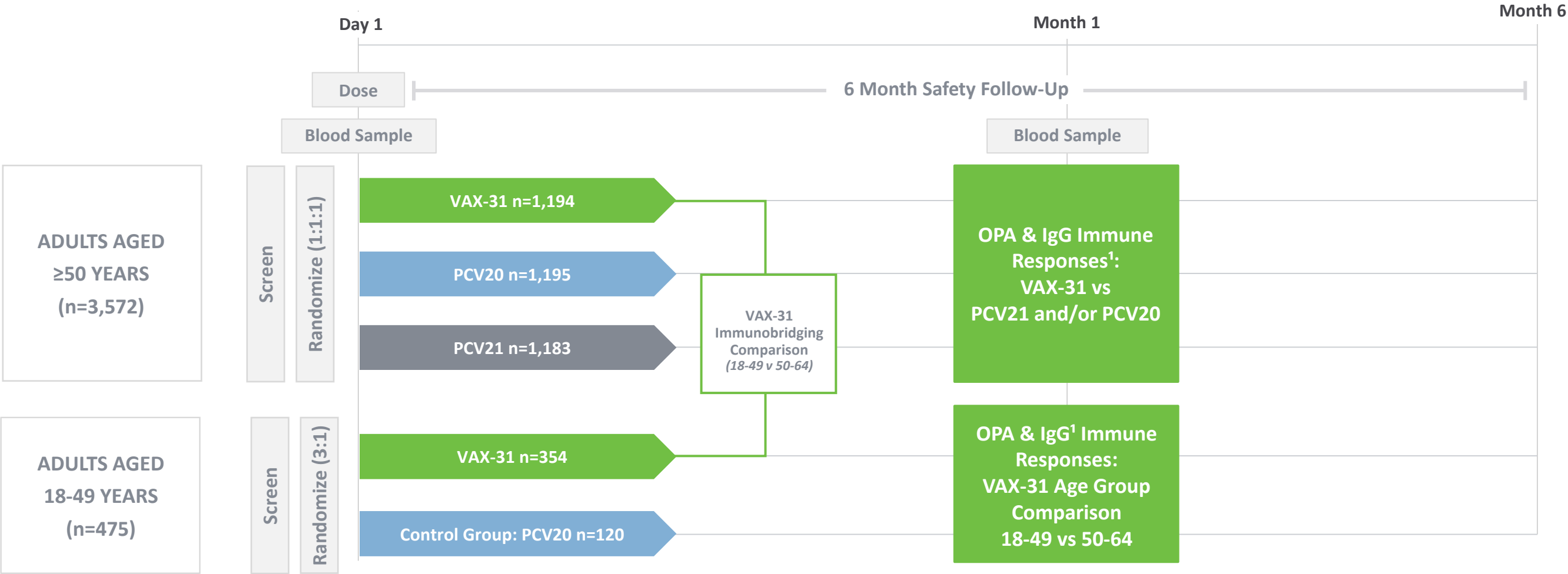
	VAX-31 vs PCV20 <u>20 of 20</u> shared serotypes met noninferiority criterion (OPA GMR LBCI >0.667)	VAX-31 vs PCV21 <u>17 of 19</u> shared serotypes met noninferiority criterion (OPA GMR LBCI >0.667)	
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OPUS-1 Study and Topline Results

Trial Design, Disposition and Demographics

OPUS-1 Phase 3 Pivotal, Randomized, Double-Blind, Active-Controlled Clinical Trial in Adults Aged 18 and Older (n=4,047*)

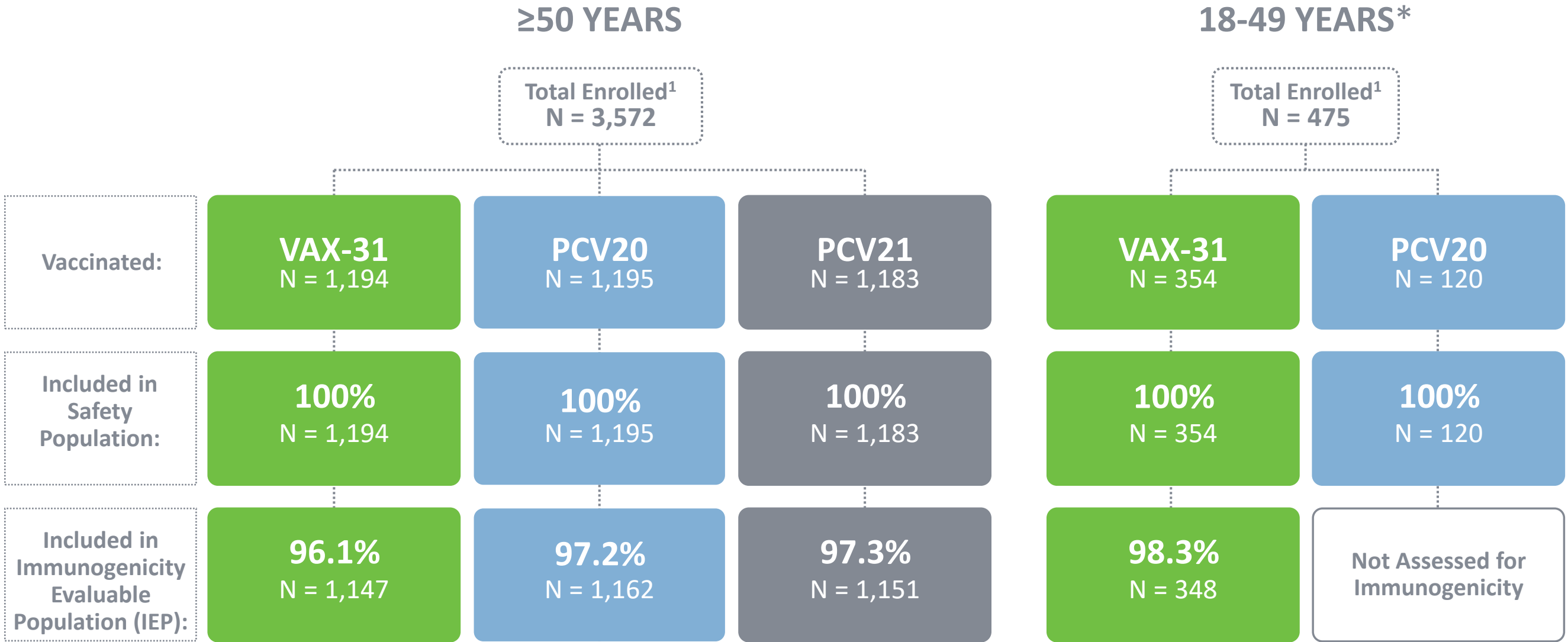
Designed to Establish New PCV Standard of Care for Adults Aged 50 and Older Through Head-to-Head Safety, Tolerability and Immunogenicity Comparisons of VAX-31 with PCV20 and PCV21; Evaluated Immunobridging to Adults Aged 18-49



Safety and tolerability assessed through Month 6, including solicited local reactions and systemic events (Day 1-7), unsolicited AEs (Day 1-Month 1), and SAEs, NOCIs and MAAEs (Day 1-Month 6)

Study Disposition

~97% of Vaccinated Subjects Included in Immunogenicity Evaluable Population



Population Demographics in Adults Aged 50 Years and Older

Well-Balanced Across Cohorts and Similar for the Safety and Immunogenicity Populations

	VAX-31		PCV20		PCV21	
	Safety	Immunogenicity	Safety	Immunogenicity	Safety	Immunogenicity
Number of Subjects	1194	1147	1195	1162	1183	1151
Median Age, Years (range)	60.0 (50, 97)	60.0 (50, 97)	60.0 (50, 86)	60.5 (50, 86)	60.0 (50, 85)	60.0 (50, 85)
50 to 64 Years	795 (66.6)	763 (66.5)	793 (66.4)	770 (66.3)	793 (67.0)	770 (66.9)
≥65 Years	399 (33.4)	384 (33.5)	402 (33.6)	392 (33.7)	390 (33.0)	381 (33.1)
At Risk for Pneumococcal Disease, n (%)	313 (26.2)	301 (26.2)	350 (29.3)	341 (29.3)	333 (28.1)	321 (27.9)
Female, n (%)	686 (57.5)	663 (57.8)	720 (60.3)	703 (60.5)	680 (57.5)	661 (57.4)
Race, n (%)						
White	730 (61.1)	706 (61.6)	776 (64.9)	760 (65.4)	752 (63.6)	737 (64.0)
Black or African American	395 (33.1)	373 (32.5)	356 (29.8)	341 (29.3)	380 (32.1)	366 (31.8)
Asian	17 (1.4)	17 (1.5)	9 (0.8)	8 (0.7)	11 (0.9)	10 (0.9)
American Indian or Native Alaskan	26 (2.2)	25 (2.2)	25 (2.1)	25 (2.2)	23 (1.9)	22 (1.9)
Native Hawaiian or Other Pacific Islander	3 (0.3)	3 (0.3)	3 (0.3)	3 (0.3)	1 (0.1)	1 (0.1)
Multiracial	5 (0.4)	5 (0.4)	10 (0.8)	10 (0.9)	7 (0.6)	7 (0.6)
Ethnicity, n (%)						
Hispanic or Latino	324 (27.1)	308 (26.9)	326 (27.3)	315 (27.1)	297 (25.1)	291 (25.3)
Median BMI, kg/m2 (range)	29.3 (16.6, 62.7)	29.4 (16.6, 62.7)	29.5 (16.6, 59.3)	29.6 (16.6, 59.3)	30.1 (16.2, 70.7)	30.1 (16.2, 70.7)

Population Demographics in Adults Aged 18-49

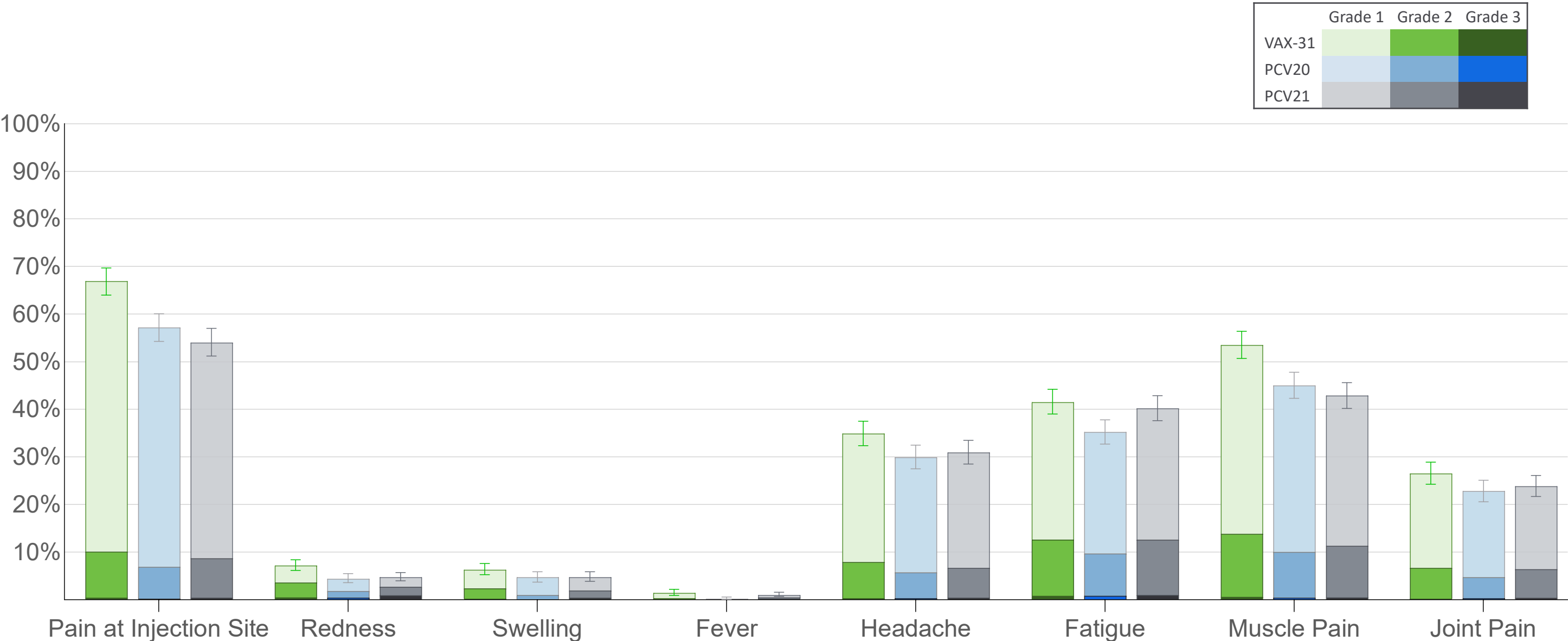
Well-Balanced Across Cohorts and Similar for the Safety and Immunogenicity Populations

	18-49 YEARS SAFETY POPULATION		VAX-31 RECIPIENTS (IEP)	
	VAX-31	PCV20	18-49 Years	50-64 Years
Number of Subjects	354	120	348	763
Median Age, Years (range)	37 (18, 49)	39 (18, 49)	37 (18, 49)	57 (50, 64)
At Risk for Pneumococcal Disease, n (%)	63 (17.8)	23 (19.2)	62 (17.8)	193 (25.3)
Female, n (%)	197 (55.6)	63 (52.5)	193 (55.5)	467 (61.2)
Race, n (%)				
White	176 (49.7)	56 (46.7)	173 (49.7)	449 (58.8)
Black or African American	131 (37.0)	50 (41.7)	129 (37.1)	268 (35.1)
Asian	9 (2.5)	4 (3.3)	9 (2.6)	14 (1.8)
American Indian or Native Alaskan	23 (6.5)	7 (5.8)	23 (6.6)	16 (2.1)
Native Hawaiian or Other Pacific Islander	1 (0.3)	1 (0.8)	1 (0.3)	2 (0.3)
Multiracial	11 (3.1)	2 (1.7)	11 (3.2)	3 (0.4)
Ethnicity, n (%)				
Hispanic or Latino	65 (18.4)	23 (19.2)	63 (18.1)	178 (23.3)
Median BMI, kg/m2 (range)	29.5 (17.0, 67.6)	30.2 (18.8, 58.8)	29.5 (17.0, 67.6)	29.6 (16.6, 62.7)

Tolerability and Safety Data

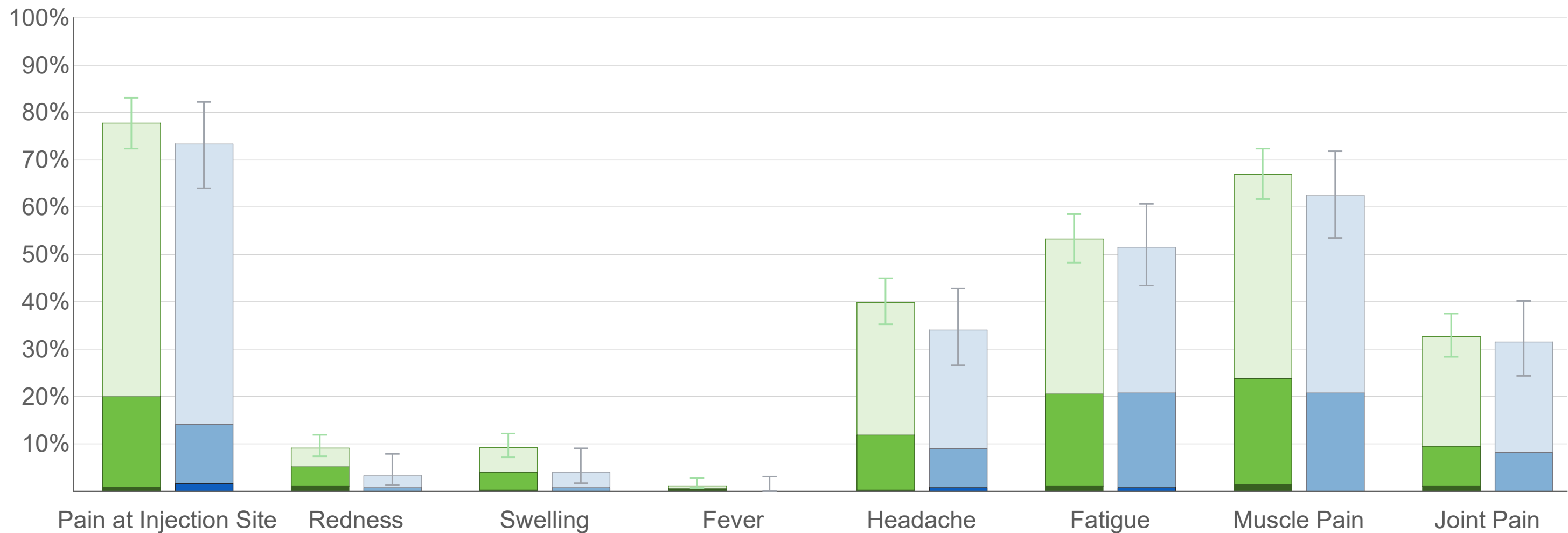
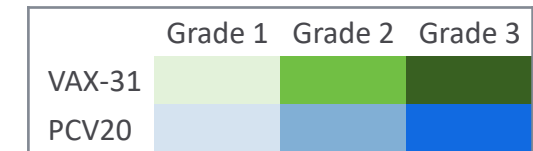
Local and Systemic Solicited AEs in Adults Aged 50 Years and Older

VAX-31 was Well-Tolerated and Consistent with PCV20 and PCV21, Majority of AEs Resolved Within 48 Hours



Local and Systemic Solicited AEs Similar to PCV20 in Adults Aged 18-49

VAX-31 was Well-Tolerated and Consistent with PCV20, Majority of AEs Resolved Within 48 Hours



Overall Safety Profile Similar to PCV20 and PCV21

	50 YEARS AND OLDER SAFETY POPULATION			18-49 YEARS SAFETY POPULATION	
	VAX-31	PCV20	PCV21	VAX-31	PCV20
Number of Subjects	1194	1195	1183	354	120
Unsolicited AE (1-Month), n (%)	75 (6.3)	99 (8.3)	96 (8.1)	37 (10.5)	11 (9.2)
Related, n (%)	19 (1.6)	24 (2.0)	28 (2.4)	9 (2.5)	3 (2.5)
MAAE, n (%)	71 (5.9)	104 (8.7)	90 (7.6)	26 (7.3)	10 (8.3)
Related, n (%)	2 (0.2)	5 (0.4)	3 (0.3)	0	0
NOCI, n (%)	7 (0.6)	9 (0.8)	12 (1.0)	2 (0.6)	3 (2.5)
Related, n (%)	0	0	0	0	0
SAE, n (%)	14 (1.2)	13 (1.1)	13 (1.1)	2 (0.6)	0
Related, n (%)	0	0	0	0	0
Death ¹ , n (%)	2 (0.2)	0	2 (0.2)	0	0
Related, n (%)	0	0	0	0	0
Discontinuation, n (%)	0	0	0	0	0
Related, n (%)	0	0	0	0	0

Immunogenicity Data

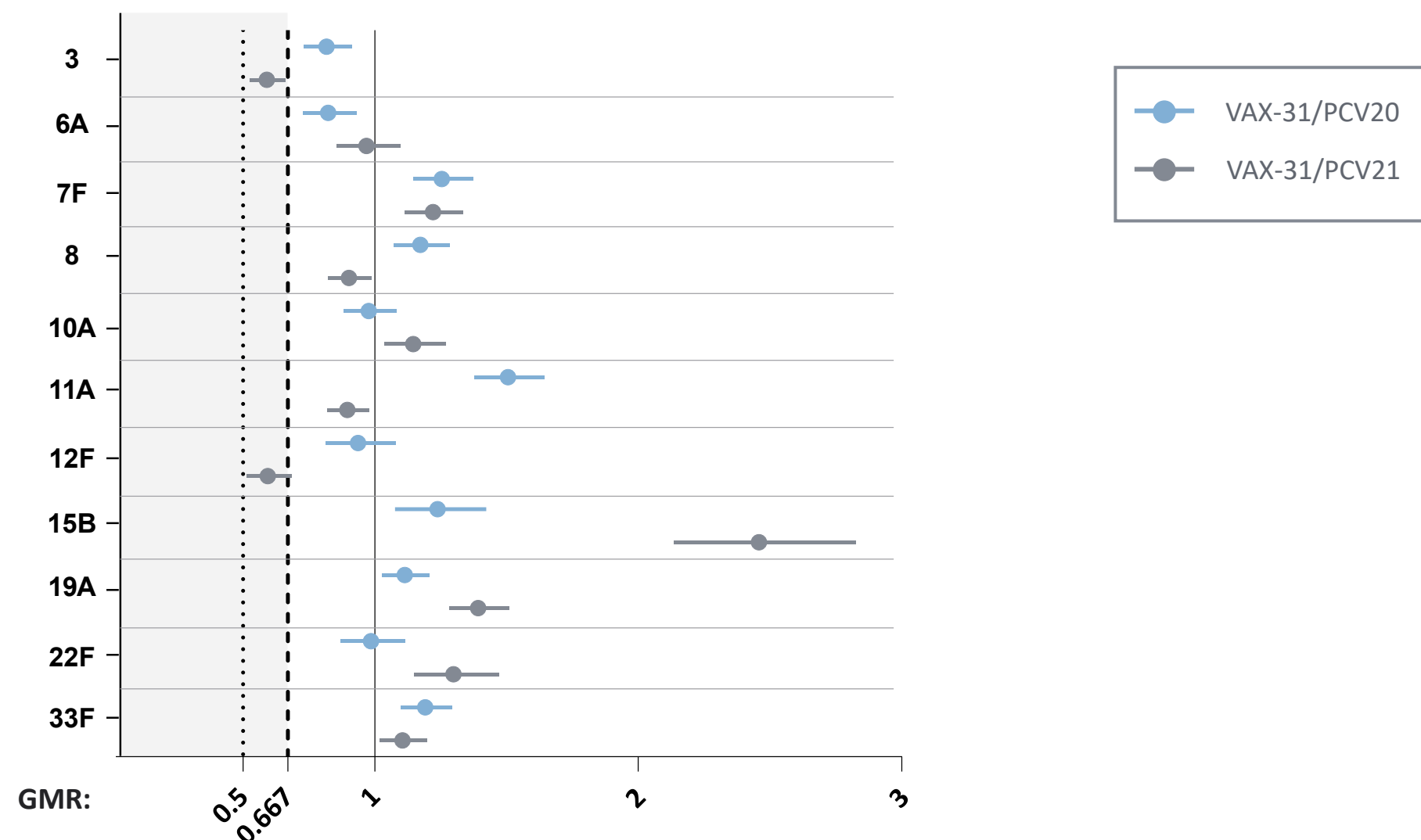
In Adults Aged ≥ 50 Years and 18-49 Years

11 STs in Common With PCV20 and PCV21

Met 11 of 11 ST OPA GMR Comparisons Per Prespecified NI Criterion¹ (LBCI >0.667) vs PCV20 and/or PCV21

CO-PRIMARY ENDPOINT GROUP 1

VAX-31 vs PCV20 & PCV21 on Common 11 STs

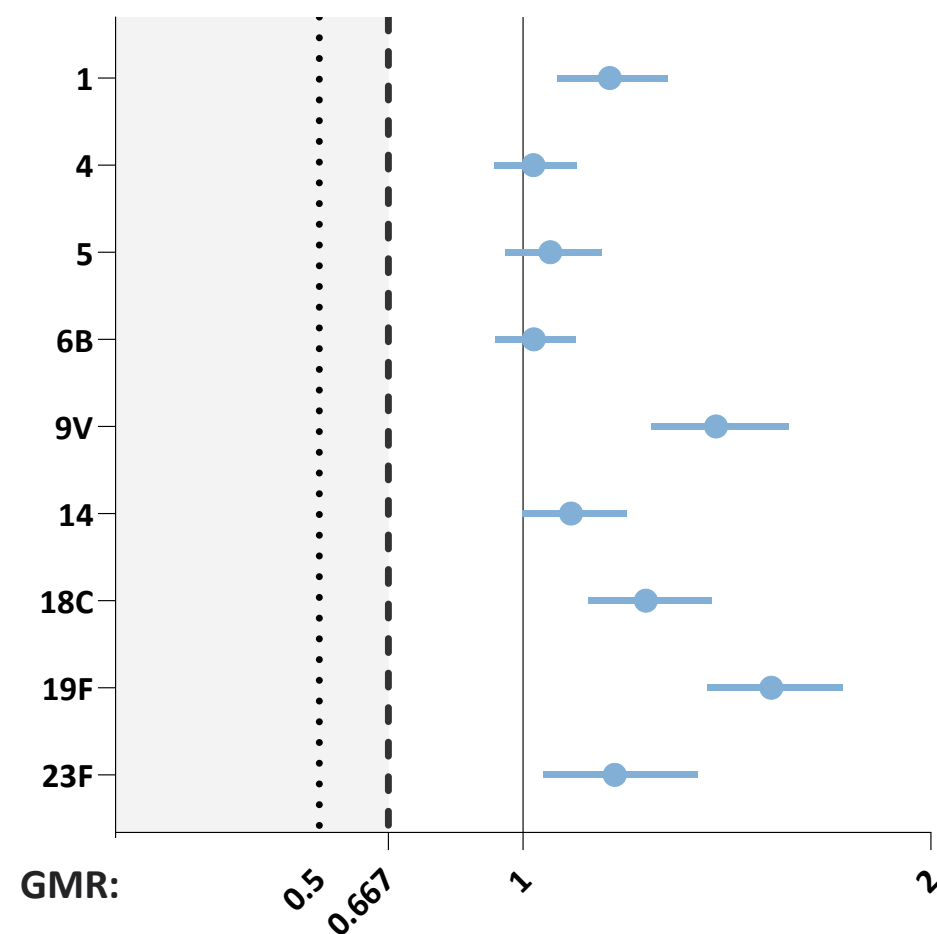


9 STs in Common With Only PCV20 and 8 STs Common With Only PCV21

Met 9 of 9 ST OPA GMR Comparisons vs PCV20 and 8 of 8 vs PCV21 Per Prespecified NI Criterion (LBCI >0.667)

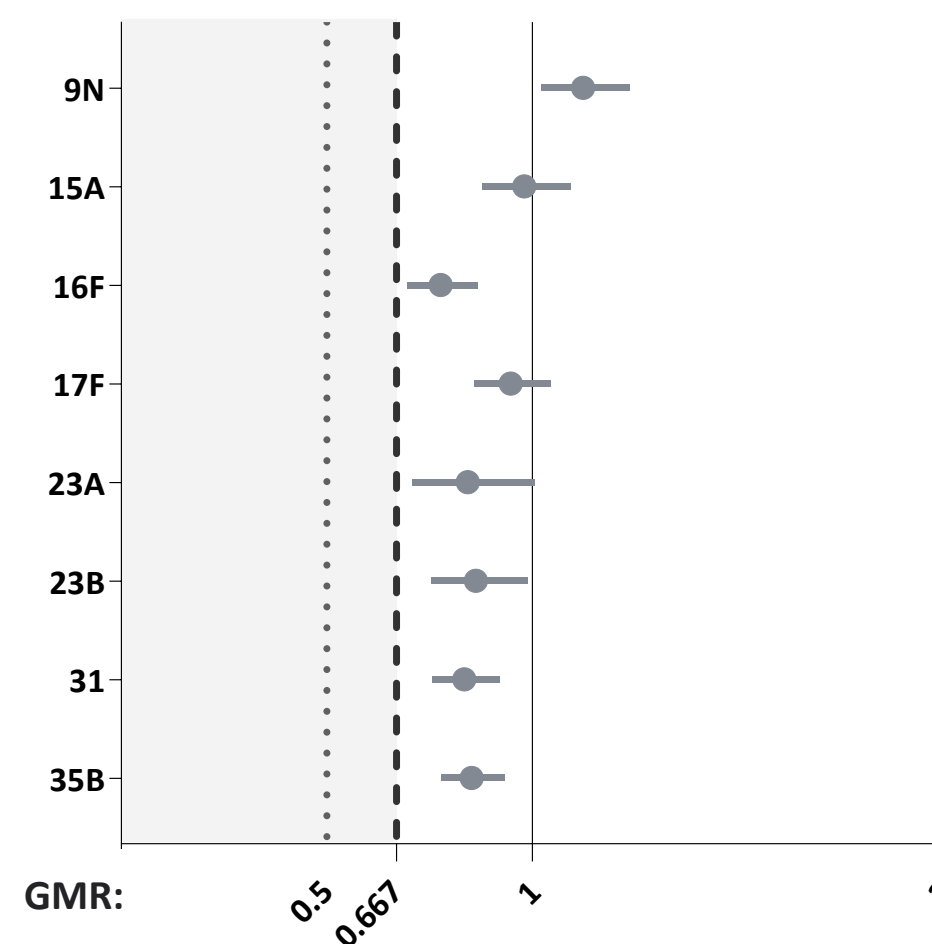
CO-PRIMARY ENDPOINT GROUP 2

VAX-31 vs PCV20: Shared 9 STs



CO-PRIMARY ENDPOINT GROUP 3

VAX-31 vs PCV21: Shared 8 STs

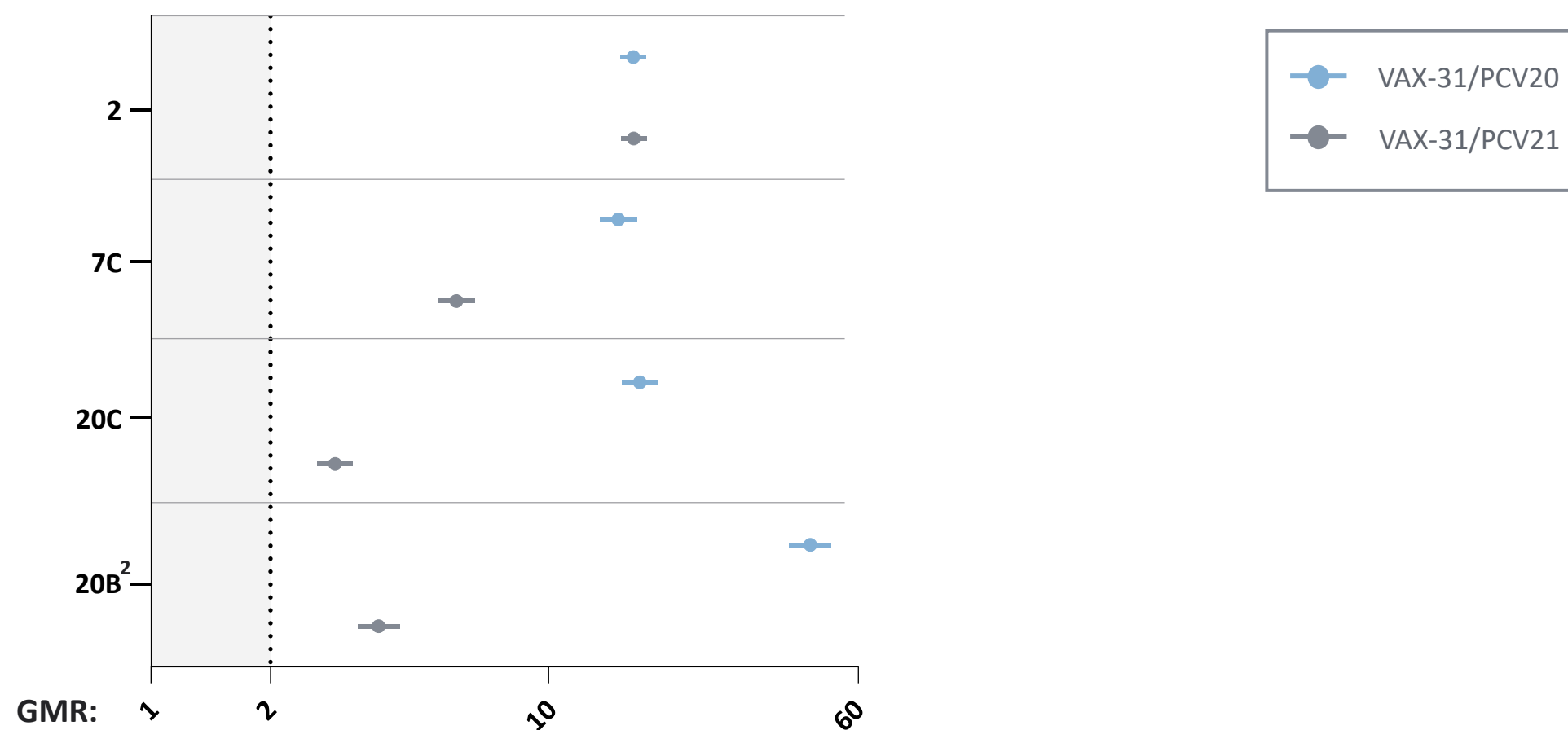


3 Unique VAX-31 STs and 20B

Met 4 of 4 ST OPA GMR Comparisons Per Prespecified Superiority Criterion (LBCI >2.0) vs PCV20 and/or PCV21¹

CO-PRIMARY ENDPOINT GROUP 4

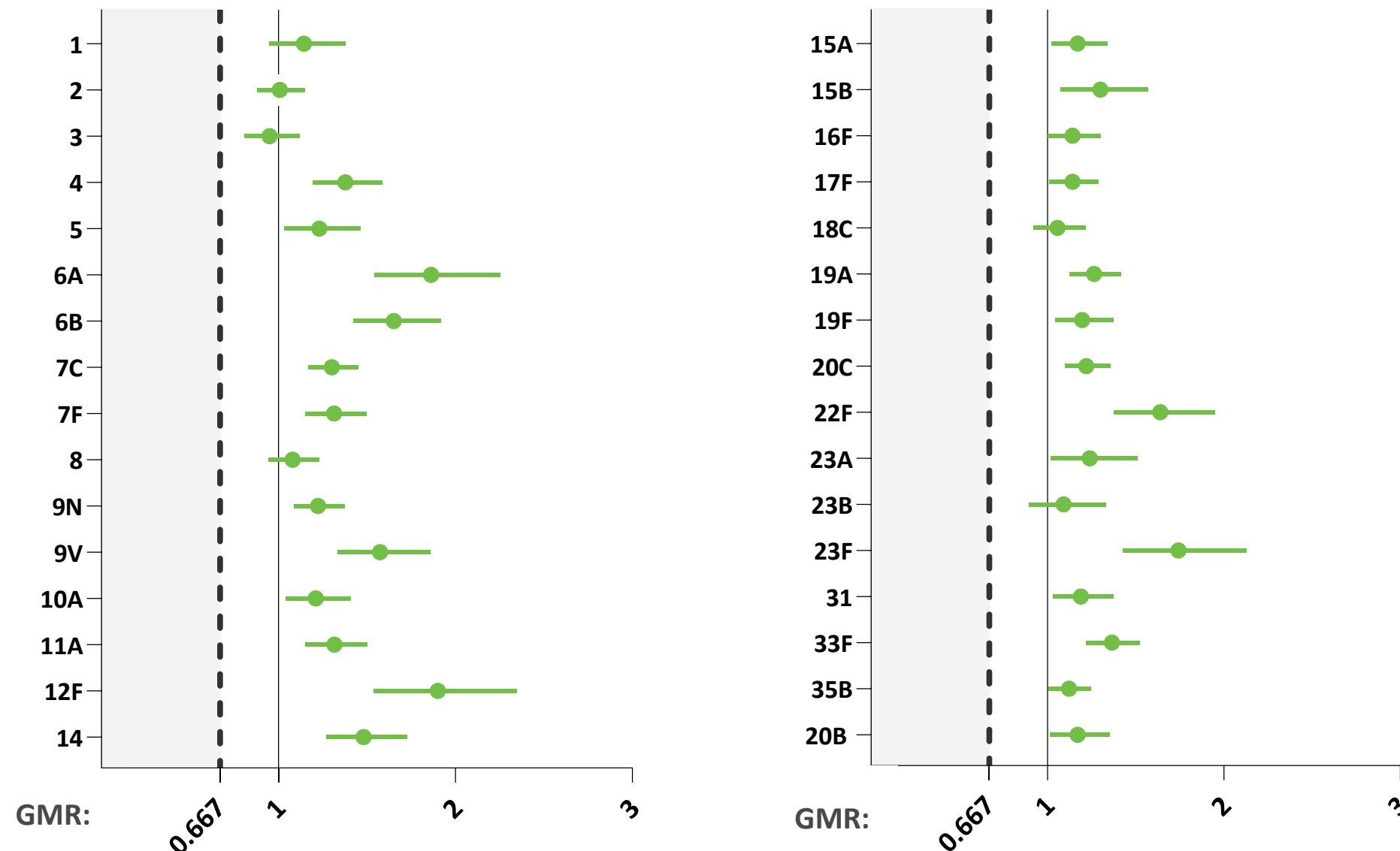
VAX-31 vs PCV20 & PCV21: 3 Unique STs + 20B²



Immunobridging Comparison in 18-49-Year-Olds vs 50-64-Year-Olds

Met Prespecified Primary Endpoint Across All 32 STs¹ (OPA GMR With LBCI >0.667)

VAX-31 Immunobridging OPA GMR Comparison (18-49 vs 50-64)

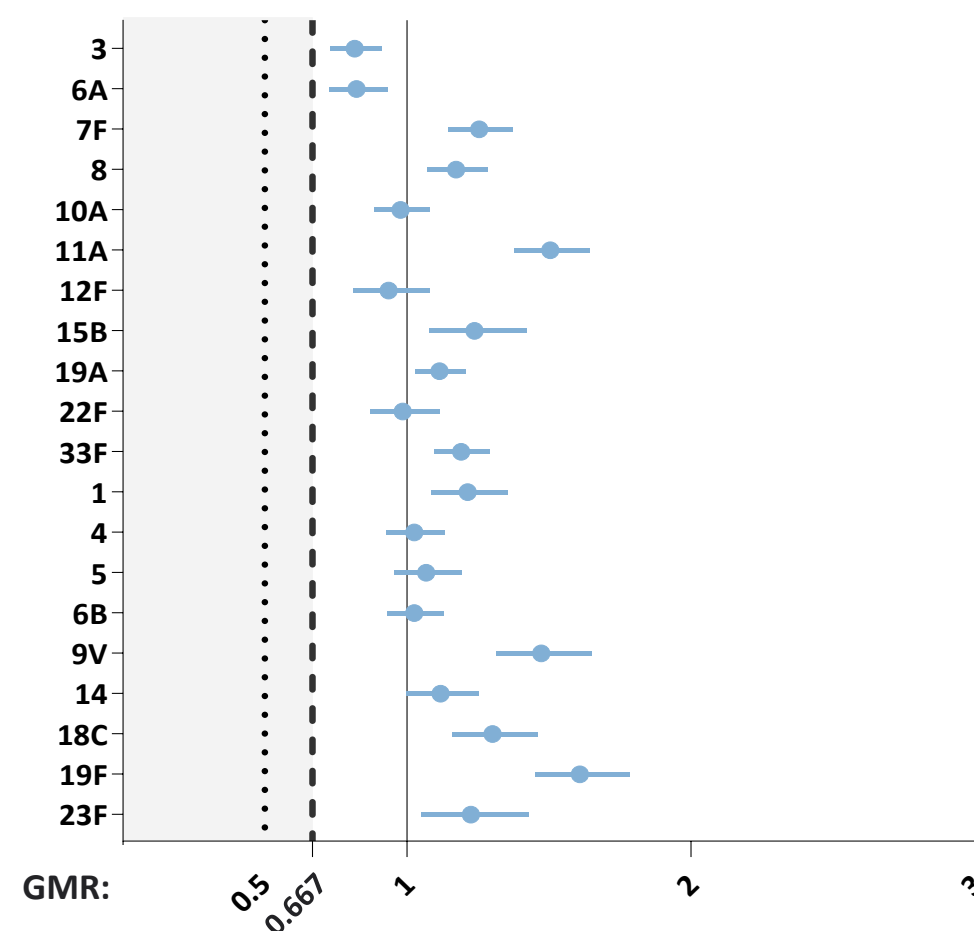


Comparator-Specific Assessments: VAX-31 Immune Responses vs PCV20 and PCV21

VAX-31 Met Noninferiority Criterion for 20/20 STs vs PCV20 and 17/19 STs vs PCV21

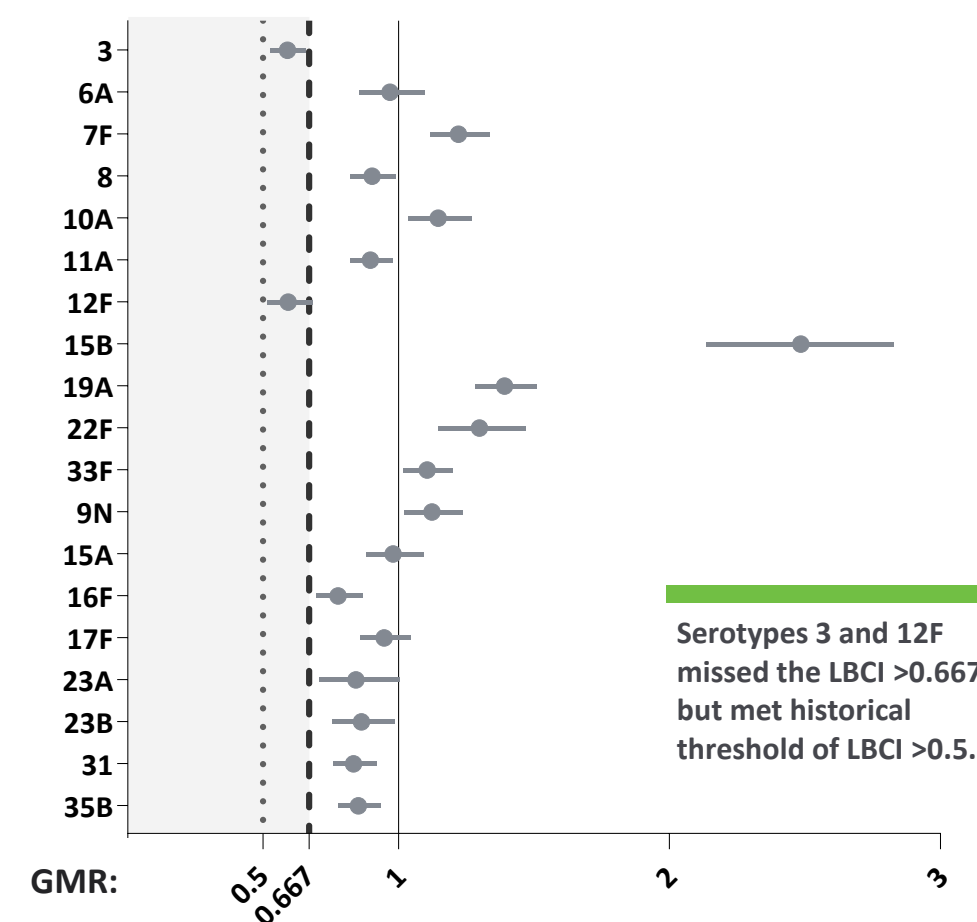
VAX-31 vs PCV20: Common 20 STs

OPA GMRs met prespecified NI criterion (LBCI >0.667) for 20 of 20 common STs



VAX-31 vs PCV21: Common 19 STs

OPA GMRs met prespecified NI criterion (LBCI >0.667) for 17 of 19 common STs



Serotypes 3 and 12F missed the LBCI >0.667 but met historical threshold of LBCI >0.5.

In the U.S., as PCV21 serotypes account for a larger share of adult disease coverage, U.S. regulators may focus more on the individual PCV21 comparison to VAX-31 in review of BLA submission.

VAX-31 Data Support Potential Best-in-Class Adult PCV Profile with Broadest Coverage Relative to SoC; Advancing Toward BLA Submission



Broad and robust immune responses observed across all 31 STs + 20B for all ages evaluated.
Met all prespecified co-primary and immunobridging endpoints.



VAX-31 was well-tolerated with a safety profile similar to PCV20 and PCV21.



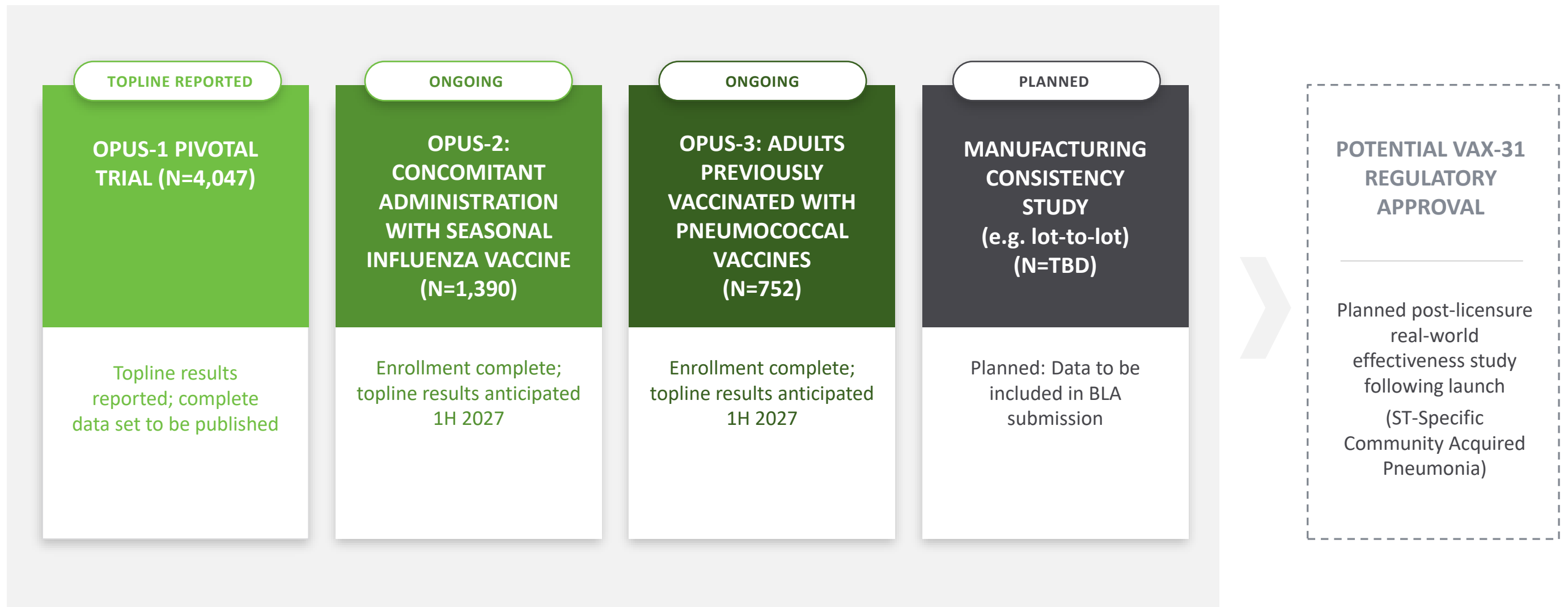
VAX-31 has the potential to offer significantly broader ST and disease coverage vs SoC vaccines.
Represents incremental 13-36% of IPD coverage¹ and incremental 19-31% of pneumococcal pneumonia coverage².



The OPUS-1 results support VAX-31's potential best-in-class profile, serving as cornerstone of the planned BLA, and further validate Vaxcyte's cell-free platform technology.

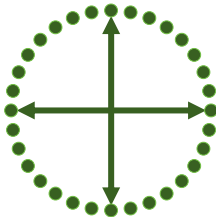
VAX-31 Program Next Steps

OPUS Phase 3 Program Serves as Cornerstone of Planned BLA Submission



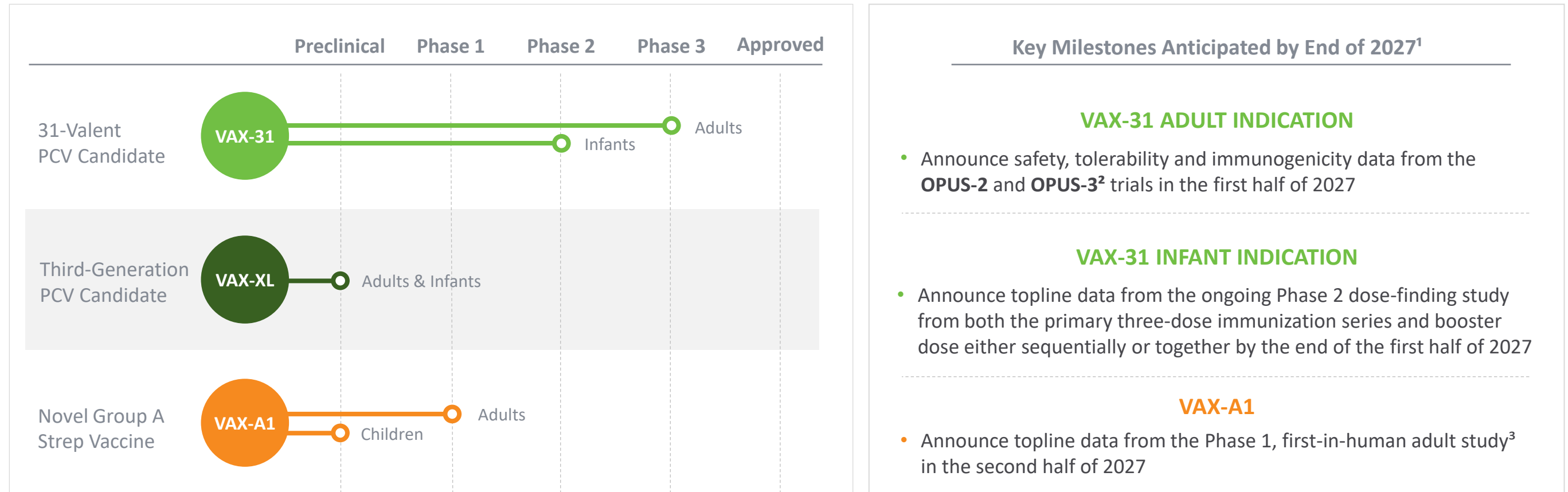
Foundation to Support Expected U.S. Commercial Launch

Integrated Manufacturing, Medical and Commercial Execution

Potential Best-in-Class Profile	Manufacturing Execution	Commercial Readiness for U.S. Launch
 Designed to cover 95% of IPD¹ and 88% of pneumococcal pneumonia² in U.S. adults 50 and older, an incremental 13-36% and 19-31% broader disease coverage than standard of care vaccines	 Establish commercial manufacturing readiness, including: - Existing supply chain sufficient to meet demand for U.S. adult launch - Expanding commercial-scale capacity to support future U.S. demand	 Medical affairs and commercial infrastructure buildout and launch strategy underway, including: - Engaging the scientific community - Defining the contracting and distribution strategy, including for U.S. retail pharmacies and large health systems

Pipeline of Vaccines with Multiple Near-Term Milestones

Leveraging Cell-Free Platform to Develop Broad-Spectrum Vaccines to Prevent Bacterial Diseases



Cell-Free Protein Synthesis Platform Unlocks Multiple Vaccine Applications

Facilitates design and production of vaccines beyond the reach of conventional methods, enabling:

- ✓ Superior site-specific conjugation chemistry
- ✓ Production of “tough-to-make” protein antigens that conform to target pathogens
- ✓ Speed, flexibility and scalability

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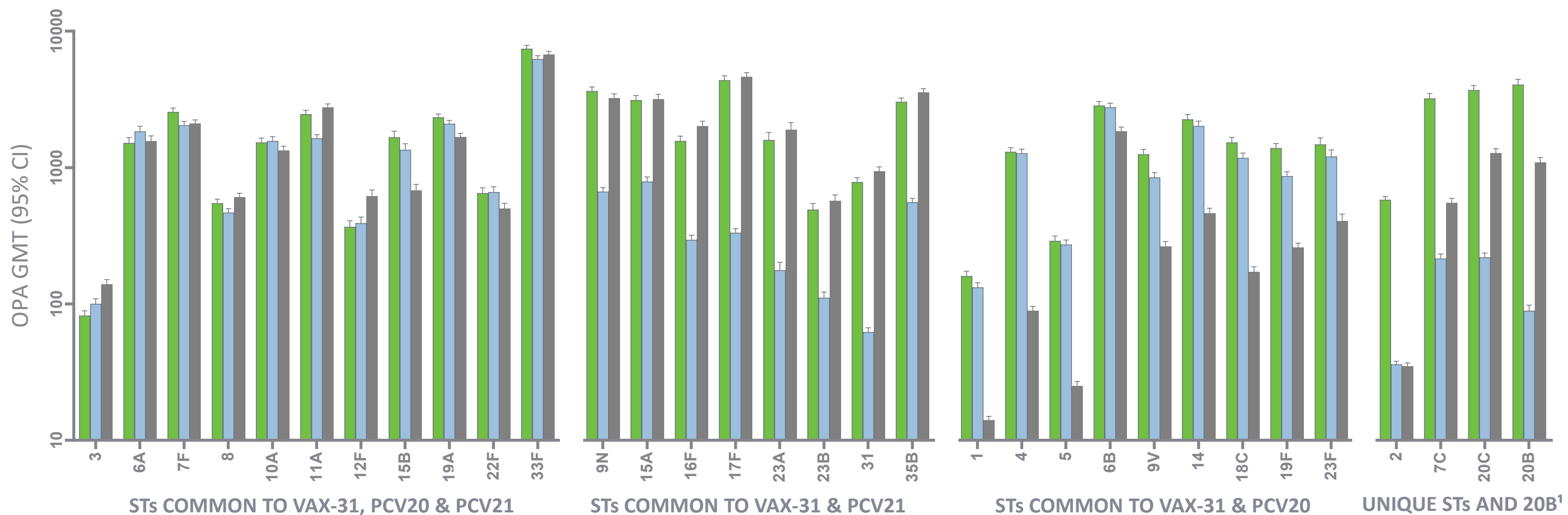
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Appendix

VAX-31 Demonstrated Robust OPA GMT Immune Responses

OPA GMTs Compared Across VAX-31, PCV20 and PCV21

VAX-31
PCV20
PCV21



VAX-31 Demonstrated Robust IgG GMC Responses

