

## Novartis Vaccines: diverse early stage pipeline will force rivals to act

**LONDON, UK----09 June 2008----ExpertREACT.** At its recent Vaccine R&D day, Novartis Vaccines announced progress on its promising pipeline of novel vaccines (1). Beyond the well publicized near term highlights Menveo and MenB, the company also revealed a rich early stage pipeline with several first-in-class vaccine candidates that may lead to the emergence of new categories of vaccines for nosocomial infections, RSV, *Helicobacter pylori* and Streptococcal Group A and B infections

Novartis entered the global vaccines market in 2005 with the takeover of California-based Chiron and since has strengthened its presence in the influenza (Fluad/Fluvirin) and travel vaccine segments (Encepur for Tick-borne encephalitis and Ixiaro for Japanese Encephalitis virus). The company generated sales of \$1.5 billion in 2007 (2), representing around 10% of the total global sales of the five major players, which include GSK Biologicals, Sanofi Pasteur, Merck & Co, and Wyeth.

Unlike its main rivals, Novartis Vaccines currently lacks a significant presence in the core paediatric market which accounts for just over half of all vaccines sales. The company is looking to address this weakness through the greatly accelerated development of Menveo (tetraivalent conjugated ACWY-CRM vaccine) and a MenB vaccine both predicted to be blockbusters.

*Neisseria meningitidis*, which is classified by five main serogroups (ACWY & B) is the only bacterium capable of generating meningitis epidemics. Novartis Vaccines recently announced encouraging new data for the investigational recombinant meningococcal group B (MenB) vaccine (2). MenB remains the only major disease-associated serogroup for which there is currently no licensed vaccine available in the US or European markets. With a significant head start on its competitors, VacZine Analytics believes Novartis Vaccines will file for the first broad coverage MenB vaccine in early 2010.

Novartis Vaccines reiterated the clinical trial results for Menveo, which showed the vaccine, produced a strong protective immune response in individuals from two months to 17 years of age. Menveo's most commercially significant feature is that it covers infants under the age of two. Nevertheless, Menveo will face substantial competition from Sanofi Pasteur which is expected to file Menactra Toddler for use between 1-2 years of age in early 2009 and has started a phase I study with a 2<sup>nd</sup> generation ACWY vaccine which targets the infant primary series schedule.

Novartis also gave an update on its progress with a broad range of vaccines in preclinical or early clinical trials that are targeting infectious diseases for which no vaccines are currently available. Indeed a recent review of vaccine intellectual property (IP) revealed that the company had one of the broadest portfolios in the industry in terms of types of pathogens being studied (3). For the new programs the most advanced project is targeting nosocomial infections caused by the problematic difficult to treat Gram-negative pathogen *Pseudomonas aeruginosa*. *Pseudomonas aeruginosa* is a common pathogen in the intensive care unit especially in late-onset ventilator-associated pneumonia (VAP) where it is associated with high patient mortality (~50%). It also causes a significant proportion blood stream infection (BSIs), wound infections (SSIs) and is a prevalent colonizer in COPD/Cystic fibrosis patients. Novartis Vaccines is planning a Phase II trial in "at risk" patients in ICUs to start at the end of 2008. The program originated from Vienna based Intercell AG, which Novartis Vaccines formed a strategic alliance with in July 2007. Interestingly, the program has come "full circle" because Intercell AG acquired the program from small biotech Pelias AG who bought the program from Chiron prior to the Novartis acquisition. Other preclinical candidate vaccines for nosocomial diseases being developed include *Candida Sp.*, *Enterococcus* and *Klebsiella* infections. Of these the *Candida Sp* program originated "in house".

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Novartis's second major area of announced research interest is *Streptococcal* infections, which cause a wide spectrum of clinical syndromes. A vaccine for Group B *Streptococcus* (GBS) started Phase I clinical trials in November 2007, targeting young females planning pregnancy that may prevent early onset newborn blood infections (sepsis), pneumonia, and meningitis. According to the US Centers For Disease Control and Prevention (CDC) approximately 2,725 cases of neonatal sepsis and meningitis each year are caused by GBS despite widespread intrapartum antibiotic prophylaxis of colonized pregnant women (4). Although disease incidence of GBS (0.5/1000) is considered as low as possible with current measures preventative vaccination will save the approximate 200-300 neonates which die each year from the disease in the US.

A second vaccine in preclinical development is for Group A *Streptococcus* (GAS), which can cause a wide range of skin and upper respiratory tract infections (pharyngitis). The majority of infections are harmless but GAS can cause invasive diseases of which toxic shock syndrome (STSS) and necrotizing fasciitis (NF) are associated with high mortality. The Novartis GAS vaccine is also expected to enter Phase I clinical trials in 2010 but is likely to face competition from Wyeth, Merck and GSK Biologicals who also have preclinical intellectual property (3).

Novartis Vaccines, along with GSK and Sanofi Pasteur is also attempting to develop a universal protein based *pneumococcal* vaccine (Pneumo), which may enter phase I trials in 2010. The company has its own pneumo antigens based on bacterial pillus components but also has access to the components of the Intercell program. Notably, the company did not give an update on the status of its hepatitis C virus therapeutic or prophylactic programs. Whether this signals potential delays with the programs, which are inherently more technically challenging than prophylactic approaches, is uncertain.

Perhaps the most significant news was the proof of concept (POC) trial planned for the end of 2008 targeting *Helicobacter pylori*, a causative agent in gastric ulcers and gastric. Given the high global prevalence of *Helicobacter pylori* especially in SE Asia the commercial and strategic prospects for this vaccine appear promising; especially considering that both prophylactic and therapeutic use of the vaccine may be possible. It is of note however, that many *H.pylori* programs have failed in the past e.g. Oravax/Sanofi Pasteur albeit based on different technologies.

In summary, the ambitious breadth of Novartis Vaccines pipeline suggests it will become an increasingly important player in the vaccines business. With near term opportunities boosting the company's presence in the important paediatric market and an unrivalled pipeline of novel vaccines extending preventative strategies to other areas of medical need, **VacZine Analytics** believes the company is serious about becoming number 1. Other leading players such as Merck & Co and Wyeth, with high revenues but thin pipelines are recommended to ramp up R&D.

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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.

