Pnuemococcal vaccines – universal coverage is the future but with big investment

LONDON, UK----11 January 2008----ExpertREACT. Intercell (ICLL), the small Austrian based vaccine company who have a strategic partnership with Novartis Vaccines have recently published data in the Journal of Experimental Medicine (1) highlighting novel *Streptococcus pneumonaie* protein antigens. The antigens are reported highly conserved among *Streptococcus pneumonaie* clinical isolates and are immunogenic in both elderly and young children. Although the generation of a protein-based universal *pneumococcal* vaccine will face many challenges during development, **VacZine Analytics** believes vaccine candidates with this profile will shape the long-term future of *pnuemococcal* vaccination. They could eventually surpass current polysaccharide-protein conjugates e.g. Wyeth's Prevnar (PCV-7, 13-v) and GSK's Synflorix (10-v), which will dominate current and near-term vaccination schedules.

Streptococcus pneumoniae is a gram positive encapsulated bacterial coccus of which ~90 different serotypes have been identified. The bacterium causes a wide range of diseases which are a major global public health problem affecting the either very young or elderly. *Pnuemococcal* diseases can be serious and invasive in nature e.g. pnuemonia, meningitis and febrile bacteremia or non-invasive, such as more common infections such as otitis media, sinusitis and bronchitis. At least 1 million children die of *pneumococcal* related diseases each year especially in developing countries where the pathogen causes around 30% of the 2.5 million vaccine preventable deaths (WHO Figures).

The development of conjugated-polysaccharide vaccines such as Prevnar (PCV-7) to prevent invasive *pnuemococcal* disease (IPD) in infants and toddlers has been one of the greatest success stories in the vaccine industry from both a medical and commercial perspective. The success story will be complete when Prevnar is available to children in those countries with limited resources. Recently at the 45th Annual Meeting of the Infectious Diseases Society of America (IDSA, October 2007) studies reported the broad public health impact of routine use of the vaccine in the United States, including a 98 percent reduction in vaccine-type invasive pneumococcal disease (IPD) among children younger than five years of age compared with a pre-vaccine baseline.

Prevnar contains polysaccharide antigens against serotypes 4, 6B, 9V, 14, 18C, 19F and 23F which are 65-80% associated with invasive disease. It is given within the routine childhood schedule at 2, 4, 6 and 12-15 months of age. The vaccine has been a resounding commercial success (~$1.9 bn sales per annum) for US-based Wyeth due to premium pricing (~$350 per course) and high rates of uptake. Because of this success many companies including GSK and Wyeth themselves have been looking to the next generation of pneumococcal vaccines to defend and expand a growing global market. Newer *pnuemococcal* vaccines are designed to have greater serotype coverage (13-valent and 10-valent) making the vaccines more applicable in SE Asia where non-Prevnar serotypes 1 and 5 are more prevalent. Higher serotype coverage will also allow utility in the vast elderly (>65 yrs) age group where the burden of *pnuemococcal* disease is still high and current polysaccharide vaccines such as Merck & Co's Pnuemovax (23-valent) have had little impact. With Synflorix (Phase III) GSK have also been cleverly positioning the inclusion of Non-typable *Haemophilis influenzae* (NTHi) as added pathogen coverage in the carrier protein of their vaccine. NTHi can be responsible for around 30-40% of otitis media cases so giving "extra" protection over Prevnar in this common childhood indication.

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Wyeth and GSK's pending new vaccines make it incredibly difficult to enter the near-term market for *pneumococcal* vaccines despite its huge long-term potential. For this reason other players have been experimenting with protein based-antigens that might provide universal coverage and avoid the complex and expensive protein-polysaccharide manufacturing process associated with current vaccines. A universal vaccine will also guard against "serotype" replacement where non-vaccine serotypes have emerged possibly in response to current vaccines.

Companies that in the past have announced protein-based pneumococcal programs have been Sanofi-Pasteur (PspA), Ace Biosciences, GSK with ID Biomedical Assets and Novartis (formerly Chiron). Most of these have been at early stages and it has been difficult to compare the relative strengths and weaknesses of program each without extensive clinical data.

The recent data presented by Intercell gives renewed encouragement to the field of universal *pneumococcal* vaccines. The observation that the antigens elicit the production of opsonophagocytotic antibodies is also important to establishing a potential serological correlate of protection. However, despite this encouraging data the biggest challenge to a new protein based *pneumococcal* vaccine will be the necessity of an expensive large-scale efficacy trial versus current vaccines. This would require tens of thousands of subjects with lengthy follow-up. In order to commit to such an investment a future sponsor, possibly Novartis Vaccines, will have to be confident that the new vaccine can gain enough share from incumbents to justify it's development. The vaccine is unlikely to be launched before 2014.

1. Giefing C., et al Discovery of a novel class of highly conserved vaccine antigens using genomic scale antigenic fingerprinting of *pneumococcus* with human antibodies. *J. Exp. Med.*.2007; 0: jem.20071168-15

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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.