Universal Influenza Vaccine

One ● For All

The First WHO Integrated Meeting on Development and Clinical Trials of Influenza Vaccines that Induce Broadly Protective and Long-lasting Immune Responses

Hong Kong Baptist University, January 2013
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 17, 2012.

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.
BiondVax’s Universal Flu Vaccine candidate M-001:

• In advanced Phase 2 clinical development
• Synergistic with current influenza vaccines
• Prepares for pandemics (incl. H5N1)
BiondVax at a glance

Dedicated to improving global protection against influenza
BiondVax in Focus

Dedicated to improving global protection against flu

Publicly-traded on Tel Aviv Stock Exchange since June 2007 (TASE:BNDX)

Comprehensive patent portfolio includes exclusive, worldwide license agreement with Weizmann Institute

Passed European QP GMP audit

4 successful Phase I/II & II clinical trials involving 440 people

M-001 significantly improves efficacy of pandemic H5N1 vaccine (pre-clinical)

1 http://www.tase.co.il/TASEEng/General/Company/companyDetails.htm?subDataType=0&companyId=001468&ShareId=01105204#SummaryLink
2 Qualified Person (QP) Good Manufacturing Practices (GMP)
One • For All - A Universal Flu Vaccine

More than 15 years of R&D at Weizmann Institute in lab of Prof Ruth Arnon

Phase I/II
2008
Phase II
2010
Phase III
2012 milestones:
✓ Phase II in elderly completed
✓ European QP GMP audit passed

2013 milestones:
➢ Submit USA IND (FDA)
➢ Start Phase II under IND

BiondVax today

BiondVax Operational

BiondVax Pharmaceuticals Ltd.

Pivotal Phase III clinical trials likely require strategic partner
BiondVax’s approach

Developing a universal vaccine to protect against A and B, seasonal and pandemic, present and future influenza 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

**The Influenza Virus**

- **HemAgglutinin (HA)**
- **NucleoProtein (NP)**
- **Matrix protein (M₁)**
Additional Use for M-001

M-001 improves current influenza vaccines

Immunize with M-001 (PRIME)  →  Immunize with current flu vaccine (BOOST)  →  More people respond to current flu vaccine

Clinically important:

- reduces vulnerability of elderly: who need improved vaccines urgently
- enables pre-pandemic preparedness: people could be vaccinated (‘primed’) before the pandemic strain-specific vaccine is manufactured

Commercially important:

- serves as an alternative regulatory pathway: could prove shorter & cheaper
- facilitates commercialization of M-001 as universal flu vaccine
Pre-Clinical Studies
M-001 Protects Against Lethal Flu Infection

Peptide-based Influenza Vaccine
Animal studies at the Weizmann Institute showed that a mixture of B-cell + T-helper + CTL peptides provides optimal protection against influenza infection:

![Graph showing survival rates](image)

(●) Untreated control
(x) B-cell epitope
(■) B-cell epitope & CTL epitope
(▲) B-cell & CTL & T helper epitope

M-001 Recombinant Vaccine
Animal studies at BiondVax showed that a single recombinant protein comprising select peptides conserved & common among type A and B influenza strains activates cellular and humoral immunity and affords protection against lethal influenza challenge:

![Bar chart showing survival rates](image)

HLA A*0201 transgenic mice immunized IM x3 with adjuvanted M-001 (Multimeric) vaccine were infected with highly lethal (30LD50) dose of H3N2
M-001 Enhances Immunity to Natural Infection

**Higher Levels of HAI Antibodies**

<table>
<thead>
<tr>
<th>Fold Increase in HAI GMT</th>
<th>Adj PBS &amp; PR8 infection</th>
<th>Adj M001 &amp; PR8 infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>5.0</td>
<td>30.0</td>
</tr>
</tbody>
</table>

**More mice seroconverted**

<table>
<thead>
<tr>
<th>% Seroconversion</th>
<th>Adj PBS &amp; PR8 infection</th>
<th>Adj M001 &amp; PR8 infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>0%</td>
<td>5%</td>
<td>90%</td>
</tr>
</tbody>
</table>

**Notes:**

HAI GMT – hemagglutinin inhibition geometric mean titer is the serial dilution of serum that after incubation with a fixed amount of a certain influenza strain is no longer capable of preventing agglutination of erythrocytes; regulatory authorities consider the dilution 1:40 indicative of protective immunity

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

Adj - Freund’s adjuvant

**M-001 immunization results in elevated HAI immune responses to sub lethal intranasal infection with PR/8/34**

*Universal Flu Vaccine - One • For All*
M-001 Enhances Efficacy of Pandemic H5N1 Vaccine

Higher Levels of HAI Antibodies

More Mice Seroconverted

M-001 priming potentially enables one instead of two doses H5N1 vaccine per person

1 0.67 mcg (2.25%) H5N1 A/Vietnam/1203/04 in naïve mice
Human Trials
4 Successful Clinical Trials – Positive Safety

**Design:**
- Randomized and placebo-controlled
- Blinded: single BVX-002, -003 and double BVX-004, -005

**Endpoints:**
- Primary endpoint: safety
- Secondary (exploratory) endpoint: immune responses

<table>
<thead>
<tr>
<th>Trial</th>
<th>Year</th>
<th>Population (age)</th>
<th>N (M-001)</th>
<th>N (Placebo)</th>
<th>Total N</th>
</tr>
</thead>
<tbody>
<tr>
<td>BVX-002</td>
<td>2009</td>
<td>Younger Adults (18-49)</td>
<td>43</td>
<td>20</td>
<td>63</td>
</tr>
<tr>
<td>BVX-003</td>
<td>2010</td>
<td>Older Adults (55-75)</td>
<td>40</td>
<td>20</td>
<td>60</td>
</tr>
<tr>
<td>BVX-004</td>
<td>2011</td>
<td>Younger Adults (18-49)</td>
<td>112</td>
<td>88</td>
<td>200</td>
</tr>
<tr>
<td>BVX-005</td>
<td>2012</td>
<td>Elderly (65+)</td>
<td>90</td>
<td>30</td>
<td>120</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>285</td>
<td>158</td>
<td>443</td>
</tr>
</tbody>
</table>

**Safety:**
- No treatment-related Severe Adverse Events
- Most adverse events were **mild** and all were **transient**

No significant differences between treatment and control groups

*Universal Flu Vaccine - One • For All*
M-001 Activates Multi-Strain Cellular Immunity

M-001 Activates Cell Mediated Immunity (CMI) to Various Flu Antigens

**BVX-005**: 500 mcg M-001 administered twice with interval of 21 days; Placebo (PBS) once
M-001’s Universality Measured Indirectly by HAI

More people are seroconverted to all tested TIV viruses

**Breadth** of immunogenicity supported by M-001 priming of different TIV boosts

**BVX-003**
- 55-75 Y

**BVX-005**
- 65-91 Y

Minimum required for regulatory approval

1. In **BVX-003**: 500 mcg M-001, TIV (Vaxigrip 2009) and Placebo (either PBS or adjuvanted PBS)
2. In **BVX-005**: 500 mcg M-001, TIV (Vaxigrip 2011) and Placebo (PBS).

* = P<0.05

Universal Flu Vaccine - One • For All
Competitive Advantages of BiondVax’s M-001

✓ **SAFETY:** Demonstrated good safety profile in advanced clinical trials with 440 people

✓ **ACTIVITY:** Triggers anti-influenza immune responses in people aged 18-91 without any added adjuvant

✓ **MULTIPLE PRODUCTS:** Universal influenza vaccine and primer for current influenza vaccines

✓ **PRACTICAL:** Quick and easy, year-round production and stockpiling
The Road Ahead
**M-001: Three Products, Large Market Potential**

<table>
<thead>
<tr>
<th>Seasonal Primer for Elderly</th>
<th>Pre-Pandemic Primer</th>
<th>Universal Flu Vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Given to elderly each year before boosting with seasonal flu vaccine</td>
<td>Given to entire population upon pandemic alert while pandemic strain-specific vaccine is manufactured</td>
<td>Given to entire population every 3-5 years to protect against seasonal &amp; pandemic flu strains</td>
</tr>
<tr>
<td>Potential price/dose: ~$10</td>
<td>Potential price/dose: ~$10</td>
<td>Potential price/dose: ~$50</td>
</tr>
<tr>
<td>Assuming given yearly to 70% of OECD elderly: ~$1.3B&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Assuming given to half of OECD population: ~$6B&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Assuming 500M yearly vaccine doses: ~$5B&lt;sup&gt;3&lt;/sup&gt;</td>
</tr>
</tbody>
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<sup>1</sup>Population in OECD is 1.2B. ~15% are elderly. (OECD Factbook 2011) Calculation: 1.2x15%x70%x$10

<sup>2</sup>Population in OECD is 1.2B. (OECD Factbook 2011) Calculation: 1.2x50%x$10

A Game-Changer for Influenza Vaccines

Thank You!

BiondVax’s Universal Flu Vaccine candidate M-001:

• In advanced Phase 2 clinical development
• Synergistic with current influenza vaccines
• Prepares for pandemics (incl. H5N1)

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