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**New studies indicate GSK's pre-pandemic influenza vaccine can protect against different strains of H5N1**

**Philadelphia, PA, London, UK, Rixensart, Belgium, March 5, 2007** – GlaxoSmithKline (NYSE: GSK) announces clinical trial data from two new studies, which show, for the first time, that GSK's candidate pre-pandemic split antigen H5N1 vaccine, formulated with GSK's proprietary adjuvant system, provides a substantial level of cross-immunity against a 'drifted' (diverse) strain of H5N1. It is hoped that the immune response elicited with this vaccine, could help prepare or 'prime' the immune system to rapidly respond against variants of the H5N1 strain and therefore protect the vaccinated population in the event of an H5N1 human pandemic.

In the first study presented at the *IX International Symposium on Respiratory Viral Infections (ISRVI)*, data demonstrated GSK's proprietary adjuvanted candidate pre-pandemic vaccine, containing very low levels of the Vietnam H5N1 antigen (3.8µg), elicits a strong cross-immune neutralizing antibody response in humans against the Indonesian strain of the virus. The neutralizing antibody seroconversion factor at Day 42 was shown to be 25 times greater when the vaccine contained the adjuvant system compared with that observed in the control group immunized with a non-adjuvanted vaccine (77.1% vs. < 3%).

GSK's proprietary adjuvant system also displays powerful antigen-sparing properties as the strong neutralizing response in this study was obtained with only two doses of 3.8µg HA antigen administered 3 weeks apart. This could mean, in effect, that by adding GSK's proprietary adjuvant system, vaccine manufacturing capacity could be increased more than tenfold. The vaccine was shown to have an acceptable safety profile when compared to the control group. As expected, reactogenicity (injection site tenderness) was slightly higher in the vaccine group due to the use of the adjuvant system.

In a second study presented at ISRVI, the data showed that GSK's proprietary adjuvanted pre-pandemic vaccine could protect against two diverse H5N1 flu strains, again at very low levels of antigen. The *in vivo* data from the pre-clinical studies demonstrated that GSK's adjuvanted vaccine, containing the Vietnam H5N1 strain, was not only able to protect against challenge with the vaccine virus strain, but also provides 96% (22/23) cross-protection against a lethal challenge with the drifted Indonesia strain of H5N1, giving an additional boost to hopes that pre-pandemic vaccination is a viable strategy for inclusion in pandemic preparedness plans.

**Jean Stéphenne, President, GlaxoSmithKline Biologicals**, the vaccine division of GSK, commented, "I am extremely encouraged by the new trial data that has been reported today on GSK's candidate pre-pandemic influenza vaccine. The data confirm that our pre-pandemic influenza vaccine has the ability to recognize and kill an H5N1 strain that is different to the one contained in the vaccine. This means that proactive administration of our pre-pandemic vaccine before or just after the start of the pandemic could help to substantially slow down the spread of disease."

Pandemic influenza poses a serious global public health threat with substantial estimated morbidity and mortality. The exact strain that may cause an influenza pandemic cannot be accurately predicted. Many experts, however, believe that the avian H5N1 strain, now endemic in many bird species across the world, is the most likely candidate pandemic strain.

"We believe this vaccine will provide governments with a new option to help protect their populations against the threat of a future human influenza pandemic," commented **David Stout, President, GSK Pharmaceuticals**.

## **Trial Study Designs**

### **First Study**

#### ***Cross-reactive immunity with an adjuvanted H5N1 candidate vaccine***

This pivotal observer-blind, randomized study was conducted in 400 adults (18 to 60 years) to evaluate the reactogenicity and the immune response of GSK's pre-pandemic candidate vaccine administered at four antigen concentrations (3.8µg, 7.5µg, 15µg or 30µg HA of H5N1 clade 1\* A/**Vietnam**/1194/04 split virion) either non-adjuvanted, or in combination with GSK's novel proprietary adjuvant system, against the drifted clade 2 A/**Indonesia**/5/05 strain. Two doses were administered 21 days apart and blood samples collected on Days 0, 21 and 42. The conventional 4-fold increase in neutralizing titers, before and after vaccination, was used to assess seroconversion.

\* A clade is the name given to groups of viral variants that are closely related from an evolutionary standpoint

### **Second Study**

#### ***Protection against challenge with a variant H5N1 strain in an animal model with a low dose adjuvanted split H5N1 vaccine***

Four animal test groups (N=23) were immunized intramuscularly with 15, 7.5, 3.8 or 1.7µg of H5N1/A/Vietnam/1194/04 (clade 1; NIBRG-14) vaccine containing a novel proprietary adjuvant system. The 2 control groups were immunized with either the adjuvant alone or the non-adjuvanted H5N1/A/Vietnam/1194/04 vaccine (15 µg). Animals were vaccinated on days 0 and 21 and challenged on day 49 with 105 TCID<sub>50</sub> (50% Tissue Culture Infective Dose\*) of H5N1/ A/ **Indonesia**/5/05 (clade 2).

\* The quantity of a cytopathogenic agent, i.e. such as a virus, that will produce degenerative changes (or a diseased condition) in 50% of the cell cultures inoculated.

#### About GlaxoSmithKline

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#### About GSK Biologicals

GSK Biologicals, based in Rixensart, Belgium, is the vaccine division of GlaxoSmithKline. As one of the world's leading vaccine manufacturers, GSK Biologicals employs more than 1,500 scientists devoted to discovering new vaccines and developing more cost-effective and convenient combination products to prevent infections that cause serious medical problems.

#### Editor's Note

##### **GSK's 2005-2007 Milestones in Pandemic Preparedness**

- 2005: GSK made three important acquisitions in North America: a vaccine manufacturing site in Marietta for cell-culture-based flu vaccines and secondary operations; Corixa Corporation, for its work in developing innovative adjuvants designed to stimulate immunity; and ID Biomedical, which offered a significant increase in flu vaccine manufacturing capacity to help address both seasonal and pandemic influenza threats.
- May 2006: GSK received an HHS contract worth \$274 million to develop cell-culture technology to speed the development of new cell culture-based seasonal and pandemic influenza vaccines, and to scale-up cell culture manufacturing capability at GSK's Marietta, PA site.
- July 2006: Clinical studies announced by GSK showed promising preliminary results on the potential antigen-sparing properties of its candidate pre-pandemic influenza vaccine.
- September 2006: GSK reached an agreement with the Simcere Pharmaceutical Group of Nanjing, China, granting the right to manufacture and sell the anti-viral influenza treatment zanamivir in China, Indonesia, Thailand, Vietnam and all Least Developed Countries.
- October 18, 2006: GSK signs contracts with Switzerland to supply its split pre-pandemic antigen and proprietary adjuvant for stockpiling, in addition to an Advanced Purchase Agreement (APA) for its pandemic vaccine in the event a pandemic is declared.

- November 2006: GSK received a \$40 million initial order for bulk H5N1 antigen from HHS.
- December 15, 2006: GSK announces that *Daronrix™* its alum-adjuvanted whole virus candidate pandemic vaccine; received a positive opinion from the Committee for Medicinal Products for Human Use.
- January 2007: GSK receives from the HHS a \$63.3 million contract to develop antigen-sparing H5N1 pandemic influenza vaccines.
- January 2007: GSK begins supplying its antiviral, *Relenza®* (zanamivir for inhalation), to the U.S. government and begins working with private-sector businesses and other organizations to provide *Relenza®* as part of their business continuity planning.
- January 4, 2007: GSK entered into an APA with the Danish government to supply its split candidate pandemic antigen and proprietary adjuvant once a pandemic has been declared.
- January 23, 2007: GSK announced that the file for their proprietary adjuvanted split antigen pre-pandemic vaccine has been accepted for review by the CHMP.

*Relenza* and *Daronrix* are registered trade marks of the GlaxoSmithKline group of companies

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