

#### ACTIVATING THE POWER WITHIN

#### Safety & Immunogenicity of a new 3-Antigen Hepatitis B Vaccine, PreHevbrio™ *[Hepatitis B Vaccine (Recombinant)]*

World Vaccine Congress 2022

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# Forward-Looking & Safe Harbor Statements

Certain statements in this presentation that are forward-looking and not statements of historical fact are forward-looking statements within the meaning of the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 and are forward-looking information within the meaning of Canadian securities laws (collectively "forward-looking statements").

The Company cautions that such statements involve risks and uncertainties that may materially affect the Company's results of operations. Such forward-looking statements are based on the beliefs of management as well as assumptions made by and information currently available to management.

Actual results could differ materially from those contemplated by the forward-looking statements as a result of certain factors, including but not limited to, the impact of general economic, industry or political conditions in the United States or internationally; the impact of the ongoing COVID-19 pandemic on our clinical studies, manufacturing, business plan, and the global economy; the ability to successfully manufacture and commercialize PreHevbrio; the ability to establish that potential products are efficacious or safe in preclinical or clinical trials; the ability to establish or maintain collaborations on the development of pipeline candidates and the commercialization of PreHevbrio; the ability to obtain appropriate or necessary regulatory approvals to market potential products; the ability to obtain future funding for developmental products and working capital and to obtain such funding on commercially reasonable terms; the Company's ability to manufacture product candidates on a commercial scale or in collaborations with third parties; changes in the size and nature of competitors; the ability to retain key executives and scientists; and the ability to secure and enforce legal rights related to the Company's products.

A discussion of these and other factors, including risks and uncertainties with respect to the Company, is set forth in the Company's filings with the SEC and the Canadian securities authorities, including its Annual Report on Form 10-K filed with the SEC on March 7, 2022, and filed with the Canadian security authorities at sedar.com on March 7, 2022, as may be supplemented or amended by the Company's Quarterly Reports on Form 10-Q.

Given these risks, uncertainties and factors, you are cautioned not to place undue reliance on such forward-looking statements, which are qualified in their entirety by this cautionary statement.

All such forward-looking statements made herein are based on our current expectations and we undertake no duty or obligation to update or revise any forward-looking statements for any reason, except as required by law.



## **About VBI Vaccines**

VBI Vaccines is a global biotechnology company driven by immunology in the pursuit of powerful prevention and treatment of disease





# Introduction to VBI's 3-Antigen HBV Vaccine – PreHevbrio™ )///

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# PreHevbrio is the Only 3-Antigen HBV Vaccines

PreHevbrio is scientifically differentiated from other HBV vaccines – expressing the three hepatitis B surface antigens (S, pre-S1, and pre-S2), and manufactured in mammalian cells (vs. yeast)





# **Extensive History of 3-Antigen HBV Vaccine**

- U.S. Activity :
  - Phase 3 program (PROTECT & CONSTANT), designed to achieve licensure in adults in U.S., Europe, and Canada, initiated at end of 2017 and completed in 2020
  - November 30, 2021 : U.S. FDA approved PreHevbrio™ for the prevention of infection caused by all known subtypes of hepatitis B virus (HBV) in adults age 18 and older
  - American Medical Association (AMA) Current Procedural Terminology (CPT®) Panel established a unique CPT code for a 3-antigen (S, Pre-S1, Pre-S2) Hepatitis B (HBV) vaccine (90759)
  - February 2022 : PreHevbrio recommended by CDC Advisory Committee on Immunization Practices (ACIP), joining the list of recommended products for prophylactic adult vaccination against HBV infection
  - Ex-U.S. History :
    - Originally developed at Weizmann Institute in Israel
    - Supported by data from 20+ clinical studies in neonates, children and adults ("legacy studies"), initial marketing authorization received in Israel in 2000
- **Distribution Data :** 750,000+ individuals estimated to have received vaccine in Israel



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# $\in$ **PROTECT & CONSTANT Studies**

**Design & Enrollment** 

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## Pivotal Phase 3 Program Designed to Achieve Licensure in the U.S., Europe, and Canada

Pivotal Phase 3 program was comprised of two studies – PROTECT & CONSTANT

Phase 3 Study	<b>PROTECT</b> 2-arm safety and immunogenicity study	CONSTANT 4-arm lot-to-lot consistency study				
N size	1,607	2,838				
Study Population	18-90 years (including those with well- controlled chronic conditions)	18-45 years				
Control Vaccine	Engerix-B (GSK)	Engerix-B (GSK)				
Primary Endpoint(s)	Based on seroprotection rates (SPR) at Day 196: i. Non-inferiority <sup>1</sup> in adults ≥ age 18 ii. Superiority <sup>2</sup> in adults ≥ age 45	Consistency of Geometric Mean Concentration (GMC) of antibodies at Day 196 across three consecutively manufactured lots of VBI's vaccine				
Secondary and Exploratory Endpoint(s)	<ul> <li>Safety and tolerability</li> <li>Serum concentrations of anti-HBs titers, kinetics of SPR, and immunogenicity in subgroups</li> </ul>	<ul> <li>Safety, tolerability, and reactogenicity</li> <li>SPR, serum concentrations of anti-HBs titers, kinetics of immunogenicity, and subgroup analyses</li> </ul>				



<sup>1</sup>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% <sup>2</sup>Statistical superiority: The lower bound of the same 95% CI is >0% - Clinical superiority: The lower bound of the same 95% CI is >5%

#### Enrolled Subjects in Phase 3 Program : PROTECT : ~80% Age 45+ | CONSTANT : 100% Age 18-45

	PRO	PROTECT			TANT		
Individuals Screened	2,4	2,472			4,452		
- Screened Failure	865 (	865 (35%)			1,614 (36%)		
Participants Randomized	1,607 at 28	study sites		2,838 at 35 study sites			
Clinical Study Interventions	PreHe∨brio™ 10 µg	PreHevbrio™ Engerix-B® 10 µg 20 µg		PreHevbrio™ 10 µg	Engerix-B® 20 µg		
Participants Randomized Mean Age	796 56.6	796 811 56.6 56.6		2126 33.5	712 33.4		
Age Segmentation - 18-44 years - 45-64 years - 65+ years	145 (18%) 355 (45%) 296 (37%)	154 (19%) 361 (45%) 296 (37%)		100% age 18	3-45 years		
- Male - Female	315 (40%) 481 (60%)	303 (37%) 508 (63%)		907 (43%) 1219 (57%)	291 (41%) 421 (59%)		
Mean BMI Diabetic Subjects	29.4 54 (7%)	29.1 60 (7%)		25.9	25.7		
Race - White - Asian - Black or African American - Other	715 (90%) 8 (1%) 66 (8%) 7 (1%)	730 (90%) 4 (0.5%) 65 (8%) 12 (1.5%)		1943 (91%) 37 (2%) 123 (6%) 23 (1%)	654 (92%) 9 (1%) 38 (5%) 11 (2%)		
Ethnicity - Hispanic or LatinX - Non-Hispanic/LatinX - Not collected	79 (10%) 714 (90%) 3 (0.4%)	75 (9%) 732 (90%) 4 (0.5%)		195 (9.2%) 1926 (90.6%) 5 (0.2%)	74 (10%) 636 (89%) 2 (0.3%)		
Country/Region - United States - Europe - Canada	338 (43%) 332 (42%) 126 (16%)	342 (42%) 336 (41%) 133 (16%)		564 (27%) 1472 (69%) 90 (4%)	188 (26%) 493 (69%) 31 (4%)		
Withdrew Completed Study	40 (5.0%) 756 (95%)	42 (5.2%) 769 (94.8%)		228(10.7%) 1898 (89.3%)	69 (9.7%) 643 (90.3%)		



# $\mathbf{x}$ PROTECT & CONSTANT Studies

**Immunogenicity Results** 

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#### PROTECT Phase 3 Results: 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 PreHevbrio arm minus the SPR in the Engerix-B arm is > -5%
- *Statistical superiority: T*he lower bound of the same 95% CI is >0%
- *Clinical superiority: T*he lower bound of the same 95% CI is >5%

## PROTECT Phase 3 Results: Higher SPRs and Anti-HBs Titers Across Subgroups

	# of Sub	jects (N)		Seroprotection Rates (SPR) at Day 196		GMC of Anti-HBs Titers at Day 196		
Population	PreHevbrio (VBI)	Engerix-B (EB)	VBI	EB Difference in SPRs : VBI – EB		VBI	EB	X-Fold Increase
All Subjects	718	723	91.4%	76.5%		1148.2	192.6	6.0x
Age					-			
18-44 years	125	135	99.2%	91.1%		4570.4	720.6	6.3x
45-64 years	325	322	94.8%	80.1%		1577.3	276.5	5.7x
>= 65 years	268	266	83.6%	64.7%	<b>⊢</b>	410.2	63.7	6.4x
18-39 years	71	72	100.0%	93.1%		5164.2	903.3	5.7x
40-49 years	158	143	98.7%	89.5%	<b>⊢♦</b> −−1	2869.6	645.7	4.4x
50-59 years	153	164	92.8%	78.1%	·	1250.0	211.6	5.9x
60-69 years	221	229	89.1%	72.1%		780.5	122.9	6.4x
>=70 years	115	115	78.3%	56.5%	·	241.8	34.8	6.9x
Diabetes					Ì			
Yes	54	60	83.3%	58.3%	· · · · · · · · · · · · · · · · · · ·	222.3	41.3	5.4x
No	664	663	92.0%	78.1%	<b>⊢</b> ,	1312.2	221.4	5.9x
BMI					1			
> 30 kg/m2	269	254	89.2%	68.1%	·	884.0	110.0	8.0x
≤ 30 kg/m2	449	469	92.7%	81.0%		1343.0	260.9	5.1x
				-10%	<b>I</b> 0% 10% 20% 30% 40%			



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## PROTECT Phase 3 Results: Higher SPRs and Anti-HBs Titers Across Subgroups (2)

	# of Sub	jects (N)	Seroprotection Rates (SPR) at Day 196		GMC of Anti-HBs Titers at Day 196			
Population	PreHevbrio (VBI)	Engerix-B (EB)	VBI	EB Difference in SPRs : VBI – EB		VBI	EB	X-Fold Increase
Daily Alcohol Consumption								
0-1 Drinks	663	662	91.0%	77.0%	<b>→</b>	1093.4	202.0	5.4x
2-3 Drinks	51	57	100%	70.2%	·	2643.8	110.6	23.9x
Smoking Status								
Current Smoker	92	95	85.9%	70.5%	↓ <b>↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ ↓ </b>	449.4	161.9	2.8x
Past Smoker	187	198	89.3%	77.3%	·◆1	1162.9	141.1	8.2x
Non-Smoker	439	430	93.4%	77.4%	<b>⊢</b>	1390.1	231.0	6.0x
Gender								
Male	282	269	86.9%	69.5%	└ <b>─</b> ◆──1	761.0	106.6	7.1x
Female	436	454	94.3%	80.6%	⊢ <b>↓</b>	1498.2	273.5	5.5x
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## PROTECT Phase 3 Results: Higher SPRs and Anti-HBs Titers Across Subgroups (3)

	# of Sub	jects (N)	Seroprotection Rates (SPR) at Day 196		GMC of Anti-HBs Titers at Day 196					
Population	PreHevbrio (VBI)	Engerix-B (EB)	VBI	EB	EB Difference in SPRs : VBI – EB		VBI	EB	X-Fold Increase	
Race										
White	648	660	92.0%	76.7%		<b>⊢♦</b> −1		1229.6	187.8	6.5x
Black/African American	57	51	86.0%	76.5%	 	<b>4</b>		535.9	291.4	1.8x
Other	13	12	84.6%	66.7%		•		1066.4	131.8	8.1x
Ethnicity					l I					
Hispanic/LatinX	67	65	89.6%	69.2%				820.9	81.1	10.1x
Non- Hispanic/LatinX	648	655	91.5%	77.1%		<b>⊢♦</b> −1		1189.2	206.4	5.8x
Region										
U.S.	297	304	85.9%	67.4%		<b></b>		544.0	95.7	5.7x
Europe	302	299	94.4%	83.3%		ı— <b>—</b> •		1851.2	274.5	4.7x
Canada	119	120	97.5%	82.5%		-		2204.5	468.1	6.7x



-20% -10% 0% 10% 20% 30% 40% 50%

## PROTECT & CONSTANT Phase 3 Results: Higher SPR after Both 2 and 3 Doses in Adults Age 18-45

On average, ~90% of adults age 18-45 vaccinated with PreHevbrio were protected after 2 doses (Day 168) vs. ~40-50% of those who received Engerix-B





#### PROTECT Phase 3 Results: Higher SPR at All Timepoints in All Age Groups



### CONSTANT Phase 3 Results: Rapid Induction of High Anti-HBs Titers

#### Kinetics of Mean Anti-HBs Titers in Participants Age 18-45 Years



# $\mathbf{x}$ PROTECT & CONSTANT Studies

Integrated Safety Analysis

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## Reactogenicity: Solicited Local and Systemic Adverse Events

#### Local (Injection Site) Solicited AEs Within 7 Days After Vaccination

Systemic Solicited AEs Within 7 Days After Vaccination



- Higher rates of mild-to-moderate pain and tenderness at injection site and myalgia for PreHevbrio generally resolved without intervention in 1-2 days
- No increase in reactogenicity symptoms over the 3-dose vaccination schedule
- Very low rates of vaccine discontinuation due to AEs (0.4% for PreHevbrio; 0.3% for Engerix-B)

# **Unsolicited Adverse Events**

No unexpected safety signals associated with either vaccine and no unusual patterns or concerning clusters of SAEs, medically-attended AEs, or NOCIs

Overview of Unsolicited Adverse Events Through End of Study (Day 336) <i>Subjects With at Least 1:</i>	PreHevbrio™ N=2,920 N (%)	Engerix-B° N=1,523 N (%)	Overview of SAEs Reported Through End of Study (Day 336) Subjects with ≥ 1 SAE
Adverse Event (AE)	1546 (52.9)	812 (53.3)	SAEs reported by ≥ 2 subjects
AE within 28 days of vaccination	1411 (48.3)	737 (48.4)	Appendicitis
Vaccine-related AE	445 (15.2)	198 (13.0)	Intervertebral disc protrusion
Medically-attended AE (MAAE)	663 (22.7)	356 (23.4)	Back pain
New Onset of Chronic Illness (NOCI)	59 (2.0)	38 (2.5)	Cardiac failure congestive
AE leading to treatment withdrawal	15 (0.5)	6 (0.4)	Vertigo
Vaccine-related AE leading to treatment withdrawal	5 (0.2)	1 (0.1)	Erysipelas Pneumonia
AE leading to study withdrawal	8 (0.3)	3 (0.2)	Joint dislocation
Vaccine-related AE leading to study withdrawal	3 (0.1)	1 (0.1)	Tendon rupture
Serious Adverse Event (SAE)	74 (2.5)	24 (1.6)	Atrial fibrillation
AE leading to death	1 (0.0)	0	Colon cancer



PreHevbrio™

N=2,920

N (%)

74 (2.5)

4 (0.1)

3 (0.1)

2 (0.1)

2 (0.1)

2 (0.1)

2 (0.1)

2 (0.1)

2 (0.1)

2 (0.1)

2 (0.1)

2 (0.1)

1 (0.0)

0

Engerix-B<sup>®</sup>

N=1,523

N (%)

24 (1.6)

0

0

1 (0.1)

0

0

0

0

0

0

0

0

2 (0.1) 2 (0.1)

# Consistent Safety Profile Across Both Phase 3 Studies & Comparable to Engerix-B

- High 3-dose <u>completion rates</u> for both vaccines
- <u>AEs</u>:
  - Most common were local reactogenicity symptoms, mostly of mild-to-moderate severity
  - Resolved without intervention within 1-2 days no increase with subsequent dosing
  - Most frequently reported reactogenicity symptoms : injection site pain & tenderness
- MAAEs :
  - Similar incidence in both studies across both study arms
  - PROTECT 25.4% and 28.5%; CONSTANT 21.7% and 17.6% for PreHevbrio and Engerix-B, respectively
- <u>SAEs</u>:
  - Uncommon for both vaccines
  - No clustering or unusual pattern of SAEs
  - Two SAEs assessed as possibly related by site investigators PROTECT gastroenteritis viral; CONSTANT ankyloglossia congenital (an infant born to a female study participant)
- Deaths :
  - No deaths reported in PROTECT
  - In CONSTANT, one sudden cardiac death secondary to preexisting hypertrophic heart disease in a participant randomized to PreHevbrio





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**₹** Summary

#### Supported by an Extensive Dataset, PreHevbrio Has Demonstrated Benefit for Adults

In adults vaccinated with PreHevbrio, data against Engerix-B demonstrated:

- ✓ A well-established safety profile
- Higher rates of seroprotection in adults
- ✓ Robust immunogenicity regardless of age
- ✓ Rapid onset of protection
- ✓ Higher immunogenicity in key high-risk populations





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