Emerging of the first NOVEL CANADIAN ADJUVANT and its potential in vaccine development and immunotherapy
Outline

- Science
  - Manufacture and Structure of PAL
  - Mechanism of action
  - Products derived from PAL:
    - Adjuvant
    - Immune modulator
    - Vaccine platform
- Tech transfer/ FOLIA
  - Overview last 6 years
  - FOLIA Business Model
  - Agreements/ Licenses
  - Products Portfolio
  - Universal Pandemic Flu Vaccine
- Concluding remark
Manufacture and Structure

Composition (biologic)
- Protein + RNA

Structure
- Crystalline and highly repetitive
  - 15x100nm

Low cost of production
- Production in *E. coli* (BD-792)*
  - Yield >150mg/L

Very stable
- Can be stored > 3 years without loss of activity and integrity

Immune receptors
- PAL is a TLR7/8 agonist
Mechanism of Action

Attractive to immune cells

Alveolar macrophage filled with PAL (white) in the endosome.
Mechanism of Action

- Antiviral response
- Cytokines
- Chemokines

TLR7 or 8

PAL subunits

PAL RNA

Endosome

Immune cell

Nucleus
Product 1: Adjuvant
Increase speed of the response

![Graph showing IgG2a titers over time post-immunization for TIV + PAL, TIV, and Placebo groups. The graph indicates a statistically significant increase in response for the TIV + PAL group compared to TIV and Placebo groups.](image-url)
Product 1: Adjuvant

Induce a broad immune response

![Survival rate percentage over days post-challenge graph]

- Flu + 60 µg PAL
- Flu + 30 µg PAL
- Flu + 15 µg PAL
- Flu + 7.5 µg PAL
- Flu
- 60 µg PAL
- Placebo
Product 1: Adjuvant

Induce long lasting memory response

![Graph showing initial weight percentage over days post-infection with two lines representing TIV and TIV + 30μg PAL.](image-url)
**Product 1: Adjuvant**  
*Phase 1 Clinical trial*

<table>
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<th>Group number</th>
<th>Treatment definition</th>
<th>Number of volunteers</th>
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<td>1</td>
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<tr>
<td>2</td>
<td>Fluviral® 7.5 µg + 30 µg PAL</td>
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</tr>
<tr>
<td>3</td>
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<tr>
<td>4</td>
<td>Fluviral® 7.5 µg + 120 µg PAL</td>
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<td>5</td>
<td>Fluviral® 7.5 µg + 240 µg PAL</td>
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<tr>
<td>6</td>
<td>Fluviral® 3.75 µg + 240 µg PAL</td>
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</table>

No adverse events reported to the product

Data analysis:
- 0 days
- 7 days
- 28 days
- 120 days
- 180 days
- 365 days
- 730 days
- 1095 days
Product 2: Immune modulator

Induce production IFN-α
Product 2: Immune modulator

Trigger innate Immunity

Streptococcus Pneumoniae

Influenza virus
Product 2: Immune modulator

Decrease tumour implantation

Lungs of animals treated with:

A

PBS 6 h

PAL 6 h

B

RLU
Product 2: Immune modulator

Improve anti-PD-1 Immunotherapy
Product 3: vaccine platform

Induce protection to influenza challenge

Engineered PAL with M2e peptide

A) IgG2a titers to M2e

B) Percent survival

- PAL-M2e (10µg)
- PAL-M2e (40µg)
- PAL (40µg)
- Buffer
PAL Characteristics

- Biologic nanoparticle
- TLR7/8 agonist
- Immunogenic
- Rapidly delivered
- Crystalline and repetitive structure
- Safe
- Highly stable
- Low cost

Functions | Key Scientific Findings | Applications
--- | --- | ---
Adjuvant | Improves flu vaccines | Non-infectious and infectious diseases
| Broadens immunogenicity | Phase I completed with flu vaccine
| Increases memory response | 
| Triggers Th1 and Th2 responses | 
| Effective by mucosal and intramuscular routes | 

Vaccine platform | Increases humoral and CTL responses to fused antigens (Ex: M2e from influenza) | Non-infectious and infectious diseases

Immunomodulator | Potentiates cancer treatments (Ex: anti-PD-1) | Infectious diseases
| Prevents tumor implantation | Immune diseases
| Induces non-specific viral and bacterial protection | Immunotherapy
| Stimulates systemic and mucosal innate immunity | Systemic or respiratory diseases
Tech transfer
Overview last 6 years

- Protect the invention-Dev Patent portfolio
- Agreement with University
- Founded in 2006 and first financing in 2008 (28 angels)
- STEPS:
  - **Dev. manufacture process***
  - Transfer process Therapure
  - cGMP manufacturing of clinical lot (12L) Therapure Mississauga, On
- Phase 1 clinical trial (first in human/NOVEL ADJUVANT)
  - Get permission from HEALTH CANADA
  - PREVENT- Halifax (Johan Langley)
Corporate

- Maximum investments directed to product development
  - Virtual & outsourcing
- Focused on project management rather than company building

Product Development Program: focused, efficient & risk sharing

Internal Program
- Focused on universal pandemic influenza vaccine
- Bring through Phase 2 (human proof of concept)
- Partner for Phase 3+ activities

External Program
- Scope PAL product opportunities
- In collaborative partnerships
  - Folia provides PAL & know-how
  - Partner provides model and assay systems & know-how
Laval University (Intellectual Property)
- Folia has exclusive worldwide ownership of all IP (present & future) covered under broad “IP umbrella” agreement;

PREVENT (vaccine development partner)
- certain commercialization rights, royalties and other revenue sharing terms
### Tech transfer

**FOLIA product portfolio**

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>R&amp;D</th>
<th>Preclinical</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
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<tr>
<td><strong>In-house vaccine</strong></td>
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<td>Universal pandemic influenza</td>
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<td><strong>Collaborations</strong></td>
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<td>Seasonal influenza (PAL – TIV)</td>
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<td>Chlamydia</td>
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<td>Cancer</td>
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<td>Conjunctivitis</td>
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2009 H1N1 exemplified unpredictability & rapidity of new influenza strain & impact on world population
- Raised the urgent need for preparedness & more efficient pandemic vaccines

H5N1 & H7N9: present & evolving threat of next pandemic – high mortality, morbidity & health costs

Estimates of a deadly pandemic flu: 175-350 million deaths worldwide
- Russian flu (1989-90): 1 million (H2N2?)
- Spanish flu (1918-20): 50 million (H1N1)
- Asian flu (1957-58): 2 million (H2N2)
- Hong Kong flu (1968-69): 1.5 million (H3N2)
- Swine flu (2009-10): 20,000 (‘new’ H1N1)

According to WHO:
Will there ever be a new influenza pandemic? ——‘YES’ (WHEN unknown?)
Are we prepared? ---‘NO’
Tech transfer
Universal Pandemic Vaccine

ELISA

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<tr>
<td>IgG2a titers</td>
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ELISPOT

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<th>30 µg N-NLP</th>
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<tr>
<td>Nb spots/500x10^3 cells</td>
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*** *** *
Universal Pandemic Influenza Vaccine

- Broader & longer protection: Folia’s PAL adjuvanted vaccine
- Rapid deployment in pandemic infections
- Prevention/mitigation of a pandemic
- Rapid containment of infection spread in pandemic outbreak geographical foci
- Rapid & cost effective manufacturing: Folia’s fermentation process & long term (>3 yrs.) stability-

Pandemic influenza infection health countermeasures: stockpiling
CONCLUDING REMARK

• What do you need for an efficient and successful Tech Transfer?
  • Chose the right project
    - Unmet medical need
    - Platform with potential for several products and partnership
  • Chose the right people
    Pierre Savard  Jacques Bernier  Louis Lamontagne
    (Manufacture)  (CEO 2008-2014)  (CEO)

• Control your Manufacture
• Have the faith—Never let anybody take you down—Follow your gut feeling