High HBsAb Titers Consistent Across 3 Lots of the Tri-antigenic Hepatitis B (HBV) Vaccine, Sci-B-Vac®:

Results from the Second Pivotal Phase 3 Double-Blind, Randomized Controlled Trial Designed to Assess the Lot-to-Lot Consistency of Sci-B-Vac® in Adults (CONSTANT)

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Disclosure Information

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Disclosure Information :

Financial disclosure :

- The presenter of this presentation was a Principal Investigator of this study and his institution received financial support for the services performed in conducting the study at his study center(s)
- The presenter's institution also received financial compensation for his participation as a consultant on one of the Company's Advisory Board Meetings

Investigational/unapproved use disclosure:

- The presenter will be discussing Sci-B-Vac® which is an investigational vaccine and has not been approved for use by the U.S. Food and Drug Administration, the European Medicines Agency, or by Health Canada. The data shown are from a Phase 3 study.

Trial Sponsor : VBI Vaccines Inc.

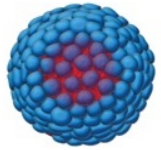
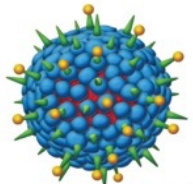
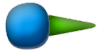
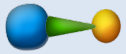
Hepatitis B Disease Burden

- Hepatitis B Virus (HBV) is a leading cause of chronic hepatitis, liver cirrhosis, and hepatocellular carcinoma worldwide
- HBV infection is the most common blood-borne infection, with recent estimates of chronically-infected people ranging from **240-350 million worldwide**, 4.7 million of whom are in the European Union/European Economic Area (EU/EEA), and with more than **2 billion** people ever having been infected
- The initial HBV infection is often asymptomatic and, as a result, **millions of people are unaware of their disease status**, increasing their likelihood of transmission –WHO estimates that only 13% of all HBV infection in Europe have been diagnosed
- In 13 EU/EEA countries that consistently report, **the rate of chronic HBV cases increased** from 6.7/100,000 in 2008 to 10.2/100,000 in 2017
- With no functional cure available for chronic HBV, active immunization against HBV, including adults, remains the primary means of further reducing the transmission of HBV and the associated morbidity and mortality
- Additional tools are needed, however, to support public health efforts to eliminate new HBV infections, including **improved and cost-effective HBV vaccines capable of quickly and safely providing robust immune response in all adults**

CONSTANT Study Overview & Objectives

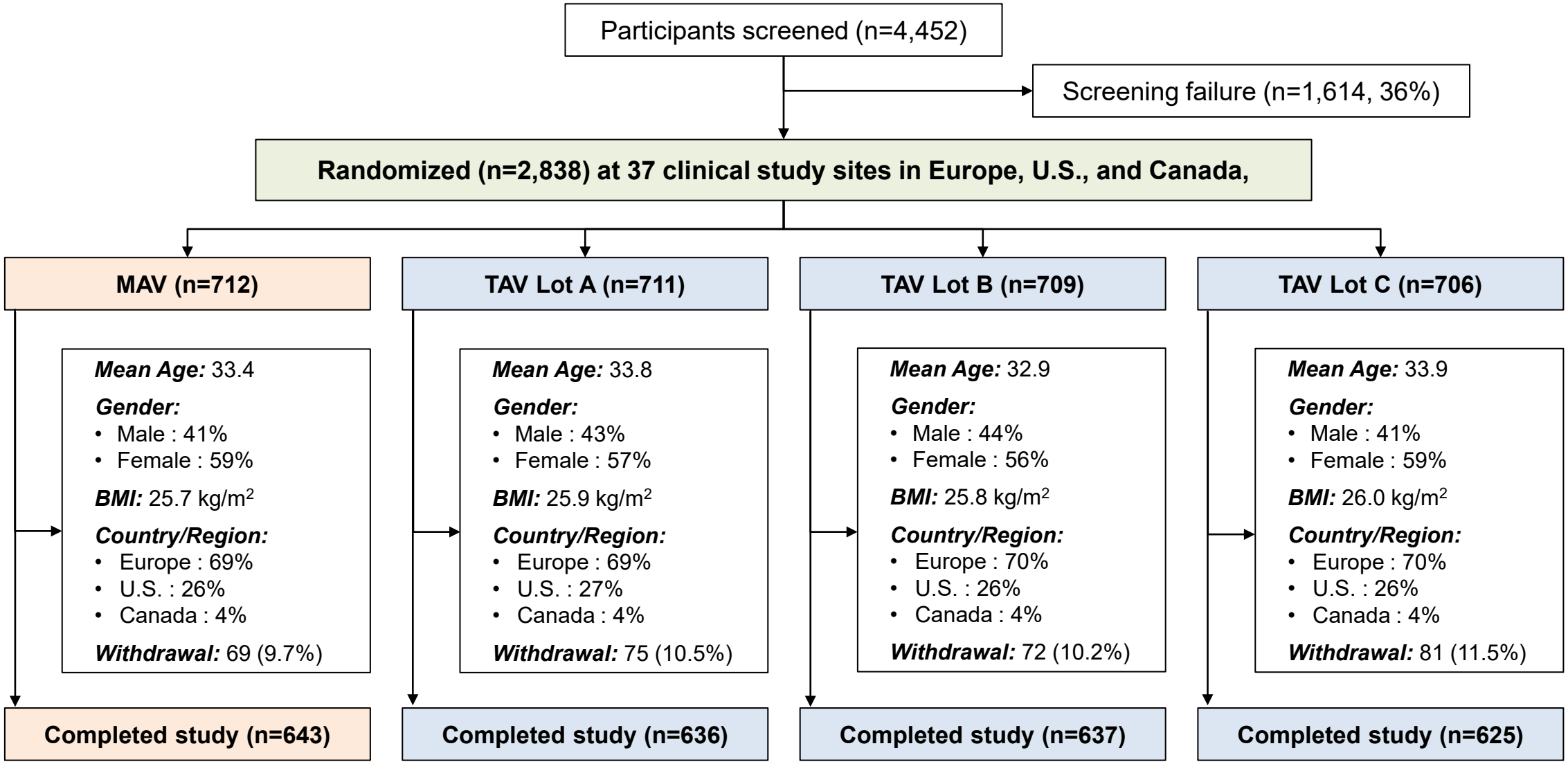
- Pivotal Phase 3, randomized, controlled, blinded, multi-center, lot-to-lot consistency study *[NCT03408730]*
- Designed to assess the manufacturing equivalence of 3 independent consecutive lots of the tri-antigenic HBV vaccine, Sci-B-Vac® (**TAV**), and to compare safety and immunogenicity to a mono-antigenic HBV vaccine, Engerix-B® (**MAV**)
- **2,838 subjects,** aged 18-45 years and in stable health were enrolled and randomized 1:1:1:1 to receive a 3-dose course of either 10 µg of TAV Lot A, 10 µg of TAV Lot B, 10 µg of TAV Lot C, or 20 µg of MAV at days 0, 28, and 168
- **Primary Endpoint**: Consistency of immune response as measured by the ratio of Geometric Mean Concentration (GMC) of HBsAb across the three lots of TAV, at day 196, 4 weeks after the 3rd vaccination
- **Secondary Endpoints**:
  - *Immunogenicity*: Non-inferiority of seroprotection rate (SPR), defined as percentage achieving HBsAb levels ≥ 10.0 mIU/mL, at Day 196 of TAV *vs*. MAV
  - *Safety and tolerability*: Standardized methods for local and systemic vaccine reactions, repeated vital signs and physical examinations, 48 weeks follow-up for serious adverse events (SAEs), medically-significant events or NOCI, and changes in concomitant medication

TAV *vs.* MAV : Vaccine Design and Function

	Mono-antigenic (MAV) *Engerix-B®*	Tri-antigenic (TAV) *Sci-B-Vac®*
		
Viral antigens mimicked:		
S Antigen 	✓	✓
Pre-S2 		✓
Pre-S1 		✓
Dose of S Antigen:	20µg	10µg
Adjuvant:	Alum	Alum
Derivation:	rDNA yeast	Mammalian cell

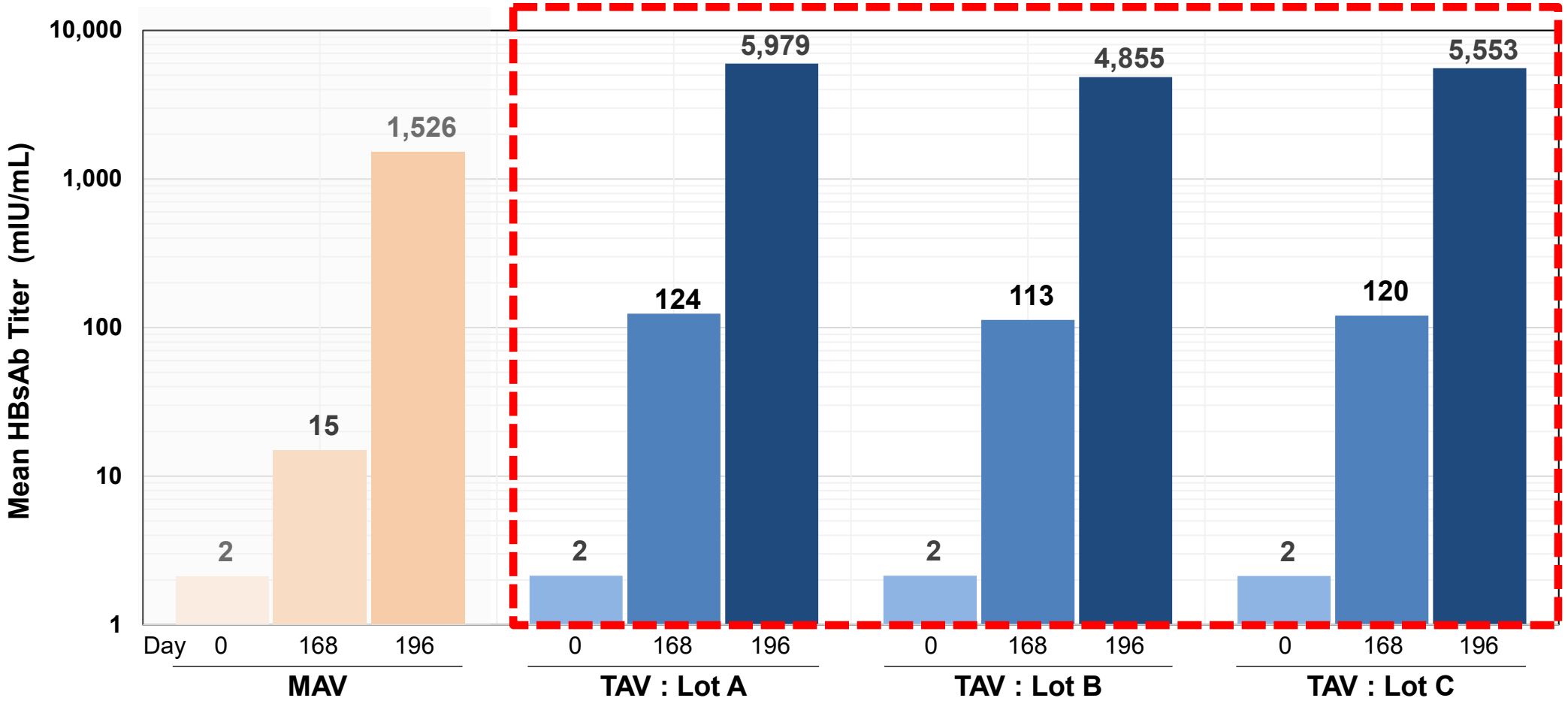
- Pre-S1 antigen induces key neutralizing antibodies that block virus receptor binding (Rendi-Wagner, 2006; Krawczyk, 2014)
- T cell responses to pre-S1 and pre-S2 antigens can further boost responses to the S antigens, resulting in a greater immune response (Hellström UB et al., 2009).

CONSTANT Study Participant Disposition



TAV: Lot-to-Lot Consistency of HBsAb Titers (GMC)

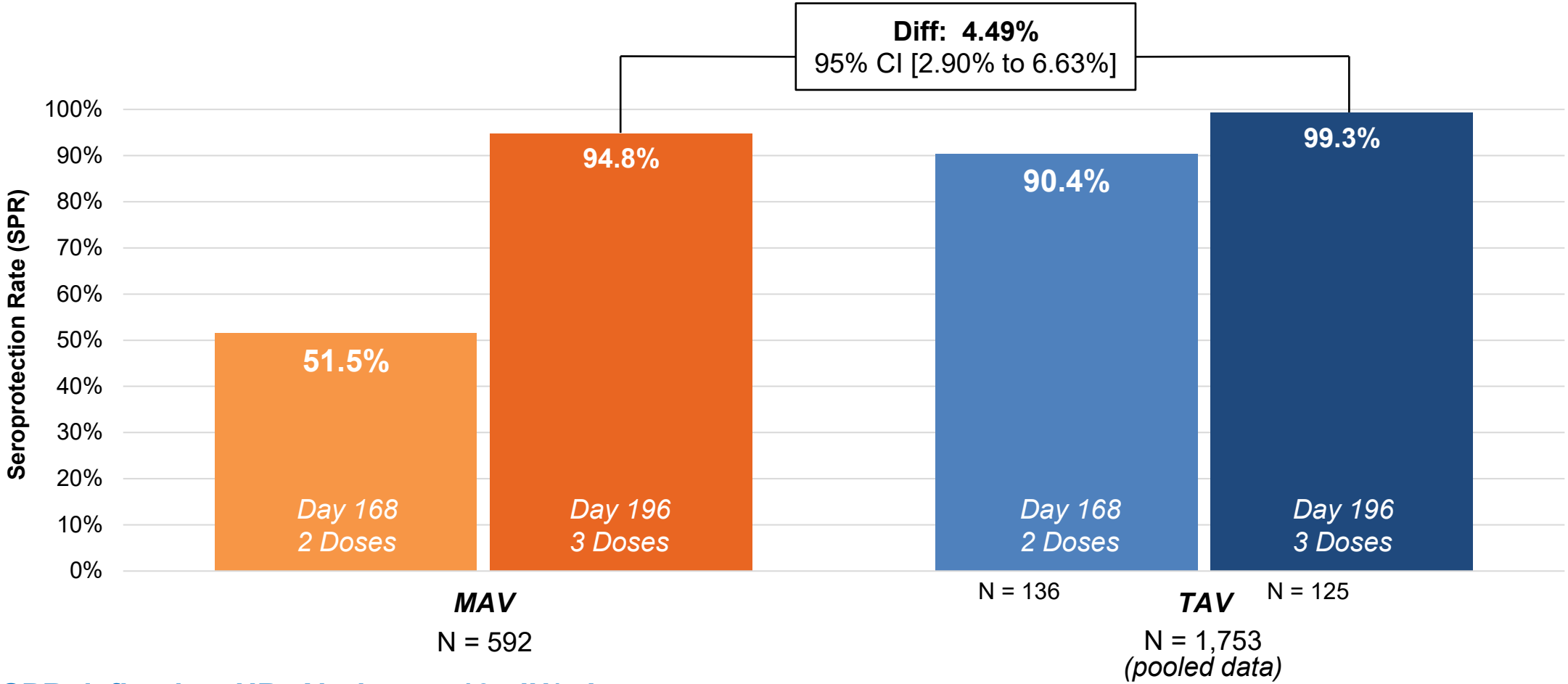
The primary objective met: TAV lot-to-lot consistency demonstrated



Greater HBsAb titers (GMC) for TAV vs. MAV after 2 vaccinations (Day 168) and after 3 vaccinations (Day 196)

Immunogenicity – Kinetics of SPR

The secondary objectives met: SPR for TAV was non-inferior to MAV at Day 196 (4 weeks after 3 vaccinations)



SPR defined as HBsAb titers ≥ 10mIU/mL

Summary of Safety Data (1)

	Pooled TAV n=2124 (% of subjects)	MAV n=712 (% of subjects)
Vaccine withdrawal due to AE/SAE	0.5	0.3
Study discontinuation due to AE/SAE	0.4	0.1
Local Reactogenicity (most common)		
Injection site pain	75.6	53.9
Injections site tenderness	75.1	54.9
Systemic Reactogenicity (most common)		
Myalgia	44.4	32.4
Fatigue	40.1	39.9
Headache	38.2	37.6
Treatment-emergent AEs	53.1	52.1
Medically-attended AEs	21.7	17.6
New Onset of Chronic Illness	1.6	1.1
SAEs	2.0	0.4
Death	1*	0

* Sudden cardiac death secondary to pre-existing hypertrophic heart disease, unrelated to the study vaccine

Summary of Safety Data (2)

- High 3-dose-vaccination completion rates: TAV 92.5% and MAV 94.2%
- No new or unexpected safety signals and comparable safety for TAV and MAV
- TAV safety profile consistent with previous clinical studies and commercial use
- Most common AEs mild to moderate local reactogenicity symptoms, which resolved without intervention within 1-2 days and with no increase of reactogenicity with subsequent dosing
    - Higher rate of injection site pain, tenderness and myalgia for TAV
- SAEs uncommon with either vaccines
    - No clustering or unusual pattern of SAEs;
    - SAEs in $\geq$ 2 subjects in TAV arm: Appendicitis, Erysipelas, Intervertebral disc protrusion,
    - 1 Death - Sudden cardiac death secondary to pre-existing hypertrophic heart disease, unrelated to the study vaccine
    - 1 post-study SAEs: “tongue-tie” (ankyloglossia congenital in an infant born to a female subject) reported as possibly vaccine-related (TAV)

Conclusions

- **Primary Endpoint Met**: Lot-to-lot manufacturing consistency of TAV was demonstrated
- **Secondary Endpoint Met:** The SPR for TAV was non-inferior to MAV after 3 vaccinations (99.3% vs. 94.8%)
- **Safety:** No new or unexpected safety signals – safety profile remains consistent with known profile of TAV
- **Exploratory Endpoints & Post Hoc Analyses:**
  - TAV induced robust immune responses, with HBsAb titers > 7.5x higher after the 2nd vaccination and > 3x higher after the 3rd vaccination, compared with MAV
  - More than 90% of individuals vaccinated with TAV were seroprotected after the 2nd vaccination (vs. 51.6% with MAV)

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Questions?