



# **VBI VACCINES**



## **CORPORATE PRESENTATION**

# Forward-Looking 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 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 therapeutic candidates; the ability to obtain appropriate or necessary governmental approvals to market potential products, including the approval of Sci-B-Vac® in the U.S., Europe, and Canada following the completion of its recent Phase 3 studies; 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, including patent protection. 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 Securities and Exchange Commission and the Canadian securities authorities, including its Annual Report on Form 10-K filed with the Securities and Exchange Commission on March 5, 2020, and filed with the Canadian security authorities at [sedar.com](https://www.sedar.com) on March 5, 2020, and may be supplemented or amended by the Company's Quarterly Reports on Form 10-Q. The company disclaims any intention or obligation to revise any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.*



# Overview of VBI Vaccines

- Leveraging significant immunology expertise to address unmet medical needs in both **INFECTIOUS DISEASE** and **IMMUNO-ONCOLOGY**
- Advancing prevention and treatment of **HEPATITIS B**:
  - *Sci-B-Vac*<sup>®</sup> : Only tri-antigenic Hepatitis B vaccine; recently completed a Phase III program in the U.S., Europe, and Canada; approved and marketed in Israel
  - *VBI-2601* : Immuno-therapeutic in development in a collaboration with Brio Biosciences for a functional cure for chronic Hepatitis B
- Leveraging a proprietary enveloped virus-like particle (eVLP) platform technology to develop next-generation vaccines:
  - *VBI-1901* : **GLIOBLASTOMA** (GBM) vaccine immunotherapeutic candidate (currently in Phase I/IIa study)
  - *VBI-2901* : **PAN-CORONAVIRUS** (COVID-19, SARS, MERS) vaccine candidate in development in a collaboration with the National Research Council of Canada
  - *VBI-1501* : Prophylactic **CMV** vaccine candidate (positive topline Phase I data announced in May 2018)



# VBI Vaccines Pipeline

		PRE-CLINICAL	PHASE I	PHASE II	PHASE III	APPROVED	STATUS
INFECTIOUS DISEASE							
Hepatitis B – Prophylaxis	Sci-B-Vac® VLP						• Approved for use and commercially-available in Israel
							• Regulatory submissions in U.S., Europe, and Canada expected to begin Q4 2020
Hepatitis B – Therapeutic	VBI-2601 VLP						• License & collaboration agreement with Bii Biosciences • Initial Phase Ib/IIa data expected H2 2020
Cytomegalovirus (CMV)	VBI-1501 eVLP						• Positive Phase I data announced May 2018
Pan-Coronavirus (COVID-19, SARS, MERS)	VBI-2901 eVLP						• Development collaboration with NRC announced March 2020
Zika	VBI-2501 eVLP						• Candidate selected from NRC collaboration
IMMUNO-ONCOLOGY							
Glioblastoma (GBM)	VBI-1901 eVLP						• Ongoing Phase I/IIa • Expanded immunologic data expected mid-year 2020 and Q4 2020
Other CMV+ Tumors	VBI-1901 eVLP						• Preclinical work ongoing



# Recent Key Achievements

## JUNE 2019 – MARCH 2020

<b>March 2020</b>	Announcement of pan-coronavirus vaccine development collaboration with the NRC of Canada
<b>March 2020</b>	Announcement of 12-month overall survival (OS) and median OS data from Part A of the ongoing Phase I/IIa study of VBI-1901 (GBM)
<b>March 2020</b>	First patient dosed in Phase IIa portion of ongoing study of VBI-1901 + GSK's AS01 <sub>B</sub> adjuvant system (GBM)
<b>January 2020</b>	Announcement of positive top-line data from the CONSTANT Phase III study of Sci-B-Vac®
<b>November 2019</b>	First patient dosed in Phase Ib/IIa study of BRIL-179 (VBI-2601) in patients with chronic hepatitis B
<b>November 2019</b>	Announcement of positive initial Phase I/IIa Part B data of VBI-1901 (GBM) at SNO Annual Meeting
<b>October 2019</b>	Announcement of late-breaking poster at AASLD's The Liver Meeting® detailing immunogenicity and safety data from the PROTECT Phase III study of Sci-B-Vac®
<b>October 2019</b>	Announcement of late-breaking oral presentation at IDWeek 2019™ highlighting detailed seroprotection data from the PROTECT Phase III study of Sci-B-Vac®
<b>September 2019</b>	Closed Public Offering for gross proceeds of \$40.3 million
<b>September 2019</b>	Announcement of GSK collaboration to evaluate VBI-1901 + GSK's AS01 <sub>B</sub> adjuvant system in additional study arm of ongoing Phase I/IIa study in patients with glioblastoma (GBM)
<b>July 2019</b>	First patient dosed in Phase IIa portion of ongoing study of VBI-1901 + GM-CSF (GBM)
<b>June 2019</b>	Announcement of addition to Russell 2000® and 3000® Indexes
<b>June 2019</b>	Announcement of positive top-line data from the PROTECT Phase III study of Sci-B-Vac®
<b>June 2019</b>	ASCO presentation of data from Part A of ongoing Phase I/IIa study of VBI-1901 (GBM)





# Hepatitis B - Prophylaxis

## a. **SCI-B-VAC®**

Only commercially-available tri-antigenic vaccine containing pre-S1, pre-S2, and S antigens of Hepatitis B virus

# Chronic HBV is a Significant and Increasing Unmet Need in US & EU

There are more than **2,000,000,000** individuals WW with serological evidence of Hepatitis B, of these **~292M** are chronic carriers

## U.S.

CDC estimates that anywhere from **850,000 – 2.2M people** in the U.S. are chronically infected with Hepatitis B



Estimated new cases of Hepatitis B have been **increasing since 2012, from roughly 18,800 new cases in 2012 to 21,000 in 2016**



The CDC has determined this increase is largely due to the **ongoing opioid epidemic**

## Europe

The European Centre for Disease Prevention and Control (ECDC) estimates that in the EU/EEA **~5M people** are chronically infected with Hepatitis B



Among EU/EEA countries that consistently report, the rate of new cases **increased from 6.7/100,000 in 2008 to 10.2/100,000 in 2017**, with UK reporting roughly 62% of all new chronic cases



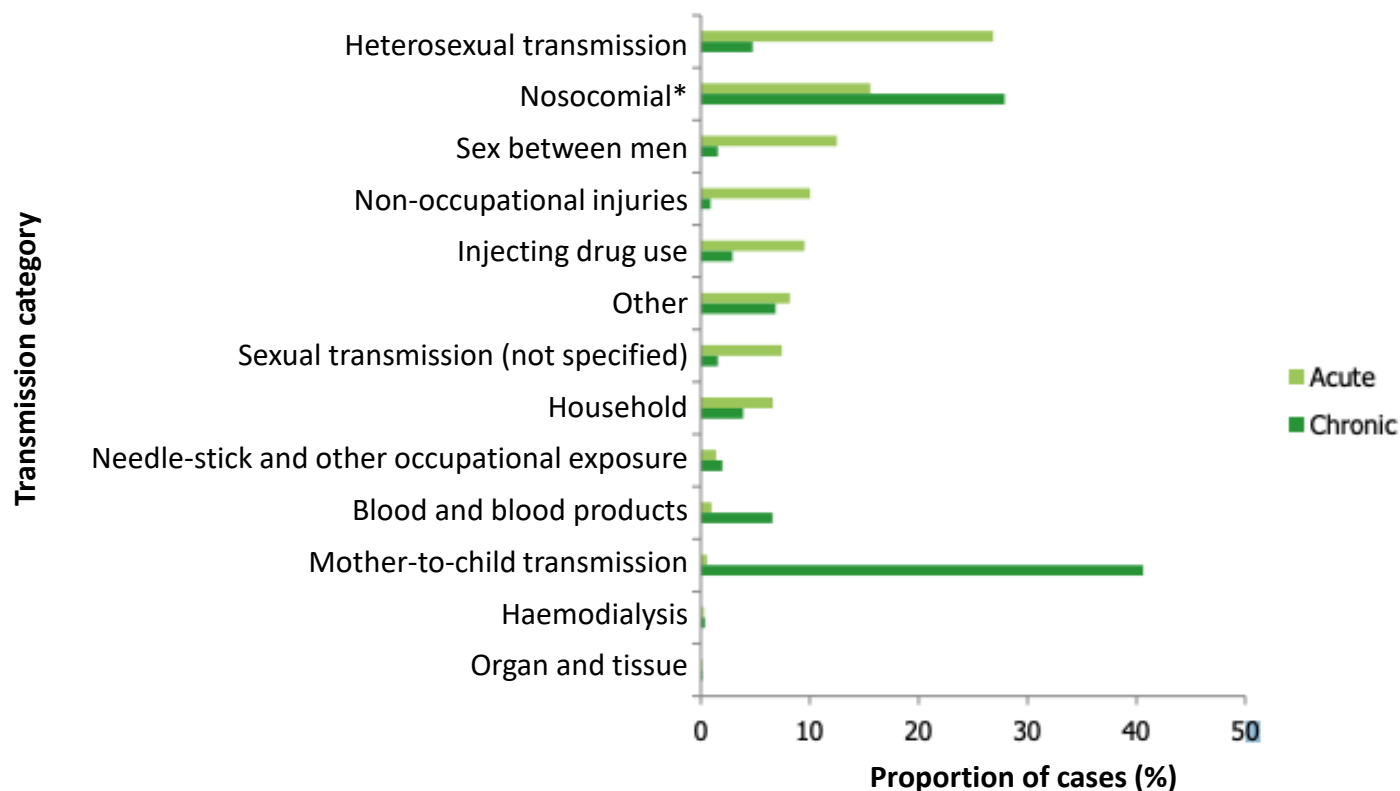
The increase in Europe is largely due to the **increased population migration and refugee crises** – a 2012 study noted the prevalence of HBsAg in the base EU population varied (0.01-0.7%), but the prevalence of HBsAg in the three largest migrant groups in each country was similar, **~4%**

Sources: U.S. Center for Disease Control and Prevention (CDC), Disease Burden of Hepatitis B 2010-2016; European Centre for Disease Prevention and Control (ECDC) Systematic Review on Hepatitis B in the EU/EAA 2005-2015 & Hepatitis B – Annual Epidemiological Report for 2017; <https://academic.oup.com/eurpub/article/23/4/642/426712/Changing-epidemiology-of-Hepatitis-B-and-migration>

# Transmission of Chronic Hepatitis B

Chronic Hepatitis B is most commonly transmitted from mother to child (pediatrics) or through nosocomial transmission (i.e. patients exposed in the healthcare setting)

## 2017 Transmission of Hepatitis B Cases by Acute and Chronic Disease Status (EU/EEA)



\*Nosocomial transmission includes hospitals, nursing homes, psychiatric institutions, and dental services. This category refers mainly to patients exposed through healthcare settings, distinct from “needle-stick and other occupational exposure” which refers to staff

Source: European Center for Disease Prevention and Control (ECDC) Hepatitis B Annual Epidemiological Report for 2017



# HBV Vaccination Rates : U.S.

- In 1991, the ACIP recommended a comprehensive HBV vaccination program : universal vaccination for children and for high-risk populations
- Despite this recommendation being in place for ~15 years, coverage rates among US adults remains low
- During 2010-2015, hepatitis B vaccination coverage decreased among all adults aged  $\geq 19$  years
- Vaccination rates have remained stable, however, among adults aged  $\geq 19$  years with chronic liver conditions and among health care providers

Reported US Hepatitis B Vaccination Coverage - 2015	
<b>Otherwise Healthy</b>	
Adults aged $\geq 19$ years	24.6%
Adults aged 19-49 years	32.0%
Adults age $\geq 50$ years	16.5%
<b>High-Risk</b>	
Chronic Liver Conditions	27.4%
Diabetics – Age 19-59 years	24.4%
Diabetics – Age $\geq 60$ years	12.6%
Healthcare Providers $\geq 19$ years	64.7%

Source: 2015 CDC Surveillance of Vaccination Coverage Among Adult Populations

# HBV Vaccination Rates : Europe

- In 1992, the World Health Assembly recommended the inclusion of Hepatitis B vaccination in all national immunization programs
- By 2004, the majority of European member states had introduced the vaccine, either as universal infant, universal newborn, or universal adolescent
- A number of EU member states, however, had not introduced the vaccine into the routine program – all of these were northern European countries

## RECOMMENDATION FOR HEPATITIS B VACCINATION BY COUNTRY (VENICE II SURVEY)



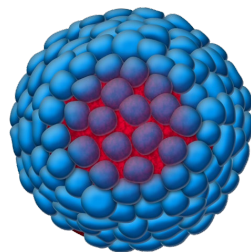
- HBV vaccination included in the routine childhood vaccination & recommended for high risk groups incl. healthcare workers (HCWs):
  - 74% of surveyed countries (20/27)
- HBV vaccination only recommended for high-risk groups incl. HCWs
  - 26% of surveyed countries (7/27)
- Countries not included in VENICE II survey

***Despite recommendations, estimated adult HBV vaccine coverage rates vary greatly (e.g. 8% in Denmark, 33% in Germany)***

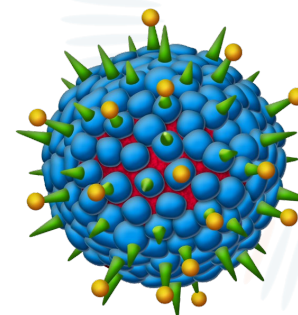
Note: Since this survey, the UK implemented routine childhood vaccination against Hepatitis B (in Aug. 2017)

Sources: [http://venice.cineca.org/Report\\_Hepatitis\\_B\\_Vaccination.pdf](http://venice.cineca.org/Report_Hepatitis_B_Vaccination.pdf); <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3840285/>

# Sci-B-Vac® : Importance of Tri-Antigenic Conformation



2<sup>ND</sup> GENERATION VACCINES



SCI-B-VAC®

Viral antigens mimicked:

S Protein 

✓

✓

Pre-S1 

✓

Pre-S2 

✓

Adjuvant:

Next-generation Adj. (e.g. TLRs)

Alum

Derivation:

rDNA yeast

Mammalian cell

- Pre-S1 antigen induces key neutralizing antibodies that block virus receptor binding
- Published data demonstrates that T cell response to pre-S1 and pre-S2 antigens can further boost responses to the S antigens, resulting in a more immunogenic response

# Sci-B-Vac®: Two Phase III Studies to Support Approval in U.S., Europe, and Canada

Phase III Study	PROTECT <i>2-arm safety and immunogenicity study</i>	CONSTANT <i>4-arm lot-to-lot consistency study</i>
N size	1,607	2,838
Age Range	18+ years	18-45 years
Control Vaccine	Engerix-B® (GSK)	Engerix-B® (GSK)
Primary Endpoint(s)	Based on seroprotection rates (SPR): i. Non-inferiority in adults $\geq$ age 18 ii. Superiority in adults $\geq$ age 45	Consistency of immune response as measured by Geometric Mean Concentration (GMC) of antibodies across three consecutively manufactured lots of Sci-B-Vac®
Secondary Endpoint(s)	i. Safety and tolerability ii. Non-inferiority of SPR after 2 doses of Sci-B-Vac® vs. 3 doses of Engerix-B®	i. Safety and tolerability ii. Non-inferiority of SPR after 3 doses of Sci-B-Vac® vs. 3 doses of Engerix-B®
Top-Line Data Readout	June 2019	January 2020

# Phase 3 Study Subject Disposition

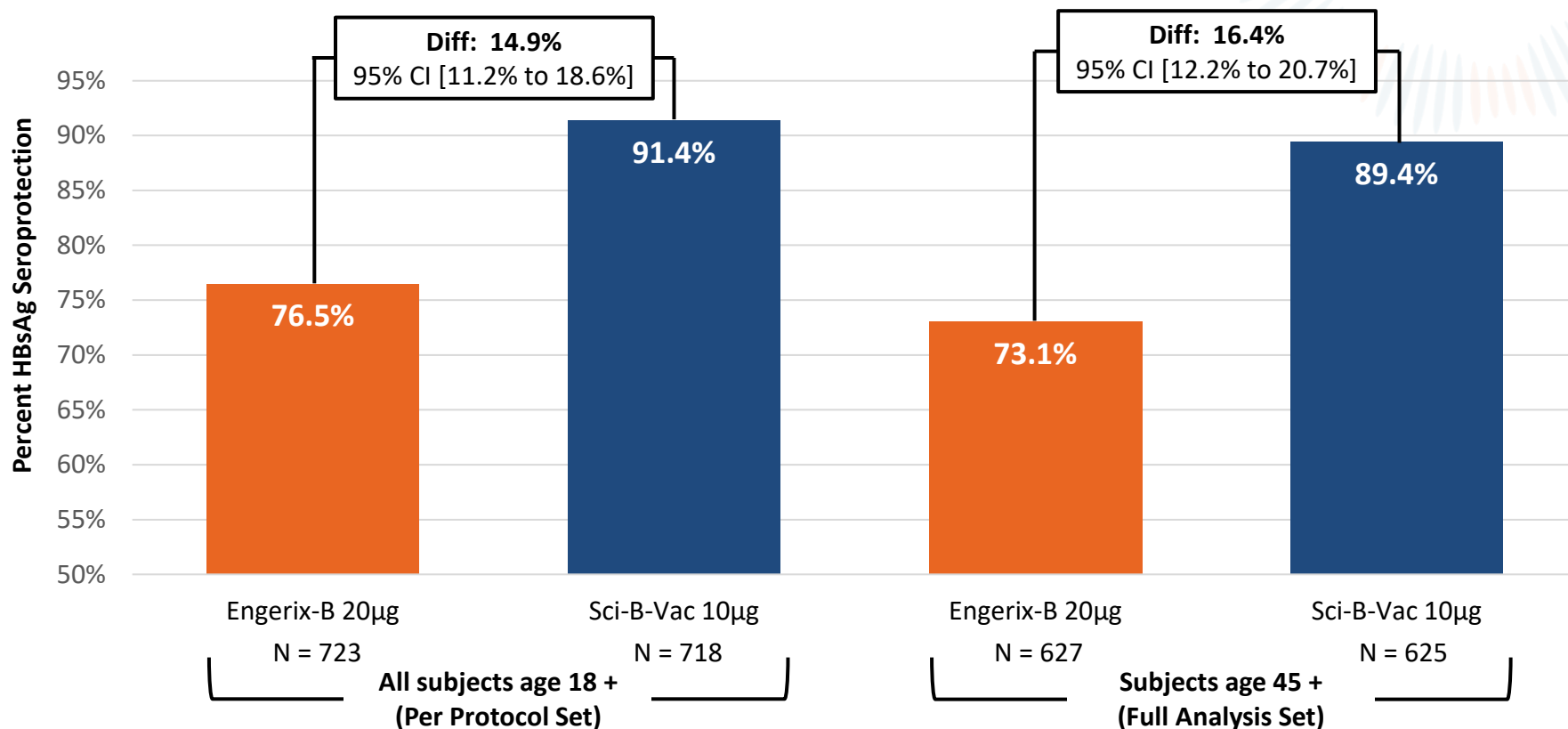
	PROTECT		CONSTANT			
Subjects Screened - Screening Failure	2,472 865 (35%)		4,452 1,614 (36%)			
Subjects Randomized	1,607 at 28 clinical study sites		2,838 at 35 clinical study sites			
Clinical Study Arms	Engerix-B 20µg	Sci-B-Vac 10µg	Engerix-B 20µg	Lot A Sci-B-Vac 10µg	Lot B Sci-B-Vac 10µg	Lot C Sci-B-Vac 10µg
Subjects Randomized	811	796	712	711	709	706
Mean Age	56.6	56.6	33.4	33.8	32.9	33.9
Age Segmentation:			100% age 18-45 years			
- 18-44 years	154 (19%)	145 (18%)				
- 45-64 years	361 (45%)	355 (45%)				
- 65+ years	296 (37%)	296 (37%)				
Gender:						
- Male	303 (37%)	315 (40%)	291 (40.9%)	303 (42.6%)	313 (44.1%)	291 (41.2%)
- Female	508 (63%)	481 (60%)	421 (59.1%)	408 (57.4%)	396 (55.9%)	415 (58.8%)
Mean BMI	29.1	29.4	25.7	25.9	25.8	26.0
Withdrew	42 (5.2%)	40 (5.0%)	69 (9.7%)	75 (10.5%)	72 (10.2%)	81 (11.5%)
Completed Study	769	756	643	636	637	625

# Both PROTECT Co-Primary Endpoints Successfully Met

Co-Primary Endpoints at Day 196, 4 weeks post-3<sup>rd</sup> vaccination:

1. Non-Inferiority of seroprotection rate (SPR) achieved in all subjects age 18+

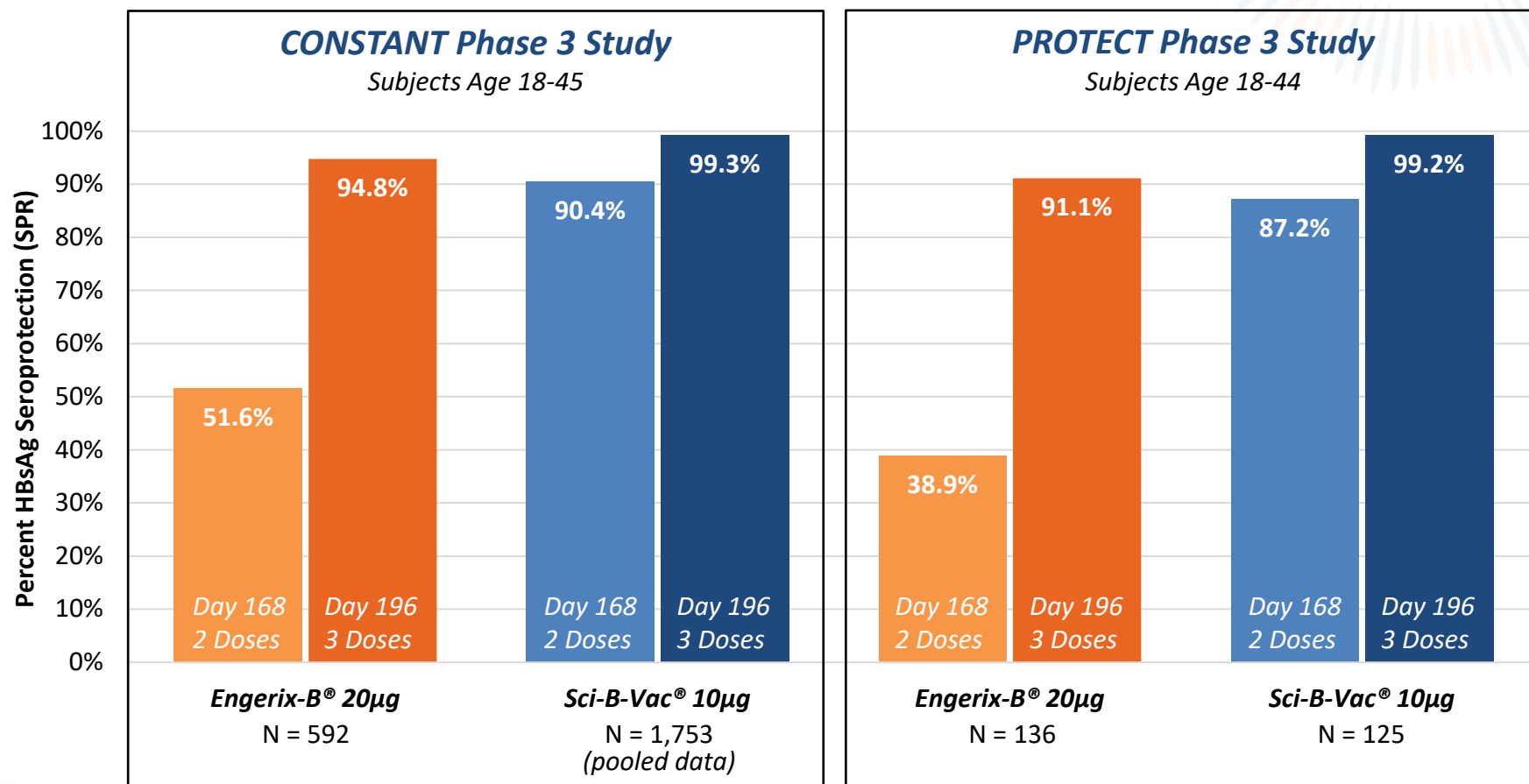
2. Statistical and clinical superiority, as defined in the protocol, achieved in subjects age 45+



- *Non-inferiority* : If the lower bound of the 95% confidence interval (CI) of the difference between the SPR in the Sci-B-Vac® arm minus the SPR in the Engerix-B® arm is > -5%, Sci-B-Vac® will be declared non-inferior to Engerix-B®
- *Statistical superiority* : If the lower bound of the same 95% CI is greater than 0%, Sci-B-Vac® will be declared statistically superior to Engerix-B®
- *Clinical superiority* : If the lower bound of the same 95% CI is > 5%, Sci-B-Vac® will be declared clinically superior to Engerix-B®

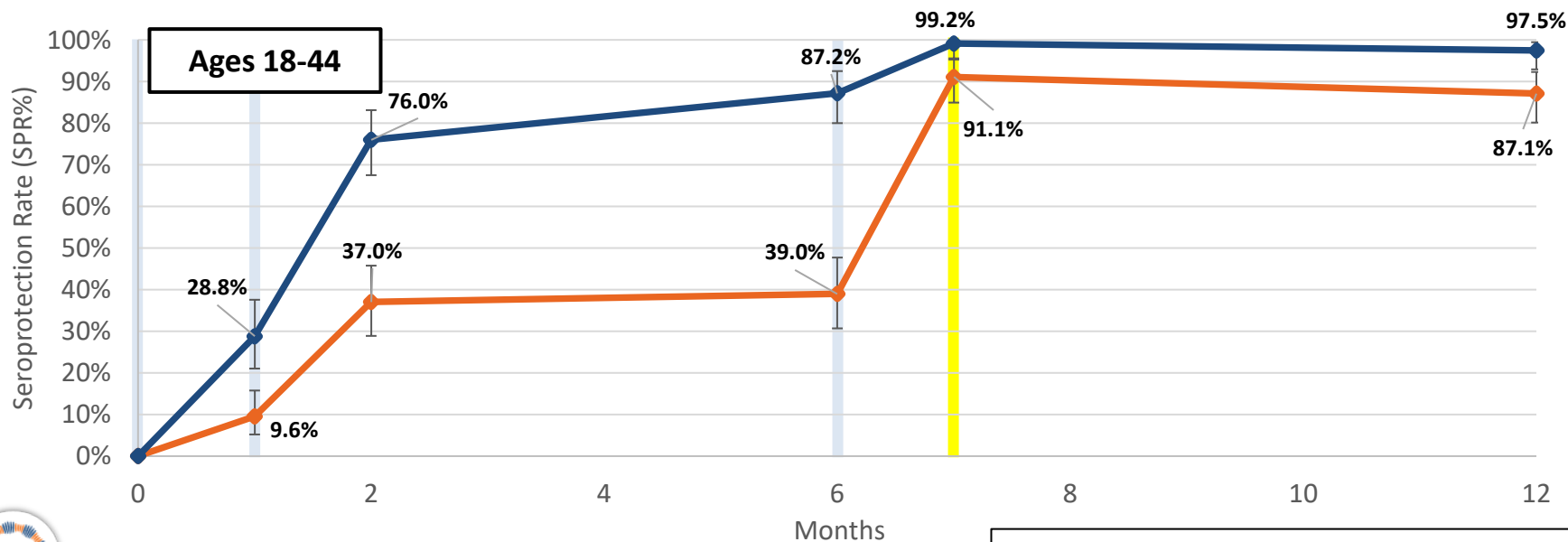
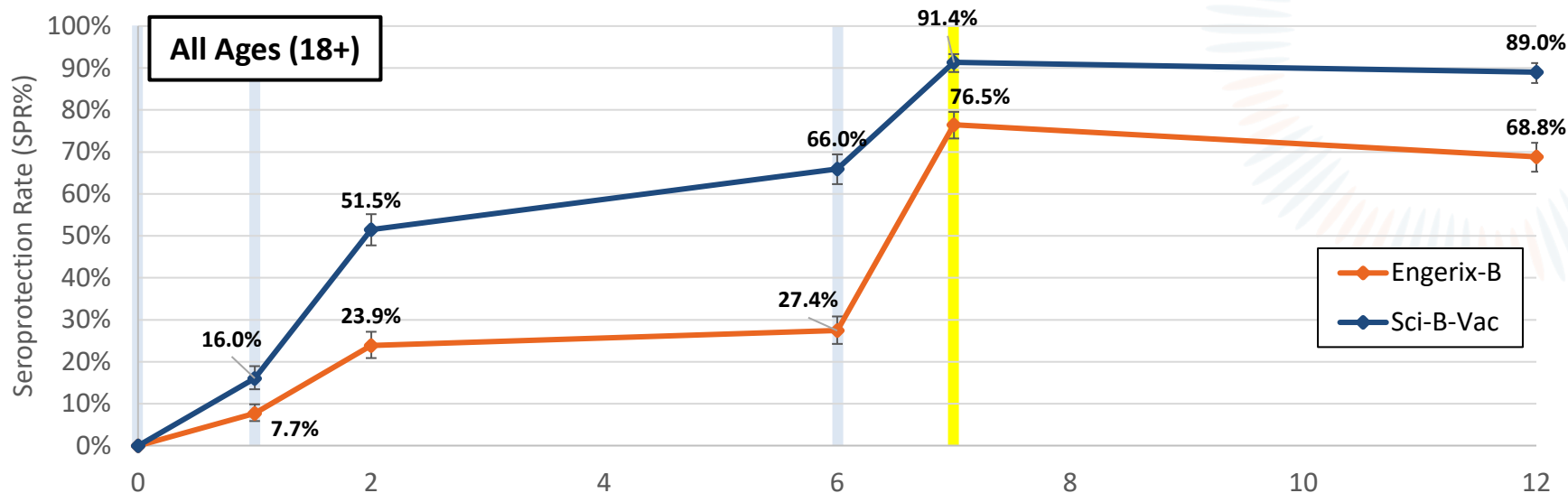
# Kinetics of Seroprotection Rates (SPR) in Younger Adults – Age 18-45 Years

At each time point, day 168 after two vaccinations and day 196 after three vaccinations, the SPR achieved with Sci-B-Vac® was higher than the SPR achieved with Engerix-B®



NOTE : SPR defined as percent (%) of subjects with anti-HBsAg titers > 10mIU/mL

# Kinetics of Seroprotection Rates by Age Groups





# Seroprotection Rates in Subgroup Populations

SPR of Sci-B-Vac® vs. Engerix-B® was statistically significantly higher in all key subgroup analyses of adults age ≥ 18 years, at Day 196, 4 weeks post-3<sup>rd</sup> vaccination, including:

## Diabetics

**58.3%** Engerix-B® vs. **83.3%** Sci-B-Vac®

*SPR difference: 25.0%; 95% CI [8.4%, 40.4%]*

## Subjects with a Body Mass Index (BMI) > 30

**68.1%** Engerix-B® vs. **89.2%** Sci-B-Vac®

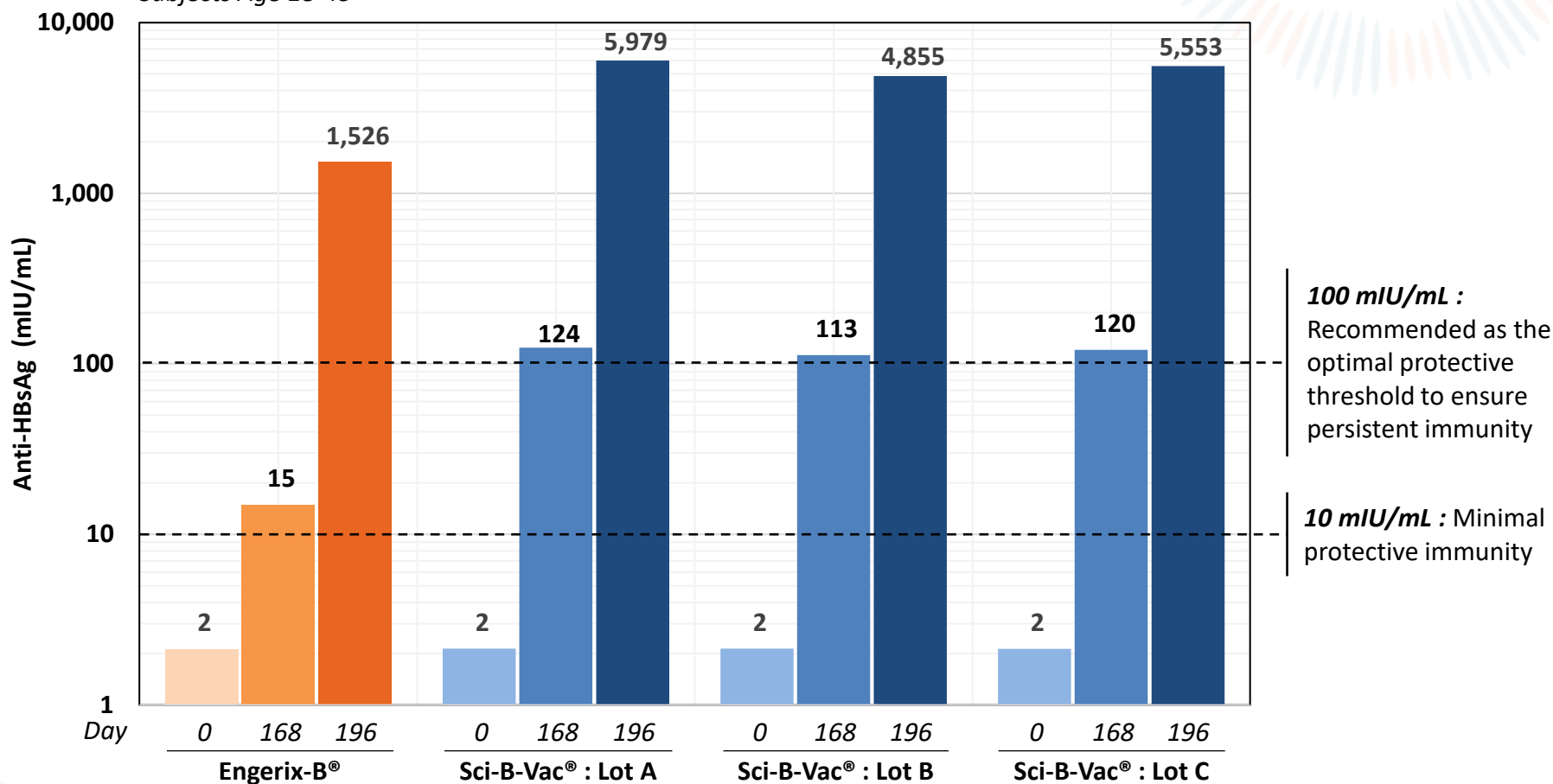
*SPR difference: 21.1%; 95% CI [14.3%, 28.0%]*

# Anti-HBsAg Antibody Titters After 2 & 3 Vaccinations

Antibody GMC achieved with Sci-B-Vac® was more than 7.5x that achieved with Engerix-B® after 2 vaccinations (day 168) and more than 3x after 3 vaccinations (day 196)

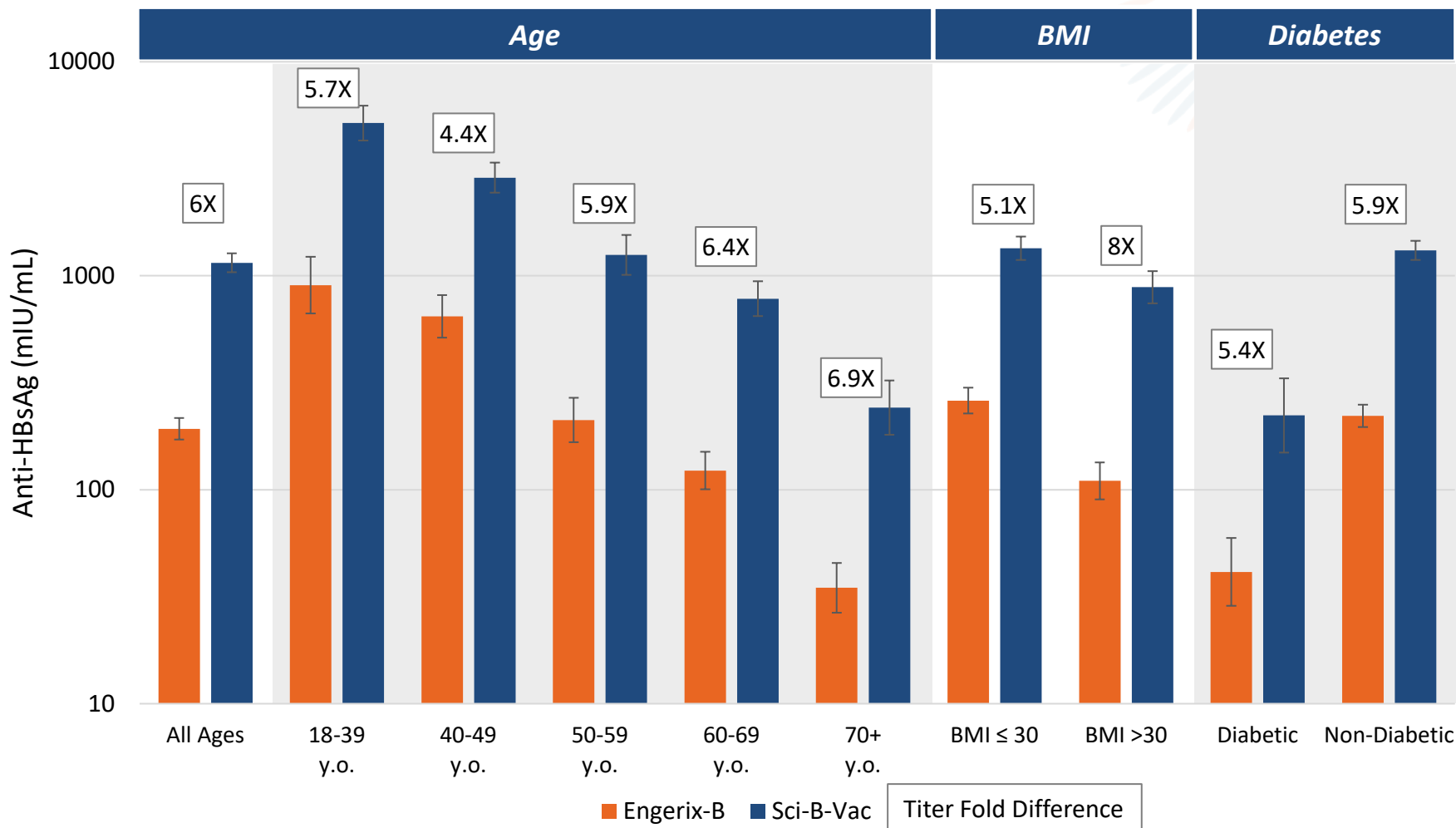
## *CONSTANT Phase 3 Study – Anti-HBsAg Antibody Titters*

*Subjects Age 18-45*



# Anti-HBsAg Titers in Subgroup Populations

5-8x fold higher antibody GMC is maintained for patients who received Sci-B-Vac vs. Engerix-B regardless of age, BMI, or diabetes status



Error bars = SE; The GMC and SE are calculated based on log10-transformed data, then transformed back to Anti-HBsAg Antibody titer

# Summary of Safety Data from PROTECT & CONSTANT

## OVERALL :

- No safety signals observed in PROTECT or CONSTANT
- Sci-B-Vac safety profile consistent with previous studies and post-marketing use (Israel)
- High rate of completion of vaccinations for Engerix-B and Sci-B-Vac
- Low rate of vaccine discontinuation due to non-serious adverse events (AEs) – in PROTECT, 0.4% vs. 0.4% and due to SAEs of 0.2% vs. 0.3% for Engerix-B and Sci-B-Vac, respectively

## REACTOGENICITY – SOLICITED AEs :

- Higher rates of mild-to-moderate injection site pain, tenderness and myalgia reported by subjects receiving Sci-B-Vac compared to Engerix-B
- Reactogenicity symptoms generally resolved without intervention within 1-7 days
- No increase in reactogenicity symptoms over the 3-dose vaccination schedule

# Key Unmet Medical Need and Market Segmentation

	Target Population	Key Product Attributes Driving Use	Est. Unvaccinated Population
<b>ADULT POPULATION (AGE 18+)</b>			
<b>Young, “Otherwise Healthy”</b>	<ul style="list-style-type: none"> <li>Public service sector workers (incl. HCWs)</li> <li>Military</li> <li>Pre-diabetics</li> </ul>	<ul style="list-style-type: none"> <li>Earlier seroprotection</li> <li>Cost</li> </ul>	US : 5M+   EU : 5M+ <b>TOTAL: 10M+</b> [conservative estimate]
<b>Older Adults</b>	<ul style="list-style-type: none"> <li>Age 45+</li> </ul>	<ul style="list-style-type: none"> <li>Superior seroprotection rates</li> <li>Safety</li> </ul>	US : 50M   EU : 35M <b>TOTAL: 85M</b>
<b>Immuno-Compromised/High-Risk</b>	<ul style="list-style-type: none"> <li>Diabetics</li> <li>CKD/ESRD patients</li> <li>Other high-risk populations</li> </ul>	<ul style="list-style-type: none"> <li>Higher seroprotection rates</li> <li>Safety</li> </ul>	US : 30M   EU : 20M <b>TOTAL: 50M</b>
<b>PEDIATRIC POPULATION (AGE 0-17)</b>			
<b>High-risk, Immuno-compromised Newborns</b>	<i>Children born:</i> <ul style="list-style-type: none"> <li>with immuno-compromising conditions (e.g. Thalassemia)</li> <li>to HBV-infected mothers</li> <li>in high endemic areas</li> </ul>	<ul style="list-style-type: none"> <li>Higher seroprotection rates</li> <li>Safety</li> </ul>	<ul style="list-style-type: none"> <li>~8M births each year in US/EU</li> <li>~75,000 births to HBV+ mothers</li> <li>~1/2,000 children are born with a primary immuno-compromising condition</li> </ul>

Sources: U.S. Center for Disease Control, U.S. Department of Health and Human Services, European Centre for Disease Prevention and Control, World Health Organization, U.S. Census Population Data

# PROTECT/CONSTANT Data Summary & Next Steps

When comparing Sci-B-Vac® at 10µg to Engerix-B® at 20µg, PROTECT and CONSTANT top-line data showed:

- ✓ **Higher rates of protection in all adults**, at all time points on a per-visit basis, with statistical and clinical superiority in adults age 45 years and older
- ✓ Higher seroprotection in **key immunocompromised populations** including obese individuals, diabetics, and elderly
- ✓ Confirmation of **robust immune response elicited with Sci-B-Vac®** – including with respect to both SPR and anti-HBsAg antibody titers – after both two and three vaccinations
- ✓ **Lot-to-lot manufacturing consistency**, required as part of the chemistry, manufacturing, and control (CMC) portion of the BLA
- ✓ **Clean safety profile** of the vaccine, with no new safety risks identified

## Next Steps:

- **Q2 2020** : Pre-BLA discussion expected with FDA

*Subject to outcome of pre-BLA discussion and discussions with other regulatory bodies:*

- **Q4 2020** : Submissions of applications for regulatory approvals in the U.S., Europe, and Canada expected to begin



# Hepatitis B - Therapeutic

## b. VBI-2601

Potential to contribute to a functional cure by inducing and sustaining broad and effective immunity against chronic Hepatitis B infection

# Functional Cure Combination for Hepatitis B

Scientific consensus is that a functional cure is within reach, but will likely be achieved through a combination approach

A functional cure will likely require the achievement of the below:

1. Drive down hepatitis B virus (HBV) DNA
2. Drive down immuno-suppressive HBV S-antigen
3. Achieve long-term immunologic control

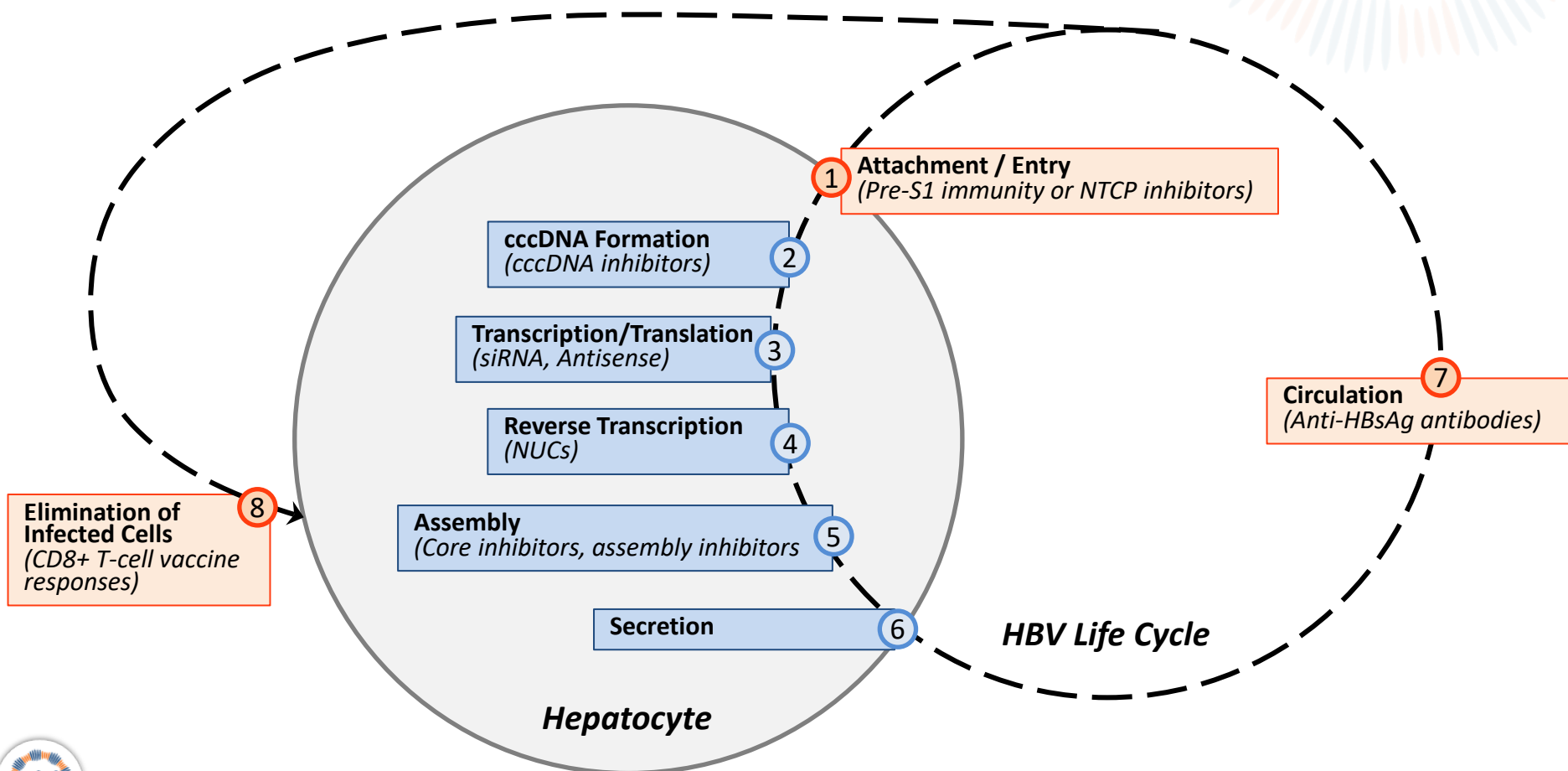
*Consensus is building that an immuno-therapeutic would be needed to achieve long-term immunologic control and restore the body's defense against hepatitis B infection*



# VBI-2601 Well Positioned as an Immuno-Therapeutic Component of a Functional Cure for Hepatitis B

VBI-2601 is designed to impact circulating virus (via anti-S immunity – step 7), viral entry (via pre-S1 immunity – step 1), and infected hepatocytes (via T-cell immunity – step 8)

Current NUCs & next-generation therapies impact intracellular steps downstream of transcription (steps 3, 4, & 5)



# Development Rationale for VBI-2601

**New therapeutic formulation (VBI-2601) enhances T-cell response – foundation for safe intervention in combination with next-generation antivirals and immunomodulators**

- Sci-B-Vac has demonstrated ability to restore HBV immunity in Chronic HBV & other non-responsive populations [Hoa et al., 2009]
  - Restoration of HBV immunity is considered a key element of HBV “functional cure”
- VBI-2601 is a novel formulation of Sci-B-Vac that provides enhanced Th1 immunity, including improved T-cell responses and increased IgG2a production
  - Builds on safety and potency of Sci-B-Vac
  - Foundation of safety data (Sci-B-Vac in over 500,000 individuals) makes VBI-2601 ideal for a combination study
  - Preclinical studies support enhanced immunity of distinct formulation

# Brii Biosciences License & Collaboration Agreement

**In December 2018, VBI announced a license and collaboration agreement with Brii Biosciences (“Brii Bio”) to develop a functional cure for Hepatitis B**

- Under the agreement, VBI and Brii Bio will collaborate in the development of the product candidate through to completion of a proof-of-concept clinical trial, following which, Brii Bio will be responsible for funding all development in the licensed territory – China, Hong Kong, Macau, and Taiwan
- VBI received gross proceeds of \$11 million, consisting of a \$4M upfront payment and a \$7M equity investment at \$3.05 per share
- VBI is eligible to receive an additional \$117.5 million in potential milestone payments and potential low double-digit royalties on commercial sales in the licensed territory
- VBI will retain all rights outside of the licensed territory with respect to the treatment of hepatitis B

# Tx HBV Phase Ib/IIa Clinical Study Design

**Two-part, multi-center, controlled, dose-escalation study of VBI-2601 in patients with chronic hepatitis B to assess safety, tolerability, and antiviral activity**

- The study is expected to enroll up to 65 subjects, across 5 cohorts:
  - Cohort A : NUC-only control
  - Cohort B : VBI-2601 (dose level 1)
  - Cohort C : VBI-2601 (dose level 1) + Bii adjuvant
  - Cohort D : VBI-2601 (dose level 2)
  - Cohort E : VBI-2601 (dose level 2) + Bii adjuvant
- The study is being conducted at clinical study sites in Australia, New Zealand, Thailand, South Korea, Hong Kong, and China
- Key outcomes:
  - Restimulation of HBV immunity – antibodies to S, T-cell immunity
  - Virologic measures: S antigen, DNA, RNA
- Enrollment in the study initiated in November 2019

# Program Milestones : VBI-2601 (Tx HBV)

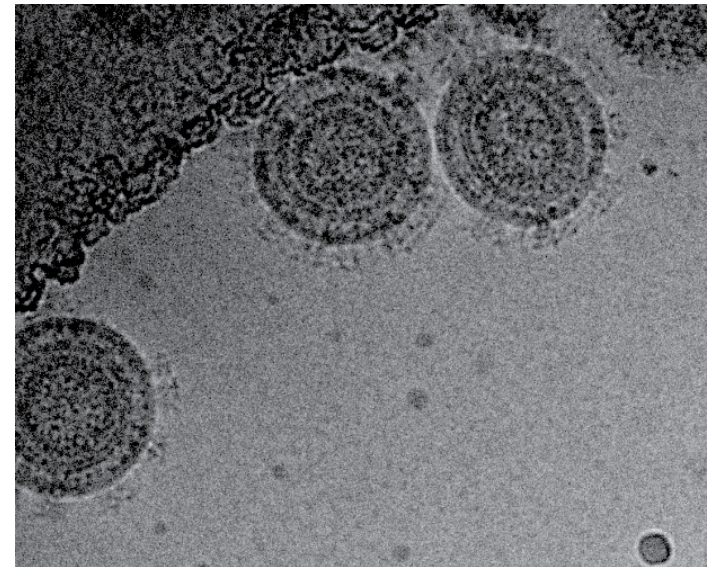
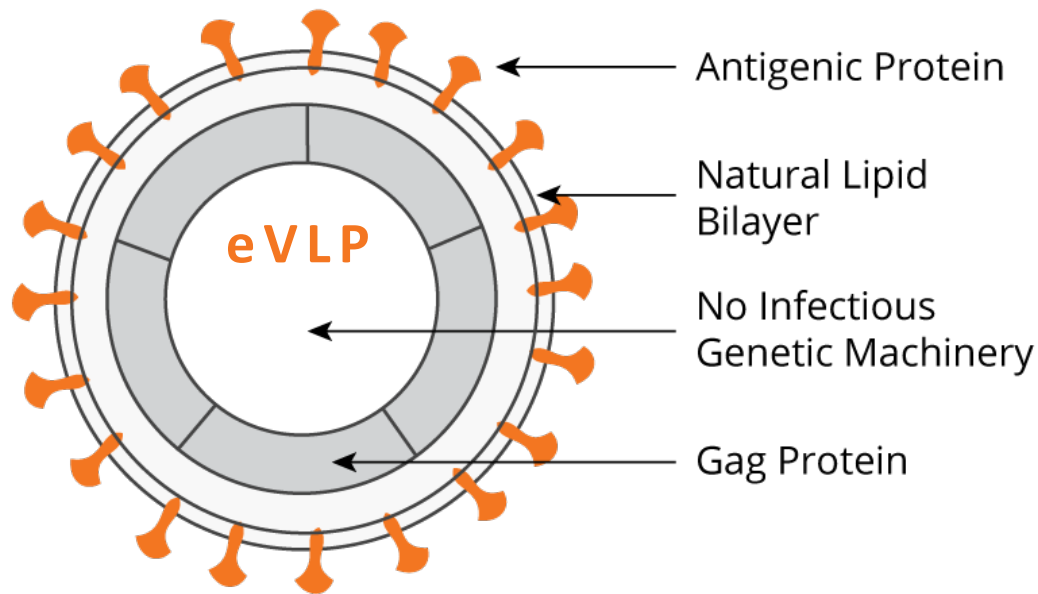
- ✓ *December 2018* : License and collaboration agreement announced with Bii Biosciences for up to \$129M + royalties to develop a functional cure for hepatitis B
- ✓ *January 2019* : Initiation of pre-clinical studies
- ✓ *Q4 2019* : Initiation of proof-of-concept Phase Ib/IIa study in subjects with chronic hepatitis B
- *H2 2020* : Initial human proof-of-concept Phase Ib/IIa data expected



# **Enveloped Virus-Like Particle (“eVLP”) Vaccine Technology**

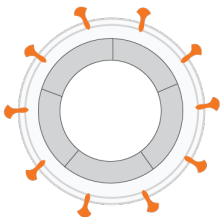
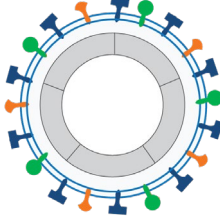
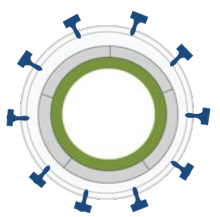
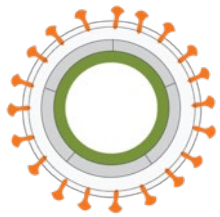
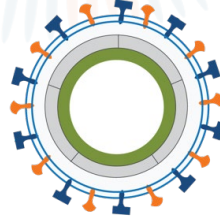
# eVLPs are a 3<sup>rd</sup>-Generation Class of Synthetic Vaccines

- eVLPs are the same size and structure as enveloped viruses, presenting antigens in their natural state for an improved immune response
- The foundation of the eVLP Platform is a stable, protein-based core which has the flexibility to express additional vaccine antigens of interest



*Electron Microscopy image of VBI's CMV eVLPs captured at Scripps Institute.*

# Multiple eVLP Candidates have Clinical & Preclinical Proof-of-Concept

	<i>Infectious Disease</i>			<i>Immuno-Oncology</i>	
	- VBI-1501 - Px CMV	- VBI-2901 - Px Pan-Coronavirus	- VBI-2501 - Px Zika	- VBI-1901 - Tx CMV+ Tumors	- VBI-2701 - Immuno-Oncology
<b>Schematic</b>					
<b>Construct Design</b>	<i>Monovalent:</i> Modified gB-G	<i>Trivalent:</i> Spike proteins for COVID-19, SARS, MERS	<i>Bivalent:</i> Modified-E / NS1	<i>Bivalent:</i> gB / pp65 (major CD4, CD8 & Ab epitopes)	<i>Bivalent with</i> Immunomodulatory protein
<b>Adjuvant</b>	Alum	Undisclosed	Alum	GM-CSF	Self Adjuvanted
<b>Most Advanced Dev. Stage</b>	Ph I complete	Preclinical	Preclinical	Ph I/II ongoing	Preclinical
<b>Key Features</b>	Modified gB elicits fibroblast & epithelial cell neutralization  Qualitatively enhanced neutralizing response	Broadly neutralizing antibodies against most clinically relevant human coronaviruses and potential new variants	Modified-E enhances neutralizing responses  NS1 T cell response enhances antibody response & protection	Internal antigen expression elicits T cell immunity  Stimulates innate immunity	Immunomodulatory proteins can enhance antigen-specific Th1 immunity







# Glioblastoma (GBM) – VBI-1901

Targeting CMV as a foreign viral antigen approach to Immuno-Oncology (GBM)  
with a bivalent eVLP expressing two potent CMV antigens – pp65 and gB

# Impact and Risks of Cytomegalovirus (CMV)

## ONCOLOGY

### Solid Tumors:

- 90%+ of some solid tumors, incl. glioblastomas, breast cancers, and medulloblastomas are CMV+
- CMV is not causative, but does influence disease progression of CMV+ tumors
- In multiple clinical studies, CMV-targeting vaccines have increased overall survival in GBM patients
- Because CMV is so broadly (and differentially) expressed on tumor cells, but not on healthy cells, a potent CMV vaccine has potential to make “cold tumors hot”
- GBM is one of the most aggressive cancers with few therapeutic options and no standard of care in the recurrent setting

# GBM Phase I/IIa Clinical Study Design

Two-part, multi-center, open-label, dose-escalation study of VBI-1901 in patients with recurrent glioblastoma (GBM)

## PART A : Dose-Escalation Phase

*Patient population :*

Recurrent GBM (any # of recurrences)

Study Arm 3:  
High Dose – 10.0µg + GM-CSF

N=6

Enrollment completed December 2018

**VS.**

Study Arm 2:  
Intermediate Dose – 2.0µg + GM-CSF

N=6

Enrollment completed September 2018

**VS.**

Study Arm 1:  
Low Dose – 0.4µg + GM-CSF

N=6

Enrollment completed April 2018

## PART B : Extension Phase

*Patient population :*

First Recurrent GBM

Study Arm 1:  
10.0µg + GM-CSF

N=10

Enrollment initiated July 2019

**VS.**

Study Arm 2:  
10.0µg + GSK's AS01<sub>B</sub> adjuvant system

N=10

Enrollment initiated February 2020

## Outcome Measures : Part A & B

- *Safety*
- *Immunogenicity* : (1) T-cell immunity (gB, pp65), (2) serum anti-gB antibody titers, (3) other immune correlates and biomarkers
- *Tumor and clinical responses* : Based on MRIs and survival data
- *Quality of life* : Change from baseline

# Part A : Safety, Immunologic, and Tumor Responses

## SAFETY :

- VBI-1901 was well-tolerated at all doses, with no safety signals observed
- Grade 2, 3, or 4 adverse events occurred in 66%, 22%, and 11% of participants, respectively – none were related to the vaccine immunotherapeutic

## IMMUNOGENICITY AND TUMOR RESPONSES :

- Six (6) patients immunologically responded to VBI-1901, with evidence of robust boosting of CMV-specific immune responses against both gB and pp65 antigens
- Three out of six (3/6) patients in the high-dose cohort had evidence of stable disease (SD) by magnetic resonance imaging (MRI), compared to one out of six (1/6) in the low-dose cohort and zero out of six (0/6) in the intermediate-dose cohort

# Part A : Clinical Responses

## MEDIAN PROGRESSION-FREE SURVIVAL (PFS) :

- Median PFS was longer among vaccine responders (14.5 weeks) vs. vaccine non-responders (6.0 weeks)

## OVERALL SURVIVAL (OS) :

- 12-month OS rate in vaccine responders was 83% (n=5/6) vs. 33% among non-responders (n=3/9)<sup>1</sup>
- 6-month OS was 100% among vaccine responders (n=6/6) vs. 63% among non-responders (n=5/8)

## MEDIAN OVERALL SURVIVAL (OS) :

- Median OS was longer among vaccine responders (14.0 months) vs. non-responders (7.75 months)<sup>1</sup>

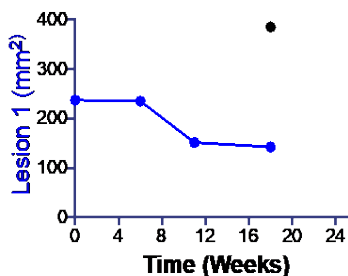
<sup>1</sup>Current commonly-used regimens, including chemotherapy and VEGF-A inhibitors, have demonstrated 12- month OS rates below 50% and median OS of 8-12 months

# Tumor Response Data

## DATA FROM SNO 2019 POSTER PRESENTATION

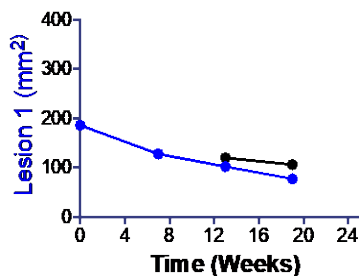
### Part A : Tumor Responders in High-Dose Cohort

**Subject 03-004**  
1 recurrence



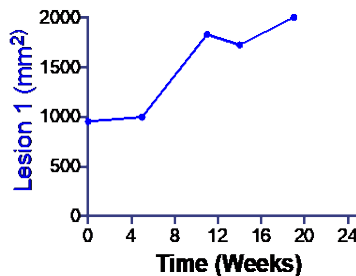
- ~60% reduction seen in Lesion 1
- Lesion 2 appeared after 4.5 months, defined PD per protocol, though patient was clinically stable

**Subject 03-006**  
1 recurrence



- ~60% reduction seen in Lesion 1
- Appearance of Lesion 2 with associated cyst required surgical resection of lesions

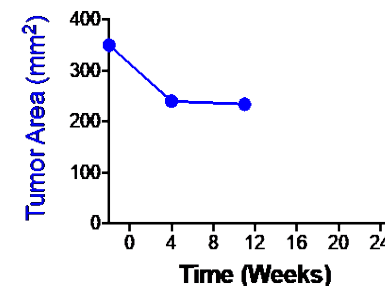
**Subject 03-003**  
1 recurrence



- Initial tumor progression later presumed to be pseudo-progression due to subsequent tumor stabilization (atypical of rGBM)

### Part B : Available Data

**Subject 04-002**  
1 recurrence



- ~33% reduction in tumor seen to-date
- Stable Disease (SD) based on 2 consecutive scans

# VBI-1901 (GBM) : Program Milestones

- ✓ **November 2018** : Announcement of initial immunologic data from Part A of the ongoing Phase I/IIa at the Society for Neuro-oncology (SNO) Meeting
- ✓ **December 2018** : Completion of enrollment in Part A of the Phase I/IIa
- ✓ **June 2019** : Presentation of expanded immunologic data and tumor and clinical responses at ASCO Annual Meeting
- ✓ **July 2019** : Initiation of enrollment in Part B of the Phase I/IIa study
- ✓ **September 2019** : Announcement of GSK collaboration to clinically evaluate VBI-1901 + GSK's AS01<sub>B</sub> adjuvant system in additional study arm of ongoing Phase I/IIa study
- ✓ **Q4 2019** : Initial immunologic data from VBI-1901 + GM-CSF Part B and expanded Part A data expected
- ✓ **Q1 2020** : Initiation of enrollment in VBI-1901 + GSK's AS01<sub>B</sub> study arm expected, subject to FDA acceptance of the amended protocol and investigational site institutional review board approval
- **Mid-year 2020** : Expanded immunologic data and clinical and tumor responses expected from VBI-1901 + GM-CSF study arm



# Pan-Coronavirus – VBI-2901

Trivalent eVLP vaccine candidate co-expressing SARS-CoV-2, SARS-CoV, and MERS-CoV spike proteins



# Impact and Risks of Coronavirus

## INFECTIOUS DISEASE

### Coronaviruses :

- Coronaviruses are a large family of viruses that usually cause respiratory illness of varying severity, including the common cold and pneumonia
- Seven coronaviruses are known to be pathogenic in humans, with three of those seven causing serious outcomes:
  - SARS-CoV-2 – the novel coronavirus identified as the cause of COVID-19
  - MERS-CoV – identified in 2012 as the cause of Middle East respiratory syndrome (MERS)
  - SARS-CoV – identified in 2002 as the cause of severe acute respiratory syndrome (SARS)<sup>1</sup>

### COVID-19 :

- COVID-19 spreads primarily through droplets of saliva or discharge from the nose of an infected individual
- COVID-19 is responsible for the most widespread coronavirus outbreak to-date, with over 1 million confirmed cases worldwide<sup>2</sup>
- Most people infected with COVID-19 experience mild to moderate respiratory illness
- Older people, along with those who have underlying medical issues such as cardiovascular disease, diabetes, chronic respiratory disease, etc., are more likely to develop serious illness<sup>1</sup>

1. "Coronavirus." World Health Organization, <https://www.who.int/health-topics/coronavirus>.

2. "Coronavirus COVID-19 Global Cases." Center for Systems Science and Engineering at Johns Hopkins University, <https://coronavirus.jhu.edu/map.html>

# eVLP Approach to a Pan-Coronavirus Vaccine Candidate

Coronaviruses are members of the “enveloped” class of viruses

- *Morphology:*

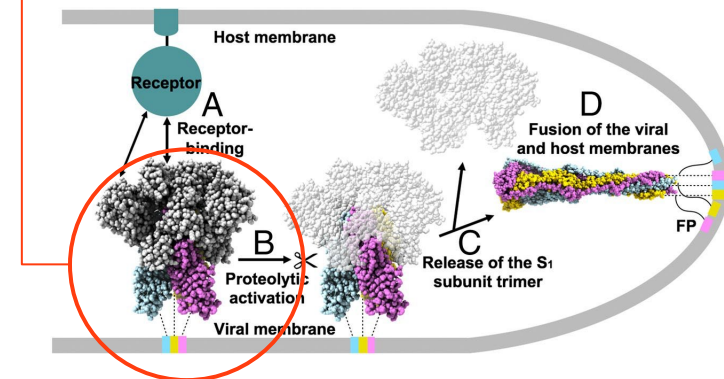
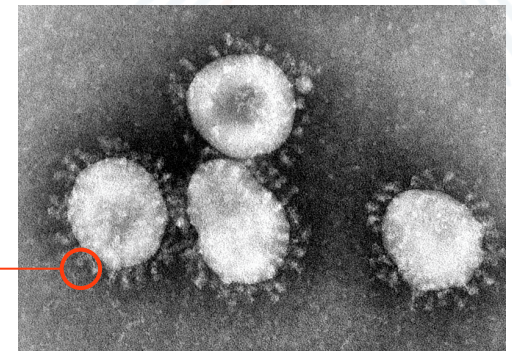
- Enveloped RNA virus with a predominant S1/S2 spike
- RNA viruses are prone to genetic drift/shift (though coronaviruses seem to be more stable than most)

- *Key Target Antigen:*

- Based on knowledge of SARS and MERS, it is anticipated that the spike protein (S1/S2) is likely a neutralizing determinant and an ideal target for inclusion in a vaccine

- Based on past experience with the eVLP platform, VBI expects that a multivalent eVLP vaccine candidate, co-expressing SARS-CoV-2, SARS-CoV, and MERS-CoV spike proteins on the same particle, will be possible

COVID-19



# VBI-2901 (Pan-Coronavirus) : Program Milestones

- ✓ *March 2020* : Announcement of collaboration with the National Research Council of Canada (NRC) to develop a pan-coronavirus vaccine candidate targeting COVID-19, severe acute respiratory syndrome (SARS), and Middle East respiratory syndrome (MERS)
- *Q4 2020* : Clinical study materials expected to be available for human clinical studies



# Cytomegalovirus (CMV) – VBI-1501

eVLP vaccine candidate potently expresses a modified-form of the gB antigen, which is functionally differentiated from other gB approaches

# Impact and Risks of Cytomegalovirus (CMV)

## INFECTIOUS DISEASE

### **Birth Defects (*Congenital Infection*):**

- Congenital CMV is a leading cause of birth defects worldwide
- A first exposure during pregnancy can lead to death, blindness, deafness, and developmental delays of the newborn
- ~30,000 infants are born in U.S. with CMV annually
- 5,000+ will develop permanent impairments (more impacted births than Downs Syndrome)
- Direct economic costs of CMV infection exceeds \$3.0B per year in U.S.
- No approved treatment or prevention
- ~\$1B U.S. annual market with a \$5B catch-up market opportunity

### **Transplant Rejection/Mortality:**

- CMV is also a leading cause of transplant rejection in both the solid organ transplant and the stem-cell transplant settings
- Over 100,000 individuals in the U.S. are on the waiting list to receive a solid-organ transplant
- Matching based on CMV sero-status is not practical given other constraints (e.g. timely organ supply)
- Despite anti-viral pretreatment, CMV status of both recipient and donor still has a major impact on organ and recipient survival

# Summary of Phase I Study Results

## Phase I Study in 128 CMV-Negative Healthy Adults (18-40 years)

- VBI-1501 is safe and well tolerated at all doses tested, with and without the adjuvant alum, with no concern about evaluating VBI-1501A at higher doses
- VBI-1501A is immunogenic, even at a low dose
  - **gB antibody binding titers** induced at all dose levels, with clear evidence of dose-dependent boosting after each vaccination
  - **Neutralizing antibodies against fibroblast cell infection** were comparable to those from CMV-positive controls in 100% of subjects receiving the highest dose
  - **Neutralizing antibodies against epithelial cell infection** had a correlation with higher gB binding titers and fibroblast cell neutralizing activity, suggesting the modified form of the gB-G used in VBI-1501A qualitatively enriches for functional nAb activity
  - **Highest dose** tested (2.0µg) is 1/10<sup>th</sup> that of several other licensed VLP-based vaccines and past non-VBI CMV candidates
- There is strong scientific rationale to support that higher doses of VBI-1501A could improve the immunogenicity and efficacy



# Summary

# VBI Vaccines Leadership

## MANAGEMENT



**Jeff Baxter**  
*President & CEO*



**Dr. David Anderson, Ph.D.**  
*Chief Scientific Officer*



**Dr. Francisco Diaz-Mitoma, M.D., Ph.D.**  
*Chief Medical Officer*



**Chris McNulty**  
*Chief Financial Officer*



**Nell Beattie**  
*Chief Business Officer*



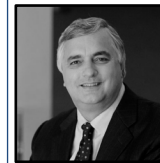
**Avi Mazaltov**  
*Global Head of Manufacturing  
SciVac General Manager*



## BOARD OF DIRECTORS



**Dr. Steve Gillis, Ph.D.**  
*Chairman*



**Damian Braga**



**Joanne Cordeiro**



**Dr. Michel De Wilde, Ph.D.**



**Blaine H. McKee, Ph.D.**





# VBI Vaccines Global Footprint



## HEADQUARTERS – CAMBRIDGE, MA

- 7 FTEs (Incl. CEO, CSO, CFO, CBO)
- Central location in biotechnology hub

## RESEARCH OPERATIONS – OTTAWA, CANADA

- ~35 FTEs (Incl. CMO)
- R&D team and facility

## MANUFACTURING FACILITY – REHOVOT, ISRAEL

- ~80 FTEs
- GMP manufacturing facility for the production of Sci-B-Vac®



# Summary

## ANTICIPATED CATALYSTS THROUGH 2020 YEAR-END:

1

### **Sci-B-Vac®: Hepatitis B Prophylactic Vaccine**

- **Q2 2020** – Pre-BLA discussions expected with FDA
- **Beginning Q4 2020** – Submissions of applications for regulatory approvals in the U.S., Europe, and Canada expected to begin

2

### **VBI-1901: GBM Vaccine Immunotherapeutic (Immuno-Oncology)**

- **Mid-year 2020** – Expanded immunologic data, tumor and clinical responses expected from VBI-1901 + GM-CSF Phase IIa (Part B) study arm
- **Q4 2020** – Initial immunologic data expected from VBI-1901 + AS01<sub>B</sub> Phase IIa (Part B) study arm

3

### **VBI-2601: Hepatitis B Immunotherapeutic**

- **H2 2020** – Initial human proof-of-concept Phase Ib/IIa data readout expected

4

### **VBI-2901: Pan-Coronavirus Prophylactic Vaccine**

- **Q4 2020** – Clinical study materials expected to be available



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