VBI VACCINES

ACTIVATING THE POWER WITHIN

# Higher seroprotection rates (SPRs) and higher anti-HBs concentrations in adults age 18+ achieved with 3-antigen hepatitis B vaccine (3A-HBV) compared to 1-antigen hepatitis B vaccine (1A-HBV):

## Results from the pivotal, double-blind, randomized Phase 3 study (PROTECT)

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Tuesday, May 4, 2021 @ 13:30 - 14:30 ET

# Hepatitis B Disease Burden

## Hepatitis B Virus (HBV) is a leading cause of chronic hepatitis, liver cirrhosis, and hepatocellular carcinoma worldwide

- Chronic HBV infections worldwide range from 240 million to 350 million with more than 2 billion people globally ever infected with HBV (acutely or chronically) [1]
- New reported HBV infections in Canada are the highest among males and adults ages 30 - 59 years [2]
- Of all reported chronic HBV infections in Canada, the rate is highest among adults age 30 - 39 years, following closely by adults age 25 - 29 years, and adults age 40 - 50 years [2]
- Healthcare workers, injection drug users, the military, and travelers to endemic regions are most in need of a HBV vaccine that ensures rapid seroprotection
- With no currently - available functional cure for HBV, vaccination is a critical pillar of the public health response to HBV
- And yet, the overall prevalence of HBV vaccine - induced immunity in Canada in ages 14 - 70 is 29%[3]
- Improved HBV vaccines are needed to ensure safe and effective seroprotection against HBV for those who are older, obese, or those with impaired immune function, including diabetics

References : [1]World Health Organization. Hepatitis B Fact Sheet. https:// www.who.int /en /news - room/fact - sheets/detail/hepatitis - b#. Accessed June 2020; [2]Report on Hepatitis B and C in Canada: 2016, Government of Canada; 32007 - 2009 and 2009 - 2011;[3]Canadian Health Measures Survey, combined

# Phase 3 Clinical Program of a 3-Antigen HepB Vaccine

**Program Objective :**

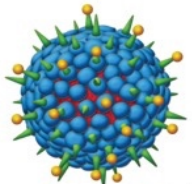
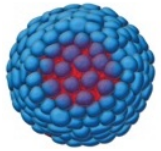
Assess the immunogenicity, safety, and manufacturing consistency of 10 µg of a 3-antigen HepB vaccine (3A-HBV), and compare it to 20 µg of Engerix-B® (1AHBV), a single antigen HepB vaccine considered to be standard-of-care:

- PROTECT: A head-to-head safety and immunogenicity study [NCT03393754]
  - Co-primary objectives of : (1) non-inferiority of seroprotection rates (SPR) in adults ⩾ age 18 years, and (2) superiority of SPR in adults ≥age 45 years

*Focus of today's presentation*

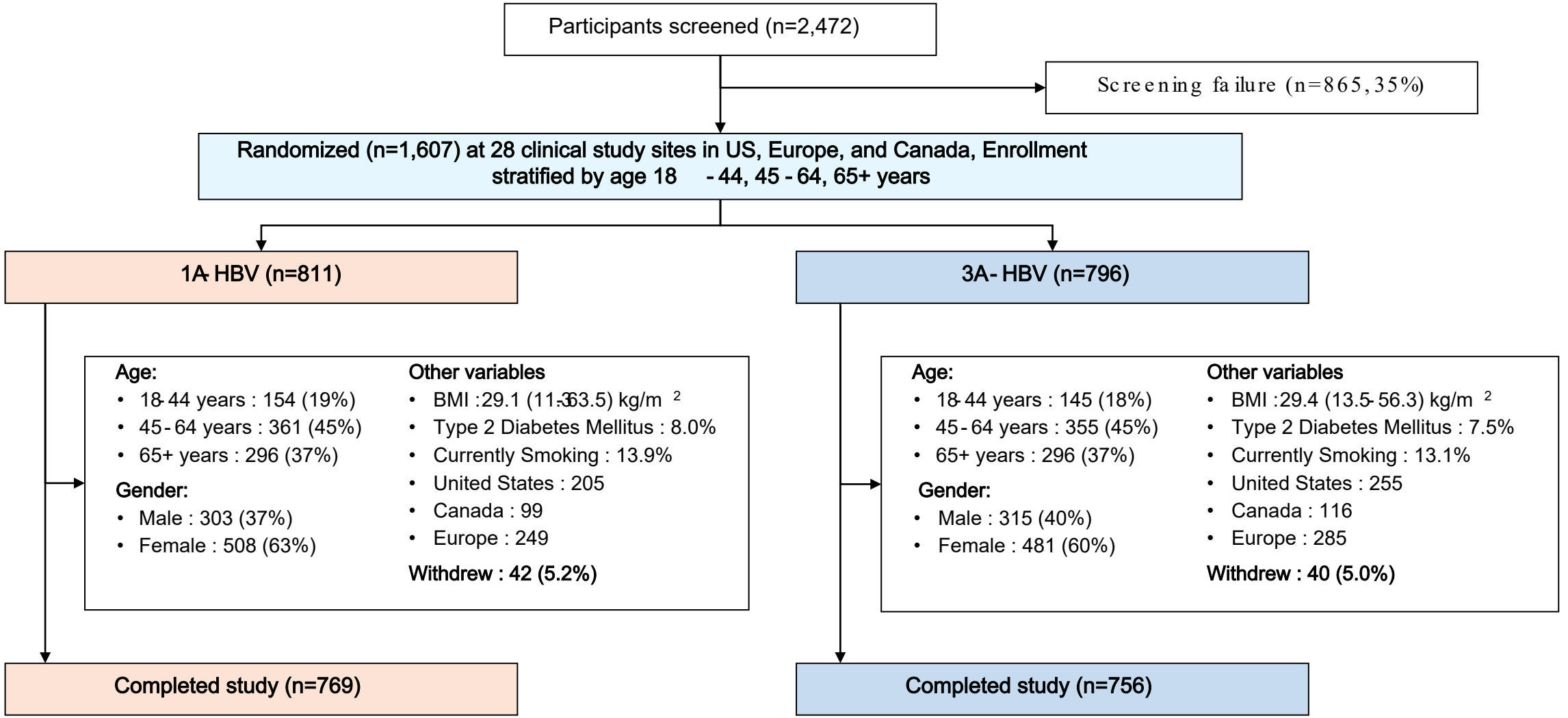
- CONSTANT : A four-arm lot-to-lot consistency study [NCT03408730]
  - Primary objective : consistency of immune response as measured by geometric mean concentration (GMC) of anti-HBs titers across three consecutively manufactured lots of 3A-HBV

# 3A-HBV vs. 1—HBV : Vaccine Design & Function

| | 3A- HBV | 1A- HBV |
|---|---|---|
| |  |  |
| **Viral antigens mimicked:** | | |
| *S Antigen* | ✓ | ✓ |
| *Pre- S2* | ✓ | |
| *Pre- S1* | ✓ | |
| **Dose of S Antigen:** | 10µg | 20µg |
| **Adjuvant:** | Alum | Alum |
| **Derivation:** | Mammalian Cell | rDNA yeast |

- **Pre- S1 antigen induces key neutralizing antibodies that block virus receptor binding** *[Neurath AR et al., 1989;* Adv Exp Med Biol; 251:237- 50 *]*
- **T cell response to pre - S1 and pre - S2 antigens can further boost responses to the S antigens, resulting in a more immunogenic response** *[*Hellström UB et al., 2009; *Virology Journal* 2009, **6**:7*]*

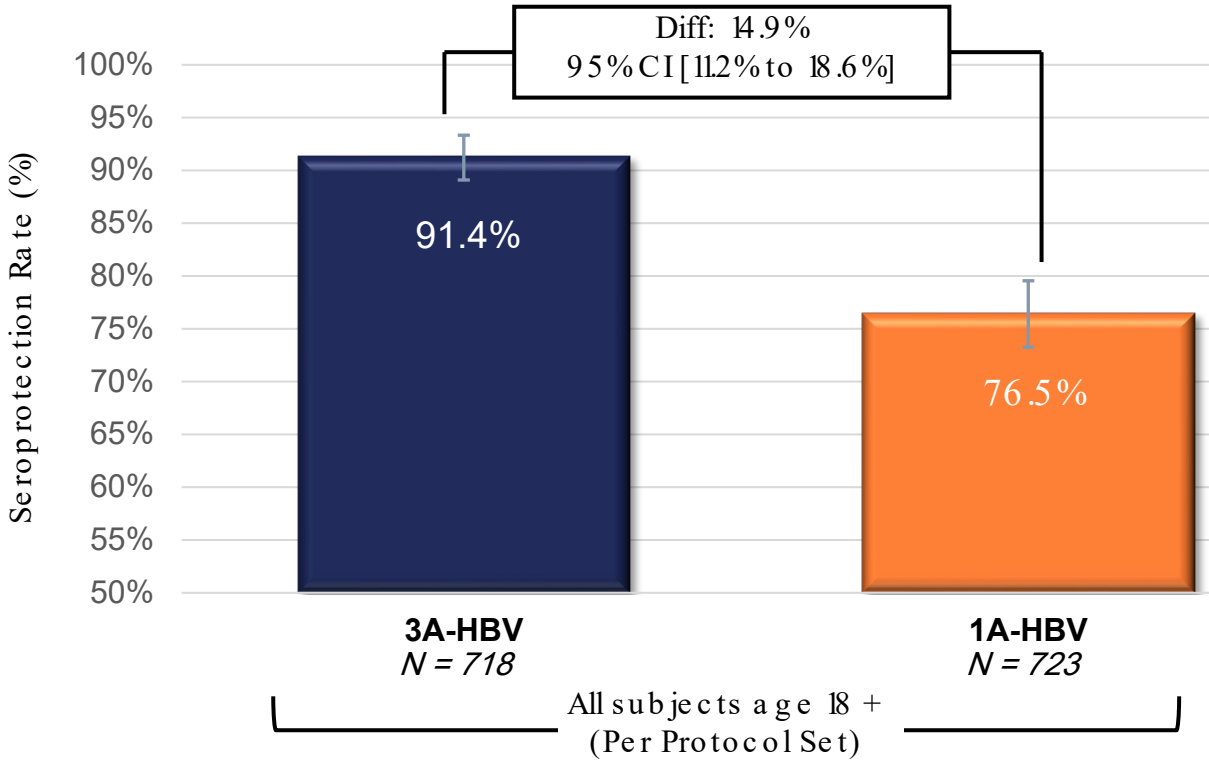
# PROTECT Study Participant Disposition



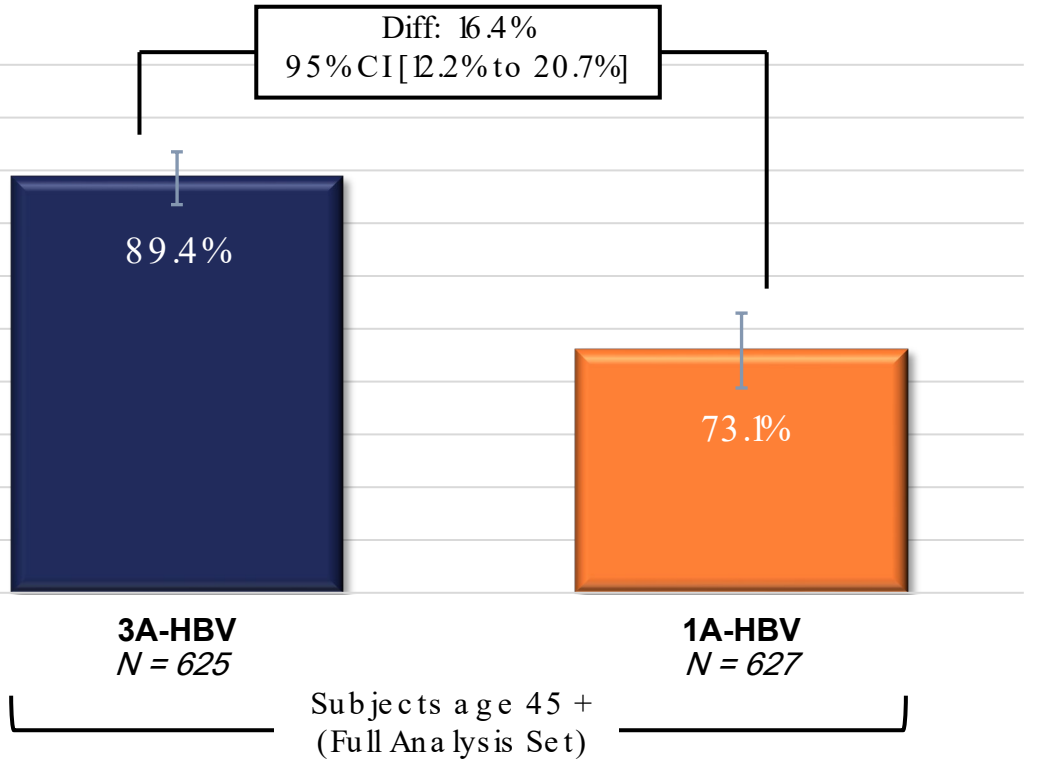
# Both Primary Endpoints Successfully Met

## Seroprotection rate (SPR) at Day 196, 4 weeks post third vaccination

**1. Non- Inferiority of SPR achieved in all subjects** age 18+

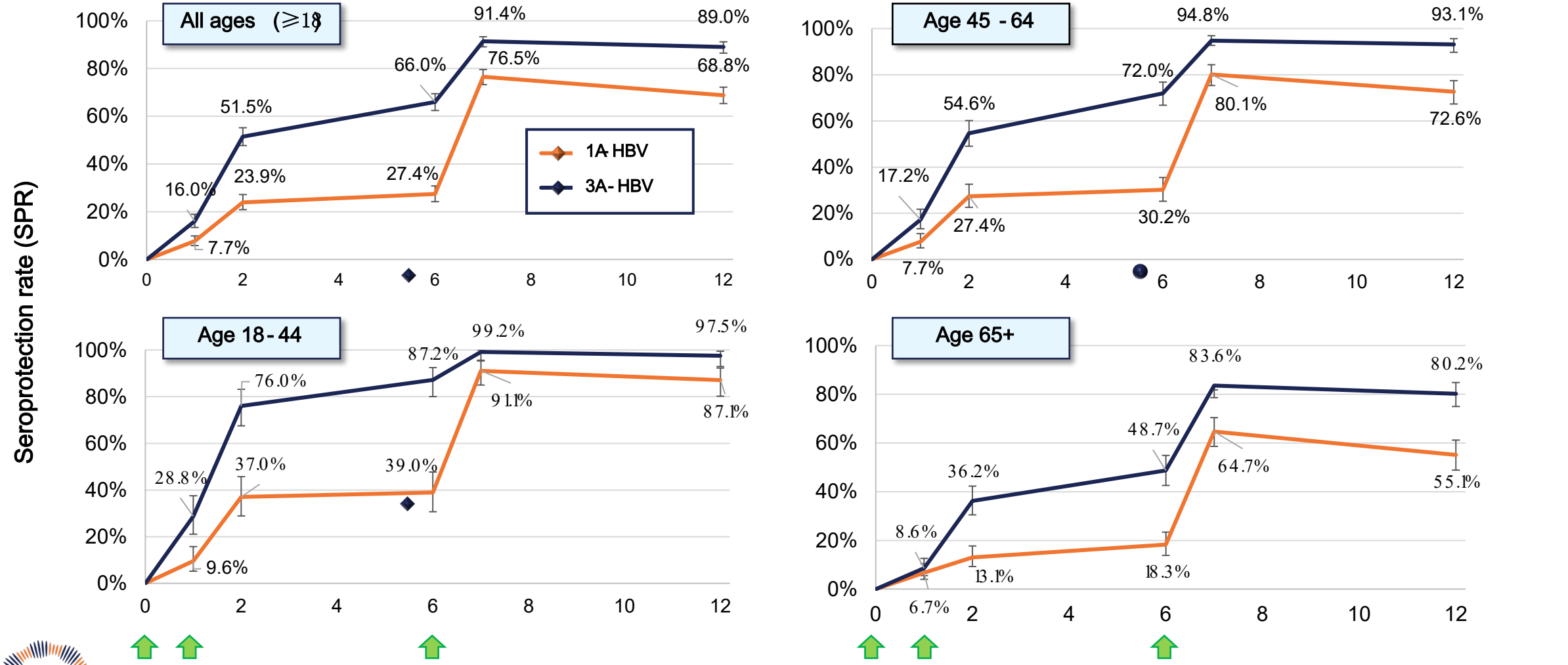



**2. Statistical and clinical superiority, as defined in the protocol, achieved in subjects** age 45+




- *Non-inferiority:* The lower bound of the 95% CI of the difference between the SPR in the VBI arm minus the SPR in the Engerix-B arm is > -5%
- *Statistical superiority:* The lower bound of the same 95% CI is >0%
- *Clinical superiority:* The lower bound of the same 95% CI is >5%

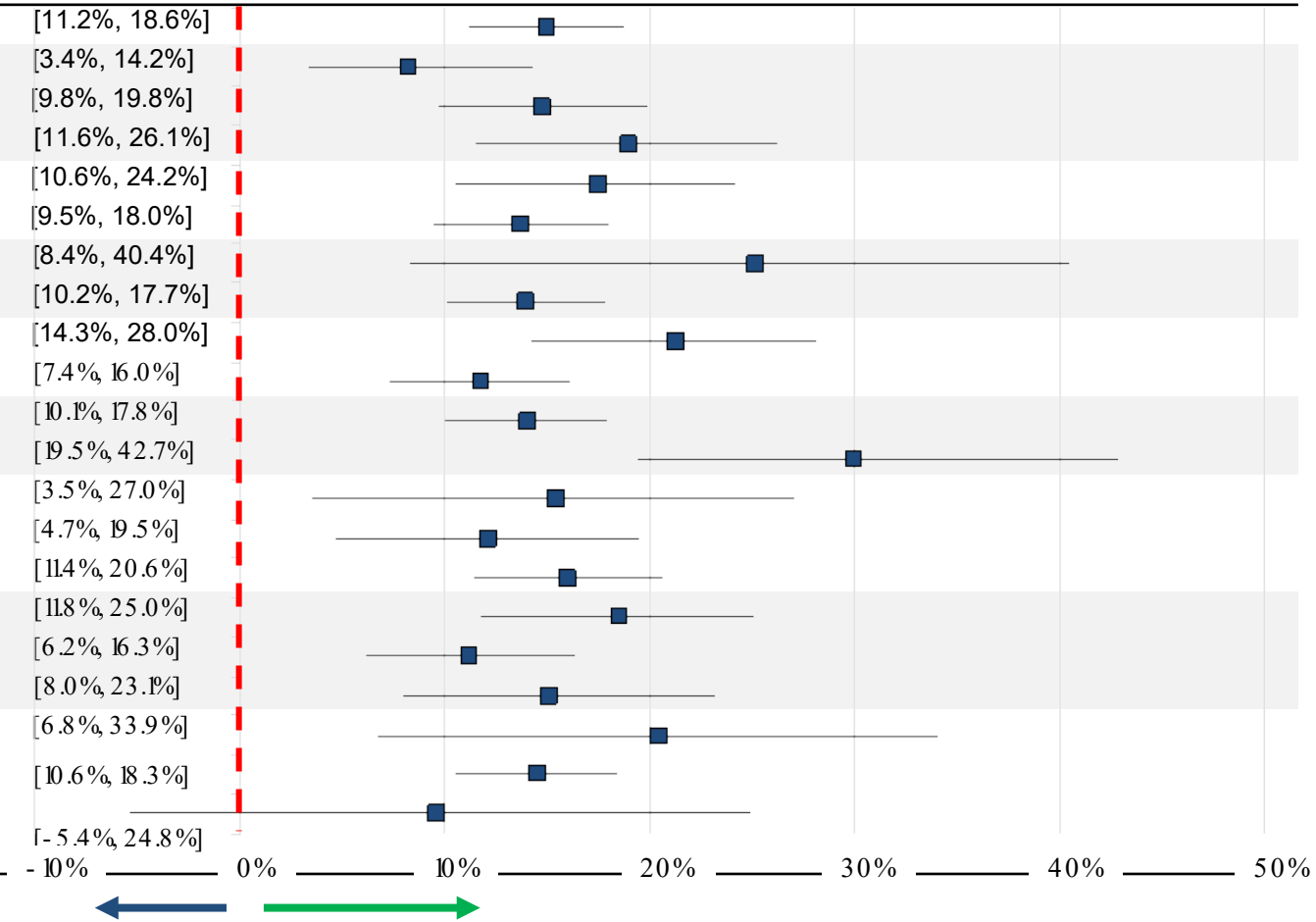
# Higher SPR at All Timepoints in All Age Groups



# PROTECT : SPR in Subgroup Populations

## 3A- HBV achieved higher SPR vs. 1A - HBV in key subgroup analyses at Day 196

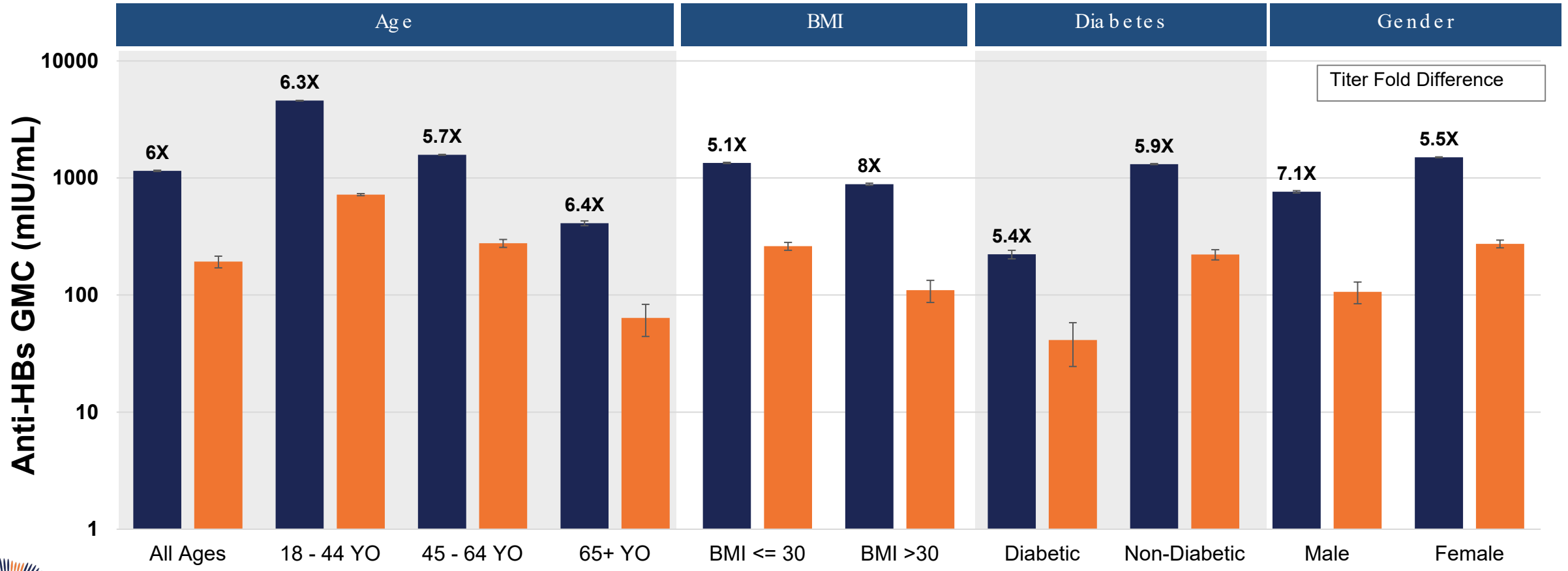
| Participant Populations* | | N | 3A-HBV | 1A-HBV | Difference in SPR (%) [95% Confidence Interval] |
|---|---|---|---|---|---|
| All Participants | | 1,441 | 91.4% | 76.5% | 14.9% [11.2%, 18.6%] |
| Age | 18-44 Years | 260 | 99.2% | 91.1% | 8.1% [3.4%, 14.2%] |
| | 45-64 Years | 647 | 94.8% | 80.1% | 14.7% [9.8%, 19.8%] |
| | 65+ Years | 534 | 83.6% | 64.7% | 18.9% [11.6%, 26.1%] |
| Gender | Men | 551 | 86.9% | 69.5% | 17.4% [10.6%, 24.2%] |
| | Women | 890 | 94.3% | 80.6% | 13.7% [9.5%, 18.0%] |
| Diabetic Status | Diabetics | 114 | 83.3% | 58.3% | 25.0% [8.4%, 40.4%] |
| | Non-Diabetics | 1,327 | 92.0% | 78.1% | 13.9% [10.2%, 17.7%] |
| Body Mass Index (BMI) | BMI > 30 (Obese) | 523 | 89.2% | 68.1% | 21.1% [14.3%, 28.0%] |
| | BMI ⩽ 30 | 918 | 92.7% | 81.0% | 11.6% [7.4%, 16.0%] |
| Alcohol Consumption | 0-1 Drinks/Day | 1,325 | 91.0% | 77.0% | 13.9% [10.1%, 17.8%] |
| | 2-3 Drinks/Day | 108 | 100.0% | 70.2% | 29.8% [19.5%, 42.7%] |
| Smoking Status | Smoker | 187 | 85.9% | 70.5% | 15.3% [3.5%, 27.0%] |
| | Past Smoker | 385 | 89.3% | 77.3% | 12.0% [4.7%, 19.5%] |
| | Non-Smoker | 869 | 93.4% | 77.4% | 16.0% [11.4%, 20.6%] |
| Geography | US | 601 | 81.9% | 58.4% | 18.4% [11.8%, 25.0%] |
| | Europe | 601 | 94.4% | 83.3% | 11.1% [6.2%, 16.3%] |
| | Canada | 239 | 97.5% | 82.5% | 15.0% [8.0%, 23.1%] |
| Ethnicity/ Race | Hispanic or Latino | 132 | 89.6% | 69.2% | 20.3% [6.8%, 33.9%] |
| | Non-Hispanic or Latino | 1,303 | 91.5% | 77.1% | 14.4% [10.6%, 18.3%] |
| | Black or African-American | 108 | 86.0% | 76.5% | 9.5% [-5.4%, 24.8%] |




* Per Protocol Set

# Higher Anti-HBs Titers Across Subgroups

## 5- 8x higher antibody GMC is maintained for participants who received 3A - HBV vs. 1A- HBV, regardless of age, BMI, gender or diabetic status at Day 196




Error bars = SE; Geometric Mean Concentration (GMC) and SE are calculated based on log10 - transformed data, then transformed back to anti - HBs titer; Data are from the Per - Protocol Set

# Comparable Safety Profile Observed Between 3A-HBV and 1A-HBV

## Serious Adverse Events (SAEs)

| | 3A- HBV | 1A- HBV |
|---|---|---|
| **SAEs occurring in ⩾ 2 participants:** | | |
| Atrial Fibrillation | 1 (0.1%) | 2 (0.2%) |
| Cardiac failure congestive | 2 (0.3%) | - |
| Colon cancer | - | 2 (0.2%) |
| Cholelithiasis | 1 (0.1%) | 1 (0.1%) |
| Ankle fracture | 1 (0.1%) | 1 (0.1%) |
| Osteoarthritis | 1 (0.1%) | 1 (0.1%) |
| Cerebrovascular accident | 1 (0.1%) | 1 (0.1%) |

- 95.2% in 3A-HBV and 96.8% participants in 1A-HBV completed full course of vaccination
- Low rate of vaccine discontinuation due to non-serious AEs of 0.4% vs. 0.4% and 0.3% vs. 0.2% due to SAEs for 3A-HBV and 1A-HBV, respectively
- Low rates of SAEs reported (1A-HBV: 2.6% and 3A-HBV: 4.0%)
- Only one SAE, viral gastroenteritis, probably related to 3A-HBV
- Higher rates of mild or moderate injection site pain, tenderness, and myalgia reported by subjects receiving 3A-HBV compared to 1A-HBV

## Unsolicited AEs

| | 3A- HBV | 1A- HBV |
|---|---|---|
| **1+ AEs reported throughout study (% of participants)** | **52.5%** | **54.5%** |
| **AEs reported by ⩾ 1% of participants:** | | |
| Headache | 8.5% | 8.3% |
| URI | 6.3% | 6.7% |
| Fatigue | 4.1% | 4.9% |
| Nasopharyngitis | 3.9% | 3.5% |
| Injection site pain | 2.9% | 1.6% |
| Back pain | 4.4% | 2.8% |
| Arthralgia | 2.1% | 2.5% |
| Diarrhea | 1.3% | 2.6% |
| UTI | 2.1% | 2.1% |
| Oropharyngeal pain | 1.9% | 2.2% |
| Dizziness | 1.5% | 1.2% |
| Sinusitis | 1.4% | 2.1% |
| Hypertension | 1.3% | 1.6% |
| Respiratory rate increase | 1.3% | 0.9% |
| Gastroenteritis | 1.3% | 0.5% |
| Nausea | 0.4% | 1.2% |
| Cough | 1.1% | 1.0% |
| Neck pain | 0.8% | 1.1% |
| Bronchitis | 1.0% | 0.7% |
| Muscle strain | 1.0% | 0.7% |

# Summary of PROTECT Data

## In PROTECT, when compared to 20 µg of 1A - HBV, 10 µg of 3A - HBV demonstrated:

- Non-inferiority in all adults age 18+ (91.4% vs. 76.5%) *[difference 14.9%; 95% CI: 11.2, 18.6%]* and superiority, as defined in the clinical protocol, in adults ⩾age 45 years (89.4% vs. 73.1%) *[difference 16.4%; 95% CI: 12.2, 20.7%]*
- Higher SPR in key high-risk and immunocompromised populations including obese individuals (89.2% vs. 68.1%), diabetics (83.3% vs. 58.3%), and subjects age 65+ (83.6% vs. 64.7%)
- A more rapid immune response, resulting in higher SPR at each time point compared
- A safety profile consistent with previous studies - no safety signals observed

## Next Steps:

- Regulatory submissions for the prevention of infection caused by all known subtypes of HBV in adults have been submitted to the FDA and EMA
- The EMA accepted the MAA for review in December 2020 – review is ongoing
- The FDA has set a Prescription Drug User Fee Act (PDUFA) target action date of November 30, 2021
- VBI expects to complete the regulatory filing in Canada in 2021

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- Michael Manns

**UK**

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Trial Sponsor :

# Questions?


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