Pandemic Influenza Vaccine Clinical Trial Abstract Minimum information:

**Title of Trial:** A Phase II, Multicenter, Randomized, Placebo-Controlled Study to Assess the Safety and Immunogenicity of an Intramuscular Influenza Vaccine (Multimeric-001) Followed by Administration of Trivalent Influenza Vaccine (TIV) to Elderly Volunteers (BVX005)

**Clinical Trial registration site if applicable (e.g. ClinicalTrials.gov):** NCT01419925

**Authors/sponsors:** BiondVax Pharmaceuticals Ltd

**Study Design:** Randomized, placebo controlled study using one or two prime immunizations with M-001 and a subsequent boost with TIV

**Vaccine:** Multimeric-001 (M-001)

- **Manufacturer:** BiondVax Pharmaceuticals Ltd

- **Type (whole virus/subvirion/subunit/live/recombinant/DNA/vector):** Recombinant

- **Adjuvant:** with and without Aluminum phosphate

- **Delivery system/site:** Intramuscular

**Doses (antigen and adjuvant):** 500mcg M-001

**Study population:**

- **Age range:** Healthy

**Specific inclusion/exclusion criteria:**

- **Inclusion criteria:**
  - Males and females at the age of ≥65 years old
  - Eligible to receive the standard seasonal influenza vaccine according to the MOH guidelines.
  - Subjects who provide written informed consent to participate in the study.
  - Subjects able to adhere to the visit schedule and protocol requirements and are available to complete the study.
  - Haematology, chemistry and urinalysis values with no clinical significance or do not reflect a medical condition which, according to the physician’s judgment, might confound the results of the study or pose additional risk to the subject by participation in the study.
  - Male subjects must agree to use a condom during the full term of the study period (including follow up) if female partner is not using an acceptable contraceptive method.
  - Subjects who are seronegative to at least one of the strains included in the seasonal vaccine against influenza for 2011-2012.

- **Exclusion criteria:**
  - Known history of significant medical disorder which, in the investigator’s judgment, might confound the results of the study or pose additional risk to the subject by participation in the study.
  - Subjects with known Guillain Barré Syndrome in the past.
  - Subjects who have been immunized with anti-influenza vaccine or infected by influenza virus within eight months prior to the screening visit.
  - Known hypersensitivity associated with previous influenza vaccination.
  - Use of an influenza antiviral medication within 4 weeks of vaccination.
- Known hypersensitivity and/or allergy to any drug or vaccine.
- Known hypersensitivity to egg proteins (eggs or egg products), chicken proteins, or any of the components of the commercial vaccine (e.g., formaldehyde, and octoxinol 9 (Triton X-100) and neomycin).
- Persons deficient in producing antibodies, whether due to genetic defect, immunodeficiency disease, or immunosuppressive therapy.
- History of any bleeding disorder or subjects with thrombocytopenia (since bleeding may occur following an intramuscular administration to these subjects).
- Any clinically significant abnormality upon physical examination or in the clinical laboratory tests at screening visit which, according to the physician's judgment, might confound the results of the study or pose additional risk to the subject by participation in the study.
- Positive serology for HIV, HCV antibody or HBsAg.
- Any acute medical situation (e.g. acute infection, ongoing flu symptoms) with or without fever within 48 hours of vaccination, which is considered significant by the Investigator.
- Subjects who participated in another interventional clinical study within 30 days prior to first dose.
- Subjects who are non-cooperative or unwilling to sign consent form.

Clinical Endpoints Assessed:

**Safety assessments:**

1. To assess the safety, tolerability, reactogenicity and local tolerance of Multimeric-001 vaccine, used as a primer to the TIV influenza vaccine administration.
2. To assess the safety, tolerability, reactogenicity and local tolerance of Adjuvanted (Aluminum phosphate) Multimeric-001 vaccine, used as a primer to the TIV influenza vaccine administration.

**Immunogenicity assessments:**

To characterize the immune responses in all study groups, including assessment of HI antibody level.

**Results:**

**Safety:**

Aluminum phosphate adjuvanted as well as non adjuvanted formulations of Multimeric-001 were well tolerated and safe across all treatment groups. The number of adverse events and the number of subjects reporting adverse events (AEs) after prime administration with M-001/adjuvanted M-001 and TIV boost was comparable to numbers in the cohorts injected with placebo and boosted with TIV.

**Immunogenicity**

**GMTs:**

500µg M-001 prime (one dose, without adjuvant) and TIV boost

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<tr>
<td>28</td>
<td>H1N1</td>
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<tr>
<td>96</td>
<td>H3N2</td>
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TIV alone

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<tr>
<td>7</td>
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<tr>
<td>31</td>
<td>H3N2</td>
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**GMT Ratios (post:pre):**
500µg M-001 prime (one dose, without adjuvant) and TIV boost
3.73 H1N1
3.03 H3N2
1.35 B
TIV alone
2.24 H1N1
2.30 H3N2
1.32 B

Per cent responding by seroconversion (4 fold or greater rise and titer ≥40 definition for reporting):
500µg M-001 prime (one dose without adjuvant) and TIV boost
37% H1N1
47% H3N2
10% B
TIV alone
17% H1N1
33% H3N2
3% B

Elevated proportions of subjects primed with M-001 and boosted with TIV were seroconverted to the boost influenza strains as compared to the control group immunized with TIV alone. Elevated HAI responses to strains contained in the TIV were observed in the group primed once without an adjuvant showing that the adjuvanted formulation is not required. M-001 priming afforded an increase in the proportion of seroconverted participants to both seasonal strains (H3N2 and influenza B) and to the pandemic strain contained in the TIV (swine H1N1 strain A/California/7/09) as well as to various influenza A and B strains not contained within the TIV (data not shown).

Others assays: CMI
Sorting of PBMCs isolated from subjects immunized with M-001 alone (FACS analysis) revealed a specific and significant increase in the proportions of IFN-gamma-secreting T-helper cells (CD4+) upon ex vivo exposure to M-001 and to influenza antigens that was not observed for PBMCs isolated from subjects immunized with placebo.

Status of trial (ongoing/completed): Completed