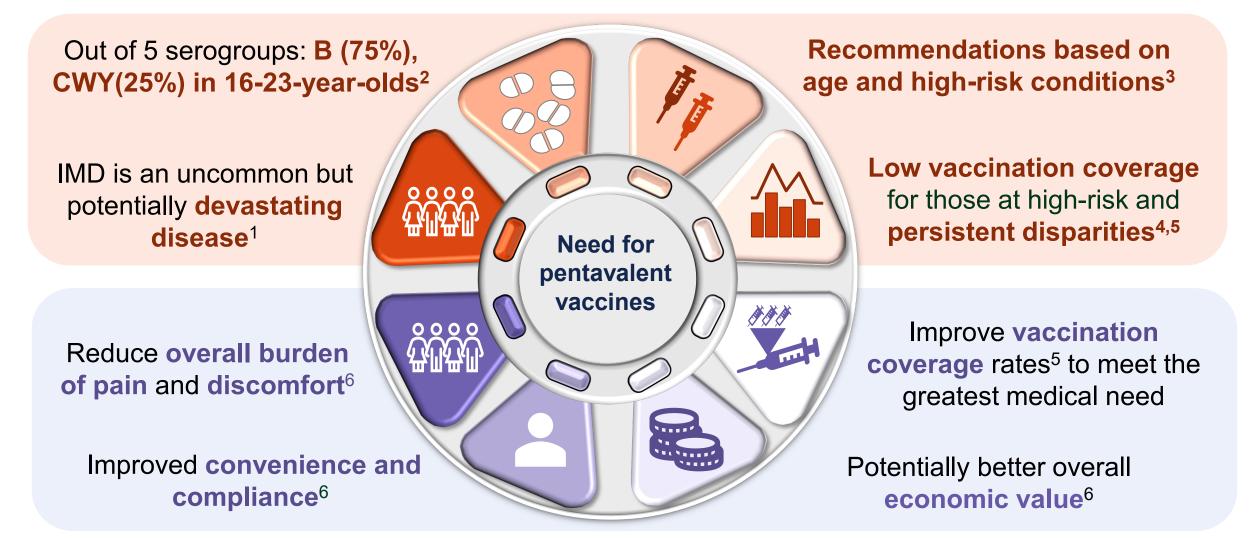


# MenABCWY for the prevention of Invasive Meningococcal Disease caused by serogroups A, B, C, W and Y

Wendy Sohn, MD Global Medical Lead Neisseria Vaccines

# **Concerted Prevention of IMD in Adolescents and Young Adults**



1. Mbaeyi S, et al. JAMA Pediatr 2020; 174 (9):843-851; 2. Enhanced Meningococcal Disease Surveillance Reports 2015-2022; 3. CDC Immunization Schedule 2024; 4. Pingali C, et al. MMWR Morb Mortal Wkly Rep 2023; 72(34):912-919; 5. Marshall G, et al. Clin Infect Dis 2022, 75(1):155-158; 6. Kroger A, et al. General Best Practice Guidelines for Immunization. [www.cdc.gov/vaccines/hcp/acip-recs/general-recs/downloads/general-recs.pdf]. Accessed on February 28<sup>th</sup>, 2024.

# MenABCWY Program Built on Antigenic Components of MenACWY<sub>CRM</sub> (Menveo) and MenB-4C (Bexsero)

Lyophilized MenACWY <sub>CRM</sub> (vial)	+	Liquid MenB-4C (prefilled syringe)	=	MenABCWY <sup>1</sup>
MenACWY <sub>CRM</sub> <sup>2</sup> 2010		MenB-4C <sup>3</sup> 2015		Anticipated 2025 <sup>1</sup>
Immunogenicity and Safety in Healthy 2 months-55 year-olds <sup>2</sup>		Immunogenicity and Safety in Healthy 10-25 year-olds <sup>3</sup>		Immunogenicity and Safety in Healthy 10-25 year-olds
Immunogenicity in high-risk patients <sup>4-6</sup>		Immunogenicity in high-risk patients <sup>7,8</sup>		
Persistence of immune response after 4-6 years <sup>9-11</sup>		Persistence of immune response after 4-7.5 years <sup>12</sup>		
Real-world effectiveness <sup>13</sup>		Real-world effectiveness <sup>14-16</sup>		

1. GSK Press Release April 16, 2024. https://www.gsk.com/en-gb/media/press-releases/gsk-s-5-in-1-meningococcal-abcwy-vaccine-candidate-accepted-for-regulatory-review-by-us-fda/; 2. Prescribing Information for <u>BEXSERO</u>; 4. Isitt C et al, *HIV* Med. 2023; 24(9):979-989; 5. Kimura A et al, *Clinical and Vaccine Immunology*. 2011; 18(3):483-486; 6. Findlow J et al, *Vaccine*. 2015; 33(29):3322-30; 7.Martinon-Torres F et al, *Pediatrics*. 2018; 142(3): e207174250; 8. Robin C et al, *Clin Microbiol Infect*. 2022, 28(12):1609-1614; 9. Tipton et al, *Vaccine*. 2019; 37(42):6171-6179; 10. Baxter et al, *Pediatr Infect Dis J*. 2014; 33(11):1169-1176; 11. Jacobson et al *Pediatr Infect Dis J*. 2013; 32(4):e170-177; 12. Watson PS et al. *Expert Review of Vaccines*. 2019; 18:4, 343-352; 13. Hyoung Im J et al, *Vaccine*. 2020; 38 (730-732); 14. McMillan M et al, *Clin Infect Dis*. 2021; 73(1):e233–7; 15. Wang B et al *Lancet Infect Dis*. 2022; 22:1011–20; 16. Wang B et al. *J Infect*. 2023; 22:S0163–4453

# MenABCWY Program Built on Antigenic Components of MenACWY<sub>CRM</sub> (Menveo) and MenB-4C (Bexsero)

Lyophilized MenACWY<sub>CRM</sub> (vial) Liquid MenB-4C (prefilled syringe)

= MenABCWY<sup>1</sup>

#### **MenABCWY Proposed Indication<sup>2</sup>**

Vaccine indicated for active immunization to prevent invasive disease caused by Neisseria meningitidis serogroups A, B, C, W, and Y in individuals **10 through 25 years** of age

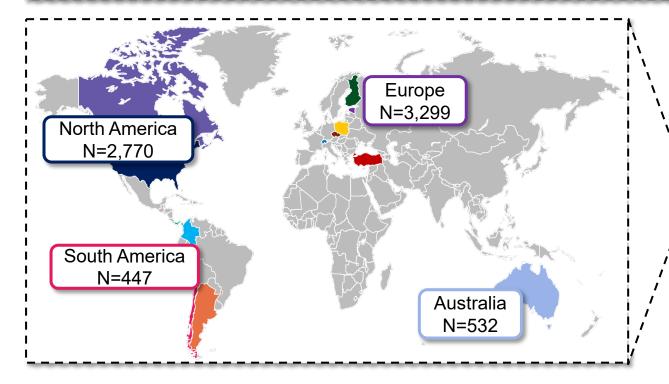
Administer 2 doses (0.5 mL each) intramuscularly at least 6 months apart

1. GSK Press Release April 16, 2024. https://www.gsk.com/en-gb/media/press-releases/gsk-s-5-in-1-meningococcal-abcwy-vaccine-candidate-accepted-for-regulatory-review-by-us-fda/;

<sup>2.</sup> MenABCWY Candidate Vaccine Draft Prescribing Information, February 2024

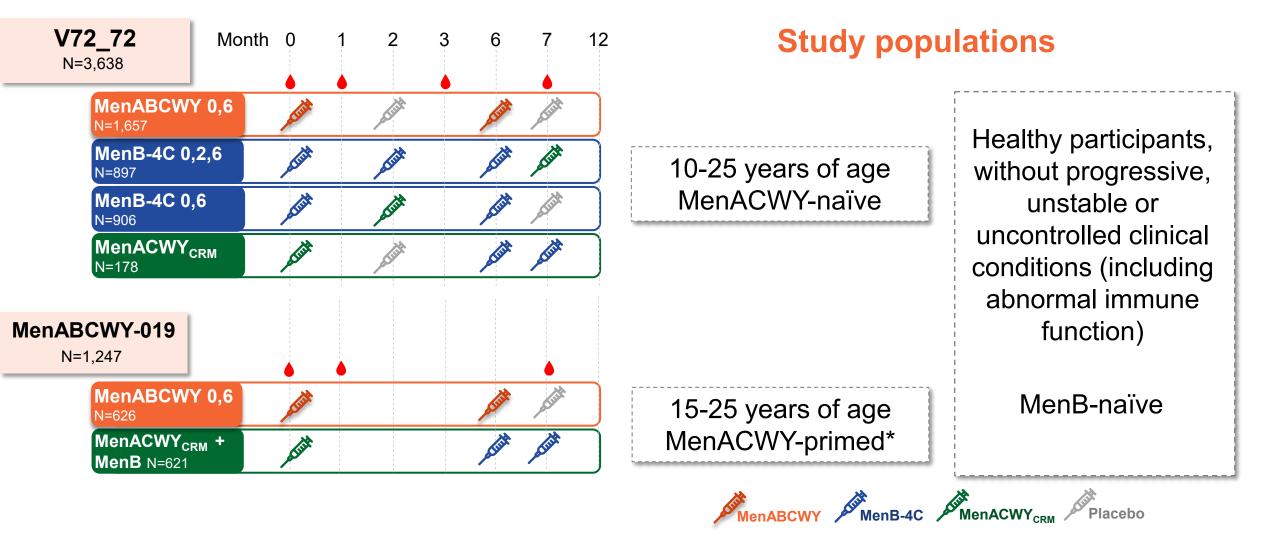
### **Comprehensive MenABCWY Clinical Development Program** *12 Studies, >7,000 Participants, 13 Countries*

- > 10 completed Ph1-2 studies: different formulations and administration schedules in ages 9 42 years<sup>1</sup>
- 2 completed Ph3 studies: safety and immunogenicity of MenABCWY in MenACWY-naïve and primed 10-25 yrs<sup>2-3</sup>
- ➤ 1 ongoing Phase 2 study: evaluating 2 doses administered 2 or 4 years apart in ages 11 14 years<sup>4</sup>



Vaccine exposed set <sup>1</sup>	N		
MenABCWY (Total)	3,718		
MenABCWY	<b>→</b> 1,216		
MenB-4C	2,969		
<b>MenACWY</b> <sub>CRM</sub>	361		
<b>TOTAL</b> receiving ≥ 1 dose of study vaccine	7,048		

### Phase 3 Studies Assessed Safety and Immunogenicity of MenABCWY Compared to MenB-4C, MenACWY<sub>CRM</sub> Administered per CDC Schedule at Study Onset



N for each study arm depicts the exposed set. \*MenACWY-primed participants received dose of licensed MenACWY vaccine  $\geq$  4 years prior to study start Clinicaltrials.gov identifier <u>NCT04502693</u>, accessed May 31<sup>st</sup>, 2024 and Clinicaltrials.gov identifier <u>NCT04707391</u>, accessed May 31<sup>st</sup>, 2024.

## **Demographics and Baseline Characteristics of Phase 3 Studies**

		V72_72		MenABCWY-019		
		MenABCWY N=1,657	MenB-4C 0-6 N=906	<b>MenACWY<sub>скм</sub></b> N=178	MenABCWY N=626	<b>MenACWY<sub>скм</sub></b> N=621
Median age	At 1 <sup>st</sup> vaccination, years (range)	<b>16</b> (9–26)	<b>16</b> (9–26)	<b>16</b> (10–25)	<b>16</b> (15–25)	<b>16</b> (15–25)
Age group	10–11 years	320 <b>(19%)</b>	172 <b>(19%)</b>	27 <b>(15%)</b>	0	0
	12–17 years	666 <b>(40%)</b>	368 <b>(41%)</b>	76 <b>(43%)</b>	450 <b>(72%)</b>	441 <b>(71%)</b>
	18–25 years	671 <b>(40%)</b>	366 <b>(40%)</b>	75 <b>(42%)</b>	176 <b>(28%)</b>	180 <b>(29%)</b>
Region	US	491 <b>(30%)</b>	270 <b>(30%)</b>	52 <b>(29%)</b>	366 <b>(59%)</b>	365 <b>(59%)</b>
Sex	Female	933 <b>(56%)</b>	446 <b>(49%)</b>	100 <b>(56%)</b>	343 <b>(55%)</b>	325 <b>(52%)</b>
Race	White	1492 <b>(90%)</b>	791 <b>(87%)</b>	162 <b>(91%)</b>	474 <b>(76%)</b>	467 <b>(75%)</b>
	Asian	71 <b>(4%)</b>	60 <b>(7%)</b>	9 <b>(5%)</b>	22 <b>(4%)</b>	33 <b>(5%)</b>
	Black or African American	59 <b>(4%)</b>	29 <b>(3%)</b>	6 <b>(3%)</b>	94 <b>(15%)</b>	86 <b>(14%)</b>
	Other	35 <b>(2%)</b>	26 <b>(3%)</b>	1 <b>(1%)</b>	36 <b>(6%)</b>	38 <b>(6%)</b>
Ethnicity	Not Hispanic or Latino	1546 <b>(93%)</b>	852 <b>(94%)</b>	172 <b>(97%)</b>	447 <b>(71%)</b>	432 <b>(69%)</b>
	Hispanic or Latino	92 <b>(6%)</b>	41 <b>(5%)</b>	6 <b>(3%)</b>	179 <b>(29%)</b>	192 <b>(31%)</b>
	Not reported	19 ( <b>1%)</b>	13 <b>(1%)</b>	0	0	0





# Evidence Supporting Safety and Immunogenicity of MenABCWY

### Serogroups A C W Y

### Serogroup B

Solicited and unsolicited adverse events after each dose of MenABCWY, MenB-4C or MenACWY<sub>CRM</sub>

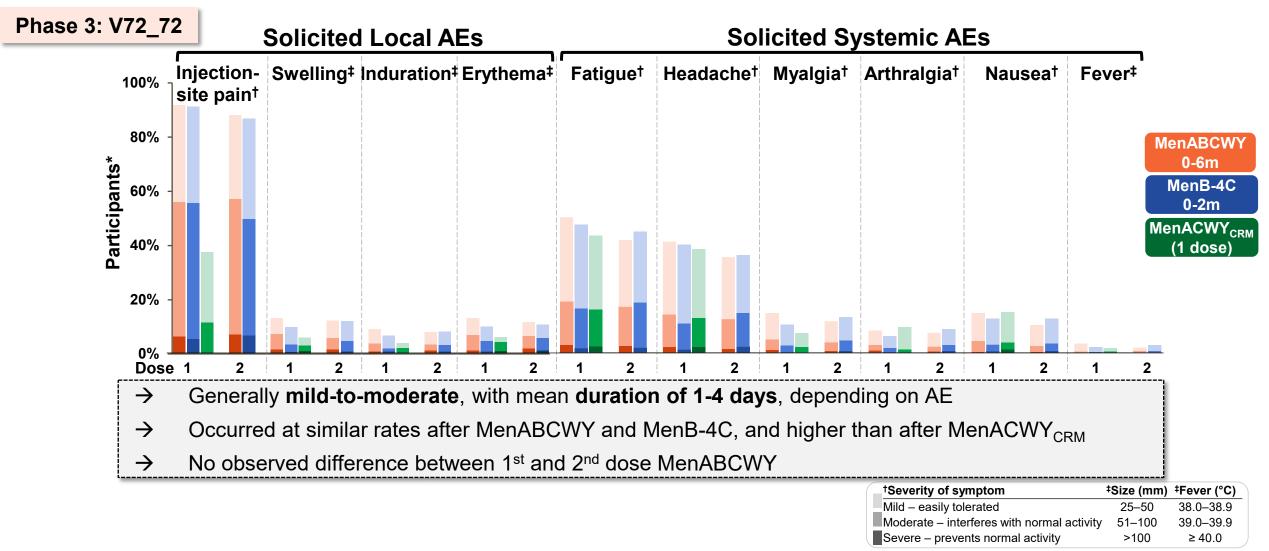
Non-inferiority vs MenACWY<sub>CRM</sub> in MenACWY-naïve and -primed

GSK's MenABCWY Immunogenicity of MenABCWY against 110 serogroup B strains

> Immunological noninferiority of MenABCWY vs MenB-4C

Persistence and booster immune response up to 24 months

# Solicited Local and Systemic AEs within 7 Days, after Each Vaccination with MenABCWY, MenB-4C or MenACWY<sub>CRM</sub>



## MenABCWY Demonstrated a Well-Tolerated Safety Profile Comparable to MenB-4C

Integrated Safety Analysis (Pooled)	MenABCWY N=3,718	MenB-4C <sub>N=2,969</sub>	MenACWY <sub>CRM</sub> N=361	
N =7,048	n (%)	n (%)	n (%)	
<b>Unsolicited AEs</b> (within 30 days of any vaccination)	1,072 <b>(29%)</b>	736 <b>(25%)</b>	47 <b>(13%)</b>	
Related*	256 <b>(7%)</b>	155 <b>(6%)</b>	10 <b>(3%)</b>	
AEs leading to withdrawal	8 <b>(0.2%)</b>	4 <b>(0.1%)</b>	0	
Medically attended AEs <sup>†</sup>	416 <b>(12%)</b>	302 <b>(11%)</b>	8 (4%)	
Related medically attended AEs <sup>†</sup>	22 <b>(0.6%)</b>	15 <b>(0.5%)</b>	0	
SAEs (entire study period)	70 <b>(1.9%)</b>	58 <b>(2%)</b>	5 <b>(1.4%)</b>	
Related*	3 <b>(0.1%)</b>	2 <b>‡ (0.1%)</b>	0	
Deaths (all unrelated)	1§	2¶	1§	

\*Assigned as related by investigator; † Medically attended flags for AEs are not available in studies V102P1, V102\_02, V102\_02E1 and V102\_03. Participants from these studies are not included. Therefore, the denominator is different for the 3 groups (MenABCWY N=3488, MenB N=2861, MenACWY N=213); ‡2 SAEs occurred in the MenB-4C arms of the studies included in the pooled safety analysis: 1 SAE followed a MenB-4C and 1 followed a MenACWY-CRM vaccination; \$Suicide; ¶Deaths by poisoning and drug overdose; AE: adverse event; SAE: serious adverse event GSK, Data on File 2024N555058.

# Evidence Supporting Safety and Immunogenicity of MenABCWY

### Serogroups A C W Y

### Serogroup B

Solicited and unsolicited adverse events after each dose of MenABCWY, MenB-4C or MenACWY<sub>CRM</sub>

Non-inferiority vs MenACWY<sub>CRM</sub> in MenACWY-naïve and -primed GSK's MenABCWY Immunogenicity of MenABCWY against 110 serogroup B strains

#### Immunological noninferiority of MenABCWY vs MenB-4C

Persistence and booster immune response up to 24 months

# **Assays Used to Infer Meningococcal Vaccine Protection**

**Traditional hSBA** 

#### Vaccine targets

### N. meningitidis capsule polysaccharide Highly abundant, conserved antigens<sup>1</sup>

#### hSBA against serogroupspecific polysaccharide capsule reference strain infers protection against all strains in serogroup<sup>2</sup>

#### Surrogate of protection:

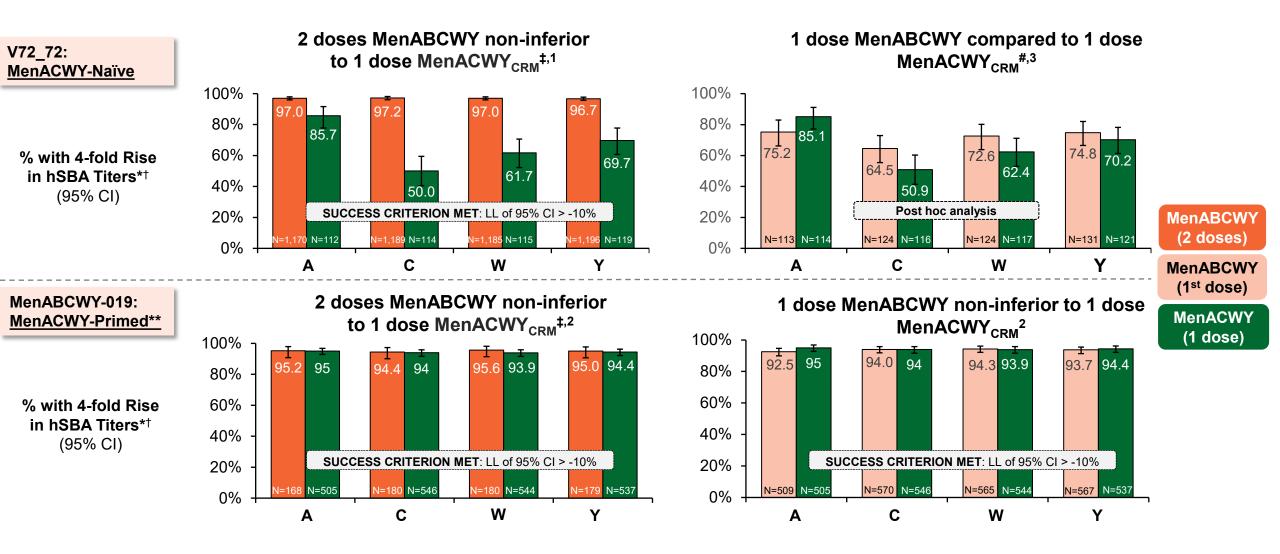
titer ≥4 threshold for protection<sup>2,3,4,5,6</sup>

hSBA, human serum bactericidal assay

1. CDC, 2022. About meningococcal vaccines. https://www.cdc.gov/vaccines/vpd/mening/hcp/about-vaccine.html; 2. Donald RGK et al. Hum Vaccin Immunother. 2017;13:255–265; 3. Balmer P et al. Postgrad Med. 2020;132:184–191;

4. Goldschneider I, et al. J Exp Med. 1969;129(6):1307-1348; 5. Bröker M et al. Vaccine. 2009;27:5574–5580; 6.Ferlito et al. Clin Exp Immunol. 2018;194(3): 361-370; 6. Muzzi A et al. MSphere. 2022;e00385223

# MenABCWY Non-Inferior to MenACWY<sub>CRM</sub> in MenACWY-Naïve and MenACWY-Primed Participants



\*At 1 month after 1 or 2 doses of MenABCWY or after single MenACWY vaccination; <sup>†</sup>Defined as a post-vaccination titer ≥4-fold the LOD or ≥LLOQ, whichever is greater if pre-vaccination titer <LOD, a post-vaccination titer ≥4-fold the pre-vaccination titer ≥4-fold the pre-vaccination titer ≥LOD and <LLOQ, and a post-vaccination titer ≥4-fold the pre-vaccination titer ≥LOQ. LOD: 4 for MenA, MenC, MenW, and MenY. LLOQ = 12 for MenA; 8 for MenC; 8 for MenW; 10 for MenY, except for the post-hoc analysis for which LLOQs were 8 for MenA and 11 for MenC; \*Licensure criteria agreed with CBER; #full set analysis; \*\*Primed participants had received a dose of MenACWY vaccine at least 4 years prior. CI – confidence interval, hSBA - human serum bactericidal assay, LOD – limit of detection; LLOQ – lower limit of quantitation 1. Clinicaltrials.gov identifier NCT04502693, accessed May 31<sup>st</sup>, 2024; 2. Clinicaltrials.gov identifier NCT04707391, accessed May 31<sup>st</sup>, 2024; 3. GSK, Data on File 2024N555056.

# **Assays Used to Infer Meningococcal Vaccine Protection**

#### Vaccine targets

MenACWY Vaccines *N. meningitidis* capsule polysaccharide

Highly abundant, conserved antigens<sup>1</sup>

#### **Traditional hSBA**

hSBA against serogroupspecific polysaccharide capsule reference strain infers protection against all strains in serogroup<sup>2</sup>

hSBA does not assess

vaccine induced immune

response against many

diverse strains expressing

more than 1 antigen<sup>4</sup>

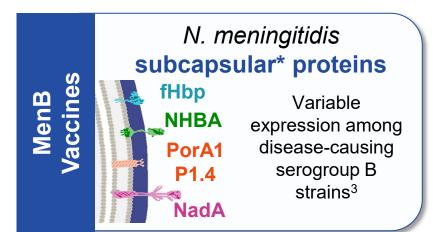
enc-hSBA

14

GSK developed enc-hSBA<sup>5</sup> to test against multiple serogroup B strains

110 strains randomly selected from 2000-2008 IMD cases, that continue to represent 95% of US disease causing serogroup B strains<sup>5</sup> collected up to 2017

hSBA, human serum bactericidal activity; enc-hSBA, endogenous complements human serum bactericidal activity, Men, meningococcal serogroup; fHbp – factor H binding protein; NHBA – Neisserial Heparin Binding Antigen; NadA – Neisseria Adhesin A; PorA1 P1.4 – porin A1 P1.4. \*A MenB capsular vaccine was poorly immunogenic due to structural similarity between the capsule and human tissue<sup>5</sup> 1.CDC, 2022. About meningococcal vaccines. <u>https://www.cdc.gov/vaccines/vpd/mening/hcp/about-vaccine.html</u>; 2. Donald RGK *et al. Hum Vaccin Immunother*. 2017;13:255–265; 3. Balmer P *et al. Postgrad Med.* 2020;132:184–191; 4. Kleinschmidt A *et al. NPJ Vaccines*. 2021;6:29; 5. Muzzi A et al. *MSphere*. 2022;e00385223



<u>enc-hSBA</u>: Immune Response Against Diverse Serogroup B Strains in MenABCWY vs MenB-4C Arms

## Immunological Vaccine Effectiveness (IVE)

**Test-Based** 

**Responder-Based** 

 $IVE = (1 - relative risk) \times 100$ 

Relative risk defined as the percentage of tests without bactericidal activity in the group receiving MenB-containing vaccine compared to controls

→ informs on breadth of MenB vaccine strain coverage at a population level

Percentage of participants whose sera killed ≥70% of strains tested<sup>†</sup>

→ percentage of participants achieving broad protection against serogroup B strains

\*relative risk = ratio between % of tests lacking bactericidal activity against 110-strain panel in group receiving MenB-containing vaccine and control (MenACWY vaccine); <sup>†</sup>Target number of strains tested for each participant was 35 strains out of the 110 strains panel. MenB: meningococcal serogroup B; enc-hSBA: endogenous complement serum bactericidal activity; IVE: immunological vaccine effectiveness Welsch et al, *Vaccine*. 2018;36(15): 5309-5317; Clinicaltrials.gov identifier NCT04502693, accessed May 31<sup>st</sup>, 2024

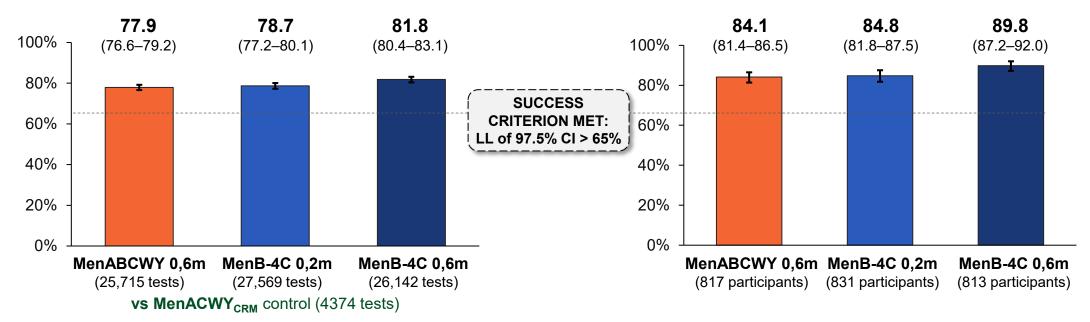
### <u>enc-hSBA</u>: Immune Response against Diverse Serogroup B Strains after 2 doses of MenABCWY or MenB-4C

#### **Test-Based IVE**

# Informs breadth of MenB vaccine strain coverage at a population level

### **Responder-Based IVE**

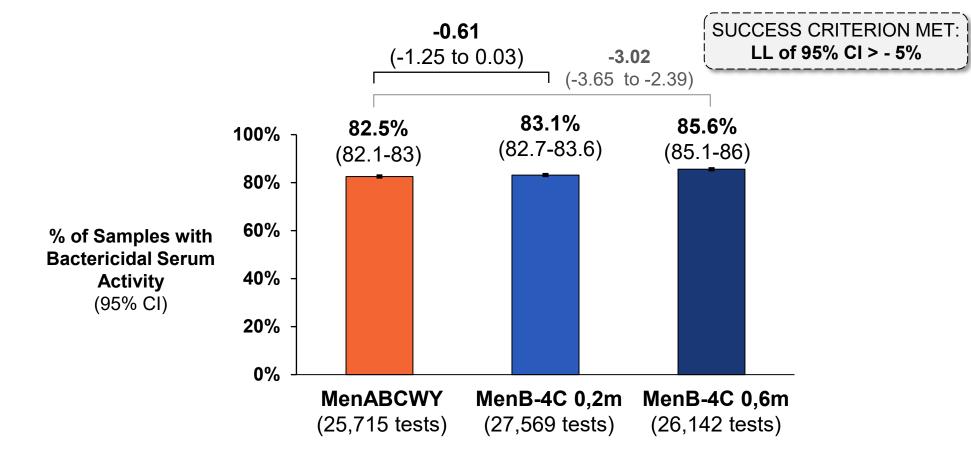
→ % participants achieving broad protection against serogroup B strains



#### MenABCWY achieved breadth of bactericidal effect against a diverse and broad panel of serogroup B strains, similar to MenB-4C 2-dose administered 2 or 6 months apart

The 3 MenB-4C schedules were hierarchically tested for IVE in the order: MenB-4C 0-2-6m → MenB-4C 0-2m. The 0-2m schedule was the last schedule to meet the predefined success criterion (LL of 95% Cl > 65%) and was hence chosen as the comparator for the MenABCWY 0-6m schedule for all subsequent statistical analyses. LL, lower limit; IVE: immunological vaccine effectiveness Clinicaltrials.gov identifier NCT04502693, accessed May 31st, 2024

### <u>enc-hSBA</u>: Noninferiority of Immune Response against Diverse Serogroup B Strains in MenABCWY vs MenB-4C



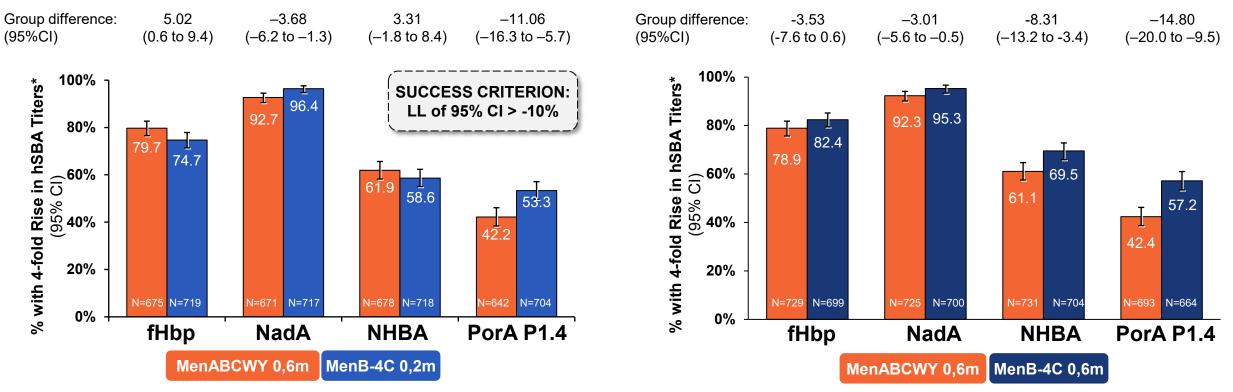
# MenABCWY was noninferior to MenB-4C, based on bactericidal effects against diverse strains assessed by enc-hSBA assay

\*The 3 MenB-4C schedules were hierarchically tested for IVE in the order: MenB-4C 0-2-6m → MenB-4C 0-2m. The 0-2m schedule was the last schedule to meet the predefined success criterion (LL of 97.5% CI > 65%) and was hence chosen as the comparator for the MenABCWY 0-6m schedule for all subsequent statistical analyses. LL, lower limit Clinicaltrials.gov identifier <u>NCT04502693</u>, accessed May 31st, 2024

### <u>hSBA</u>: MenABCWY Immune Response Against Serogroup B Reference Strains

MenABCWY 0,6m vs MenB-4C 0,2 m

MenABCWY 0,6m vs MenB-4C 0,6 m



- Secondary endpoint not met because success criterion not met for all 4 strains
- MenABCWY elicited comparable immune responses for 3 reference strains vs MenB-4C 0,2 and 2 reference strains vs MenB-4C 0,6m.

<sup>\*</sup>At 1 month after  $2^{nd}$  MenABCWY or  $2^{nd}$  MenB-4C vaccination, relative to baseline. 4-fold rise in hSBA titer for each strain was defined as a post-vaccination titer  $\geq 4$ -fold the LOQ or  $\geq$ LOQ, whichever is greater if pre-vaccination titer <LOD, a post-vaccination titer  $\geq 4$ -fold the pre-vaccination titer  $\geq 4$ -fold the LOQ or  $\geq$ LOQ, whichever is greater if pre-vaccination titer <LOD, a post-vaccination titer  $\geq 4$ -fold the pre-vaccination titer  $\geq 4$ -fold the pre-vaccina

# Evidence Supporting Safety and Immunogenicity of MenABCWY

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### Serogroup B

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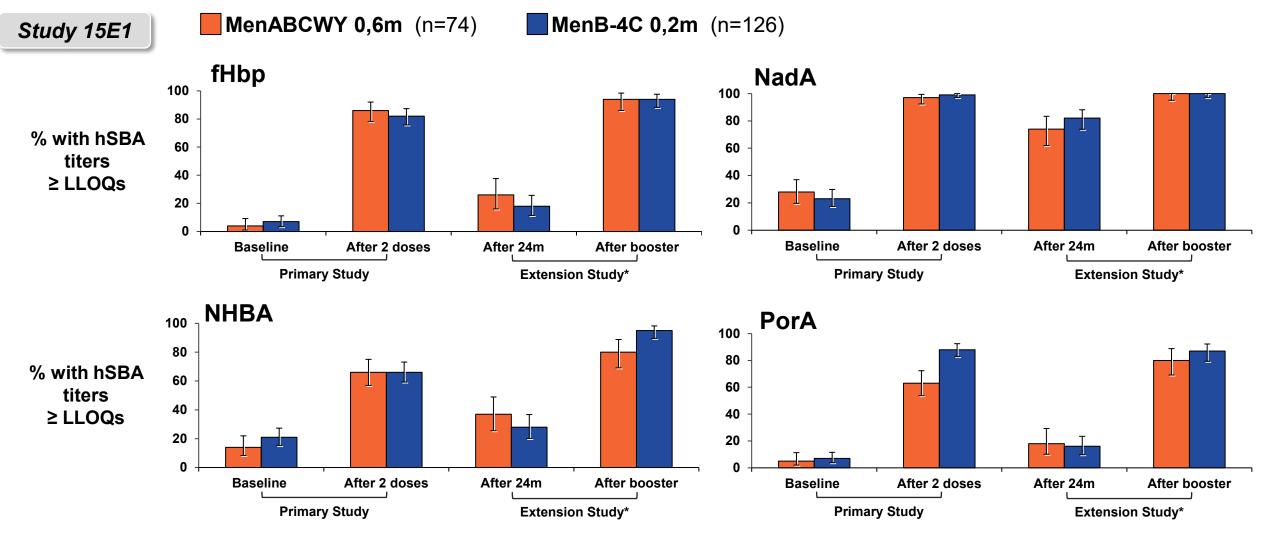
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> Immunological noninferiority of MenABCWY vs MenB-4C

Persistence and booster immune response up to 24 months

### Persistence After 24 months and Booster Response of MenABCWY Demonstrated Against Serogroup B Reference Strains



\*For follow-on group: blood draws were done at baseline and 5 days after booster dose. For the Matched Naive group: blood draws were baseline (prevaccination), 1 month after 1st dose and 5 days after 2nd dose. fHbp, factor H binding protein; hSBA, serum bactericidal assay using human complement; LLOQ, lower limit of quantitation; NadA, Neisseria adhesin A; NHBA, Neisseria heparin binding antigen; PorA, porin A. The LLOQs were 8.0 (fHbp), 8.6 (NadA), 8.9 (NHBA), 8.2 (PorA). Vesikari T et al. *Hum Vaccin Immunother*. 2021;17(11):4689-4700

# MenABCWY Summary

 $\rightarrow$  Combines two well-established vaccines licensed in the US - MenB-4C, MenACWY<sub>CRM</sub>

→ Clinical program demonstrated safety and immunogenicity in adolescents and young adults

→ Tested against a broad panel of 110 serogroup B strains, representing 95% of US serogroup B disease-causing strains

 $\rightarrow$  Demonstrated persistence of immune response up to 24 months

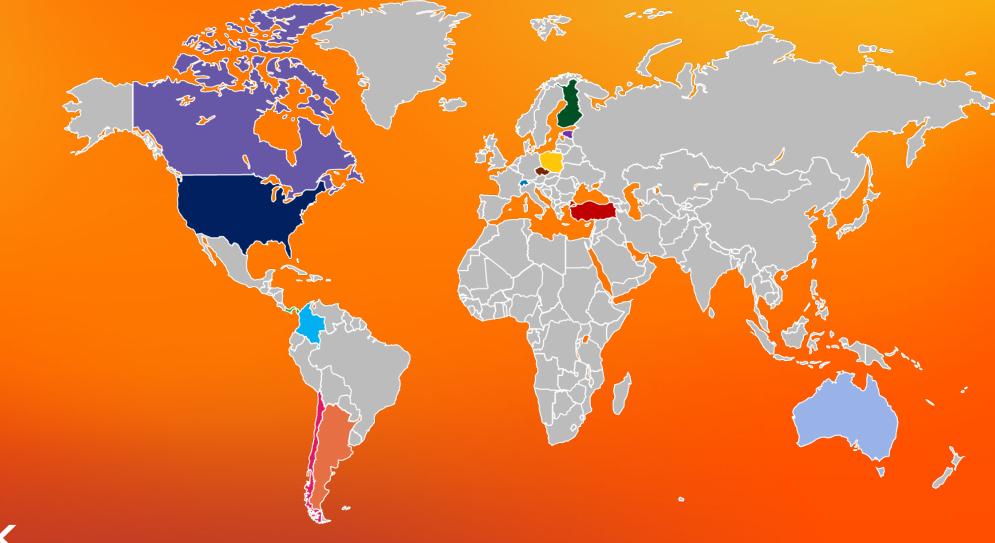
# **Summary of Data for Policy Considerations**

2 doses of MenABCWY can protect against serogroups A,B,C W,Y

- → Achieves broad coverage against strains causing endemic and outbreak disease, to meet the current and evolving US epidemiology
- → Offers the opportunity to improve vaccination coverage in adolescents and young adults
- → Represents the evolution of IMD as **one vaccine-preventable disease**

### **MenABCWY** allows for prevention of IMD with one vaccine

### Investigators, study site personnel, study participants, and their families



Thank you!