GSK files new *pneumococcal* vaccine, Synflorix in the EU – let the battle commence.

LONDON, UK----1 February 2008----ExpertREACT. GSK Biologicals recently announced that the EU regulatory authorities (EMEA) have accepted its new 10-valent *pneumococcal* vaccine, Synflorix for review. From many perspectives, **VacZine Analytics** believes that Synflorix, if approved will be one of the most closely watched new products in the vaccine industry. It challenges a powerful Wyeth monopoly and after Cervarix, is critical to the continued success of GSK in vaccines.

Synflorix is indicated for the prevention of invasive *pnuemococcal* disease (IPD) observed in childhood meningitis, otitis media and pneumonia. By virtue of a novel carrier protein (protein D) the vaccine also brings enhanced protection against non-typable *Haemophilus influenzae* (NTHi) a pathogen also common to these indications.

The vaccine, formerly known as Streptorix, entered clinical development in 1998. From the outset the program was technically complex pushing forward new untested vaccine technologies. It has also been saddled with the enormous challenge of following Wyeth's formidable Prevnar (PCV-7), which has since surpassed $2.4 billion in annual sales (1). Developing Synflorix has required tremendous organisational resolve with the program experiencing various difficulties and delays in its path to regulatory filing.

GSK persisted with the development of Synflorix because it was clear that the global market potential for pnuemococcal vaccines is large enough for two or more products (2). In addition, Prevnar has areas of potential enhancement that competitors could exploit. Firstly, Prevnar does not contain certain *pnuemococcal* serotypes that are prevalent in the fast-growing markets of SE Asia (serotypes 1 and 5). Secondly, there is potential for use of conjugated *pnuemococcal* vaccines in the vast elderly population (>65 yrs), which also suffers from invasive pnuemococcal disease. GSK state that Synflorix is now estimated to cover 80% of serotypes causing pediatric invasive disease worldwide (3).

GSK, like other competitors have taken the route of adding or "conjugating" additional *pnuemococcal* polysaccharides to their candidates in an effort to differentiate from Prevnar. Whilst conceptually this move sounds straightforward, in reality it is technically complex and expensive. Polysaccharide-protein conjugation is not an efficient process and highly depends on the type of vaccine carrier protein used, the purity of the source polysaccharides and the conjugation method. Furthermore, certain carrier proteins only have a limited capacity making it difficult to successively add additional polysaccharides without causing interference during immunogenicity studies.

To many within the industry Wyeth's success with Prevnar has been mainly due to the selection of CRM_{197} (diphtheria toxin) as their carrier protein along with their "in house" expertise in conjugation. Other manufacturers such as Sanofi-Pasteur and Merck & Co have seemingly struggled with other carrier proteins such as diptheria and tetanus toxoids and outer membrane vesicles (MenB OMV). Novartis Vaccines (formerly Chiron) also has access to CRM-conjugation technology as seen in their Meningitis vaccines (C, ACWY).

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With their NTHi carrier protein, GSK have not only challenged Wyeth in terms of number of polysaccharides (10 versus 7), they also cleverly introduced a carrier with pertinent biological activity. The NTHi provides the broader pathogen coverage of Synflorix, which will also provide protection against Non-typable *Haemophilus influenzae* (NTHi). NTHi along with *Streptococcus pnuemonaie* is responsible for approximately 40% of otitis media infections (middle ear infection); it is also a common component of bacterial meningitis and community-acquired pnuemonia (4). Current Hib vaccines only cover the encapsulated forms of *Haemophilus influenzae* (Type B) making NTHi a welcome addition.

While it is easy to be enthusiastic with regard to the novelty of Synflorix, the product will not have an easy ride. GSK do not openly have plans to file in the key US market, which accounts for around one half of current Prevnar revenues. It is not also guaranteed the product will dislodge the "tried and tested" Prevnar from existing tenders of current 19 national immunization programs. GSK will probably target the rich affluent classes of emerging economies, where Prevnar is not so entrenched and Western like prices are achievable.

GSK must act fast after launch as the most dangerous threat is Wyeth's 13-valent Prevnar (currently in Phase III), which is due for submission in early 2009. The enhanced Prevnar again demonstrates the higher flexibility of the CRM carrier protein but the product does not have the dual pathogen coverage pitched by GSK. **VacZine Analytics** believes there will be a fierce battle in pneumococcal vaccines where policy decision makers will face a difficult decision. It will be a choice between NTHi coverage and some extra *pneumococcal* serotypes.

For more information about this research please visit www.vacZine-analytics.com
Or e-mail us at info@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.