Enveloped Virus Like Particles: Third-generation VLPs for the Development of a Broadly Neutralizing Hepatitis C Vaccine

World Vaccine Congress Asia – June 2015
Forward-Looking Statement Disclaimer

This presentation contains forward-looking statements within the meaning of the provisions of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. Forward-looking statements are generally identifiable by the use of words like "may," "will," "should," "could," "expect," "anticipate," "estimate," "believe," "intend," or "project" or the negative of these words or other variations on these words or comparable terminology. The reader is cautioned not to put undue reliance on these forward-looking statements, as these statements are subject to numerous factors and uncertainties outside of our control that can make such statements untrue, including, but not limited to, inadequate capital, adverse economic conditions, intense competition, lack of meaningful research results, entry of new competitors and products, adverse federal, state and local government regulation, termination of contracts or agreements, technological obsolescence of our products, technical problems with our research and products, price increases for supplies and components, inability to carry out research, development and commercialization plans, loss or retirement of key executives and research scientists and other specific risks. We currently have no commercial products intended to diagnose, treat, prevent, or cure any disease. The statements contained in this presentation regarding our ongoing research and development and the results attained by us to date have not been evaluated by the Food and Drug Administration. There can be no assurance that further research and development, and/or whether clinical trial results, if any, will validate and support the results of our preliminary research and studies. Further, there can be no assurance that the necessary regulatory approvals will be obtained or that we will be able to develop new products on the basis of our technologies. In addition, other factors that could cause actual results to differ materially are discussed in our Annual Report on Form 10-K for the year ended December 31, 2014 filed with the SEC on March 20, 2015. Investors and security holders are urged to read these documents free of charge on the SEC's web site at www.sec.gov. We undertake no obligation to publicly update or revise our forward-looking statements as a result of new information, future events, or otherwise. NO OFFER; NO RELIANCE. This presentation does not constitute an offer to sell, or a solicitation of an offer to buy, any security and may not be relied upon in connection with the purchase or sale of any security. Any such offer would only be made by means of formal documents, the terms of which would govern in all respects. You should not rely on this presentation as the basis upon which to make any investment decision.
Platform Technologies
Two complementary vaccine platform technologies.

<table>
<thead>
<tr>
<th>Enveloped Virus-Like Particle (&quot;eVLP&quot;) Platform</th>
<th>Liquid Particle Vaccine (&quot;LPV™&quot;) Platform</th>
</tr>
</thead>
<tbody>
<tr>
<td>“Third-generation” virus-like particle vaccines that closely mimic the structure of target viruses.</td>
<td></td>
</tr>
<tr>
<td>Possible utility in both prophylactic and therapeutic vaccine applications.</td>
<td></td>
</tr>
<tr>
<td>Lead program is developing a prophylactic cytomegalovirus (&quot;CMV&quot;) vaccine (&quot;VBI-1501A&quot;) with strong preclinical proof of concept.¹</td>
<td></td>
</tr>
<tr>
<td>- CMV market could exceed $1B annually.²,³</td>
<td></td>
</tr>
<tr>
<td>- Toxicology expected to begin in Q2 2015.</td>
<td></td>
</tr>
<tr>
<td>- Phase I start anticipated in Q1 2016.</td>
<td></td>
</tr>
<tr>
<td>- Exploring other eVLP vaccine candidates for internal development.</td>
<td></td>
</tr>
<tr>
<td>Enables the development of vaccines that can withstand storage or shipment at elevated or constantly fluctuating temperatures.⁴</td>
<td></td>
</tr>
<tr>
<td>Entered into an agreement (April 2015) with Sanofi Pasteur to use LPV™ formulation technology to further the development of a key Sanofi Pasteur vaccine candidate</td>
<td></td>
</tr>
<tr>
<td>Pursuing additional partnerships, all of which are expected to be self funding.</td>
<td></td>
</tr>
<tr>
<td>- Currently, more than 90% of all vaccines require “cold chain” shipment at 4°C.⁵</td>
<td></td>
</tr>
<tr>
<td>Extensive LPV™ intellectual property extending to 2030.</td>
<td></td>
</tr>
</tbody>
</table>
Experienced Leadership

Vaccine development, commercialization, and financing expertise.

DR. STEVE GILLIS, CHAIRMAN OF THE BOARD
- Immunologist and investor with track record of blockbuster drugs and visionary corporate development success.
- Founder of Immunex, the developer of Enbrel, a $7B/year landmark innovation.
- Managing director at Arch Venture Partners, a biotech VC with $1.9B under management.

JEFF BAXTER, PRESIDENT & CEO
- A history of focused value creation, company building, and strategic management.
- Former Senior Vice President, R&D Finance and Operations at GlaxoSmithKline (“GSK”) during a period of tremendous corporate growth and shareholder returns.
- Managing Partner at The Column Group, a VC fund, responsible for start-ups and successful exits.

DR. FLORIAN SCHODEL, SAB CHAIR
- Clinical vaccinologist with extensive drug development experience.
- Former VP Vaccines Clinical Development at Merck.
- Led development of multiple complex global licensures for Measles, Mumps, and Rubella (“MMR”) and Rotavirus, each billion dollar products.

The trademarks above are the sole property of their respective owner. VBI does not claim any ownership of such marks.
eVLP Platform
## Virus-like Particle Vaccine Evolution

Virus-like particle vaccines have evolved considerably since their introduction in the early 1990s.

<table>
<thead>
<tr>
<th>1&lt;sup&gt;st&lt;/sup&gt; Generation</th>
<th>2&lt;sup&gt;nd&lt;/sup&gt; Generation</th>
<th>3&lt;sup&gt;rd&lt;/sup&gt; Generation – VBI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Design: Antigens are produced and self-assemble.</td>
<td>Design: Antigens of interest are covalently attached to the surface of a backbone protein.</td>
<td>Design: Common protein backbone and lipid membrane in which the antigen of interest can be expressed.</td>
</tr>
<tr>
<td>Key Advantage: Simple structures and repetitive pattern of antigenic epitopes.</td>
<td>Key Advantage: Can be applied to multiple different target antigens; VLP structure is not limited to the properties of the antigen.</td>
<td>Key Advantage: Enables more natural presentation of target antigen within a membrane that more closely mimics a virus; can express multiple target antigens in a single VLP.</td>
</tr>
<tr>
<td>Key Limitation: Only a very limited number of antigens spontaneously form orderly VLP structures; cannot be applied to all enveloped viruses.</td>
<td>Key Limitation: Antigen of interest is artificially bound to the structural protein and not represented in a natural configuration.</td>
<td>Limitation: More effort to meet FDA/EMA purification standards.</td>
</tr>
</tbody>
</table>

The trademarks above are the sole property of their respective owner. VBI does not claim any ownership of such marks.
eVLP Platform Overview

eVLPs are a third-generation class of synthetic vaccines that closely resemble the structure of the virus they mimic.

**eVLP PLATFORM HIGHLIGHTS**

- Same size and structure as enveloped viruses; present antigens in their natural state for an improved immune response.
- Demonstrated ability to trigger strong, broadly neutralizing antibodies in multiple preclinical models (CMV, HCV, Flu and West Nile).
- Suitable to a wide array of viruses such as RSV and Dengue.
- Strong intellectual property estate.

Top: eVLP Diagram – the foundation of the eVLP technology is a stable, protein-based core on which additional vaccine antigens of interest can be added; Bottom: Electron Microscopy image of VBI’s CMV eVLP captured at Sripps Institute.
# eVLP Platform Overview

**CUSTOMIZED DELIVERY OF ANTIGENS IN THEIR NATURAL STATE TO TAILOR IMMUNE RESPONSE**

<table>
<thead>
<tr>
<th>Attributes</th>
<th>Monovalent</th>
<th>Bivalent – Multiple Surface proteins</th>
<th>Bivalent – Internal Protein</th>
<th>Trivalent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present antigen in natural conformation</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Broadly Reactive Neutralizing Antibodies</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Polyvalent Immune Response</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>Potent Cellular Immunity for Therapeutic Applications</td>
<td>+</td>
<td>+</td>
<td>+++</td>
<td>+++</td>
</tr>
</tbody>
</table>
eVLP Platform Characteristics

eVLP Platform provides VBI with a novel technology designed to address unmet vaccine needs.

KEY CHARACTERISTICS

- **Highly Immunogenic**: eVLP immune responses comparable to or better than natural infection by closely mimicking structure of target virus.

- **Customizable**: eVLPs provide ability to rationally design a vaccine by including different antigens and controlling their relative expression.

- **Safe**: Unlike live-attenuated vaccines, eVLPs cannot revert back to an infectious state.

- **Commercially Viable**: Manufactured and purified using scalable methods; demonstrated high yields and purity.

VBI’s Ottawa, Canada-based research facility.
Therapeutic HCV eVLP Vaccine Candidate
## Therapeutic HCV Vaccine Opportunity

HCV market analysis: critical numbers infected in many established & growing economies

<table>
<thead>
<tr>
<th>Region</th>
<th>Example Countries</th>
<th>Total Infected</th>
<th>GDP/Capita</th>
<th>Infection Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>China &amp; Southeast Asia</td>
<td>China</td>
<td>20,000,000</td>
<td>$8,862</td>
<td>1.50%</td>
</tr>
<tr>
<td></td>
<td>Vietnam</td>
<td>2,600,000</td>
<td>$3,503</td>
<td>2.90%</td>
</tr>
<tr>
<td></td>
<td>Thailand</td>
<td>1,900,000</td>
<td>$9,371</td>
<td>2.80%</td>
</tr>
<tr>
<td></td>
<td>Taiwan</td>
<td>1,000,000</td>
<td>$30,874</td>
<td>4.40%</td>
</tr>
<tr>
<td></td>
<td>Korea</td>
<td>635,000</td>
<td>$19,890</td>
<td>1.30%</td>
</tr>
<tr>
<td>Middle East &amp; India</td>
<td>Egypt</td>
<td>10,700,000</td>
<td>$4,753</td>
<td>14.90%</td>
</tr>
<tr>
<td></td>
<td>India</td>
<td>9,500,000</td>
<td>$1,330</td>
<td>1.50%</td>
</tr>
<tr>
<td></td>
<td>Pakistan</td>
<td>8,800,000</td>
<td>$2,976</td>
<td>4.70%</td>
</tr>
<tr>
<td>Russia &amp; Eastern Europe</td>
<td>Russia</td>
<td>4,252,500</td>
<td>$9,900</td>
<td>3.00%</td>
</tr>
<tr>
<td></td>
<td>Romania</td>
<td>770,000</td>
<td>$9,446</td>
<td>3.50%</td>
</tr>
<tr>
<td>North America &amp; Europe</td>
<td>Italy</td>
<td>3,400,000</td>
<td>$30,791</td>
<td>5.50%</td>
</tr>
<tr>
<td></td>
<td>USA</td>
<td>2,500,000</td>
<td>$45,218</td>
<td>1.00%</td>
</tr>
<tr>
<td></td>
<td>Spain</td>
<td>1,200,000</td>
<td>$28,810</td>
<td>2.60%</td>
</tr>
</tbody>
</table>

Therapeutic vaccination is a cost effective alternative to expensive antivirals

1)  *Liver International, v31 suppl 2, July 2011; IMF WEO Online Database*
Global Distribution of HCV Genotypes – One Solution for All?

- Viral resistance and genotype distribution requires a broadly active solution
- Example: Southeast Asia experiencing a dramatic rise in Genotype 6

Current Interferon-based HCV Therapy is Associated with Significant Toxicity & Side Effects

- Fatigue
- Flu like symptoms
- Rash
- Anemia
- Depression

Therapeutic Vaccine Rationale: Eliminate use of interferon while effectively managing viral load (and transmission)
HCV Market Dynamics – Cost of New Therapies is a Critical Barrier to Addressing Unmet Medical Need

**LATE 90’S**

U.S. & EU Markets

- **Ribavirin + Interferon**
  - Viral suppression
  - Highly toxic – compliance issues

**RECENT PAST**

- **2nd Gen Small Molecules + Interferon**
  - Viral clearance in certain populations
  - Very expensive
  - Tox issues remain
  - Anti-viral resistance

**PRESENT**

- **3rd Gen Oral Small Molecules**
  - Promising efficacy without interferon/toxicity
  - Oral administration

**BRICM & Growing Economies**

- Few treatment options
- **Ribavirin & Interferon now available**
  - As above, tox issues & compliance are issues
  - Viral resistance
  - Expensive 2nd Gen small molecules may not be an efficient use of Public Healthcare dollars
- **Ribavirin + Therapeutic Vaccine**
  - Reduced toxicity (interferon-free)
  - Multi-genotype efficacy
  - Clear health economic benefits

NASDAQ: VBI
Is a Therapeutic Vaccine for HCV Possible and How Would it be Evaluated?

- There is significant evidence that immune control and clearance of HCV is possible
  - Approximately 25% of those infected can “spontaneously” clear the virus\(^1\)
  - Virus-specific neutralizing antibodies contribute to clearance
  - Genotype of HCV influences spontaneous viral clearance

- Concepts for clinical development
  - Phase I trial designed to compare standard antiviral therapy (ribavirin + interferon) vs Tx vaccine + ribavirin
    - Demonstrate non-inferiority in terms of virus control with reduced toxicity/greater compliance
  - Experimental groups will be removed from traditional therapy following Tx vaccination
  - Inclusion criteria: patients early in onset of infection, with controlled viremia

# Therapeutic HCV Vaccine Target Product Profile

<table>
<thead>
<tr>
<th>Target Profile</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Indication</strong></td>
<td>Therapeutic use in patients infected with HCV (any genotype) to eliminate use of interferon</td>
</tr>
<tr>
<td><strong>Regions</strong></td>
<td>Vietnam/Southeast Asia where a therapeutic vaccine has clear health economic benefit</td>
</tr>
<tr>
<td><strong>Ages/classes</strong></td>
<td>Seropositive adults</td>
</tr>
<tr>
<td><strong>Regimen</strong></td>
<td>6 monthly immunizations + ribavirin (improvement from current daily regimens given up to 48 weeks)</td>
</tr>
<tr>
<td><strong>Efficacy</strong></td>
<td>Non-inferior to current standard of care (interferon + ribavirin), improved efficacy against non-genotype 1 or drug-resistant HCV</td>
</tr>
<tr>
<td><strong>Safety</strong></td>
<td>Significantly reduced toxicity due to lack of interferon</td>
</tr>
</tbody>
</table>
HCV Imaging: Detection of Envelope Glycoprotein on HCV eVLPs vs. Virions Using Immunogold EM Staining

HCV eVLP
(Garrone et al., Science Translation Medicine 2011)

HCV virions isolated from patients
(Petit et al. Virology 2005)
Macaques primed with adenoviral vector to induce suboptimal HCV immunity (no induction of nAbs) that mimics infected individuals

Strong cross-reactive neutralizing antibody responses against divergent genotypes of HCV

- Neutralizing Ab titers measured at week 12 after 1st eVLP immunization

**Divergent Circulating HCV Isolates**

Neutralization response in sera from vaccinated macaques (n=4)


*Internal Reference: VAC0805 CrossNeutral*
eVLP Vaccines: Scalable manufacturing process established with exceptional purity

**eVLP PURIFICATION SCHEME**

1. Clarification (Depth filtration)
2. Concentrate particles (Tangential flow filtration)
3. Inactivate residual host DNA and adventitious virus (Benzonase/βPL Tx & diafiltration)
4. Wash and Concentrate (Diafiltration & ultracentrifugation)
5. Sterilize (filter)

Current Scale with Lead Program: 50L
Current Yield – Lead Program: ~150 purified doses / liter

- eVLP density = 9.60x10^6 particles/mL
- 1.44x10^{12} particles/mL
- 1.15x10^{10} particles/mL
HCV eVLP Program Summary

- HCV eVLP proof-of-concept (Garrone et al. 2011)
  - Strong induction of neutralizing antibody responses in monkeys
  - Broadly reactive against multiple HCV genotypes

- eVLP production and purification development
  - Substantial knowledge & expertise gained from CMV eVLP program
  - VBI has licensed a GMP-compliant HEK 293 cell line (serum-free, cell suspension growth)
  - VBI has developed a scalable, cost-effective purification process that provides:
    - High yields
    - High purity (residual DNA and host cell protein content meet regulatory targets)