VBI-2601: Immunotherapeutic HBV Program

HBV Forum & ICE-HBV Therapeutic Vaccines Webinar
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 PreHevrio; 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 PreHevrio; the ability to obtain appropriate or necessary regulatory approvals to market potential products; the ability to obtain future funding for development 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 2, 2021, and filed with the Canadian security authorities at sedar.com on March 2, 2021, 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.
### VBI’s Pipeline: Comprehensive Approach to HBV

**VBI’s broad spectrum of vaccine and immunotherapeutic candidates are designed to power the immune system to prevent and treat disease.**

<table>
<thead>
<tr>
<th>Hepatitis B Programs</th>
<th>Program</th>
<th>Preclinical</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
<th>Registration/Commercial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Approved Prophylactic Vaccine</td>
<td>PreHevbro 12</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment Candidate</td>
<td>VBI-2601(BRII-179)</td>
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</tbody>
</table>

**Other pipeline candidates include:**

- **COVID-19/Coronavirus vaccine candidates**: A suite of multivalent pan-coronavirus and monovalent coronavirus vaccine candidates supported by CEPI and the Government of Canada.
- **VBI-1901**: Glioblastoma (GBM) cancer vaccine immunotherapeutic candidate in Phase 1/2a study
- **VBI-1501**: Prophylactic CMV vaccine candidate, completed Phase 1 study

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1. Approved for use in the U.S. for the prevention of infection caused by all known subtypes of hepatitis B virus in adults 18 years of age and older.
2. Approved for use in Israel, under the brand name Sci-B-Vac®, for active immunization against hepatitis B virus (HBV) infection.
PreHevbrio is the Only 3-Antigen HBV Vaccine

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)

**Pre Hevbrio:**

- Pre-S1 Antigen
- Pre-S2 Antigen
- S Antigen

**The pre-S1 and pre-S2 regions of the hepatitis B virus contain hepatocyte receptor binding sites**

**VBI-2601** has a similar conformation to PreHevbrio, but has been reformulated to enhance B and T cell responses, with the aim of restoring defective HBV-specific humoral and cellular immunity in chronic HBV patients.
VBI-2601: Potential to be a Critical Component of a Functional Cure for Chronic HBV Infection

Scientific consensus is that a functional cure for HBV is within reach, but will likely require the use of an immunotherapeutic as part of a combination approach.

A functional cure will likely require the achievement of:

1. Drive down hepatitis B virus (HBV) DNA
2. Drive down immuno-suppressive HBV S-antigen
3. Achieve long-term immunologic control
**VBI-2601 Development Plan & Status**

Studies Designed & Executed in Partnership with Brili Biosciences

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**Phase 1b/2a Study**  
Completed in 2021

- Two-part, multi-center, controlled, dose-escalation study (n=44)
- Assessed VBI-2601 safety, tolerability, and immunologic antiviral activity in non-cirrhotic patients with chronic HBV infection
- Conducted in Australia, New Zealand, Thailand, South Korea, Hong Kong, China, and Taiwan

Data demonstrated that VBI-2601 induced both B cell and T cell responses and was well tolerated with no safety signals observed

**Phase 2 Combination Study**  
Initiated April 2021

- First-in-class study to evaluate safety and efficacy of VBI-2601 in combination with an HBV-targeting siRNA (VIR-2218)
- Multi-center study to be conducted in Australia, New Zealand, Thailand, South Korea, Hong Kong, China, Singapore, and Taiwan
- Expected enrollment of ~135 adults aged 18-60 years with chronic HBV infection
- **Interim Phase 2 data expected H2 2022**  
  
ClinicalTrials.gov Identifier: NCT04749368

**Phase 2a/2b “Add-On” Study to Standard of Care**  
Initiated December 2021

- Two-part Phase 2 study designed to evaluate the clinical effect of adding VBI-2601 to existing standard of care therapy (PEG-IFN-α and Nrtl) in non-cirrhotic HBV patients
- Expected enrollment of ~600 subjects in China
- **Initial data expected H1 2023**  

China DrugTrials.org.cn Identifier: CTR202B100
Completed Phase 1b/2a Study

- Two-part, multi-center, controlled, dose-escalation study of VBI-2601 (BRII-179) in non cirrhotic patients with chronic HBV infection to assess safety, tolerability, and immunologic antiviral activity

- The study was conducted at clinical study sites in Australia, New Zealand, Thailand, South Korea, Hong Kong, and China

- Key objectives: re-stimulate HBV immunity, including HBV-specific antibody and T cell responses

- Study Design: VBI-2601 (BRII-179) was administered at 2 dose levels as IM monthly injections over 4 months

  - **Study Part 1** (n=25):
    - Cohort A (n=5 **): NUC-only control
    - Cohort B (n=10): VBI-2601 (20 µg) Q4W
    - Cohort C (n=10): VBI-2601 (20 µg) + interferon alpha (IFN-α) Q4W

  - **Study Part 2** (n=24):
    - Cohort D (n=12): VBI-2601 (40 µg) Q4W
    - Cohort E (n=12): VBI-2601 (40 µg) + IFN-α Q4W

Q4W: every 4 weeks; NA: not applicable; NUC: Nucleos(t)ide analogue. ** Including 3 subjects from Cohort A randomized to Cohort E after Part 1 Week 16 visit
### Phase 1b/2a Study Results: Safety and Tolerability

#### Frequency and Severity of Treatment Emergent Adverse Events

| BRII-179 (VBI-2601) – 4-dose regimen, administered monthly at months 0, 1, 2, and 3 |
|---|---|---|---|---|---|
| **Cohort A** | **Cohort B** | **Cohort C** | **Cohort D** | **Cohort E** |
| Nuclos(t)ide analogue (Nrtl) (n=5) | 20 µg + Nrtl (n=10) | 20 µg + IFN-α + Nrtl (n=10) | 40 µg + Nrtl (n=12) | 40 µg + IFN-α + Nrtl (n=12) |
| TEAEs | 2 (40.0) | 7 (70.0) | 10 (100.0) | 10 (83.3) |
| Severe AE or SAE | 0 | 0 | 0 | 0 |
| Drug Related AE | 6 (60.0) | 9 (90.0) | 8 (66.7) | 11 (91.7) |

#### TEAEs (any grade) in ≥2 patients in any treatment

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Cohort A</th>
<th>Cohort B</th>
<th>Cohort C</th>
<th>Cohort D</th>
<th>Cohort E</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>0</td>
<td>4 (40.0)</td>
<td>4 (40.0)</td>
<td>5 (41.7)</td>
<td>8 (66.7)</td>
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<tr>
<td>Headache</td>
<td>0</td>
<td>2 (20.0)</td>
<td>5 (50.0)</td>
<td>0</td>
<td>8 (66.7)</td>
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<tr>
<td>Injection site reaction</td>
<td>0</td>
<td>4 (40.0)</td>
<td>4 (40.0)</td>
<td>5 (41.7)</td>
<td>7 (58.3)</td>
</tr>
<tr>
<td>Myalgia</td>
<td>0</td>
<td>1 (10.0)</td>
<td>4 (40.0)</td>
<td>1 (8.3)</td>
<td>7 (58.3)</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>0</td>
<td>0</td>
<td>3 (30.0)</td>
<td>0</td>
<td>6 (50.0)</td>
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<tr>
<td>Nasopharyngitis</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>3 (25.0)</td>
<td>0</td>
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<tr>
<td>Influenza like illness</td>
<td>1 (20.0)</td>
<td>1 (10.0)</td>
<td>2 (20.0)</td>
<td>0</td>
<td>1 (8.3)</td>
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<tr>
<td>Chills</td>
<td>0</td>
<td>0</td>
<td>2 (20.0)</td>
<td>0</td>
<td>1 (8.3)</td>
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<tr>
<td>Nausea</td>
<td>0</td>
<td>1 (10.0)</td>
<td>2 (20.0)</td>
<td>0</td>
<td>2 (16.7)</td>
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<tr>
<td>Diarrhea</td>
<td>0</td>
<td>0</td>
<td>2 (20.0)</td>
<td>0</td>
<td>2 (16.7)</td>
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<tr>
<td>Dizziness</td>
<td>0</td>
<td>1 (10.0)</td>
<td>0</td>
<td>0</td>
<td>2 (16.7)</td>
</tr>
</tbody>
</table>

**VBI-2601 generally well-tolerated, with no SAEs, deaths or signs of hepatotoxicity observed**

Sources: Brili Biosciences and VBI Vaccines Present Positive Data from Completed Phase 1b/2a Study on BRII-179 (VBI-2601) in Patients with Chronic Hepatitis B at the International Liver Congress 2021; June 23, 2021 (press release); additional data presented in ILC poster by Brili Bio.
Phase 1b/2a Data Demonstrated Significant Restoration of Antibody and T Cell Responses

- **Potent re-stimulation of T cell responses** to HBV surface antigens (S, Pre-S1, Pre-S2) seen in 67% (Cohort B n=6/9) and 78% (Cohort C n=7/9) of evaluable patients in the low-dose VBI-2601 unadjuvanted and adjuvanted, respectively.

- **Boosting of antibodies** to HBV surface antigens observed in 19/43 (44.2%) of evaluable patients.

**VBI-2601 Unadjuvanted Data - Responders**

Sources: Brii Biosciences and VBI Vaccines Present Positive Data from Completed Phase 1b/2a Study on BRB-179 (VBI-2601) in Patients with Chronic Hepatitis B at the International Liver Congress 2021; June 23, 2021 (press release); additional data presented in ILC poster by BriiBio.
VBI-2601 Ongoing Partnership & Upcoming Milestones

**Brii Partnership:**

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

- **Upfront:** $11M - $4M upfront payment + $7M equity investment

- **Milestones & Royalties:** Up to $117.5M in potential milestone payments and potential low double-digit royalties on commercial sales in the licensed territory

- **Licensed Territories:** China, Hong Kong, Macau, and Taiwan

- VBI will retain all rights outside of the licensed territory with respect to the treatment of Hepatitis B

**Upcoming Milestones:**

- **H2 2022:** Top-line interim clinical data from Phase 2 combination study of VBI-2601 (BRII-179) and BRII-835 (VIR-2218) expected

- **H1 2023:** Initial data from Phase 2a/2b “add-on” study of VBI-2601 (BRII-179) + current standard-of-care therapy expected