



L I F F E Y

V A X

EXECUTIVE SUMMARY
JULY 8TH, 2018

Liffey/Vax Expanded Coverage Twenty-Valent Pneumococcal Conjugate Vaccine (ePCV20)

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New “Liffey/Vax ePCV20”: Simplifying Coverage Expansion

- Separate standalone vaccine
- Replaces **BOTH** Prevnar 13[®] (Pfizer) and Pneumovax[®] 23 (Merck) in older adults
- Novel *Streptococcus pneumoniae* Conjugate Vaccine
- Composition reflects current IPD serotypes causing 93% of invasive disease in US adults
 - Contains clinically relevant serotypes identified by CDC from 2016-2017
- Indication: Prevention of pneumococcal diseases in adults ≥50 years
 - Provides expansion option for children ages 2 to 18 years

Liffey/Vax ePCV20 Description

- Pneumococcal conjugate vaccine containing 20 polysaccharides conjugated to CRM₁₉₇
- CRM₁₉₇ carrier protein
- Established CDAP chemistry
- Aluminum salt free (No adjuvant)
 - Vials
 - Non-siliconized syringes
- Administration: single 0.5mL IM injection

Liffey/Vax ePCV20: Addresses Antimicrobial Resistance

- Covers major contributing serotypes to antimicrobial resistance
- Serotypes 3, 6C, 19A, 23A, 23B, and 35B
- 35B a major emerging cause of antimicrobial resistance IPD

“Original Liffey/Vax ePCV15”: Adapting to a Changing Epidemiology

- Original Liffey/Vax ePCV15
 - Complemented Prevnar 13[®]
 - One dose of “Liffey/Vax ePCV15” for EACH dose of Prevnar 13[®] in Adults
 - Dose 1: Prevnar 13[®]; Dose 2: Liffey/Vax ePCV15
 - Proposed to replace Pneumovax[®] 23 in adults aged 65 years and older
 - Novel *Streptococcus pneumoniae* Conjugate Vaccine
 - Contained only clinically relevant serotypes not found in Prevnar 13[®]
 - IPD serotypes causing invasive disease (all ages) in 2005-2015
 - Serotypes: 6C, 8, 9N, 10A, 11A, 12F, 15A, 15B, 15C, 16F, 22F, 23A, 23B, 33F, 35B

MEDICAL NEED: COVERAGE

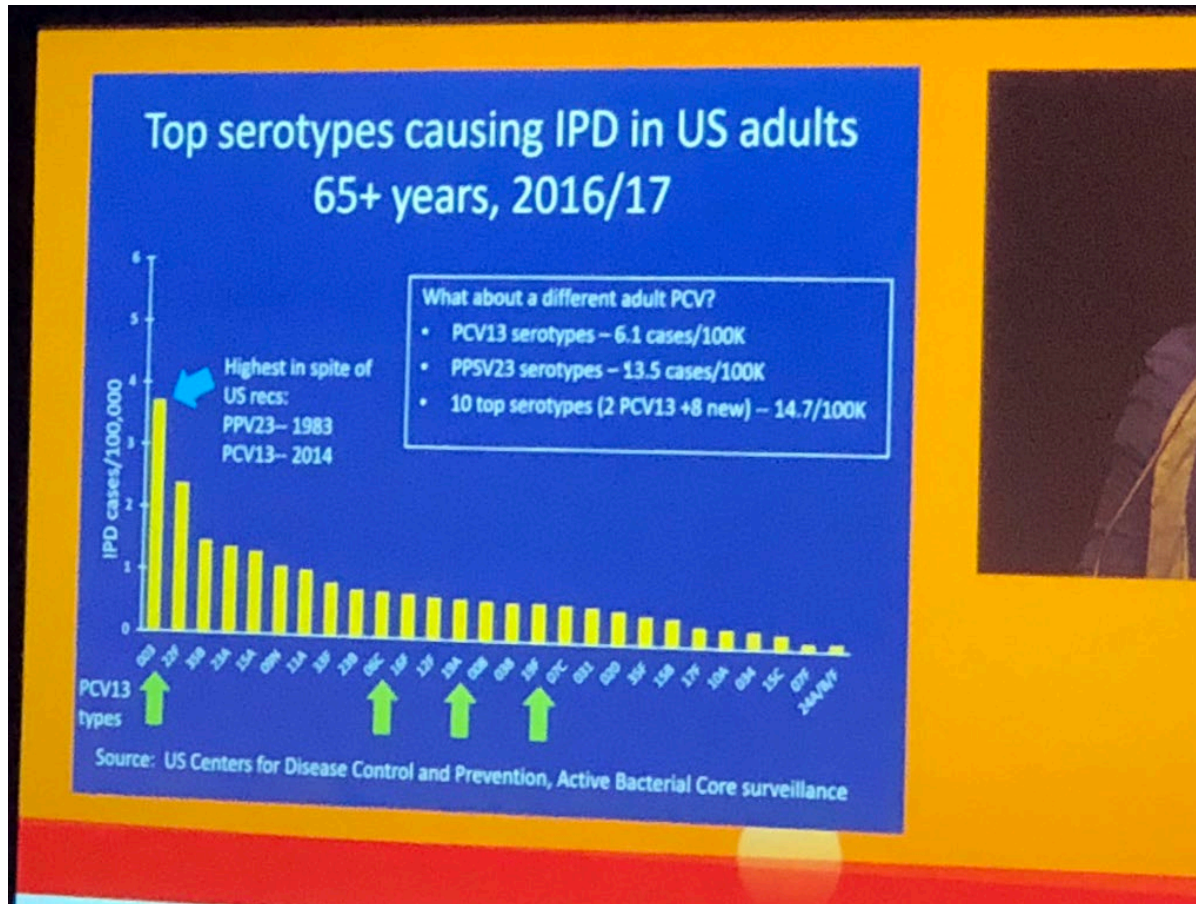
Prevnar 13[®]: Coverage Problem

- Pevnar 13[®] provides inadequate coverage
 - Significant residual disease & selective pressure increasing disease caused by excluded serotypes
 - >13,500 IPD cases in adults aged ≥ 65 years in US (2013)
 - Pevnar 13[®] does not protect against circulating strains causing ~75% of disease in adults
 - 18 pneumococcal strains cause ~ 90% current clinical disease
 - Only 3 serotypes of Pevnar 13[®] in top 90% of US adult disease

Current CDC US Recommendation

- Current ACIP (US CDC) pneumococcal vaccine recommendation
 - Adults aged ≥ 65 years
 - Two-dose schedule at least a year apart
 - Dose 1: Prevnar 13[®]
 - Dose 2: Pneumovax[®] 23
- The sole purpose of Pneumovax[®] 23 is to expand coverage
- One dose of Pneumovax[®] 23 given for EACH dose of Prevnar 13[®]
 - Major market driver is for a Pneumovax[®] 23 replacement

Changing Epidemiology of US Adult IPD



Serotypes Causing Invasive Disease: New issues in Developed and Developing Countries

Plenary Session: BMGF Symposium: Future Strategies for Pneumococcal Conjugate Vaccination

11th International Symposium on Pneumococci and Pneumococcal Diseases, Melbourne, Australia 15-19 April, 2018

Cynthia G. Whitney, MD, MPH

Chief, Respiratory Diseases Branch

Division of Bacterial Diseases

National Center for Immunization and Respiratory Diseases

Centers for Disease Control and Prevention

Adult PCV Composition: CDC Recommendation

Conclusions

- Children <5
 - PCVs controlling strains causing preponderance of invasive disease in developed countries
 - Adding ~7 serotypes would target small burden (~3-5 cases/100,000 children)
- Adults 65+
 - Serotype 3 remains common, even with recs for PCV13 (U.S.) and PPV23; differs from other PCV antigens
 - Indirect effects largely controlling other VTs
 - Vaccines with 8-10 antigens would target substantial burden
- Limited review – including more countries would be helpful
- Top NVTs vary between settings – why?

Serotypes Causing Invasive Disease: New issues in Developed and Developing Countries

Plenary Session: BMGF Symposium: Future Strategies for Pneumococcal Conjugate Vaccination

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Minimum composition for Adult Vaccine in the US is:

- PCV13 serotypes: 3, 19A
- New Serotypes: 6C, 9N, 11A, 12F, 15A, 16F, 22F, 23A, 23B, 33F, 35B

Cynthia G. Whitney, MD, MPH

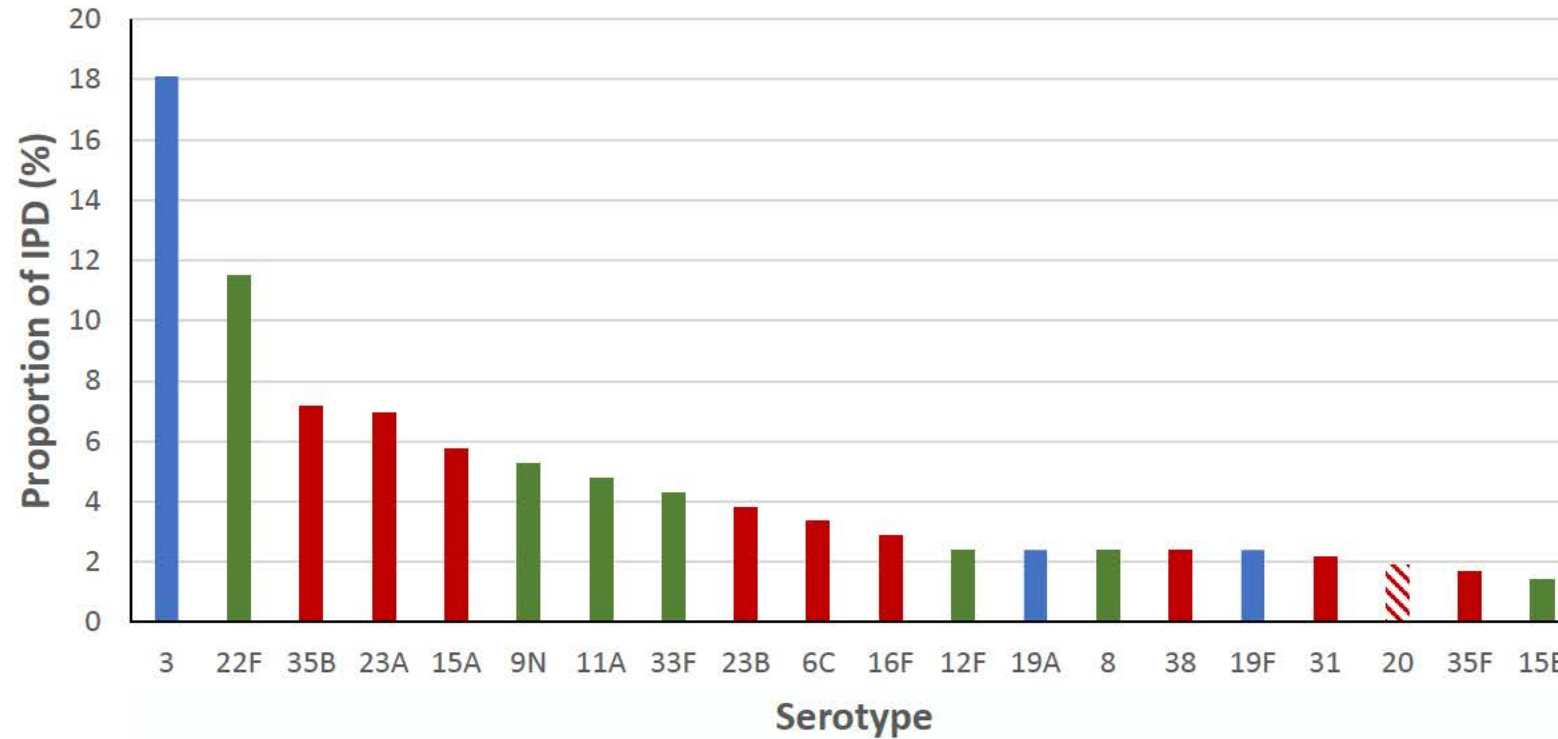
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Coverage Problem Today: US (Adults)



- Pevnar 13 Serotypes
- Pneumovax 23 Serotypes
- Unique Liffey/Vax ePCV20 Serotypes



Serotype 20: Current circulating strain is designated 20B.
Only Liffey/Vax ePCV includes 20B

Whitney, C (CDC). Serotypes Causing Invasive Disease; New issues in Developed and Developing Countries. ISPPD11, April, 2018

New “Liffey/Vax ePCV20”: Simplifying Coverage Expansion

- Composition reflects current IPD serotypes causing 93% of invasive disease in US adults
 - Contains clinically relevant serotypes identified by CDC data from 2016-2017
 - Prevnar 13[®]/Pneumovax[®] 23 Serotypes: 3, 8, 9N, 11A, 12F, 15B, 19F, 19A, 22F, 33F
 - Unique Liffey Serotypes: 6C, 15A, 16F, 20(B), 23A, 23B, 31, 35F, 35B, 38
- Serotypes in Liffey/Vax ePCV20 preferred by CDC over Pfizer PCV20 or Merck PCV24
 - Pfizer PCV20 in clinical stage of development
- Indication: Prevention of pneumococcal diseases in adults ≥50 years
 - Provides expansion option for children ages 2 to 18 years

Competitive Environment: PCV

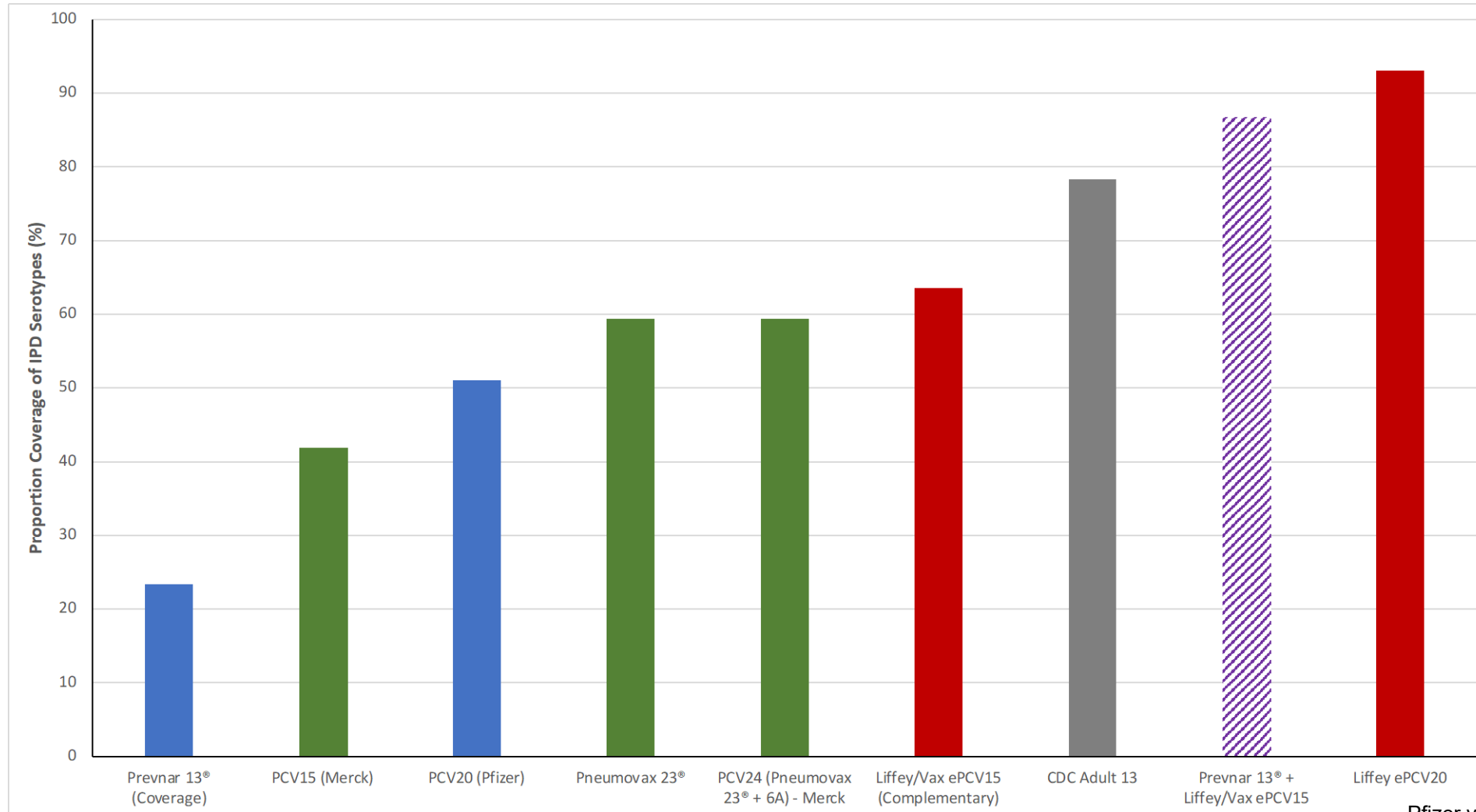
		Vaccine Serotype Composition																																		
Company	No. Serotypes	1	2	3	4	5	6A	6B	6C	7F	8	9N	9V	10 A	11 A	12 F	14	15 A	15 B	15 C	16 F	17 F	18 C	19 A	19 F	20 A	20 B	22 F	23 F	23 A	23 B	31	33 F	35F	35B	38
Pfizer	7																																			
GSK	10																																			
Serum Institute India	10																																			
Panacea Biotech	10																																			
Pfizer	13																																			
Affinivax/Astellas	13																																			
PnuVax	13																																			
SK Chemicals	13																																			
LG Life Sciences	13																																			
Walvax Biotechnology	13																																			
Biological E	14																																			
Merck	15																																			
Pfizer	20																																			
Merck	23																																			
Merck	24																																			
CDC Adult Minimum	13																																			
Liffey/Vax	15																																			
Liffey/Vax	20																																			

Yellow = Serotypes only in Liffey/Vax ePCV formulations.

Synflorix was never approved in the US but was approved ex-USA, including Europe.

Affinivax uses a novel carrier protein that they hope will get greater coverage against additional pneumococcal serotypes.

Hypothetical Coverage (%) of Serotypes Causing IPD in US Adults 65+ years (2017)



Whitney CDC
Recommendation

PCV: US Adult ≥65 years Coverage

	Coverage (%)
Liffey/Vax ePCV20	93.0
Prenvar 13[®] + Liffey/Vax ePCV15	86.9
CDC Adult Minimum	79.0
Liffey/Vax ePCV15	63.5
PCV24 (Pneumovax 23[®] + 6A; Merck)	59.4
Pneumovax 23[®]	59.4
PCV20 (Pfizer)	51.1
PCV15 (Merck/MSD)	42.0
Prenvar 13[®]	23.4

- Prenvar 13[®]: Coverage of IPD isolates provided by Prenvar 13[®] in a given region
- PCV23: Projected coverage of IPD isolates by making the Pneumovax[®] 23 serotypes into a 23-valent conjugate vaccine
- PCV24: Projected coverage in a region by a PCV comprising the serotypes of Prenvar 13[®] + the 11 serotypes of Pneumovax[®] 23
- PCV15: Merck investigational vaccine comprising serotypes in US Patent 8,192,746
- PCV20: Pfizer investigational vaccine comprising serotypes in US Patent 9,492,559
- Prenvar 13[®] + ePCV: Projected coverage by a vaccine formulation comprising Prenvar 13[®] + conjugates in Liffey/Vax ePCV

“Liffey/Vax ePCV20”: Target Product Profile

- Adults Aged ≥ 50 years
 - Expands Coverage Choices
 - No current ACIP recommendation
- Adults aged ≥ 65 years
 - Single dose Liffey/Vax ePCV20 will replace **BOTH** Prevnar 13[®] AND Pneumovax[®] 23 in current recommended ACIP Schedule
- Major new market opportunity
- IP creates opportunities for alternative regional combinations
- Estimated global annual gross revenues: >\$2.5B (USD)
- Target launch date: 2023

FDA Pre-IND Meeting

June 4th, 2017

FDA Pre IND Meeting Outcomes

June 4, 2017

- Agreement that there is an unmet medical need alternate composition vaccine
- Agreement on Phase 1-2 trial design
- Agreement that pivotal trial will be a non-inferiority trial comparing OPA responses
 - Compare common serotypes with Pneumovax[®] 23 (and Prevnar 13[®])
 - Compare new serotypes to placebo (or alternative)
- Agreement that no clinical demonstration of efficacy necessary for registration
- Agreement on conjugate QC tests for GMP release of clinical supplies

Adult Regulatory Pathway

- Licensure based on OPA responses
- No demonstration of efficacy required
- Comparison with Pneumovax[®] 23 for common serotypes
- Criteria for approval of remaining serotypes will be similar to those used for Prevnar 13[®] for a serotype not in Pneumovax[®] 23
 - Liffey/Vax team has successfully negotiated similar licensure criteria several times

Liffey IP Portfolio

“Liffey/Vax ePCV”: IP Position

- Patent Application: PCT/US2017/025621
 - Priority Date: 03/31/2016
 - Unique compositions
 - Covers all major contributing serotypes to antimicrobial resistance
 - Serotype 20B vaccine composition (current circulating strain)
- Provisional Application 62/568,164
 - Priority Date: 10/04/2017
 - Only known polysaccharide structures for 23A and 23B
 - Unique 23A and 23B containing compositions
- No competition with Pfizer, Inc.
 - Patents US 8,895,024 & US 9,399,060: Covers Serotype 3 + Prevnar 7 serotypes
 - PTAB decision 10/20/2017; Case IPR2017-01223: MSD Corp. vs. Wyeth, LLC.
- Exclusive license from UAB for serotype 6C
 - US 8,481,054
 - EP 1 976 974

Summary

Liffey/Vax ePCV20: Summary

- “Next Gen” PCV
- Replaces BOTH Prevnar 13[®] and Pneumovax[®] 23 in adults
- Expansion of Population Coverage
 - Not limited to adults ≥ 65 years
 - 140M adults aged ≥ 50 years in the US alone
- Target BLA Approval: 1H 2023

Supplementary Material

Pneumovax[®] 23

Pneumovax[®] 23

- Unconjugated polysaccharide (PS) vaccine
 - Approved in the US in 1984
 - Serotype composition covered 80%-90% of US adult IPD occurring before 1980
- Current US Indications
 - Prevention of invasive pneumococcal disease
 - Adults ≥ 65 years only
 - Limited use in <65 years
 - “Higher risk” patients (may receive one additional booster 5 years later)
- Significant local injection reactions and efficacy questions
- Does not provide long term protection
- PS suppresses immune responses to self and PCV
- Strong medical need for a conjugate vaccine “replacement”

REGULATORY STRATEGY

Target Indications: Initial

- Adults (basis for initial clinical POC and initial FDA approval)
 - For protection of adults ≥ 50 years:
 - Invasive disease caused by the serotypes in the vaccine
 - Bacteremic pneumonia
 - Single-dose regimen
 - Plus potential 5 year boosters offer significant upside potential
 - May be eligible for accelerated regulatory pathways to meet medical need
- Pediatrics
 - Aged ≥ 2 years to <18 years
 - Likely routine use at 2 years and catch-up to 5 years
 - Substantial upside potential
 - Simplified POC and regulatory approval program

Requirements for Market Authorization: Pre-Clinical

- Animal immunogenicity data
 - IgG and OPA responses for all 15 serotypes as a combination vaccine
- Safety toxicology in rabbits (N+1)
 - Human dose to be tested
 - Single dose in adults and pediatrics (aged 2 years to <18 years) = 2 human doses required in toxicology study
- GMP released clinical supplies
 - GMP facilities, process, QC tests, and QA release

Adult Regulatory Pathway

- Licensure based on OPA responses
- No demonstration of efficacy required
- Comparison with Pneumovax[®] 23 for common serotypes
- Criteria for approval of remaining serotypes will be similar to those used for Prevnar 13[®] for a serotype not in Pneumovax

Requirements for Market Authorization: Clinical Overview

- Phase 1-2 Protocol
 - Objective 1: Dose finding study based on opsonophagocytic assay (OPA)
 - Objective 2: Preliminary non-inferiority comparison to serotypes common with Pneumovax® 23 and Prevnar 13®
 - This reduces risk for Phase 3 by increasing likelihood of future success
 - Healthy adults 50 years and older
- Phase 3 protocols
 - Pivotal non-inferiority trial compared to Pneumovax® 23 and Prevnar 13®
 - Demonstration of clinical consistency of manufacturing
 - At least 3 GMP lots and at least one of each conjugate at commercial scale
 - Approximately 500 additional subjects for safety data to ~3000 total
- Additional Trials
 - Pediatrics: 2-<18 years

FDA Endorsed Regulatory Strategy



U.S. Food and Drug Administration
Protecting and Promoting Public Health

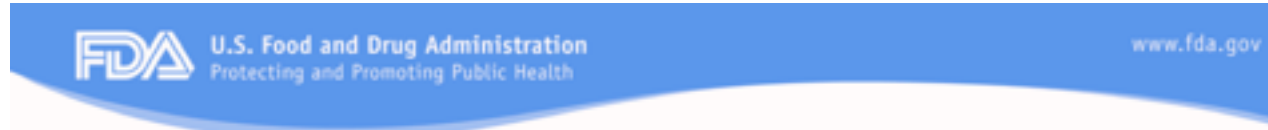
www.fda.gov

November 17, 2005 VRBPAC - Licensure Pathways for New Pneumococcal Vaccines in Adults

- Presentations
 - Changing epidemiology since PCV7
 - Use of opsonophagocytic assay (OPA)
 - Proposed development plans from manufacturers
- Committee discussion on licensure pathways
 - Immunogenicity vs clinical endpoint studies
- VRBPAC considerations
 - Emphasized the need for clinical endpoint studies while acknowledging the challenges
 - Accelerated Approval is a reasonable path to follow

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FDA Endorsed Regulatory Strategy

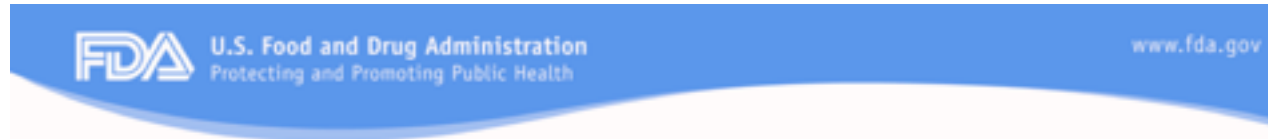


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FDA Endorsed Regulatory Strategy



Opsonophagocytic Assay (OPA)

- Opsonophagocytosis is an important mechanism of protection against pneumococcal disease.
- Opsonophagocytosis can be measured using the functional antibody assay (OPA) which is reasonably likely to predict clinical benefit.
- During Prevnar 13 studies in children OPA titers were used as exploratory endpoints.
- For Prevnar 13 studies in adults:
 - a high through-put version of the assay was validated – microcolony OPA.
 - comparison of OPA titers between the approved Pneumovax 23 vaccine and Prevnar 13 is a primary endpoint for phase 3 studies.

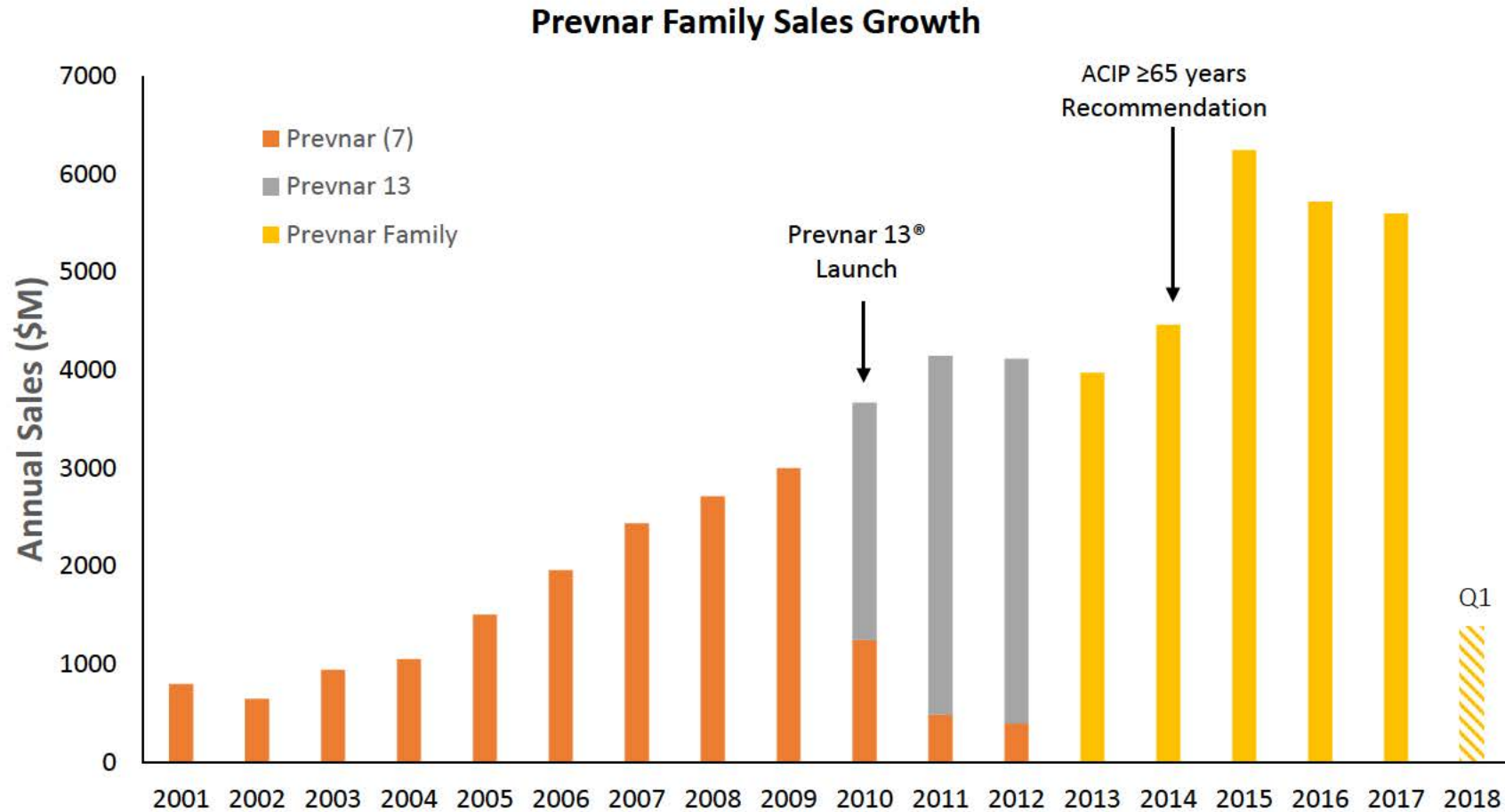
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MARKET ANALYSIS AND COMMERCIAL CONSIDERATIONS

Prevnar Family Cumulative Sales Growth

- \$55B total sales since launch (2001)
- \$5.6B sales (2017)
- ACIP Adult recommendation (2014)
 - Increase in 2015 sales by \$1.8B (39.9% increase over 2014)

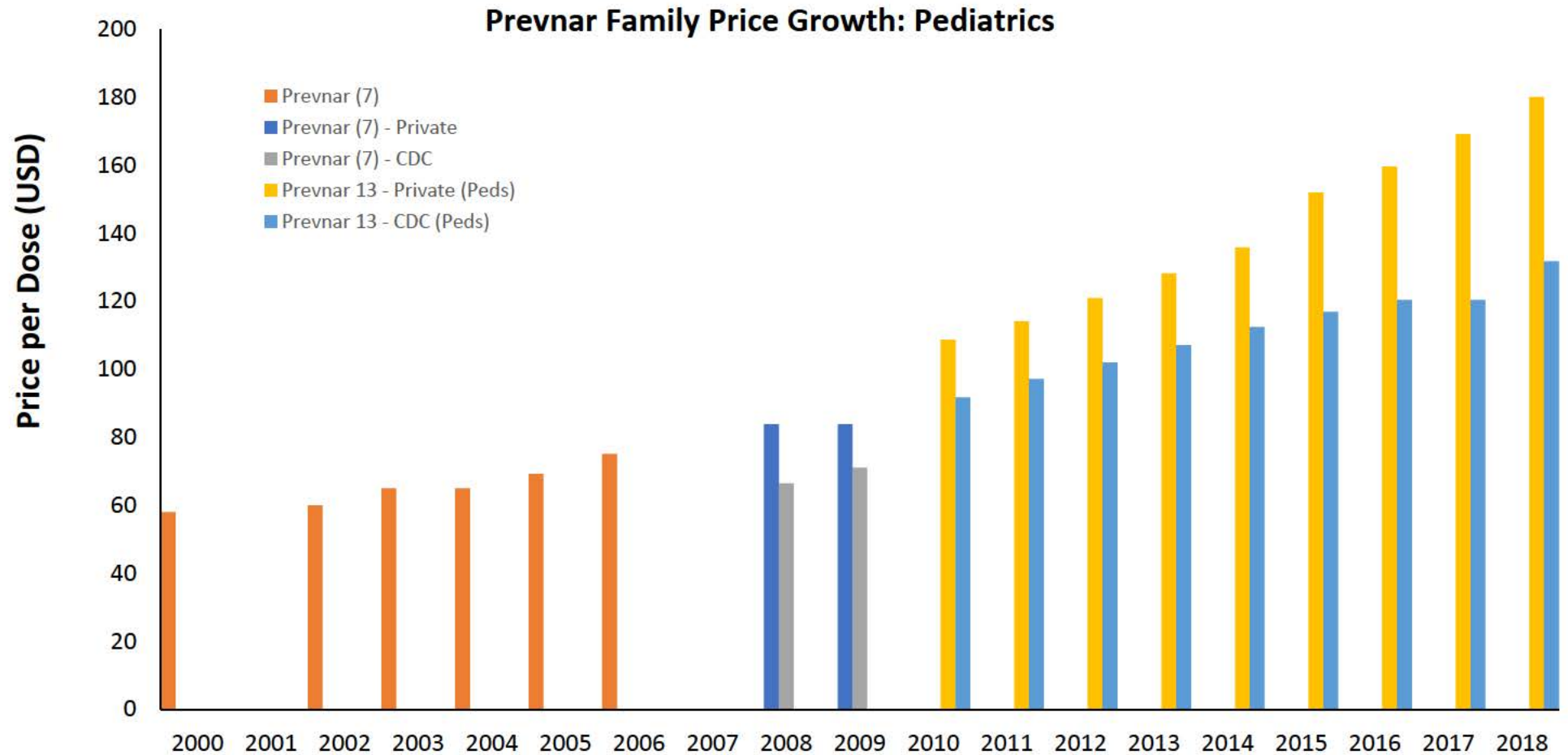
Prevnar Family Cumulative Sales Growth



Prevnar Family Sales Growth

- >300% increase in price since launch of Prevnar® (2001)
- Price growth factors:
 - Expansion of serotypes from 7 to 13 in 2010
 - 30% increase in price with launch of Prevnar 13® (2010)
 - Annual price increase
 - 6% annual price increase since 2010
 - ACIP Adult recommendation (2014)
 - Increase in 2015 sales by \$1.8B
 - 39.9% increase over 2014

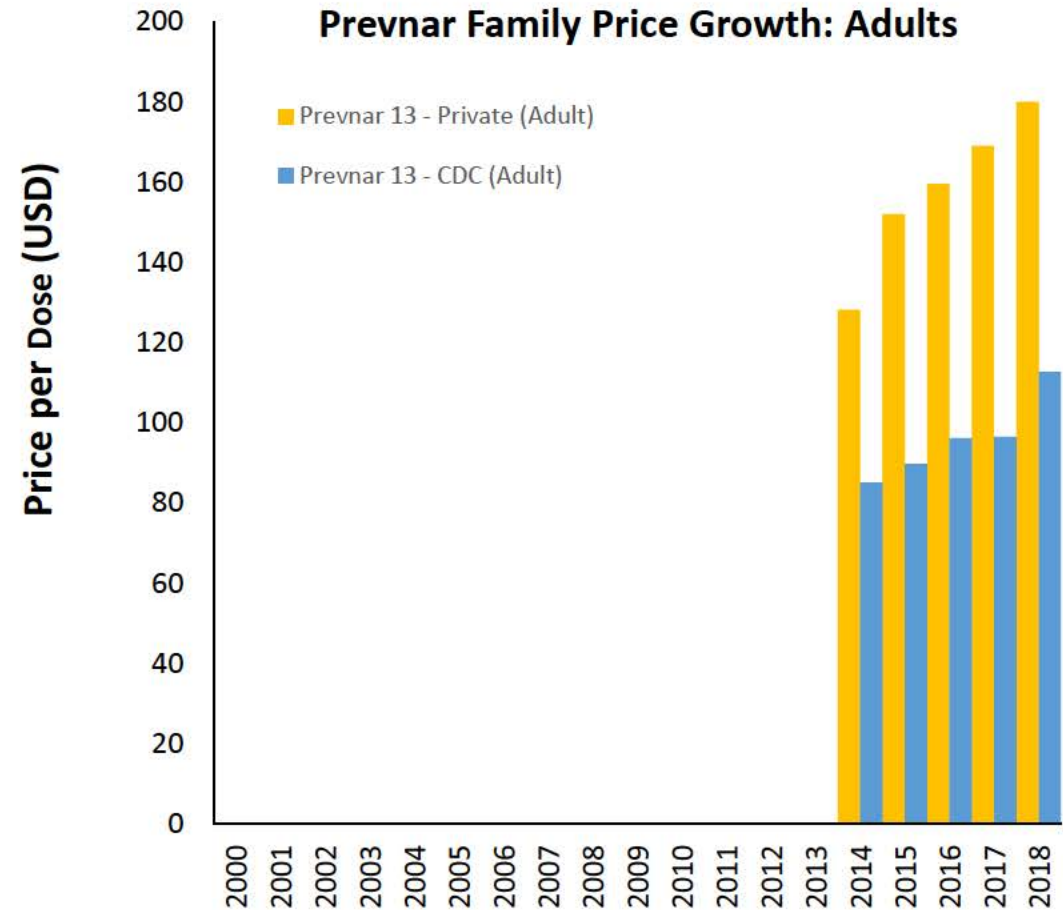
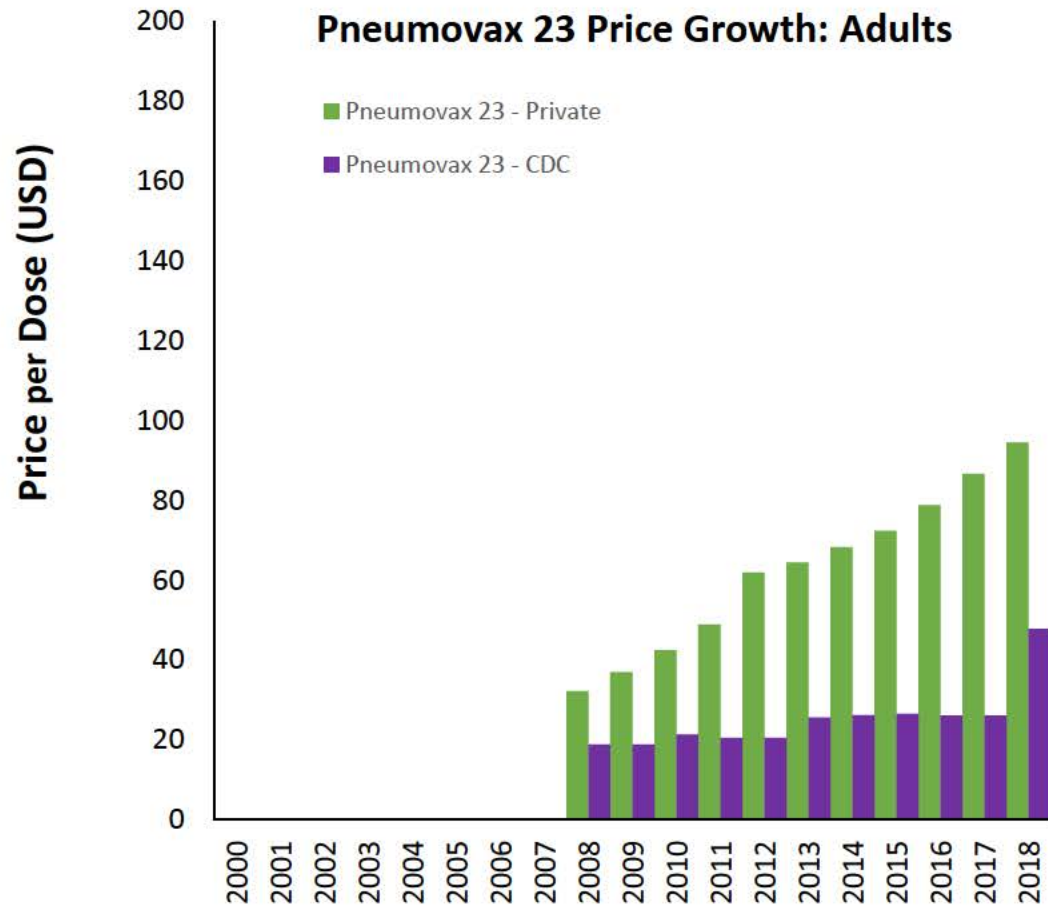
PCV13 Vaccine Pricing Growth: Pediatrics



Pneumococcal Vaccine Sales Growth: Adults

- 38% increase in sales of Prevnar 13[®] with Adult ACIP recommendation (2014)
 - 6% annual price increase
- >200% increase in price of Pneumovax[®] 23 since 2008
 - 42% increase in Medicare (CDC) price in 2018
 - 9% average annual price increase

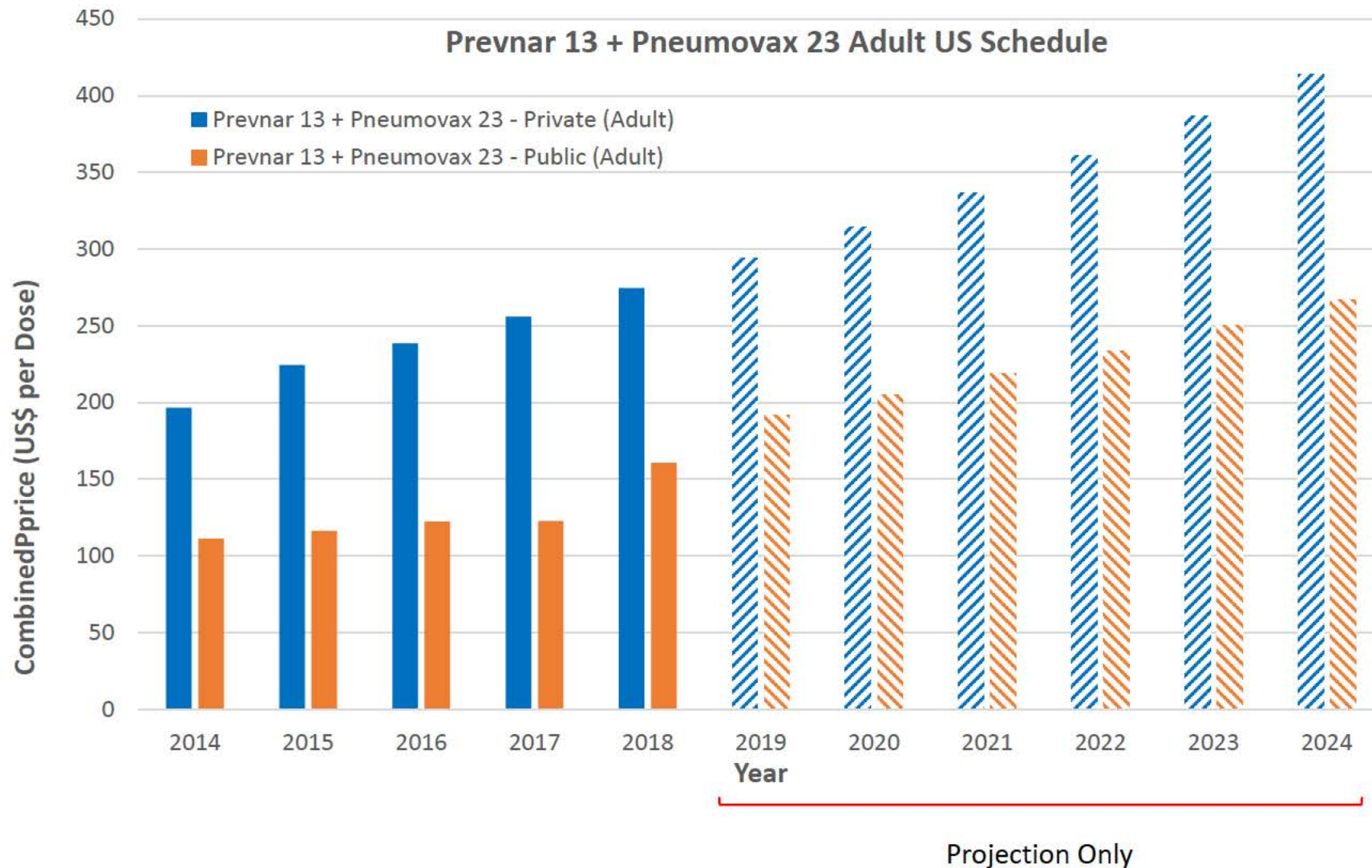
Pneumococcal Vaccine Pricing Growth: Adults



Pneumococcal Vaccines' Costs: Adults

- ACIP Schedule (Pneumovax 13[®] + Pneumovax[®] 23)
 - Total cost:
 - Medicare/CDC (≥65 years): \$160.54
 - Average 10.2% annual price increase/Median 4.8% annual price increase
 - Private market (50-64 years): \$274.56
 - Average 8.7% annual price increase/Median 7.3% annual price increase
 - Projected 2024 price of series
 - Medicare/CDC (≥65 years): \$267.08
 - Private market (50-64 years): \$413.91

Pneumococcal Vaccine Pricing Growth: Adults



Prevnar 13 Uptake: Adults ≥ 65 Years

- Medicare Parts A and B coverage
- Variable Uptake (Sep. 2016)
 - 43.2% had received one dose of Pneumovax 23
 - 31.5% had received Prevnar 13
 - 18.3% received both vaccines (ACIP schedule)
- Demographics of combined schedule uptake:
 - Hispanics: 6.8%
 - White: 19.5%
 - 65-69 years: 11%
 - 80-84 years: 24.3%

Liffey/Vax ePCV20 Commercial Drivers: Adults

- ACIP Recommendation
 - Replacing/Displacing Prevnar 13[®] & Pneumovax[®] 23
 - Simplified schedule (improves uptake)
 - Gives access to 50 to 64 years age group
- Pricing Strategy
 - Favorable positioning compared with combination Prevnar 13[®] /Pneumovax[®] 23 series

MANAGEMENT AND ADVISORY TEAM

Liffey/Vax Management Team

Bruce Forrest, MD, MBA



- SVP Wyeth Vaccines, 25 years in vaccine clinical trials and development
- Career responsibility for 25+ bacterial & viral vaccine programs at Chiron, Wyeth & Pfizer
- Clinical Team Leader, Prevnar[®] & Prevnar 13[°], FluMist[°], RotaShield[°], Menjugate[°]
- Career responsibility for 150+ vaccine clinical trials incl. 14 Phase III vaccine efficacy trials

Jack Love, Ph.D.



- Former Head, Worldwide Regulatory Affairs, Wyeth Vaccines
- Career responsibility for over 75 bacterial and viral vaccine programs
- Developed regulatory strategy for, and negotiated approval of, Prevnar[®], Prevnar 13[°] & Meningitec[°]
- 2011 Winner of Prix Galien Award for Prevnar 13[°]

Joseph Meehan



- President/Founder, Qtrade Canada Inc. (Canada's leading outsourced wealth management firm)
- M&A solicitor, Clifford Chance

Joseph O'Neill



- Former CCO ADIENNE SA
- Sanofi Genzyme Sr. Director Marketing, US Hematology & Oncology Business.
- Prior Sales and Marketing roles at J&J, Berlex Labs, Abbvie

Liffey/Vax Commercial Advisor



Geno J. Germano

- Independent Commercial Adviser
- Former President, Intrexon Corporation
- Director, Sage Therapeutics, Inc. & Bioverativ
- Former Group President, Global Innovative Pharma Business, Pfizer
- Former Corporate EVP/Group Manager, Wyeth Global Vaccines, Wyeth