



## **The New England Journal of Medicine Publishes Results of Final Landmark Phase III Efficacy Clinical Study of Sanofi Pasteur's Dengue Vaccine Candidate**

- Study successfully met primary objective and confirms high efficacy against severe dengue and hospitalization -**
- Sanofi Pasteur intends to file for registration in several endemic countries in 2015 -**
- Dengue vaccine candidate would address an urgent unmet medical need in tropical and sub-tropical regions of the world -**

**Lyon, France - 3<sup>rd</sup> November, 2014** - [Sanofi Pasteur](#), the vaccines division of [Sanofi](#), today announced the publication of the detailed results of the final landmark phase III clinical efficacy study in Latin America in *The New England Journal of Medicine*.<sup>1</sup> Overall efficacy against any symptomatic dengue disease was 60.8 percent\* in children and adolescents 9-16 years old who received three doses of the vaccine. Analyses show a 95.5 percent\* protection against severe dengue and an 80.3 percent\* reduction in the risk of hospitalization during the study. The results of this second phase III efficacy study confirm the high efficacy against severe dengue and the reduction in hospitalization observed during the 25-month active surveillance period of the first phase III efficacy study conducted in Asia<sup>2</sup>, highlighting the consistency of the results across the world.

Safety analyses (solicited reactions, unsolicited events and Serious Adverse Events SAEs) during the study showed similar reporting rates between the vaccine and control groups and are consistent with the favorable safety profile observed during the 25-month active surveillance period of the previous efficacy study conducted in Asia. The full data of the Latin American study are also presented at the American Society of Tropical Medicine and Hygiene (ASTMH) Annual Meeting, 2-6 November 2014.

Sanofi Pasteur's phase III efficacy clinical study program for its dengue vaccine candidate was conducted in over 31,000 participants across 10 endemic countries in Asia<sup>2</sup> and Latin America. Sanofi Pasteur will file for registration of its vaccine candidate and, subject to regulatory approval, the world's first dengue vaccine could be available in the second half of 2015.

*"We plan to submit the vaccine for licensure in 2015 in endemic countries where dengue is a public health priority," said Olivier Charmeil, President and CEO of Sanofi Pasteur. "We are committed to supporting countries' ambitions to significantly impact the human and economic*

*burden of dengue through comprehensive vaccination programs. Our goal is to help meet the WHO's objectives to reduce dengue mortality by 50% and morbidity by 25% by 2020."*

Dengue is a threat to over 2.5 billion people, nearly half the world's population, and is a pressing public health priority in over 100 countries in the Americas and in Asia.<sup>3</sup> Every year, an estimated 500,000 people, including children, are hospitalized due to severe dengue, which puts a huge strain on health care systems particularly during outbreaks.<sup>3</sup> Dengue has dramatically increased over the past 30 years with an acceleration over the last decade due to travel and urbanization.

*"Healthcare systems can be paralyzed when trying to cope with a dengue outbreak. The economic and societal costs can be staggering," said Dr Roberto Tapia-Conyer, Director General Carlos Slim Foundation, Mexico. "Broad public immunization programs will be critical in achieving the full benefit of a dengue vaccine within a public health perspective, to reach the control of the disease."*

*"Until now, we were only able to provide supportive care for patients with dengue. On the strength of the outcome of this phase III efficacy study, we hope this will become an effective preventive measure against dengue," said Dr. Rivaldo Cunha, MD, Infectious Disease Specialist, Associate Professor, Faculty of Medicine Universidade de Mato Grosso do Sul, Brazil, and a principal investigator in the study. "I will welcome a dengue vaccine that can prevent the personal suffering of severe disease and hospitalization."*

Sanofi Pasteur is already producing the vaccine in a newly dedicated production facility in Neuville-sur-Saône, France, which will be capable of providing timely supply of large quantities of vaccines to meet the global public health demand.

\*95 percent CIs efficacy against severe dengue [68.8 percent, 99.9 percent]; 95 percent CIs overall efficacy [52.0 percent, 68.0 percent]; 95 percent CIs reduction of the risk of hospitalization [64.7 percent, 89.5 percent]

#### **About the Phase III clinical study conducted in Latin America and the Caribbean**

The primary objective of the phase III study in Latin America and the Caribbean was to assess the efficacy and safety of the Sanofi Pasteur dengue vaccine candidate after three vaccinations in preventing symptomatic virologically-confirmed dengue cases. A total of 20,869 children aged 9 to 16 years from dengue endemic areas of Brazil, Colombia, Mexico, Honduras and Puerto Rico participated in the study and were randomized to either receive three injections of the dengue vaccine or a placebo (2 to 1 ratio) at 0, 6, and 12 months.<sup>1</sup>

#### **About Sanofi Pasteur's dengue vaccine clinical program**

Sanofi Pasteur has been working on a dengue vaccine for more than 20 years. The company's goal is to make dengue the next vaccine-preventable disease with a safe and effective dengue vaccine accessible in all regions of the world where dengue is a public health issue. The company is committed to support the WHO's ambition to reduce dengue mortality by 50 percent and morbidity by 25 percent by 2020.<sup>4</sup>

Two pivotal phase III efficacy studies involved more than 31,000 volunteers from Asia (Indonesia, Malaysia, the Philippines, Thailand and Vietnam) and Latin America and the Caribbean (Brazil, Colombia, Honduras, Mexico and Puerto Rico). The phase III evaluations provide pivotal data on efficacy, safety, and immunogenicity of the vaccine candidate in a broad

population and different epidemiological environments and assess the potential impact of the vaccine on the disease burden.

Sanofi Pasteur's dengue vaccine candidate is the most clinically and industrially advanced dengue vaccine candidate in development. Over 40,000 volunteers participated in the Sanofi Pasteur dengue vaccine clinical study program (phase I, II and III).

Additional information, photos and videos about Sanofi Pasteur's dengue vaccine candidate are available on the web at <http://www.dengue.info> and at <http://es.dengue.info/>

### **About dengue**

Dengue is caused by four distinct virus serotypes transmitted by mosquitoes. It is a threat to nearly half of the world's population. Currently, there is no specific treatment available for dengue. It is a health priority in many countries of Latin America and Asia where epidemics occur regularly. The WHO estimates that there are up to 100 million infections per year<sup>2</sup>; however, the overall number of people infected with dengue globally is not fully known. The WHO has set the goal of estimating the true public health burden of dengue by 2015.<sup>5</sup> The burden of dengue is generally underestimated. The majority of current surveillance programs are passive and are not intended to assess disease burden.<sup>5</sup> Also the similarity of dengue symptoms to other common infectious diseases may result in dengue cases being incorrectly reported.<sup>6</sup> Moreover, a large proportion of dengue infections are asymptomatic and therefore unreported.<sup>7</sup>

Each year, an estimated 500,000 people, including children, with severe dengue require hospitalization. About 2.5% affected would die.<sup>2</sup> Severe dengue (also known as dengue haemorrhagic fever) is a potentially deadly complication due to plasma leakage, fluid accumulation, respiratory distress, severe bleeding, or organ impairment.<sup>2</sup> Dengue places tremendous pressure on health systems and strains medical resources resulting in significant economic and social impact. Timely access to appropriate health care is critical to reduce the risk of mortality in case of severe dengue. The WHO has set the target to reduce dengue mortality by 50% and reduce morbidity by 25% by 2020.<sup>4</sup>

### **About Sanofi**

Sanofi, a global healthcare leader, discovers, develops and distributes therapeutic solutions focused on patients' needs. Sanofi has core strengths in the field of healthcare with seven growth platforms: diabetes solutions, human vaccines, innovative drugs, consumer healthcare, emerging markets, animal health and the new Genzyme. Sanofi is listed in Paris (EURONEXT: [SAN](#)) and in New York (NYSE: [SNY](#)).

Sanofi Pasteur, the vaccines division of Sanofi, provides more than one billion doses of vaccine each year, making it possible to immunize more than 500 million people across the globe. A world leader in the vaccine industry, Sanofi Pasteur offers the broadest range of vaccines protecting against 20 infectious diseases. The company's heritage, to create vaccines that protect life, dates back more than a century. Sanofi Pasteur is the largest company entirely dedicated to vaccines. Every day, the company invests more than EUR 1 million in research and development. For more information, please visit: [www.sanofipasteur.com](http://www.sanofipasteur.com) or [www.sanofipasteur.us](http://www.sanofipasteur.us)

## References

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3. WHO Dengue and severe dengue Fact sheet N°117 Updated March 2014. Available at <http://www.who.int/mediacentre/factsheets/fs117/en>
4. World Health Organization (WHO). Global strategy for dengue prevention control: 2012-2020. Available at: [http://reliefweb.int/sites/reliefweb.int/files/resources/9789241504034\\_eng.pdf](http://reliefweb.int/sites/reliefweb.int/files/resources/9789241504034_eng.pdf). Published 2012. Accessed September 8, 2014
5. WHO 2009: p112, para5. Beatty 2010: p3, table 1. Undurraga 2013: p2, col1, para1
6. WHO working group 2007: p38, col1, para3-col2, para1; p125, col2, para1
7. Dussart 2012: p9, col2, para3. Bhatt 2013: p505, col2, para3; p506, table1. Chastel 2012: p3, col2, para4-5

## Forward Looking Statements

*This press release contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, as amended. Forward-looking statements are statements that are not historical facts. These statements include projections and estimates and their underlying assumptions, statements regarding plans, objectives, intentions and expectations with respect to future financial results, events, operations, services, product development and potential, and statements regarding future performance. Forward-looking statements are generally identified by the words "expects", "anticipates", "believes", "intends", "estimates", "plans" and similar expressions. Although Sanofi's management believes that the expectations reflected in such forward-looking statements are reasonable, investors are cautioned that forward-looking information and statements are subject to various risks and uncertainties, many of which are difficult to predict and generally beyond the control of Sanofi, that could cause actual results and developments to differ materially from those expressed in, or implied or projected by, the forward-looking information and statements. These risks and uncertainties include among other things, the uncertainties inherent in research and development, future clinical data and analysis, including post marketing, decisions by regulatory authorities, such as the FDA or the EMA, regarding whether and when to approve any drug, device or biological application that may be filed for any such product candidates as well as their decisions regarding labelling and other matters that could affect the availability or commercial potential of such product candidates, the absence of guarantee that the product candidates if approved will be commercially successful, the future approval and commercial success of therapeutic alternatives, the Group's ability to benefit from external growth opportunities, trends in exchange rates and prevailing interest rates, the impact of cost containment policies and subsequent changes thereto, the average number of shares outstanding as well as those discussed or identified in the public filings with the SEC and the AMF made by Sanofi, including those listed under "Risk Factors" and "Cautionary Statement Regarding Forward-Looking Statements" in Sanofi's annual report on Form 20-F for the year ended December 31, 2013. Other than as required by applicable law, Sanofi does not undertake any obligation to update or revise any forward-looking information or statements.*

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