Virus-Like Particle (VLP) Based Pandemic Flu Vaccine Candidate

Rahul Singhvi, ScD
President & CEO
March 21, 2006
Safe Harbor

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Agenda

- Novavax Overview
- Pandemic Influenza Challenges
- Novavax Solution
  - Antigen: Virus-Like Particles (VLPs)
  - Adjuvant: Novasomes
  - Portable Manufacturing Scalability
- H9N2 VLP Vaccine Pre-clinical Data
Novavax: A Unique Capability Blend

- Formulation Science
- Products
- Drug Development & Manufacturing Infrastructure
- Adjuvants
- Vaccine Technologies
- Flu Vaccine
Pandemic Flu Vaccine: Challenges

Emerging Strain
- Strain Match
- Lead time

Immunogenicity
- Dose, schedule
- Adjuvants

Surge Capacity
- Limited capacity
- Cost
Pandemic Flu Vaccine: Solutions

- rDNA
- VLP, Adjuvants
- Redefine Surge Capacity
Recombinant Virus-Like Particle (VLP) Vaccine

- Exact genetic match
- Right 3D configuration of HA protein
- Efficient insect cell-based production
- Allows surge capacity
VLP Vaccine Reduces Lead Time

A/Hong Kong/1073/99 (H9N2) HA, NA, and M1 baculovirus vector

10^6 pfu influenza virus
CDC/WHO

rtPCR cloning
HA, NA, and M1 genes

Master and Working Seed stocks

Day 1 rtPCR
Day 3 Cloned
Day 7 Bacmids
Day 21 rBaculovirus
Day 30 Master stock
Day 40 Working stock
Day 45 Seed stock

Wave Bioreactors
500 L working

HA/NA/M1 VLPs Secreted

100K+ Doses per Bag

Days 47 cGMP Manufacturing
Days 52 Purification
Day 60 Formulation/Filling

Bulk VLPs
Pandemic Flu Vaccine: Solutions

- rDNA
- ✓ VLPs, Adjuvants
- Redefine Surge Capacity
VLPs Mimic Whole Influenza Virus

Influenza Virus

Purified VLPs

HA

NA

M1

100 nm
Novasomes®: A Proprietary Adjuvant

For use with vaccines for the prevention of infectious diseases

[USPTO # 6,387,373 B1, Date of issue: May 14, 2002]

Novasome  +  Influenza virus  =  “Virusome”
Pandemic Flu Vaccine: Solutions

- rDNA
- VLPs, Adjuvants
- ✓ Redefine Surge Capacity
Traditional Cell Culture Limitations

- Stainless-steel tanks
- Difficult to clean, sterilize, operate
- $ 300 – 500 MM/facility
- Difficult to expand
- No surge capacity
- 18 – 24 months to commission
Disposable Cell Culture

- Inflated plastic bag
- Disposable cultivation chamber
- Wave action
  - Large turbulent surface
  - Good oxygen transfer
  - Prevents cell settling
Proven Scale-Up to 500 Liters

- Ideal for insect cell/VLP vaccine process
- Completely closed system
- No biosafety/containment issues
- High productivity/yield
- Easy cultivation process
- Low cost medium

Wave Bioreactor System 500/1000

*Potential Influenza vaccine output per 500L batch = 0.1 – 1 MM eggs*
Minimal Infrastructure, Low Cost

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<thead>
<tr>
<th></th>
<th>Disposable</th>
<th>Tank-based</th>
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<tbody>
<tr>
<td>Construction time</td>
<td>5 months</td>
<td>12-16 months</td>
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<td>Cost</td>
<td>$ 1 million</td>
<td>$ 3-5 million</td>
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GMP cell culture capability to 500L
PacificGMP, San Diego CA
Pandemic Flu Vaccine: Solutions

- rDNA
  - Reduced Lead Time
  - Exact Strain Match

- VLP, Adjuvants
  - Single dose
  - Novasome

- Portable Mfg
  - Large capacity
  - Low cost
H9N2 Vaccine: Pre-clinical Data
H9N2 VLP Vaccine Protective Efficacy

- Protective Efficacy (A/Hong Kong/1073/1999)
  - BALB/c mice
  - Intramuscular inoculation
  - 1 dose VLP (1 ug HA) or 10 ug soluble rHA
  - 2 inoculations (Week 0 and 4)
  - Bleed Weeks (0, 3, 5)
    - HAI vs. A/HK/1073/99 (H9N2)
  - Viral Challenge (100 MID\textsubscript{50} (10^{5.5} EID\textsubscript{50}) i.n.)
    - Weight Loss
    - Viral titers in lungs
Influenza Antibody Response

![Graph showing mean ELISA titer + S.D. (log_{10}) for No Vaccine, VLP, and VLP+Novasome groups.](image)
H9N2 Hemagglutination Inhibition Assay

Serum HAI Antibody titer (log$_2$)

- 10 µg HA subunit (soluble protein)
- 10 µg HA subunit + Novasomes
- 1 µg HA in VLPs + Novasomes
- 1 µg HA in VLPs

Protective
Weight Loss after Viral Challenge

- No vaccine
- H9 VLP
- H9 VLP + Novasome

Days post infection:
- 0
- 2
- 4
- 6
- 8
- 10
- 12

% weight loss:
- 0
- 2
- 4
- 6
- 8
- 10
- 12
- 14
- 16
- 18
- 20
Lung Virus Titers after Viral Challenge

Mean virus titer EID50/ml (log_{10})

- **Lung - Day3**
  - Control: ~6.5
  - VLP Vaccine: ~5.0
  - VLP Vaccine + Novasomes: ~4.0

- **Lung - Day5**
  - Control: ~4.5
  - VLP Vaccine: ~3.0
  - VLP Vaccine + Novasomes: ~2.0
H9N2 VLP Vaccine Immunogenicity

- Immunogenicity Dose-Response (A/Hong Kong/1073/1999)
  - SD rats 6/group
  - Intramuscular inoculation
  - 4 doses (0.12, 0.6, 3.0, and 15.0 ug)
  - 2 doses (0.12/0.6 ug + 100 ug Novasome or Alum)
  - 2 inoculations Weeks 0 and 3
  - Bleed Weeks 0, 3, 5, 7
    - HAI vs. A/HK 1073/99 (H9N2)
H9N2 VLP Only Hemagglutination Inhibition

![Bar graph showing HAI titer (GMT Log2) for different VLP doses and bleed times.](image)

- **Protective** level indicated by the dashed red line.

**VLP Dose**:
- PBS
- 0.12 ug
- 0.6 ug
- 3.0 ug
- 15.0 ug

**Bleeding Schedule**:
- Pre-Bleed
- Week 3
- Week 5
H9N2 VLP +/- Adjuvant (HAI)

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<thead>
<tr>
<th>VLP Dose</th>
<th>Pre-bleed</th>
<th>Week 3</th>
<th>Week 5</th>
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Novavax Resources

- **Right People**
  - Blend of Management & Science

- **Right Partners**
  - Wave Biotech
  - Bharat Biotech
  - PacificGMP
  - University of Pittsburgh
  - Others

- **Strong Investors**
  - Kleiner Perkins Caufield & Byers
  - Prospect Ventures

- Financial stability - $50MM cash (current)
Management Team

Rahul Singhvi, ScD President & CEO
10 years with Merck & Co.

Rick A. Bright, PhD, VP Vaccine Research
10 years experience in human and avian influenza viruses, vaccine development, and antiviral drug resistance at the CDC Influenza Branch

Gale Smith, PhD, VP Vaccine Development
Inventor Baculovirus system insect cells, CSO Protein Sciences

Steve Bandak, MD VP Medical Affairs
26 years at Lilly in Clinical Research

D. Craig Wright, MD Chief Scientific Officer
Co-founder of Novavax, prolific inventor, infectious disease expert

Robert Lee, PhD, VP Pharmaceutical Development
Co-founder Nanosystems, VP at Lyotropics, Imcor

Ray Hage, SVP & COO
Various Sales & Marketing positions at Lilly & Cephalon

Dennis Genge, VP & CFO
Various Acct & Finance positions at Ligand, Picxus
Participate in the Novavax Opportunity!

- Adjuvants
- Formulation Science
- Vaccine Technologies
- Drug Development & Manufacturing Infrastructure
- Flu Vaccines
- Products