New vaccines for dengue – paying adults please

LONDON, UK----9th May 2011----ExpertREACT. With sharp increases in global incidence and huge disease/economic burden, a dengue vaccine is a much needed intervention. Recent market modelling analysis published by **VacZine Analytics** predicts global demand and highlights the importance of the adult private sector for dengue vaccine manufacturers.

Like other mosquito borne diseases such as malaria, a large proportion of the world's population (living in over 100 countries) is potentially at risk of infection with the dengue virus. Latest estimates by the Pediatric Dengue Vaccine Initiative (PDVI) suggest there are about 70 – 500 million dengue infections per year of which 36 million actually translate to symptomatic dengue fever (DF) (1). DF is an acute self-limiting febrile illness characterized by fever, rash and severe myalgia. However, in a small minority of patients severe manifestations such as dengue hemorrhagic fever (DHF), leading to dengue shock syndrome (DSS) may be fatal if supportive therapy is not administered rapidly. DHF/DSS are responsible for the estimated 21,000 deaths due to the dengue each year. Importantly, a large proportion of these deaths are in children (<15yrs).

Experts believe the incidence of dengue is increasing. Although there are many weaknesses in our ability to accurately capture the true epidemiology burden of dengue, the total reported cases of DF and DHF in the three major WHO regions (PAHO, SEA and WPR) has quadrupled since the year 2000 (2). Aside from improvements in reporting and surveillance infrastructure, this increase is thought to be mostly due to environmental factors such as rapidly increasing urbanization which in turn contribute to the extensive distribution of the vector *Aedes aegypti*. In many parts of the world all four dengue serotypes (DEN1-4) are now co-circulating. This is significant because being re-infected with a different dengue serotype from that in a previous primary infection can cause more severe dengue disease (3).

A preventative dengue vaccine is a much needed intervention. Current prevention measures such as mosquito control and personal protection measures from bites are for the most part ineffective, difficult to implement and costly. Not only would a dengue vaccine reduce a high degree of excess morbidity and mortality, stakeholders also argue it could be hugely cost effective to governments of endemic countries. A recent study conducted by Brandeis University estimated that dengue costs countries of the America's region the range of $1 – 4 billion per year. This estimate encompasses both direct and indirect costs of hospitalized and ambulatory dengue cases but not the current costs associated with vector control (4). Interestingly the authors argued that these costs exceeded those estimated for human papilloma virus and rotavirus for which now licensed vaccines are now available.

Dengue vaccine research has ongoing for sixty years and challenging with many different approaches investigated. Currently, there are around 6 dengue vaccine candidates in clinical testing (5) with the field currently at a climatic point. Back in November 2010, the French vaccine manufacturer, Sanofi Pasteur announced that its candidate (CYD) based on ChimeriVAX™ technology had entered Phase III studies in Australia (6). Sanofi state their vaccine, which has been given so far to 5000 children and adult volunteers, meets the requirements of having a good safety profile, being genetically stable and able to promote seroconversion against all four dengue serotypes. However, some commentators have stated Sanofi's extended vaccine schedule (3 doses, 6 months apart) does not meet the profile of an ideal dengue vaccine (5). If all goes to plan Sanofi's vaccine could be available certainly within 3 -5 years.

Because of the enormous public health implications linked with the availability of a new dengue vaccine, **VacZine Analytics** has recently modelled potential demand in terms of both volume required (mio doses) and financial parameters i.e. funding required/market value (7). From a manufacturer's point of view, sources of potential return associated with a new dengue vaccine are complex and interrelated. Because dengue mainly kills children, it is conceivable that a wide range of governments of endemic countries would procure vaccine for integration into national immunization programs and expanded program on immunization (EPI) as postulated elsewhere (8).

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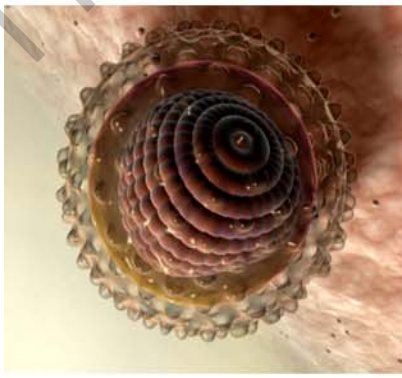

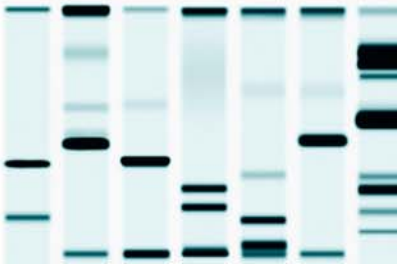

A dengue vaccine could become part of the routine schedule for 1 – 2 yrs where, ideally, the first dengue dose (at 12 months) could be alongside MCV (measles) and Hib (third dose) where already scheduled.

The timescale /phasing at which a new dengue vaccine would be adopted and, whether vaccination would extend to older children (2 – 14 yrs) as part of publically funded catch-up campaigns (school based), are much more difficult to predict. Many countries in dengue endemic regions (who can afford vaccines) have many competing health care priorities and ever increasing pressures on financial resources. The same is true for GAVI which now has a long "to do" list. It is expected that in many countries private sector use will evolve rapidly and in turn shape emergent public sector policy; a possible "wait and see" strategy already voiced by endemic countries such as Thailand. For adults (> 15 yrs), who form a much larger component of the population, demand will be predominately private sector with vaccine price per dose already estimated at ~$30 **(9)**. Due to natural priming adults may require less vaccine doses than toddlers/children.

According to **VacZine Analytics** assumptions, the global market for a dengue vaccine is substantial with blockbuster revenues achievable for the first licensed candidate. For a manufacturer, our analysis would suggest it is easy to overestimate near term public sector demand. Most market upside depends on driving private sector uptake in adults, a real possibility in the PAHO region which recently has experienced ruthless epidemics as in Brazil. For the time being, Sanofi's current vaccine appears to match this potential market more closely.

PAHO = Pan American Health Organisation, SEA = South East Asia, WPR = Western Pacific Region

References and Notes:

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