2009 and vaccines – lots of activity, and surprises.

LONDON, UK----31st December 2009----ExpertREACT. 2009 was a year of unprecedented activity for the vaccine industry. Not only did existing players have to mount a rapid response to an influenza pandemic, they also had to ramp up corporate expansion to stay ahead of newcomers. Overall it was a year of many surprises but beyond the H1N1 "blip", meningitis (now more so B) and the nosocomial segment are still the long-term growth drivers.

The vaccine industry continues to develop at a rapid pace. Nearly every month of 2009 contained a major announcement or event which contributed significantly to industry momentum. **VacZine Analytics** reviews 2009 and discusses some of the most notable events and how they might impact upon 2010. We also review how our ongoing predictions fared during the year.

2009 started out with the surprise $68 bn acquisition of Wyeth by Pfizer, announced January 26th 2009. Pfizer, who had previously made selected smaller vaccine-related acquisitions (or investments) such as those in Powdermed, Coley and Cytos suddenly, owned one of the most successful vaccine franchises to date, namely the *S.pneumoniae* vaccine Prevnar and its successor PCV-13. Throughout the year the newly merged company succeeded in progressing PCV-13, although the US FDA recently stated it would take more time to complete its review **(1).** PCV-13 is now approved Europe.

As with 2009, in 2010 it is certain that Pfizer (Wyeth) will focus on development of its Phase II vaccine for *meningococcus* B (rLP2086), which along with a more advanced candidate at Novartis Vaccines, could define a new blockbuster vaccine category. Interestingly, Pfizer also advanced a new vaccine for *Staphylococcus aureus* into Phase I (SA3Ag) **(2),** the first new clinical vaccine candidate for a number of years. Another key area to watch will be R&D productivity of the new group while it reshuffles its organization from Sandwich, UK to the US. Will the newly merged Pfizer vaccines plan for its future through further near-term acquisitions or a long-term commitment "in house" vaccine R&D projects?

Further into 2009, in March, we turned our attention to avian influenza (H5N1) sensing significant activity in terms of company and government focus. At the time the US HHS had already allotted ~$7 billion to a plethora of pandemic related activities, a legacy from the Bush administration. At the time some experts believed H5N1 could be responsible for the next pandemic although others were not certain. The experts we consulted agreed that pre-emptive or early immunological priming of certain members of the population with a "pre-pandemic" vaccine could alleviate the impact of a future pandemic **(3).** In light of this research, it then was of incredible surprise to us that in mid-April the H1N1 "swine flu" pandemic emerged then initiating the biggest public health story since that of SARS and before that, HIV.

While many agree that now the H1N1 pandemic, at least for 2009, was relatively "mild" when compared to previous pandemics, its emergence dominated the vaccine agenda with all companies mounting a significant response. In effect, H1N1 vaccine development allowed manufacturers to perpetuate licensure of many new technologies mainly cell culture production (Celtura, Celvapan) and new vaccine adjuvants (AS03, AF03 and MF-59). It also demonstrated, that even with egg-based technologies the industry could ramp production quickly. As of December 2009, major producers such as Sanofi Pasteur had secured over 250m doses of H1N1 vaccine committments for 2009-2010, while at the same time producing 180m doses of trivalent seasonal influenza vaccine **(4).** GSK Biologicals, a company experiencing a full "renaissance" in flu, achieved other significant milestones in H1N1, for example, recently gaining WHO prequalification for Arepanrix™ **(5)**.

Acquisitions, alliances, partnerships, joint ventures were very much a feature in 2009 for the vaccine industry, indeed for the decade. In approximate terms, **VacZine Analytics** calculates that during 2000-2009, around $30bn* has been spent by companies on such activity. The most recent was the $450m investment by Johnson & Johnson for a 18% stake in Dutch-based Crucell NV. In our view, for 2009, GSK Biologicals appeared the most active (and innovative) in their acquisition/alliance strategy with a broad "sweep" across every possible area of potential growth. GSK Biologicals made investments in China, needle-free patch technology, traveller's diarrhea, *Staphylococcus aureus* (NABI), nicotine vaccines (NABI) and Intercell AG, probably the last remaining attractive vaccine company. GSK also achieved significant milestones for Cervarix, Synflorix, Rotarix and most notably, were the first vaccine company to convince the cautious US FDA that they should approve a new vaccine adjuvant (monophosphoryl lipid A, MPL).

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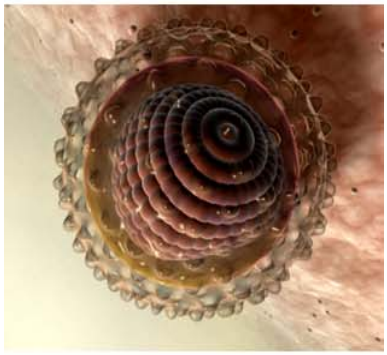

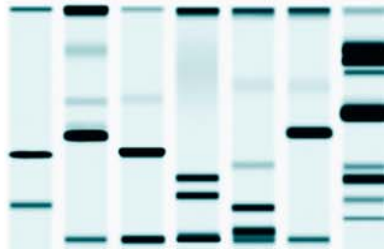

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For arch-rival Sanofi Pasteur, numerous achievements were also made in 2009. Sanofi harnesses an exciting mid-to-early stage pipeline, partly due to its acquisition of UK-based Acambis. In addition to a vaccine for Dengue, one program of high interest, especially to **VacZine Analytics** is the nosocomial vaccine for *Clostridium difficile* (ACAM-CDIFF). Sanofi recently expanded its clinical trial program to the US (Phase IIb) for prevention of disease recurrence **(4)** and importantly, is planning a Phase II prophylaxis trial during the 2nd half of 2010. Back in December 2007, we postulated that primary prevention was the most valuable indication for this vaccine both medically and commercially **(7).** To compliment their position in the nosocomial segment, Sanofi also made an investment in preclinical *Staphylococcus aureus* technology (Syntiron).

In the latter part of 2009, the US ACIP committee's hesitancy to recommend new meningitis ACWY vaccines for the US infant schedule affected the fortunes of a number of vaccine players but not more so than Novartis Vaccines' Menveo (MenACWY-CRM). While Menveo has recently received positive opinion from the EU CHMP for adolescents (11 yrs onwards), we, like many others stated that the real prize is within the US market, especially infants **(6).** There is potential to drive uptake of MenACWY in other groups on a global basis, but such a strategy will prove expensive and is best left to the incumbent Sanofi Pasteur, who are already planning a second-generation product to Menactra. Novartis Vaccines reported a negative $211m operating income for the first nine months of the year, although Q4 is important to a flu company, this was not the position last year. Novartis Vaccines needs menB to be successful, or the US ACIP to alter their ACWY stance, possibly based on cost-effectiveness. A negative on both counts will undoubtedly make the larger Novartis parent, which is busily making acquisitions elsewhere; begin to ask questions, if it is not already. Fortunately, Novartis Vaccines were the first major player to make an equity stake in Intercell AG, and while uptake of Ixiaro has been initially slow, the Austrian-based company has an encouraging outlook, especially if both the *Staphylococcus aureus* (Merck & Co) and *Pseudomonas aureginosa* nosocomial vaccines advance to market. Novartis has a stake in the latter. Earlier in the pipeline Novartis does have unique programs for *H.pylori* and GBS.

Reflecting on this year's events, and last year's predictions, in our view sources of future industry growth remain very similar. Meningitis and the nosocomial segment fare strongly, with dengue as an outlier within the travel/endemic segment. H1N1 provided a "blip" to influenza which may continue based on how the H1N1 virus evolves. It is highly possible that another health crisis may challenge the industry in 2010 and beyond. Lastly, studying vaccines related to addiction is also on our "to do" list. This may sound radical in 2009 but in 5-10 years it may sound appealing to think about vaccines preventing addiction too.

**Western based acquisitions*

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