## Sanofi's intradermal flu vaccine – the way forward?

**LONDON, UK----14 February 2008----**Recently Sanofi-Pasteur announced that they have filed with the European Medicines Agency (EMEA) their new influenza vaccine with an intradermal delivery (ID) system. The vaccine brings many possible benefits over current influenza vaccines. After observing many failed efforts to revolutionize flu vaccination, **VacZine Analytics** believes Sanofi's product has the highest chance of dominating the future market.

It is common knowledge within the vaccine industry that the current global market for influenza vaccines (~$ 3 billion, 400 million doses) is set to expand over the coming years. This expansion is mainly driven by the US market (~40% of value), where each year healthcare policy recommends more and more individuals to be vaccinated. Widening US policy then usually influences influenza vaccine recommendations around the world thus stimulating increasing demand.

Manufacturers of flu vaccines have recognised this dynamic and in response have ramped up supply. For example, for the 2007-08 season the US Centers For Disease Control and Prevention estimated that a record amount of flu doses (~132 million) were delivered. Sanofi-Pasteur, the current market leader producing about half of the world's supply estimates that the US market target demand is 200 million doses (1).

Because the market for influenza is growing other vaccine companies, not previously committed to influenza have entered the business for the first time or refocused their portfolios. Indeed, the number of approved US flu vaccine suppliers has doubled in the space of 2-3 years For example GSK rejuvenated their flu franchise with the rapid US licensing of Fluarix in 2005. The product had been available elsewhere since 1992. CSL Biotherapies, a relatively small vaccine player also licensed a new vaccine Afluria in September 2007.

Beyond increasing supply to match growing demand, many flu vaccine manufacturers are wary that the market for influenza vaccines is essentially a commodity business. Each has recognised that in order to gain an increasing future market share and maintain strong pricing they must pursue an avenue of product differentiation and generate a superior product. The classic case example of producing a new kind of flu vaccine was Wyeth/Medimmune's Flumist (LAIV*) launched in 2003.

Wyeth/Medimmune suggested that a more convenient intranasal delivery system would appeal mainly to the "worried well" segment (18-49 yrs) that were anxious not to lose working days due to influenza. Unfortunately the product initially experienced low uptake after launch. Amongst other reasons, an overly high pricing strategy (~$60 per dose) contributed to its poor start. Over recent years Medimmune have addressed the initial weaknesses of Flumist, reduced the price and now wisely focus on efficacy as the key product differentiator. Now Flumist has gained widened use in healthy children (2-4 years) but still only makes up below 10% of current supply.

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Other competitors such as Novartis Vaccines (formerly Chiron) are focused on changing the way flu vaccines are produced in order to differentiate their offering. Novartis's new mammalian cell culture system (MDCK cells) has brought Optaflu, licensed last year in the EU and due for filing in the US this year. Cell culture systems avoid the laborious egg-production based systems, which dominate current supply. Novartis is making a significant investment in building US cell culture capacity at Holly Springs, USA to augment production in Marburg, Germany.

Enthusiasm for the use of cell culture systems has undoubtedly been driven by concerns that during an influenza pandemic current egg-based systems would not "hold-up". However, in the seasonal market it is difficult to see a strong benefit of Optaflu other than use in individuals allergic to egg based vaccines (~5%), as efficacy appears no better than egg-based vaccines. Nevertheless GSK, Solvay and Sanofi are still pursuing cell culture systems.

Another possible avenue of differentiation for a flu vaccine is adjuvantation. The concept here is that in certain individuals the immune response to standard egg-based vaccines is suboptimal, normally due to immune senescence in the elderly (>65 yrs). Adding an adjuvant to a flu vaccine would give a more powerful response and possibly stimulate other immune mechanisms (T-cells) to combat the virus. For example, Novartis Vaccines already markets an adjuvanted flu vaccine; Fluad, which contains the squalene, based adjuvant MF-59. GSK are also developing "improved flu" which contains an adjuvant system with MPL. However, judging by the US regulators reaction to MPL containing AS04 in Cervarix (bivalent HPV vaccine), it is not a "sure thing" that adjuvanted flu vaccines can penetrate the US market, especially in the pediatric segment.

Considering all of the past and ongoing attempts to bring improvements to influenza vaccines, **VacZine Analytics** believes Sanofi's ID vaccine has the strongest chance to dominate. Undoubtedly the company has the strongest market and lobbying power in influenza vaccination. Although it is very early to judge, the new vaccine brings an advanced delivery system, which brings higher efficacy without the need for an adjuvant. Although the system still relies on egg-based manufacture of antigens there is nothing to stop Sanofi switching to cell culture supply possibly improving margins.

Looking forward if Sanofi's ID flu vaccine is successful, **VacZine Analytics** believes this might form a case study for other flu vaccine manufacturers. It appears that in established vaccine markets such as flu, radical product innovation might be a step too far.

Sanofi plans to file the new vaccine in the key US market in 2009.

**References:**

(1) Sanofi Aventis company presentation, Full year results 2007. Available at :http://en.sanofiaventis.com/Images/080212_presentation_results2007_en_tcm24-20285.pdf (accessed Feb 2008)

*LAIV = Live attenuated influenza vaccine

For more information about this research please visit www.vacZine-analytics.com
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**About VacZine Analytics:**

VacZine Analytics is a new strategic research agency based in the United Kingdom. Its aim is to provide disease and commercial analysis for the vaccine industry and help build the case for developing new vaccines.