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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The Company reports under IFRS. Where foreign currency equivalents have been provided for convenience in this presentation, the exchange rates applied are those used in the relevant financial statements from which the figures have been extracted.

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

I.

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 PHARMACEUTICAL COMPANIES OF Johnson & Johnson

NIH National Institutes of Health

Alios BioPharma

GILEAD

VERTEX

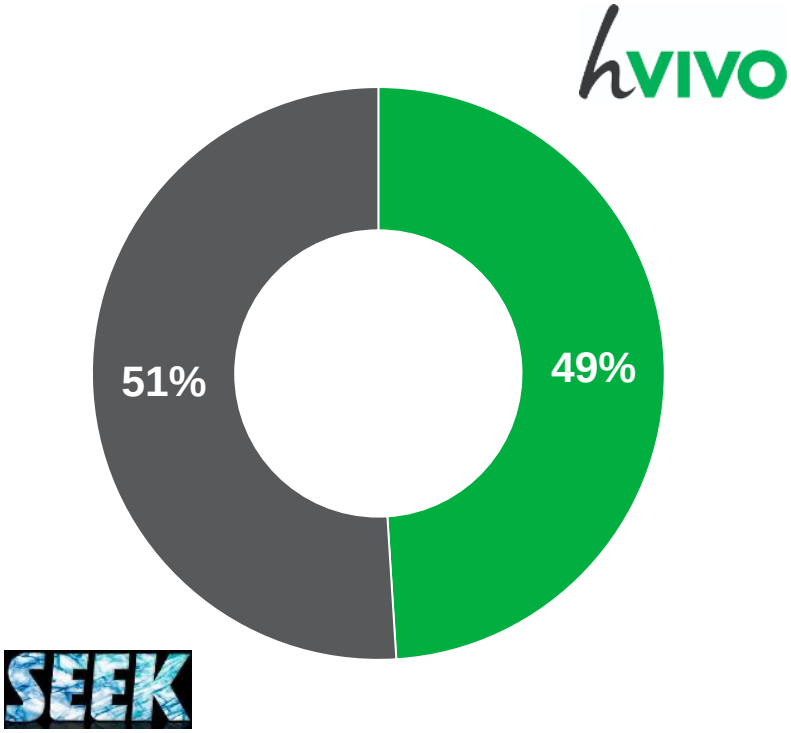
DARPA

ReViral

PULMOCIDE INHALED RESPIRATORY MEDICINE

hVIVO

Imutex – Shared Ownership Influenza Asset FLU-v



- 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

Seasonal Flu[1]

	**3,000,000** hospitalisations	**290,000-650,000** deaths	**$260bn** economic burden
	**200,000** hospitalisations	**12,000-56,000** deaths	**$87bn** economic burden
	**19,000** hospitalisations	**8,000** deaths	**£55-72bn** economic burden

Pandemic Flu[2]

- 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

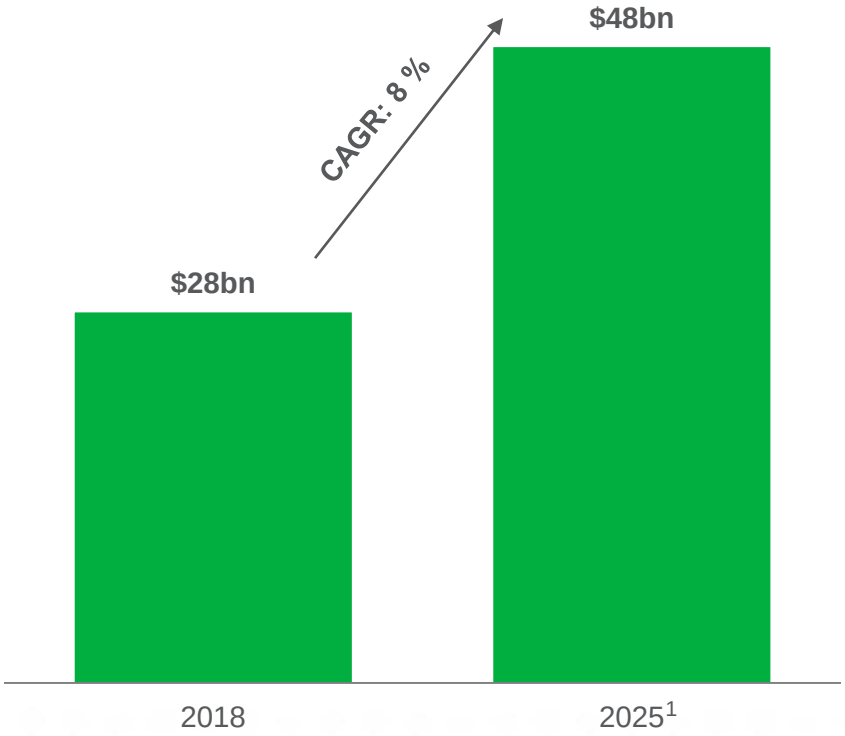
A severe pandemic can result in millions of deaths, and even the most conservative estimates suggest that pandemics reduce global GDP by up to 1%

[1] http://www.endfluenza.com[1] CDC[2], WHO[2]

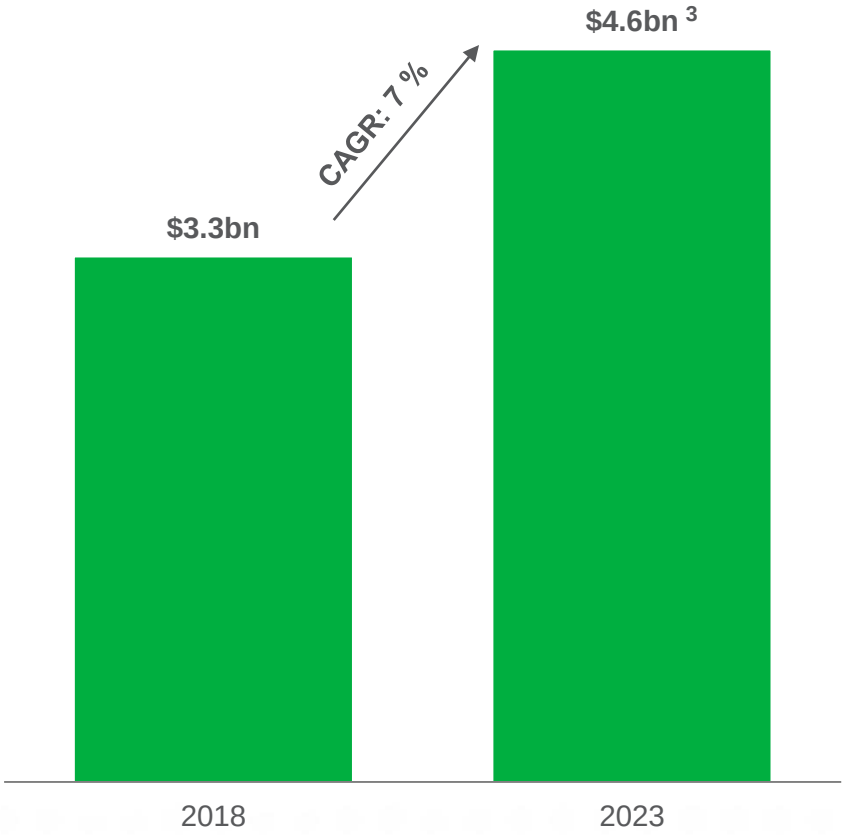
Flu Vaccine Market Opportunity

Global Vaccines

3% of Pharmaceutical Market[2]



Current Annual Flu Vaccines

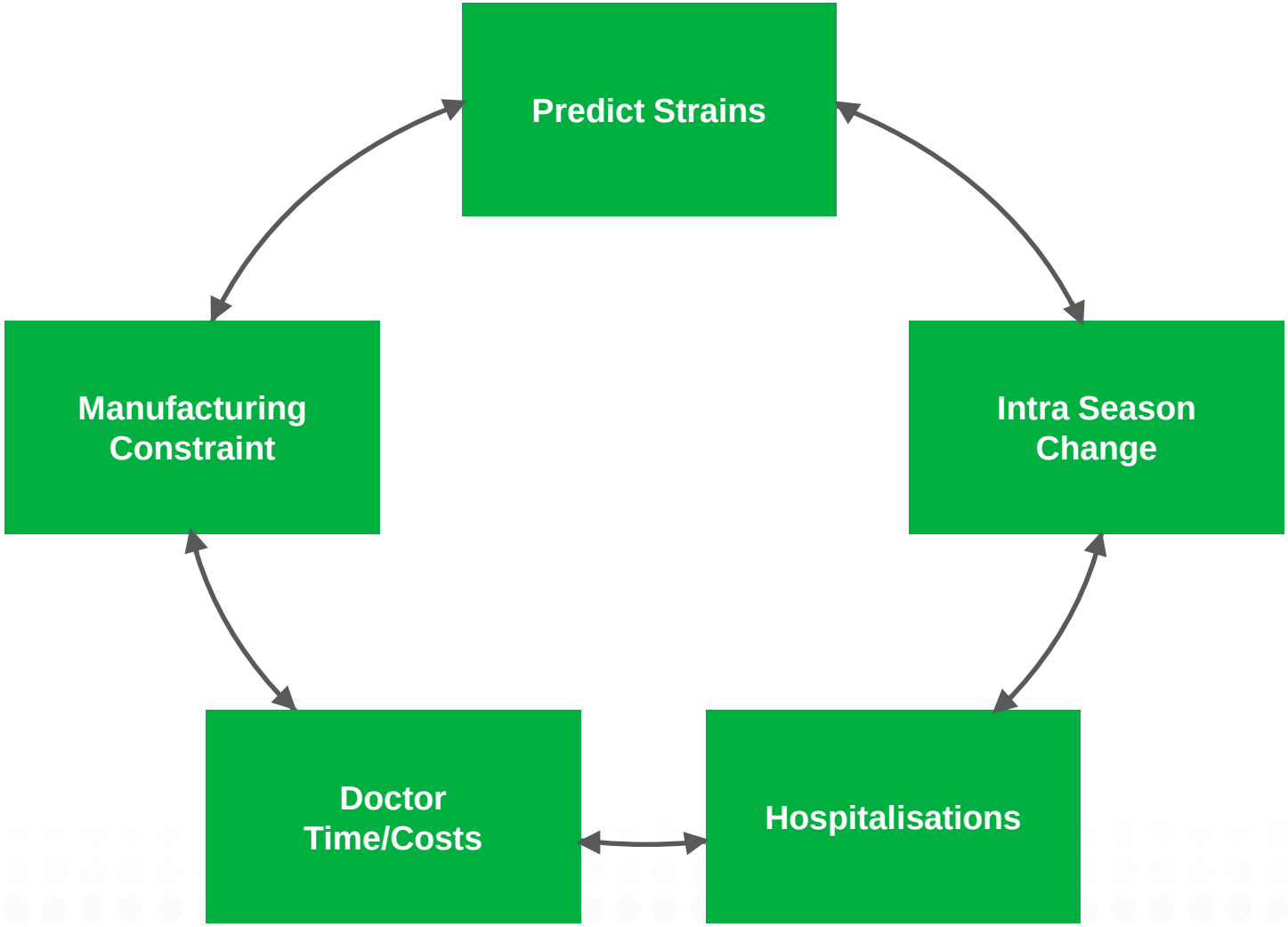


Universal flu vaccine market potential of $10-20bn[4]

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

[1] https://www.transparencymarketresearch.com/global-vaccine-market.html
[2] https://www.theatlantic.com/business/archive/2015/02/vaccines-are-profitable-so-what/385214/
[3] https://www.prnewswire.com/news-releases/global-influenza-vaccine-markets-2017-2023 [4] Management estimates.

Existing Issues with Current Flu Vaccines

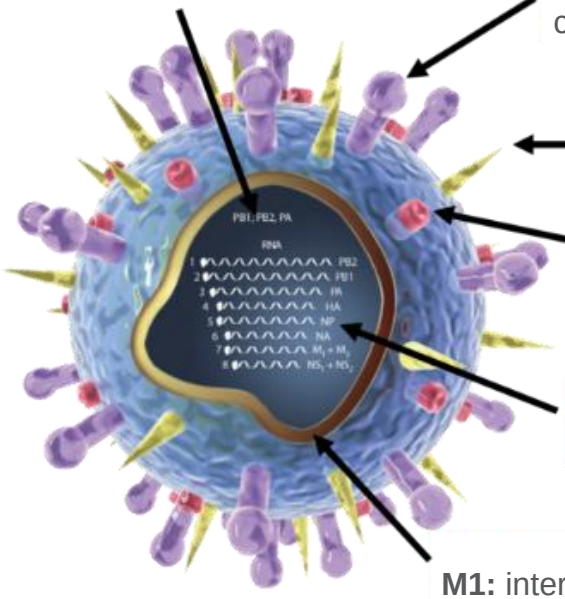


FLU-v – Broad Spectrum Stand-alone Flu Vaccine Candidate

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-medicated protection

NP: internal highly conserved. Induces CMI

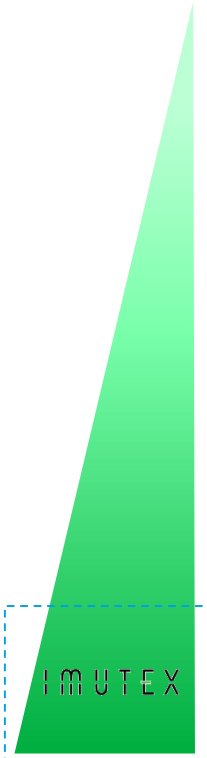
M1: internal highly conserved. Induces CMI

Differentiated Approach in the Flu Vaccine Market

Proposed Solutions

	Advantages	Considerations
Booster to Annual	• 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	• Doses limited by annual manufacturing cap • No supporting evidence that a boosted immune system can provide broad strain protection • Relies on findings from swine flu pandemic
Standalone	• Vaccines given alone, no need for annual • HA head/stem or stalk only targets certain groups of flu strains; peptide approach can target A, B or all strains	• 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 • Will not cover a pandemic strain • **If standalone covers all strains then none of the above issues arise**

NIH[1] Schematic of Solutions



Vaccine	Coverage
Strain-specific	Current circulating strains
Subtype-specific	All strains within a single HA subtype (e.g., H1)
Multi-subtype	Multi HA subtype within single group (e.g., H1/H5/H9)
Pan-group	Covering all group 1 and 2
Universal influenza vaccine	**All influenza (+/-influenza B)**

Imutex approach has full-spectrum strain coverage

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

[1] National Institutes of Health.

Robust Patent Portfolio in Place

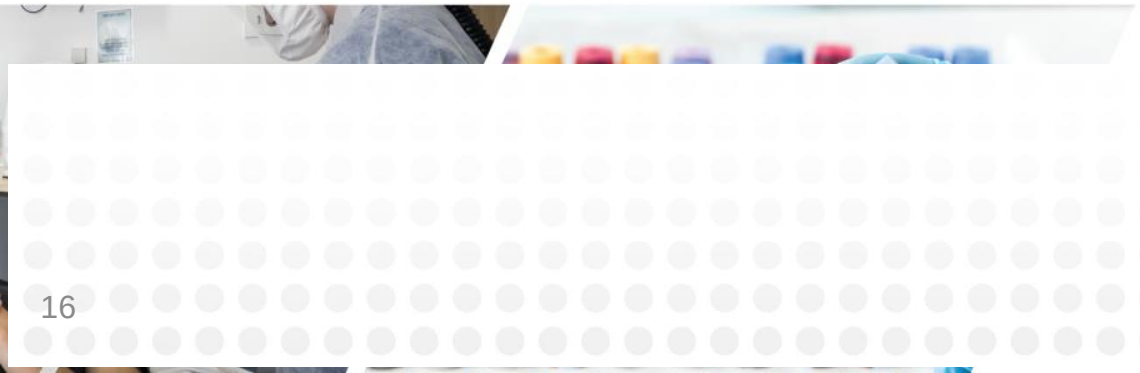
Strategy: To protect individual polypeptides as well as compositions including them. Patents also cover homologies of the peptides and compositions

- 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



II.

FLU-v 003 Phase IIb Results
Real World Study

FLU-v 003 – Phase IIb Real World Study – Design

A randomised, double-blind, placebo-controlled, real world study in 176 volunteers to evaluate safety, immunogenicity and efficacy of different formulations and dosing regimens S/C in collaboration with UNISEC[1]

Aims		
Confirm the safety and tolerability of different regimens and formulations of FLU-v	Determine the immunogenicity response (T&B cells mediated) to FLU-v vaccination	Determine the efficacy of FLU-v in a Real World setting

Vaccination – 4 groups: Day 0 and 21

Two regimes were tested:
Single dose adjuvanted FLU-v (500ug in emulsified adjuvent)

Two doses, given 21 days apart, of un-adjuvanted FLU-v (500ug in aqueous vehicle)

Both regimes had matching placebo

[1]University Space Engineering Consortium

FLU-v 003 – Phase IIb Real World Study – Results

Primary Endpoint Achieved (IFNg Responders)

- Primary endpoint of enhancing T-cell responses was met demonstrating a statistically significant enhancement of the number of responders positive for interferon gamma (IFNg) producing T-cells ($p<0.001$), at both 42 days and 180 days after single vaccination
- IFNg 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)

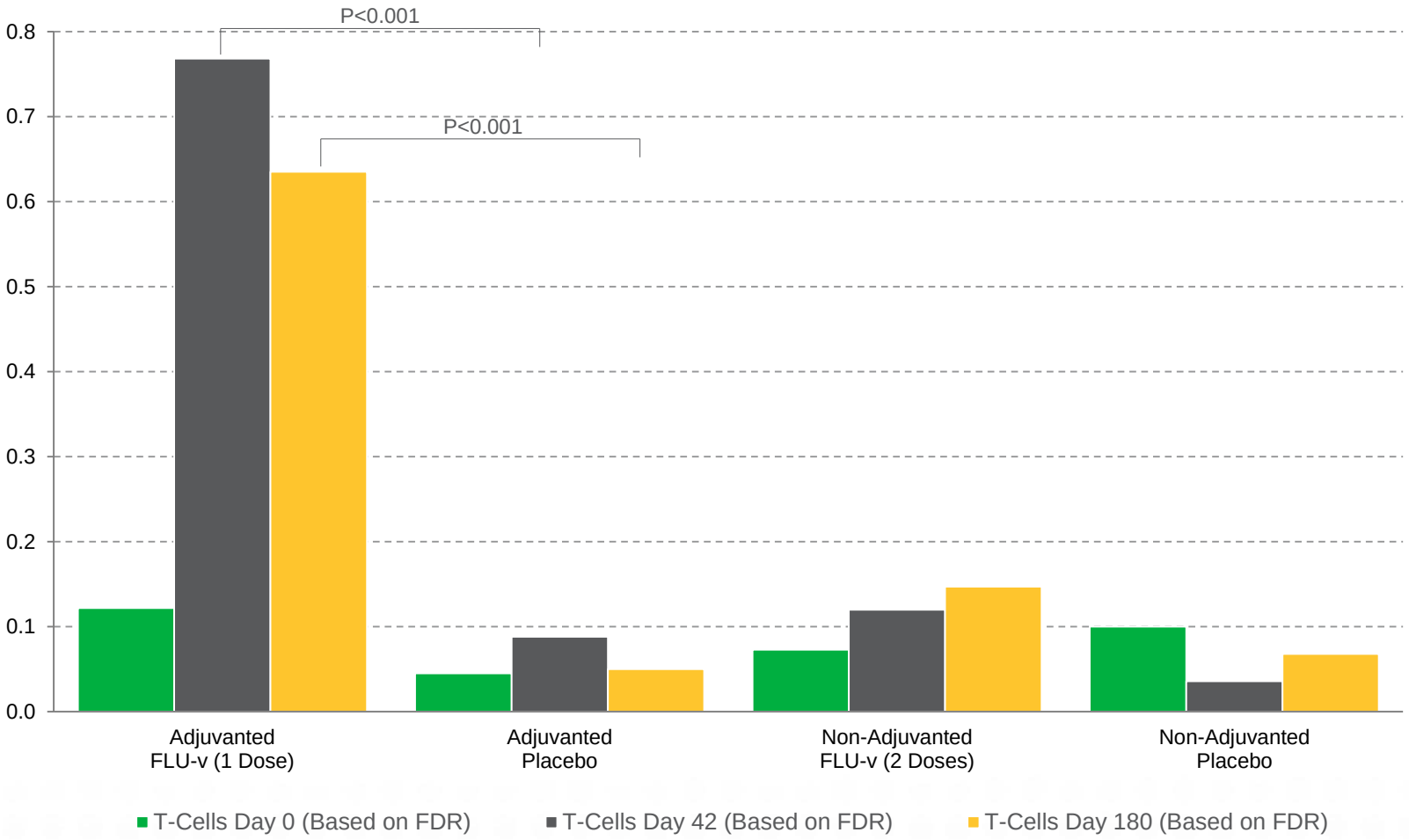
- Secondary immunogenicity related endpoint was to assess the FLU-v specific antibody, immunoglobulin (IgG) responses at both 42 and 180 days after single vaccination compared to placebo
- The secondary endpoint achieved a statistically significant increase in antibody titers of 100% of vaccinated subjects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

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

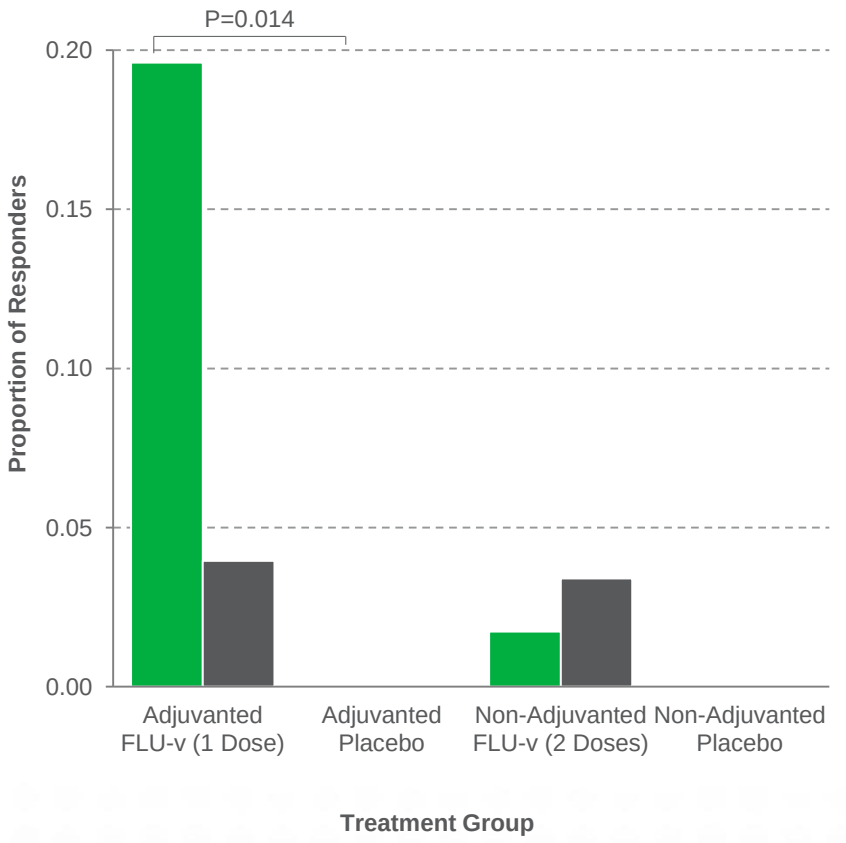


Similar results obtained with TNFa and IL-2 responders

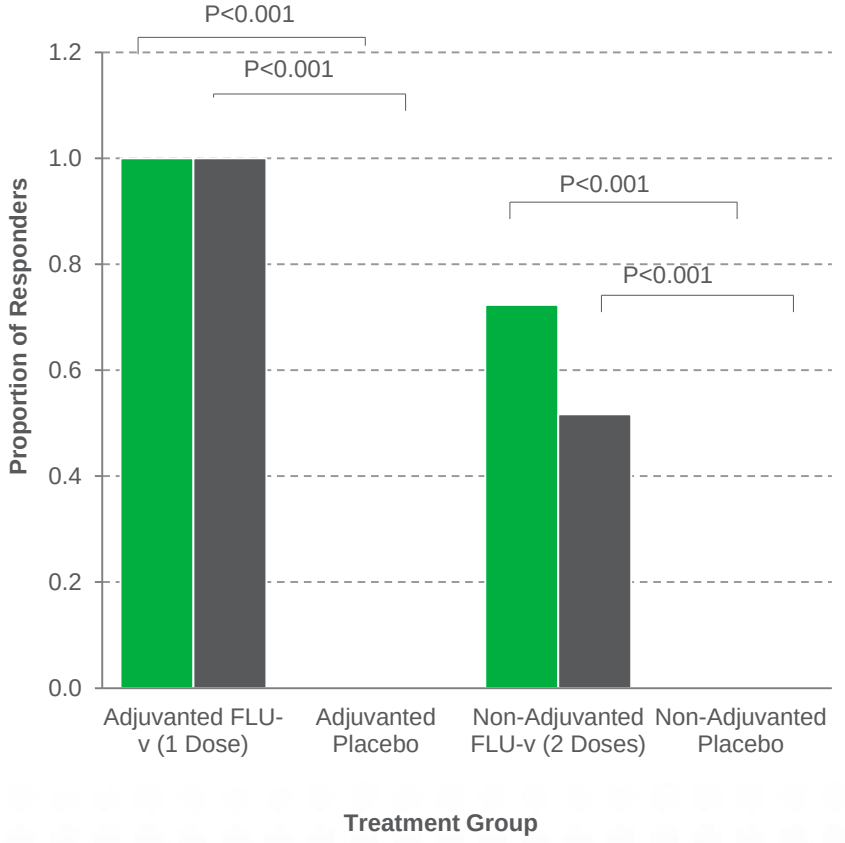
Secondary Endpoint – B-Cell Mediated Immune Response

Significant increase in key B-Cell mediated protective mechanisms

Frequency of IgM Responders



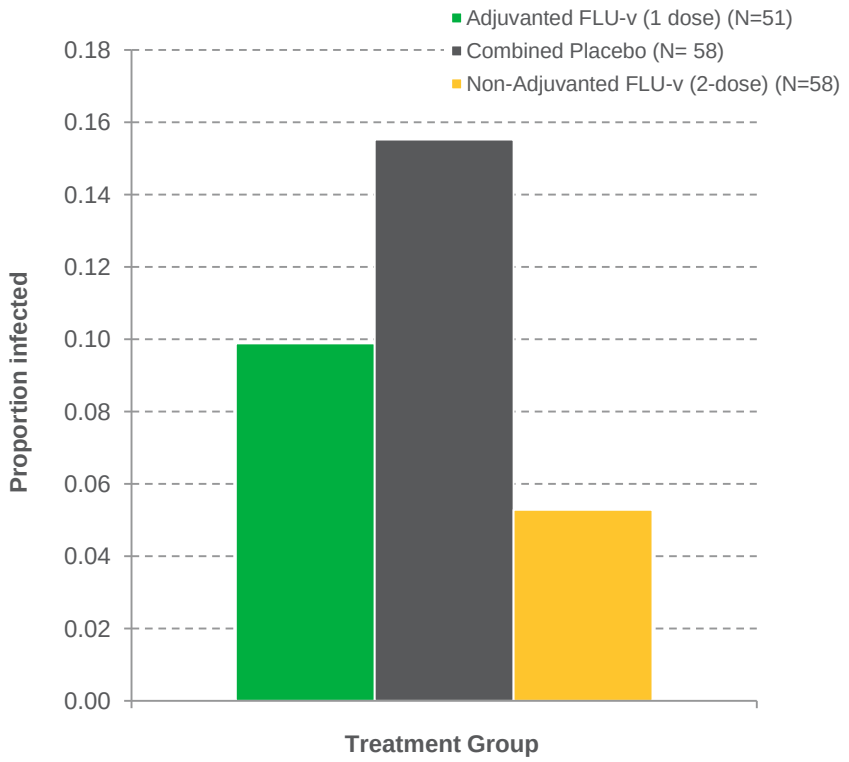
Frequency of IgG Responders



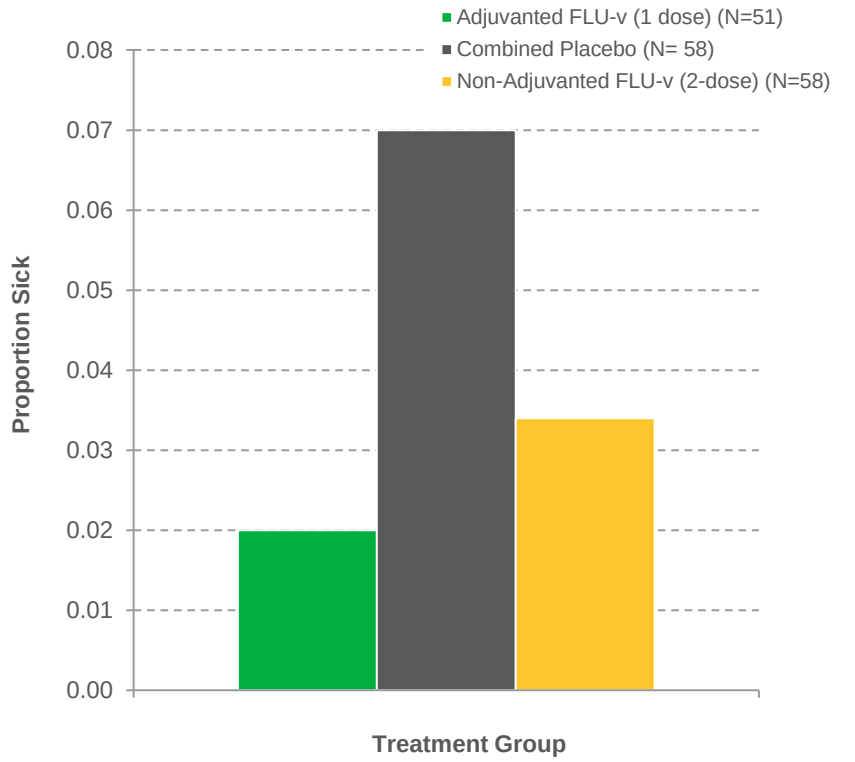
Day 42 Compared to Day 0 ■ Day 180 Comapred to Day 0

Consistent Trend in Reduction of Infections and Influenza Symptoms (Number, Severity & Duration) Following Single Dose of FLU-v

Any Strain – Proportion Sick



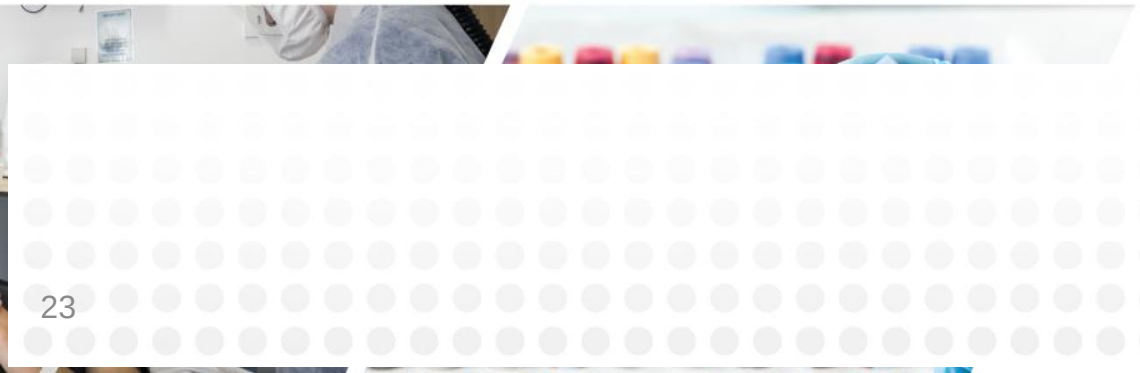
Severe Symptomatology – Proportion Sick



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



III.

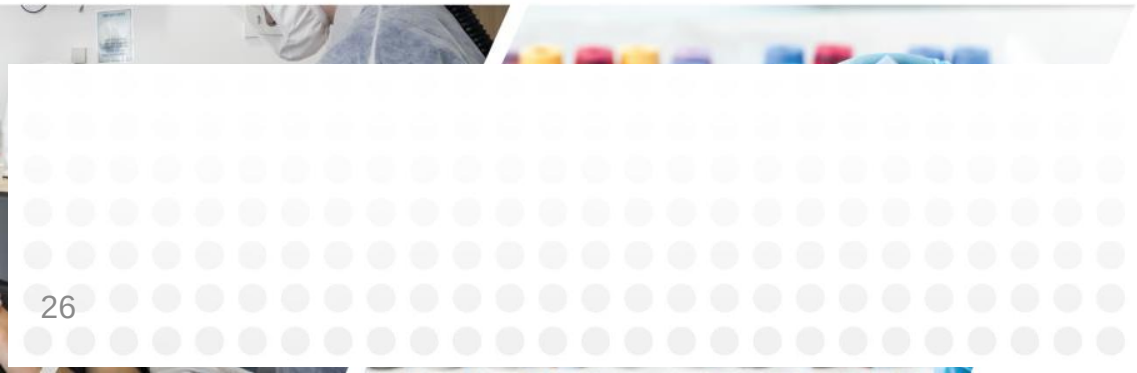
Our Vision for FLU-v

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



IV.

hVIVO Strategy

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