LEADING DENGUE VACCINE CANDIDATE
COULD CHANGE THE LIVES OF MILLIONS

A GLOBAL PUBLIC HEALTH CHALLENGE

- Dengue fever, a mosquito-borne disease caused by four types of dengue viruses, is a threat for almost half of the world’s population\(^1\).
- Dengue is a pressing public health priority in many countries in Asia and Latin America where epidemics occur\(^2\).
- Dengue fever occurs mostly in tropical and subtropical countries\(^2\) and is spreading to new parts of the globe each year. Many factors contribute to the spreading of dengue fever, including urbanization and increased travel which facilitate the dissemination and the circulation of this disease.
- Currently, there is no specific treatment available for dengue.
- The World Health Organization (WHO) has set the target to reduce dengue mortality by 50% and morbidity by 25% by 2020\(^3\).

Key figures\(^{1,4}\)...

- 3.9 billion people at risk in over 128 countries
- 390 million people infected annually, of which 96 million people show clinical symptoms
- 500,000 people, including children, develop dengue haemorrhagic fever, a severe form of the disease
- $6 billion USD in direct medical costs and indirect costs (lost productivity, absenteeism)

From early scientific discoveries....

- 1944: isolation and identification of the 1st serotype (in Hawaii, DEN1) and 2nd serotype (in N.Guinea, DEN2) by Sabin and Schelsinger(5).
- 1944-45: first monovalent dengue vaccine, a live attenuated vaccine (LAV) DEN1, developed by Sabin and Schelsinger(5).
- 1956: isolation and identification of the 3rd serotype (DEN3) and 4th serotype (DEN4) by W. Hammon(6).
- 1970-1980: development of a tetravalent LAV DEN1, DEN2, DEN3, DEN4, by Pr Natth Bhamarapravati at the Mahidol University (Bangkok - Thailand). Data from clinical investigations conducted in Thailand showed hope for a tetravalent dengue vaccine(7).

.... to the leading candidate dengue vaccine from Sanofi Pasteur

Dengue virus under electronic microscope
## 20 years of commitment from Sanofi Pasteur

1994  
Partnership between Sanofi Pasteur and the Vaccine Development Centre, University of Mahidol (Bangkok - Thailand).

2001  
Proof of concept of a tetravalent live attenuated dengue vaccine in two doses and a booster.  
Start of the development of a second generation vaccine obtained by recombinant technology.

2004  
Clinical study of classical live-attenuated vaccine stopped due to reactogenicity and under-attenuation of serotype 3. Sanofi Pasteur decides to adopt a new approach, with a second generation live attenuated vaccine.

2006  
Partnership with PDVI (Pediatric Dengue Vaccine Initiative), a consortium working to accelerate the introduction of a dengue vaccine for children in endemic countries (supported by the Bill & Melinda Gates Foundation).

2007  
Positive results in phase II clinical studies; proof of concept for Sanofi Pasteur’s candidate dengue vaccine.

2009  
Sanofi Pasteur dengue vaccine enters pediatric clinical efficacy study in Thailand.

June 2010  
The U.S. FDA grants fast track status to Sanofi Pasteur candidate dengue vaccine.

Oct. 2010  
Sanofi Pasteur dengue vaccine enters phase III clinical study.

Feb. 2011  
Partnership with the International Vaccine Institute to support the DVI (Dengue Vaccine Initiative), a non-profit advocacy group focused on raising awareness of dengue fever and supporting the introduction of dengue vaccination, funded by the Bill & Melinda Gates Foundation.

July 2012  
Results from Sanofi Pasteur’s Phase IIb clinical trial in Thailand demonstrate that a vaccine is possible.

July 2014  
World’s first Phase III dengue vaccine efficacy study including 10,275 children in Asia demonstrated protection against dengue and dengue haemorrhagic fever. Results published in *The Lancet*.

Nov. 2014  
Final landmark phase III clinical efficacy study in more than 20,000 children and adolescents in Latin America successfully completed. The study met its primary endpoint and showed efficacy against each of the four dengue serotypes. Results published in the *New England Journal of Medicine*.

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*Sanofi Pasteur dengue vaccine clinical study in Ratchaburi, Thailand*
15 endemic and non-endemic countries included in the Sanofi Pasteur global clinical study program (phase I, phase II and phase III).

Globally, nearly 40,000 volunteers participated in the clinical study program.

First vaccine candidate to successfully complete phase III clinical studies.

Sanofi Pasteur dengue vaccine candidate has been evaluated in 25 clinical studies (Phase I, II, III) in adults, adolescents and children in the United States, Australia, Asia and Latin America.

“Developing a dengue vaccine is at the heart of our public health mission. Our goal is to make dengue the next vaccine-preventable disease and to support the WHO’s ambition to reduce dengue mortality by 50% and morbidity by 25% by 2020.”

Olivier Charmeil, President and CEO, Sanofi Pasteur.

Countries hosting Sanofi Pasteur dengue vaccine clinical studies

Areas at risk of dengue: 3.9 billion people in over 128 countries
AN INDUSTRIAL PIONEER FOR GLOBAL HEALTH

In response to the global need for a dengue vaccine, Sanofi Pasteur took a bold step and built a new vaccine manufacturing facility in Neuville-sur-Saône, France. The objective is to reduce the time necessary to provide access to the vaccine once it is licensed. The site is the largest investment in Sanofi Pasteur global vaccines industrial network (300 million euros). This facility is equipped with state-of-the-art manufacturing technologies. It became operational in 2014 with a production capacity of 100 million doses of the vaccine per year.

- 2009: start of construction
- 2014: production site operational

THE NEXT STEP: ACCESS TO DENGUE VACCINATION

- Implementation of dengue vaccination programs face important challenges such as creating vaccination policies for the first dengue vaccine, as well as access and financing mechanisms for people most in need.
- It is urgent that the public health community work together to start preparing for vaccination programs.
- Sanofi Pasteur is joining efforts with international organizations to raise awareness and move dengue vaccination a higher priority on the global health agenda.
- Collaboration efforts focus on accelerating the adoption and introduction of dengue vaccination and on making it accessible to those at highest risk of dengue.

References
5 Science 1945;101(2634):640-642
6 Science 1960;131:1102-3
7 AJTMH 2003;69(Suppl 6):5-11

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