Universal Flu Vaccine
&
Pandemic Preparedness AHEAD of Outbreak

WHO meeting, May 2014
Forward Looking Statements

This presentation includes “forward-looking statements” within the meaning of applicable securities laws. These forward-looking statements involve risks and uncertainties, including those identified within the “Risk Factors” section of the Company's Shelf Prospectus dated January 8, 2014.

Although management of the Company believes the expectations reflected in such forward-looking statements are based on reasonable assumptions, the Company cannot assure investors that these expectations will prove correct, and the actual results that the Company achieves may differ materially from any forward-looking statements, due to such risks and uncertainties.
Agenda

WHY? Today’s flu vaccines are strain-specific and do not work against emerging strains

HOW? New generation flu vaccine active against seasonal and pandemic, A and B Type strains

WHAT? Pre-clinical and clinical data support safety and efficacy of BiondVax’s universal flu vaccine
# Current Vaccines vs BiondVax’s New Approach

<table>
<thead>
<tr>
<th>CURRENT</th>
<th>BiondVax’s M-001</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strain specific</td>
<td>Universal</td>
</tr>
<tr>
<td>New vaccine every year</td>
<td>Single formulation</td>
</tr>
<tr>
<td>Long production cycle</td>
<td>Short year-round production &amp; vaccination</td>
</tr>
<tr>
<td>Limited effect</td>
<td>Activates both arms of the immune system, can serve as a primer</td>
</tr>
<tr>
<td>Hen egg allergy</td>
<td>Non allergenic</td>
</tr>
</tbody>
</table>

**Universal Flu Vaccine - One • For All**
BiondVax’s Partners

Weizmann Institute of Science, Israel

OCS-Office of the Chief Scientist
State of Israel

FP7 Consortium, EU

Tel Aviv Sourasky Medical Center, Israel

Hadassah University Medical Center, Israel

MonoSol Rx, USA
A Game Changing Flu Vaccine

Both immune arms against all strains
BiondVax’s Universal Flu Vaccine (M-001)

**Design: Targets Common Regions**
Nine common regions are connected to make one recombinant protein called M-001

**Production: Quick and Robust**
Produced easily and quickly all year-round within 6-8 weeks via fermentation in *E. coli*
BiondVax’s Facility: GMP Production of M-001

**Downstream**
- Fermentation (E. coli): 3 days
- M-001 purification: 5 days
- Fill and finish: 1 day
- QC testing: 6 weeks
- Product Release: 6-8 weeks
- Stability (ongoing): 33 months

**Upstream**
- Fermentation
- IB Solubilization
- Ultrafiltration
- Lysis
- Chromatography
- Fill & Finish

*Universal Flu Vaccine - One • For All*
Universality

Pre-clinical and Clinical Data
High Homology with Seasonal & Pandemic Strains

<table>
<thead>
<tr>
<th>Epitope in M-001</th>
<th>Homology to Influenza Type &amp; Strains (representative list)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HA (T-helper)</td>
<td>A</td>
</tr>
<tr>
<td>NP (T-helper)</td>
<td>A</td>
</tr>
<tr>
<td>NP (CTL)</td>
<td>A</td>
</tr>
<tr>
<td>NP (CTL)</td>
<td>A</td>
</tr>
<tr>
<td>M1 (B-cell &amp; CTL)</td>
<td>A</td>
</tr>
<tr>
<td>HA (B-cell)</td>
<td>A</td>
</tr>
<tr>
<td>HA (B-cell)</td>
<td>A</td>
</tr>
<tr>
<td>HA (B-cell)</td>
<td>A</td>
</tr>
<tr>
<td>HA (B-cell)</td>
<td>B</td>
</tr>
</tbody>
</table>

* Homology to influenza strains was determined by Blast search in NCBI data base
M-001: Clinical trials

No significant differences between treatment and control groups

No treatment-related Severe Adverse Events
Most adverse events were mild
All adverse events observed were transient

<table>
<thead>
<tr>
<th>Trial</th>
<th>Year</th>
<th>Population (age)</th>
<th>Total N</th>
</tr>
</thead>
<tbody>
<tr>
<td>BVX-002</td>
<td>2009</td>
<td>Younger Adults (18-49)</td>
<td>63</td>
</tr>
<tr>
<td>BVX-003</td>
<td>2010</td>
<td>Older Adults (55-75)</td>
<td>60</td>
</tr>
<tr>
<td>BVX-004</td>
<td>2011</td>
<td>Younger Adults (18-49)</td>
<td>200</td>
</tr>
<tr>
<td>BVX-005</td>
<td>2012</td>
<td>Elderly (65+)</td>
<td>120</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>443</td>
</tr>
</tbody>
</table>

1Mild Side Effects:
- Local reactions: injection site pain, erythema (skin redness), swelling
- Systemic reactions: myalgia (muscle ache), malaise (general discomfort) fever
## M-001: Good Safety Profile & Well-Tolerated

<table>
<thead>
<tr>
<th>BVX-005: 120 elderly (65+ Y)</th>
<th>M-001 x2 +TIV</th>
<th>M-001 x1 +TIV</th>
<th>Alum/M-001x1 +TIV</th>
<th>Placebo x1 +TIV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rhinitis</td>
<td>3 (10%)</td>
<td>1 (3.3%)</td>
<td>6 (20%)</td>
<td>4 (13.3%)</td>
</tr>
<tr>
<td>Malaise/asthenia</td>
<td>2 (6.7%)</td>
<td>2 (6.7%)</td>
<td>4 (13.3%)</td>
<td>2 (6.7%)</td>
</tr>
<tr>
<td>Sore throat</td>
<td>1 (3.3%)</td>
<td>1 (3.3%)</td>
<td>3 (10%)</td>
<td>2 (6.7%)</td>
</tr>
<tr>
<td>Injection site pain</td>
<td>3 (10%)</td>
<td>1 (3.3%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cough</td>
<td></td>
<td></td>
<td>1 (3.3%)</td>
<td>3 (10%)</td>
</tr>
<tr>
<td>Headache</td>
<td>1 (3.3%)</td>
<td></td>
<td>2 (6.7%)</td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td></td>
<td>2 (6.7%)</td>
<td></td>
<td>1 (3.3%)</td>
</tr>
<tr>
<td>Neck pain</td>
<td>1 (3.3%)</td>
<td></td>
<td>2 (6.7%)</td>
<td></td>
</tr>
<tr>
<td>Fever</td>
<td></td>
<td></td>
<td>1 (3.3%)</td>
<td>1 (3.3%)</td>
</tr>
<tr>
<td>Back pain</td>
<td>1 (3.3%)</td>
<td>1 (3.3%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injection site erythema</td>
<td></td>
<td></td>
<td></td>
<td>1 (3.3%)</td>
</tr>
<tr>
<td>Arthralgia</td>
<td></td>
<td></td>
<td>1 (3.3%)</td>
<td></td>
</tr>
<tr>
<td>Rash</td>
<td></td>
<td></td>
<td></td>
<td>1 (3.3%)</td>
</tr>
<tr>
<td>Flushing</td>
<td>1 (3.3%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dizziness</td>
<td></td>
<td></td>
<td>1 (3.3%)</td>
<td></td>
</tr>
<tr>
<td>Decreased blood pressure</td>
<td></td>
<td></td>
<td></td>
<td>1 (3.3%)</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>13</strong></td>
<td><strong>8</strong></td>
<td><strong>23</strong></td>
<td><strong>12</strong></td>
</tr>
</tbody>
</table>
M-001 Activates CD4+ IFNg+ in Elderly 65+

Mechanism of action & potential cellular biomarker

Peripheral blood mononuclear cells (PBMCs) from whole blood were exposed ex vivo to the indicated antigens. Intracellular staining for IFN-gamma and CD4 frequencies were analysed by FACS.
M-001 Activates CD8+ IFNg+ in Elderly 65+

Mechanism of action for pandemic primer & universal products

BVX 005: Peripheral blood mononuclear cells (PBMCs) from whole blood were exposed ex vivo to the indicated antigens. Intracellular staining for IFN-gamma and CD8 frequencies were analysed by FACS.

* P<0.05
M-001 Efficacy Measured After Viral Ag Exposure

More people seroconverted (HAI) to all tested *seasonal* strains

**BVX-003**: 500 mcg M-001, TIV (Vaxigrip 2009) and Placebo (either PBS or adjuvanted PBS)

**BVX-005**: 500 mcg M-001, TIV (Vaxigrip 2011) and Placebo (PBS).

* = P<0.05

H1N1 pandemic swine flu strain
Enhanced HAI responses to strains **NOT** included in boost vaccine

<table>
<thead>
<tr>
<th>Strains not included in the boost</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>H1N1</strong></td>
<td>A/New Caledonia/20/99, A/Wuhan/371/95, A/Brisbane/59/07</td>
</tr>
<tr>
<td><strong>H3N2</strong></td>
<td>A/New York/55/04, A/California/07/07, A/Wisconsin/67/05, A/Perth/16/09, A/Brisbane/10/07</td>
</tr>
<tr>
<td><strong>Influenza B Victoria and Yamagata</strong></td>
<td>B/Malaysia/2506/04, B/Johannesburg/5/99, B/Shanghai/361/02</td>
</tr>
</tbody>
</table>
| **H5N1**                                   | Clade 2.1 (A/Duck/Hunan/795/02)  
|                                           | Clade 2.2 (A/Bar headed goose/Qinghai/1A/05) 
|                                           | Clade 2.3 (A/Duck/Laos/3295/06) |
One Protein, Multiple Pathways/Products

**Universal Flu Vaccine**
- Standalone multi-strain, multi-season
- Trial: M-001 vs placebo
- Endpoints: clinical efficacy

**Pandemic Primer**
- Enhancer of pandemic strain specific vaccines
- Trial: M-001 + pandemic vaccine vs pandemic vaccine
- Endpoint: current antibody immune marker (HAI)
M-001 as Pandemic Primer

Immediate vaccination upon any pandemic declaration
BARDA’s Model of Pandemic Preparedness

Universal Flu Vaccines Will Transform Seasonal & Pandemic Influenza Preparedness

“Priming Dose”

“Booster Dose”

Egg- & Cell-based Vaccines with Adjuvants

Universal Vaccines

Recombinant Vaccines with Adjuvants

Pan Flu Illnesses

12-16 weeks
16-20 weeks

Source:
HHS Pandemic Influenza Vaccine Program
VRBPAC Meeting November 14, 2012
Robin Robinson, PhD
Director of BARDA¹, HHS, USA

¹http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/BloodVaccinesandOtherBiologics/VaccinesandRelatedBiologicalProductsAdvisoryCommittee/UCMB30392.pptx
BiondVax’s Pandemic Preparedness Plan (PPP)

Today's situation:

Inter pandemic Phase

BiondVax's PPP:

Pandemic Declaration

Key benefits:

- Vaccination schedule starts immediately upon ANY pandemic declaration (instead of 6 months later)
- More subjects reach level of protection to pandemic and evolving strains after ONE boost
Universal Flu Vaccine - One • For All

M-001 Efficacy Measured After Viral Ag Exposure

Enhanced HAI responses to pandemic strains

**Swine H1N1**

- **Human clinical trial: Age 65+**
  - In human: 500mcg M-001 twice, TIV (Vaxigrip 2011) and Placebo (PBS).
  - In mice: 150mcg M-001 thrice, 0.67mcg H5N1 once (A/Vietnam/1203/04 Clade 1, Aventis Pasteur, non adjuvanted)

**Avian H5N1**

- **Mouse Model**
  - Seroconversion: % of mice with mean fold increase in HAI GMT ≥4x and HAI GMT ≥ 1:40 post-immunization

* * P<0.05
Primed Broadens Immunity to Drift Strains

Response to non H5N1 vaccine strains

- **In mice:** 250mcg M-001 twice, partial dose of H5N1 vaccine (A/Vietnam/1194/04)
- **Seroconversion:** % of mice with mean fold increase in HAI GMT ≥4x and HAI GMT ≥ 1:40 post-immunization
- **Strains:** Clade 2.1 (A/Duck/Hunan/795/02); Clade 2.2 (A/Bar headed goose/Qinghai/1A/05); Clade 2.3 (A/Duck/Laos/3295/06)

* P<0.05
Clinical Trials for a Universal Pandemic Primer

<table>
<thead>
<tr>
<th>Prime</th>
<th>Boost</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M-001</td>
</tr>
<tr>
<td>2</td>
<td>Saline</td>
</tr>
</tbody>
</table>

Prime Vaccine  
Boost Vaccine

Population:
- Adults eligible to receive the pandemic vaccine (H5N1 or H7N9)

Endpoints:
- Safety
- Elevated Hemagglutination inhibition (HAI)
- CMI
- 2 seasons follow up

Sample size:
- 400 Experimental and 200 Control per age group
- Planned as part of UNISEC consortium for 2015
Take Home

✓ **One • For All**: against A & B-Type, seasonal & pandemic strains

✓ **Safe**: no adjuvant required

✓ **Active**: induces cellular responses and enhances HAI responses

✓ **Pandemic Primer**: preparedness AHEAD of any outbreak & sparing

✓ **NEXT**: Clinical trials for each indication
A Game Changer for Influenza

Thank You!

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