

Safety and Immunogenicity of the Seasonal Influenza Virus-Like Particle (Trivalent) Vaccine in Healthy Adults:

Results of a Phase IIa Study



Agenda

- Design of Phase IIa Clinical Trial
- Safety Results
- Immunogenicity Results
- Conclusions and Implications



Clinical Goals of the Seasonal Influenza VLP (Trivalent) Vaccine Program

- Develop a safe and effective vaccine against the influenza sub-types responsible for yearly epidemics (H3N2, H1N1, B)
- Develop a vaccine that induces a broad immune response
 - Improved efficacy in older adults ≥ 65 years over existing vaccines
 - Cross-reactivity against drifted strains
- Develop a vaccine that is matched to the strain circulating in humans
 - Vaccines made in eggs (i.e., adapted to grow in eggs) have genetic differences from strains isolated from humans
 - Recombinant technology permits exact match



Overview of a Phase IIa Clinical Trial of the Seasonal Influenza VLP Vaccine

Objectives

- To evaluate the safety and immunogenicity of the seasonal influenza VLP vaccine

	Influenza VLP Vaccination Groups			
	mcg HA/strain/dose			
	5	15	30	0 (placebo)
n subjects/ group	50	100	100	50

Study Design

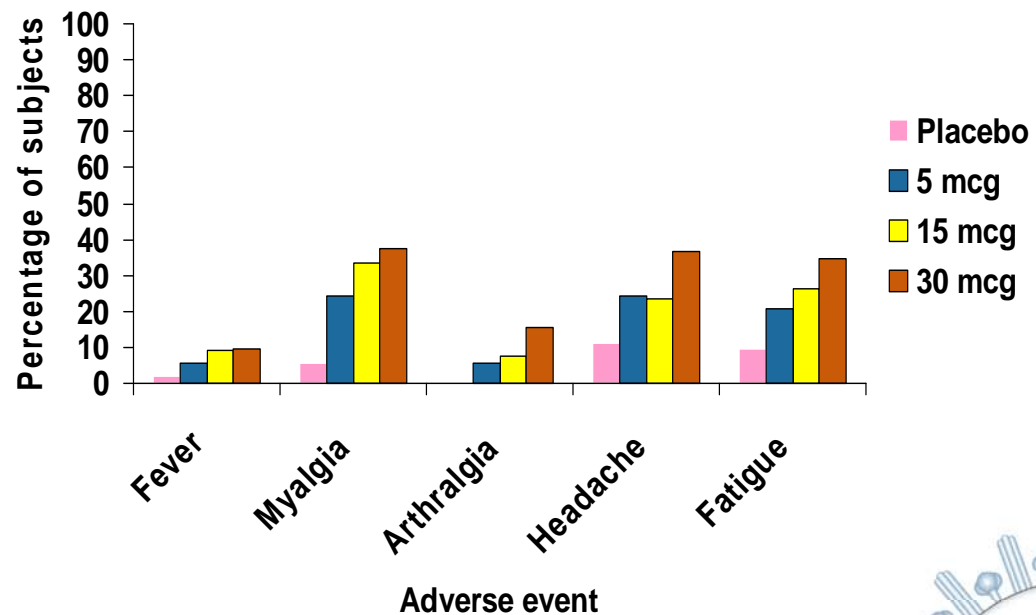
- Sample: 300 healthy adult subjects, 18 to 49 years of age
- Safety evaluation following vaccination:
 - All adverse events (AEs) through Day 22
 - Serious AEs through 6 months
- Immunogenicity evaluation:
 - HAI titers against vaccine and drifted strains
 - Additional assays to evaluate antibody and cell mediated immune responses to other vaccine components will also be evaluated



Safety of the Influenza VLP Vaccine

- The types of non-serious adverse events reported are similar to what has been observed with other influenza vaccines
- No serious adverse events (AEs) have been reported to date

Solicited Systemic AEs Within 7 Days of Vaccination



HAI Responses Against Vaccine Strains

	<u>Vaccination Group</u>	
	<u>15 mcg</u>	<u>30 mcg</u>
H3N2 (A/New York)		
- % Seroprotection*	95	97
- % Seroconversion**	100	90
- GMT*	210	324
H1N1 (A/New Cal.)		
- % Seroprotection*	83	94
- % Seroconversion**	69	78
- GMT*	132	208
B Jiangsu		
- % Seroprotection*	73	79
- % Seroconversion**	42	56
- GMT*	58	63

*All subjects

**Subjects with negative antibody titers at baseline



HAI Responses Against Drifted Strains

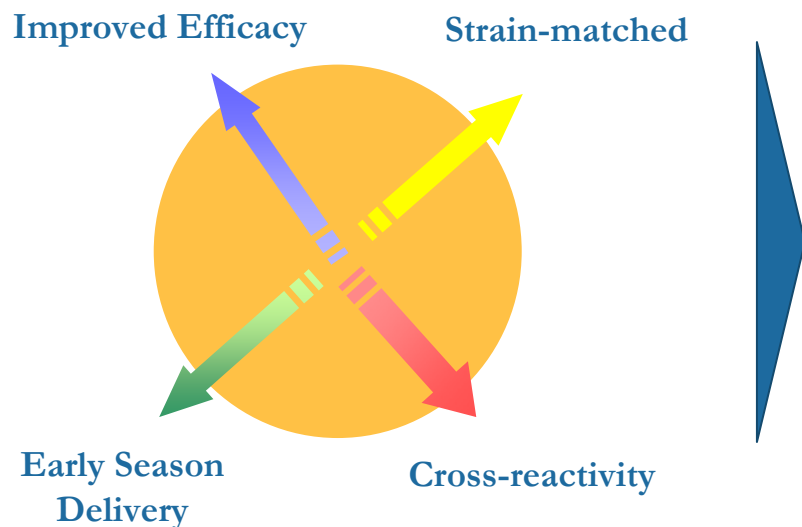
	<u>Vaccination Group</u>	
	<u>15 mcg</u>	<u>30 mcg</u>
H3N2 (A/Wisconsin)		
- % Seroprotection*	96	97
- % Seroconversion**	100	92
- GMT*	279	436
H1N1 (A/Solomon Is.)		
- % Seroprotection*	78	92
- % Seroconversion**	36	67
- GMT*	126	197
B Malaysia		
- % Seroprotection*	38	58
- % Seroconversion**	7	18
- GMT	23	35

*All subjects

**Subjects with negative antibody titers at baseline



Progress on the Goals for the Seasonal Influenza VLP (Trivalent) Vaccine Program



- Clinical data from seasonal study suggest higher doses lead to higher HAI titers
- Clinical data from the pandemic study suggest that VLPs activate CD8+ /CTLs
- Preclinical seasonal studies show VLPs induce anti-NA and NAI activity
- Clinical and preclinical data from seasonal studies show cross-reactivity against drifted strains
- Cloning process for seasonal strains has been optimized; VLPs for 3 new strains for 2008-9 vaccine made in 6 weeks



Development Plans for 2009

The data from this study support moving forward with continued development of the seasonal influenza VLP vaccine

- Conduct studies in healthy adults to finalize dose and continue evaluating safety and immunogenicity in this population
- Conduct dose ranging studies in elderly adults (≥ 65 years old) including comparison with a currently licensed influenza vaccine
- Continue to optimize manufacturing process to ensure consistency, high purity and yields

