VLP based technology for Vaccines

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What are VLPs?

- Is a recombinant-expressed viral proteins that spontaneously assemble into 3-D structures similar to parent virus
  - By electron microscopy, VLPs mimic the parent virus
  - Immune response is similar to that which would be seen if exposed to the parent virus

☑ Not contain any genetic material
☑ Can not replicate

**influenza VLP:**
- Epitope I = Hemagglutinin (HA)
- Epitope II = Neuraminidase (NA)
Partnership in VLP technology platform

- Partnership with Novavax for developing VLP based technology for vaccines
- Novavax successfully cloned several genes for different vaccine in baculo-virus and expressed the protein in Insect cell line
- Proof of concept has been established in animal model and some vaccine tested in human
- Manufacturing process, analytical characterization and stability of product has been demonstrated
Development of Recombinant Influenza VLP Vaccines

• Select proteins important for inducing protective immunity
  – Surface hemagglutinin (HA)
  – Neuraminidase (NA)
  – Matrix (M1)

Genes coding for the HA, NA, and M proteins are put into baculovirus

Infect cell culture (Sf9) with baculovirus

Recombinant proteins (HA, NA, M1) form VLPs
VLP Technology: Salient Features

- No Live pathogenic virus, Baculo Virus expression system
- Exact genetic match to circulating virus (HA, NA, M1)
- Faster Delivery- cloning & development to release (10 to 12 weeks)
- Easy to scale-up and manufacture in large quantity
- Disposable manufacturing Solutions.

<table>
<thead>
<tr>
<th>Task Name</th>
<th>Start</th>
<th>Finish</th>
<th>Apr 2009</th>
<th>May 2009</th>
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<tr>
<td>H1N1 Vaccine Starts</td>
<td>4/24/09</td>
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<td>Viral genes A/CA/04/09 received</td>
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<td>A/CA/04/09 genes cloned</td>
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<td>5/4/09</td>
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<td>Recombinant baclovirus generated</td>
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<td>5/10/09</td>
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<td>VLP Production for preclinical study</td>
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<td>5/14/09</td>
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H1N1 Virus RNA from CDC

H1N1 VLPs

HA Reagent
Influenza Vaccine (Traditional vs. VLP)

Faster Delivery of First Dose of Pandemic Vaccine

- **Recombinant VLP**
  - Virus/sequence available: 4 wks, 8 wks, 12 wks, 16 wks, 20 wks, 24 wks, 28 wks
  - First doses released in week 10 - 12

- **Traditional**
  - RG, Pathogenicity, Mfg, Reagents

Cloning & Seed Prep, Mfg & Fill 1st Lot, Release & Ship, Form/Fill, Release & Ship
Influenza vaccine - Joint Venture March 2009

- Influenza VLP Process Technology Transfer Initiated (May, 2009)
- Facility Design Initiated (June, 2009)
- Facility Ground Broken (November, 2009)
- Facility Expected Completion (May, 2010)
- Process, Analytical Transfer Ongoing in Parallel
- Facility Commissioning and Validation (July, 2010)

Implementation of a new functional modular facility ready within 1 year
Recombinant product-Process Flow Diagram

- Pre-seed
- Seed
- Production Fermentation
- Harvest/ Microfiltration/ Centrifugation
- Purification by chromatography
- Filtration of purified product

Basic Infrastructure will remain same.

Only process will change as per the product.

- Working cell bank
- Market
- Filling
- Formulation
- Final Bulk
Overview of Manufacturing Process for Recombinant Influenza VLP Vaccines

- Master Virus Seed
- P1
- P2
- 100L Wave bioreactor
- Ultrafiltration/Diafiltration
- IEX
- SEC
- 0.2 µ filter
- Filling
- Harvest
- TFF Filtration
- Inactivation BPL
Partnership in VLP technology platform

- Cadila/Novavax is open for joint venture/partnership in India and abroad for VLP based technology/product with different options-
  - Technology transfer
  - Joint development
  - Contract manufacturing
  - Product supply for CT and commercial
THANK YOU