FLU-v: Broad Spectrum
(A, B and Pandemic Strains)
Stand-alone Influenza Vaccine Candidate

Results of Phase IIb Field Study of FLU-v (FLU-v003)
Now Ready For Phase III Development

FLU-v is being developed by Imutex Ltd, hVIVO’s 49% JV with SEEK Group

18 June, 2018
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Today’s Presenters

Dr. Trevor Phillips
Executive Chairman
hVIVO

Gregory Stoloff
CEO
SEEK
Overview

- Opportunity to redefine the flu vaccine market
- Novel first-in-class, broad spectrum, true stand-alone, flu vaccine candidate
- Robust clinical data – reported positive results in immunogenicity profile and reduction of symptoms
- Positioned to enter Phase III, with clear disease and symptom-based endpoints identified
- Not dependent upon administration with annual vaccines
  - Administer at any time of year
- Synthetic product, no need for egg or cell based manufacture
- Significant market potential
Agenda

I. Introduction
II. FLU-v 003 Phase IIb Results, Real World Study
III. Our Vision for FLU-v
IV. hVIVO Strategy
V. Q&A
Introduction
## hVIVO – Uniquely Positioned Drug Discovery and Product Development Service Experts in Airways Disease

### Company Profile
- Listed in UK on AIM (HVO)
  - Established in 1989 - spin out from Queen Mary University, London
- Headquarters, London
  - Quarantine unit opened 2011
  - c. 150 employees
- Blue chip institutional investor base

### FYE 31-Dec-2017 Financials
- Revenue: £10.9m
- Gross profit: £3.6m (32.7% margin)
- Short term deposits, cash & cash equivalents: £20.3m
- Current Financial Initiatives:
  - Continued focus on cost control
  - Successfully driven operational efficiencies/cost management
  - Leveraging our know-how and service offering to grow and diversify revenue streams

### Significant Know-how and Proprietary Tools
- Pioneer of human disease models and industry leading clinical development
- Established strong reputation for expertise in providing disease insights and technical execution
- Biological insight developed into proprietary clinical services

### Established Global Customers and Collaborations
- Janssen
- NIH
- Alios BioPharma
- Gilead
- Vertex
- DARPA
- ReViral
- Pumocide
- National Institutes of Health

April 2016, hVIVO formed Imutex Limited ("Imutex") with the SEEK Group ("SEEK") to develop vaccines against influenza (FLU-V) and universal mosquito-borne diseases (AGS-v)

Imutex strengthened hVIVO’s commercial flu portfolio (FLU-v) and expanded it into the adjacent therapeutic area of mosquito-borne diseases

Anticipate progress of FLU-v programme towards monetisation
Flu is a Global Issue

<table>
<thead>
<tr>
<th>Seasonal Flu¹</th>
<th>Pandemic Flu²</th>
</tr>
</thead>
<tbody>
<tr>
<td>3,000,000 hospitalisations</td>
<td>290,000-650,000 deaths</td>
</tr>
<tr>
<td>200,000 hospitalisations</td>
<td>12,000-56,000 deaths</td>
</tr>
<tr>
<td>19,000 hospitalisations</td>
<td>8,000 deaths</td>
</tr>
</tbody>
</table>

• Pandemic strain: new to human
• We can’t predict when or where the next epidemic or pandemic will begin
• Many challenges exist worldwide that increase the risk that outbreaks will occur and spread rapidly, including:
  • Increased risk of infectious pathogens “spilling over” from animals to humans
  • Development of antimicrobial resistance
  • Spread of infectious diseases through global travel and trade
  • Acts of bioterrorism
  • Weak public health infrastructures

A severe pandemic can result in millions of deaths, and even the most conservative estimates suggest that pandemics reduce global GDP by up to 1%
Flu Vaccine Market Opportunity

Global Vaccines

Universal flu vaccine market potential of $10-20bn

<table>
<thead>
<tr>
<th>Year</th>
<th>Global Vaccines</th>
<th>Current Annual Flu Vaccines</th>
</tr>
</thead>
<tbody>
<tr>
<td>2018</td>
<td>$28bn</td>
<td>$3.3bn</td>
</tr>
<tr>
<td>2025</td>
<td>$48bn</td>
<td>$4.6bn³</td>
</tr>
</tbody>
</table>

CAGR: 8% $48bn
CAGR: 7% $4.6bn³

3% of Pharmaceutical Market²

By overcoming a number of key issues with current annual flu vaccines, FLU-v has the potential to address a much larger patient population and therefore has future blockbuster sales potential

³ Management estimates.

References:
Existing Issues with Current Flu Vaccines

- Predict Strains
- Intra Season Change
- Manufacturing Constraint
- Doctor Time/Costs
- Hospitalisations
FLU-v – Broad Spectrum Stand-alone Flu Vaccine Candidate
A, B and pandemic strains

An equimolar combination of four individual synthetic polypeptides (20 to 32 aa long) covering conserved immunogenic regions in M1, M2 and NP-A and NP-B

Non-structural proteins. Conserved Potential targets for T cell immunity

HA: surface, highly variable immunodominant head conserved stem

NA: surface, variable, slower drift

M2: surface, fairly conserved. Possible Ab-mediated protection

NP: internal highly conserved. Induces CMI

M1: internal highly conserved. Induces CMI
**Differentiated Approach in the Flu Vaccine Market**

<table>
<thead>
<tr>
<th>Proposed Solutions</th>
<th>NIH Schematic of Solutions</th>
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<tbody>
<tr>
<td><strong>Advantages</strong></td>
<td><strong>Coverage</strong></td>
</tr>
<tr>
<td>Booster to Annual</td>
<td>Vaccine</td>
</tr>
<tr>
<td>• Vaccine given alongside the annual that boosts the immune response and provides cross protection against strains if the guess is wrong or if they drift slightly during the season</td>
<td>Strain-specific</td>
</tr>
<tr>
<td>• Doses limited by annual manufacturing cap</td>
<td>Subtype-specific</td>
</tr>
<tr>
<td>• No supporting evidence that a boosted immune system can provide broad strain protection</td>
<td>Multi-subtype</td>
</tr>
<tr>
<td>• Relies on findings from swine flu pandemic</td>
<td>Pan-group</td>
</tr>
<tr>
<td>Standalone</td>
<td>Universal influenza vaccine</td>
</tr>
<tr>
<td>• Vaccines given alone, no need for annual</td>
<td>Imutex approach has full-spectrum strain coverage</td>
</tr>
<tr>
<td>• HA head/stem or stalk only targets certain groups of flu strains; peptide approach can target A, B or all strains</td>
<td></td>
</tr>
<tr>
<td>• Needs to be updated regularly and people re-vaccinated regularly, or may still need to receive the annual vaccine if the strain circulating is different</td>
<td></td>
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<tr>
<td>• Will not cover a pandemic strain</td>
<td></td>
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<tr>
<td>• If standalone covers all strains then none of the above issues arise</td>
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*Imutex has a unique solution with compelling competitive advantage over both vaccination frequency (no more than once every 5 years) and strain coverage (annual, pandemic and A & B in both humans and animals)*

Source: Company information

National Institutes of Health.
Robust Patent Portfolio in Place

**Strategy:** To protect individual polypeptides as well as compositions including them. Patents also cover homologies of the peptides and compositions

- Robust patent portfolio filed in 34 countries
- PCT Application filed in 2007
- 21 patents granted (in US, EU, Eurasia, China and many other countries)
- 13 pending patents (also in US, EU and many other countries)
- Up to 10 year market exclusivity on grant of market authorisation in certain major countries
Efficient and Scalable Chemical Manufacturing Process

No constraint on manufacturing capacity as synthetic process and not biological system allowing all year round manufacturing

- Stable at 5° Celsius for 2 years, no preservatives added
- Finished product mixed with Adjuvant and water for injection
- Freeze drying avoids cold-chain during storage and transport
- Low cost and scalable manufacturing up to kg levels and can be undertaken in multiple plants around the world
FLU-v 003 Phase IIb Results
Real World Study
## Aims

<table>
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<tr>
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<tr>
<td>Confirm the safety and tolerability of different regimens and formulations of FLU-v</td>
<td>Determine the immunogenicity response (T&amp;B cells mediated) to FLU-v vaccination</td>
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## Vaccination – 4 groups: Day 0 and 21

- Two regimes were tested:
  - Single dose adjuvanted FLU-v (500ug in emulsified adjuvant)
  - Two doses, given 21 days apart, of un-adjuvanted FLU-v (500ug in aqueous vehicle)
- Both regimes had matching placebo
Primary Endpoint Achieved (IFNγ Responders)
• Primary endpoint of enhancing T-cell responses was met demonstrating a statistically significant enhancement of the number of responders positive for interferon gamma (IFNγ) producing T-cells (p<0.001), at both 42 days and 180 days after single vaccination
• IFNγ is one of the most important markers of T-cell and immunoglobulin of B-cell mediated immunity effective against influenza infection

Secondary Endpoint Achieved (IgG Responders)
• Secondary immunogenicity related endpoint was to assess the FLU-v specific antibody, immunoglobulin (IgG) responses at both 42 and 180 days after single vaccination compared to placebo
• The secondary endpoint achieved a statistically significant increase in antibody titers of 100% of vaccinated subjects (p<0.001)

Symptom / Severity Score
• The reduction in the number and severity of symptoms observed in this study was consistent with the top-line FLU-v 004 challenge study results
• In this study a single dose of FLU-v was shown to induce the strongest immunological response rates and this group also experienced a 60% reduction in influenza confirmed infections and an 83% reduction in the number of influenza confirmed cases with severe symptoms compared to placebo
Primary Endpoint – T-Cell Mediated Immune Response
Statistically Significant Enhancement of the Number of Responders Positive for IFNg Producing T-Cells

Similar results obtained with TNFa and IL-2 responders
Secondary Endpoint – B-Cell Mediated Immune Response
Significant increase in key B-Cell mediated protective mechanisms

**Frequency of IgM Responders**

- **Adjuvanted FLU-v (1 Dose)**
- **Adjuvanted Placebo**
- **Non-Adjuvanted FLU-v (2 Doses)**
- **Non-Adjuvanted Placebo**

*Proportion of Responders*

- **P=0.014**

**Frequency of IgG Responders**

- **Adjuvanted FLU-v (1 Dose)**
- **Adjuvanted Placebo**
- **Non-Adjuvanted FLU-v (2 Doses)**
- **Non-Adjuvanted Placebo**

*Proportion of Responders*

- **P<0.001**

**Day 42 Compared to Day 0**
**Day 180 Compared to Day 0**
Consistent Trend in Reduction of Infections and Influenza Symptoms (Number, Severity & Duration) Following Single Dose of FLU-v

**Any Strain – Proportion Sick**

- Adjuvanted FLU-v (1 dose) (N=51)
- Combined Placebo (N= 58)
- Non-Adjuvanted FLU-v (2-dose) (N=58)

**Severe Symptomatology – Proportion Sick**

- Adjuvanted FLU-v (1 dose) (N=51)
- Combined Placebo (N= 58)
- Non-Adjuvanted FLU-v (2-dose) (N=58)

NB: Study not powered for efficacy
Safety

- Safe & Well Tolerated
- Main AE’s mild/moderate, some severe at site of injection only
- As expected, adjuvant formulation increases number of transient injection site reactions
Our Vision for FLU-v
## FLU-v – Excellent Profile

| Universal | • Tested across multiple A&B strains anticipate full coverage of all human strains  
• Covers all animal strains – pandemic protection  
• Both immune arms activated – T&B cells |
| --- | --- |
| Vaccination | • Single injection  
• Stand-alone vaccine, not linked to or limited by annual vaccine  
• Long lasting protection  
• Can vaccinate all year round, not limited to annual production |
| Manufacturing | • Synthetic process, low cost and efficient  
• Freeze dried, no need for cold-chain storage & transport |
| Evidence | • Immune response and clinical efficacy from two phase II studies  
• Real world and viral challenge studies  
• Phase III ready, breakthrough designation potential |
Current Environment Around FLU-v

- High confidence with two Phase IIb study results

- Definitive Primary Endpoint result from NIH expected shortly

- Supportive environment from key stakeholders:
  - FDA and EMA are both supportive for development of a universal flu vaccine; Imutex will now work with both the FDA and the EMA to progress pathway
  - Large number of academic, public and private organisations, which Imutex is working with (such as, WHO, BARDA, NIH), encourage development of a universal flu vaccine – Imutex working with these organisations
hVIVO’s Strategic Priorities
Focus on Revenue Growth and Becoming Cash Generative

- Continue to progress development of unique fee-for-service partnerships in airways disease
- Focus on revenue growth and achieving cash generation
- Fund further progression of own/part-owned programmes only through partnering / out-licensing / non-dilutive sources
- Continue to improve operational effectiveness through cost management and operational excellence
- Progress FLU-v programme towards monetisation using resultant capital to further fund strategic growth of the base business
V.

Q&A