

## VaxInnate's Influenza Vaccine Program

VaxInnate is developing novel, proprietary vaccines for seasonal and pandemic influenza using a technology platform that substantially improves the potency, manufacturing capacity, and cost efficiency of the vaccines.

This technology physically links a natural component of microbes known as flagellin to vaccine antigens, helping the human immune system to recognize the vaccine as foreign and respond with a strong, protective immune response. This boost in the immune response could overcome the poor potency of seasonal and pandemic influenza vaccines in individuals with less-than-robust immune responses, among them the elderly, children, and the immunocompromised.

The physical linkage of flagellin to vaccine antigens enables VaxInnate to use efficient, low-cost recombinant protein methodologies. The recombinant expression of VaxInnate's vaccines alleviates the manufacturing constraints that have long restricted influenza vaccine availability, making it possible to produce sufficient seasonal and pandemic influenza vaccine to meet national and even global needs.

VaxInnate's influenza vaccines use two influenza components, the hemagglutinin and M2 proteins. Hemagglutinin (HA) is well characterized and has been the key component in influenza vaccines for 50 years. HA, however, has some significant limitations.

For one thing, it changes each year as the virus evolves to evade previous immune responses against it. These annual changes in HA can require manufacturers to change some or even all of the HA antigens used in the annual vaccine formulation. Furthermore, the production of HA is dependent upon egg-based manufacturing, which has limited capacity. Finally, production relies upon development of new viral vaccine seed strains that express the target HA and are capable of growing in eggs, a process that can take months to complete.

Recent efforts to improve influenza vaccine production have focused on the production of influenza vaccine in cell culture. While this approach alleviates the need for eggs, it has its own manufacturing limitations. The focus on cell culture production stems from the historical view that protective forms of HA antigens must be manufactured using cells from animals such as humans and chickens.

However, VaxInnate has developed the proprietary insights and methods needed to produce protective forms of HA in bacterial expression systems. Our evaluations indicate that a supply of HA-based vaccines sufficient to meet national needs and even global needs, including those for H5 avian influenza, can be produced in several months without the need for major investments in manufacturing infrastructure.

To address the ever-changing nature of HA-based vaccines, one of VaxInnate's vaccine candidates uses the stable antigen, M2 ectodomain (M2e). M2e is a 24 amino-acid peptide that

protrudes from the surface of the influenza virus. Importantly, M2e remains unchanged across influenza strains and has mutated little in the last century.

Although the M2 antigen by itself is poorly immunogenic, VaxInnate's technology platform stimulates the immune system to take specific notice of it, resulting in a rapid and robust immune response that far exceeds what is possible using standard vaccine methods. Since the M2-based vaccine does not require the advance identification of specific influenza strains, it may be appropriate for vaccine stockpiling and prophylactic vaccination of populations.

VaxInnate's preclinical studies of M2e, including both active immunization and passive immunoprophylaxis, show reduced severity and duration of illness in animal models. Furthermore, our initial animal studies of M2e demonstrate survival in the face of lethal challenge.

### **Clinical Development Underway**

VaxInnate's M2e vaccine candidate has completed its first Phase I trial, with promising results accepted for presentation at a major scientific conference in 3Q 2008. VaxInnate has also validated its manufacturing processes.

Results of another Phase I study of the M2e vaccine candidate, this one comparing intramuscular, intradermal and subcutaneous routes of vaccine administration, will also become available in 2Q.

Two efficacy studies are also planned for the M2e vaccine candidate, one involving several hundred volunteers to begin in late 2008 and second with several thousand volunteers to get underway in 2009. These studies are expected to demonstrate reduced severity and duration of illness in humans following vaccination, results that have already been shown in animal models.

VaxInnate's HA-based vaccines will also enter clinical development in 3Q 2008, with initial results expected to become available late this year.

During this same time period, we expect to complete preclinical assessments, including highly predictive animal models with challenge studies and serological data, for the entire set of hemagglutinin types (H1, H3, and B) required to produce seasonal influenza vaccine. In parallel, we are continuing to develop a prototype pandemic influenza vaccine candidate using the H5 clade of virus.