Fact Sheet

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 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.

• There is no specific treatment and vaccination is the only efficient means of fighting against dengue fever.

• Sanofi Pasteur, a world leader in vaccines, has taken on the challenge of providing the first dengue vaccine for individuals living in endemic areas and developing countries as well as for those who plan to travel to those areas.

Key figures\(^{1,3}\)...

- Over 2.5 billion people at risk in over 100 countries
- Up to 100 million people infected annually
- 500,000 people, mostly children, develop dengue hemorrhagic fever, a severe form of the disease

From early scientific discoveries....

- **1944:** isolation and identification of the 1<sup>st</sup> serotype (in Hawaii, DEN1) and 2<sup>nd</sup> serotype (in N.Guinea, DEN2) by Sabin and Schelsinger<sup>(4)</sup>.

- **1944-45:** first monovalent dengue vaccine, a live attenuated vaccine (LAV) DEN1, developed by Sabin and Schelsinger<sup>(4)</sup>.

- **1956:** isolation and identification of the 3<sup>rd</sup> serotype (DEN3) and 4<sup>th</sup> serotype (DEN4) by W. Hammon<sup>(5)</sup>.

- **1970-1980:** development of a tetravalent LAV DEN1, DEN2, DEN3, DEN4, by Pr Natth Bhamarapravati at the Mahidol University (Bangkok - Thailand). At this point, data from clinical investigations conducted in Thailand showed promise for a tetravalent dengue vaccine<sup>(6)</sup>.

.... to the leading candidate dengue vaccine from Sanofi Pasteur
**A long term commitment**

<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
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<td>1994</td>
<td>Partnership between Sanofi Pasteur and the Vaccine Development Centre, University of Mahidol (Bangkok - Thailand).</td>
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<td>2001</td>
<td>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.</td>
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<td>2004</td>
<td>Classical live vaccine approach abandoned due to reactogenicity and under-attenuation of serotype 3. Sanofi Pasteur decides to adopt a new approach, with a second generation live attenuated vaccine.</td>
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<td>2006</td>
<td>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 &amp; Melinda Gates Foundation).</td>
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<td>2007</td>
<td>Positive results in phase II clinical studies; proof of concept.</td>
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<td>2009</td>
<td>Sanofi Pasteur dengue vaccine enters pediatric clinical efficacy study in Thailand.</td>
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<td>June 2010</td>
<td>The U.S. FDA grants fast track status to Sanofi Pasteur candidate dengue vaccine.</td>
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<td>Oct. 2010</td>
<td>Sanofi Pasteur dengue vaccine enters phase III clinical study.</td>
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<td>Feb. 2011</td>
<td>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 &amp; Melinda Gates Foundation.</td>
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*Sanofi Pasteur dengue vaccine clinical study in Ratchaburi, Thailand*
CLINICAL STUDIES: A PROGRAM TO COVER THE WORLD

- First vaccine to reach phase III clinical study, the ultimate steps in the clinical development of a vaccine before its introduction.

- 15 endemic and non-endemic countries included in the Sanofi Pasteur global clinical study program (completed, ongoing and planned studies).

- Globally, nearly 40,000 volunteers are participating in the Sanofi Pasteur clinical study program.

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

“Today, we are very excited to be in the last stage of clinical development. We are confident that we will be the first with a dengue vaccine within a few years. A dengue vaccine will fulfill an unmet medical need and change the lives of millions of people across the world.”

Olivier Charmeil, President and CEO, Sanofi Pasteur.

- Countries hosting Sanofi Pasteur dengue vaccine clinical studies (completed and ongoing studies)
- Areas at risk of dengue: 2.5 billion people in over 100 countries
AN INDUSTRIAL PIONEER FOR GLOBAL HEALTH

In response to the global need for a dengue vaccine, Sanofi Pasteur is building a new vaccine production center, located in France. The objective is to reduce the time necessary to provide access to the vaccine once it is licensed.

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

THE NEXT BATTLE: ACCESS TO DENGUE VACCINATION FOR EVERYONE AT RISK

- 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 groups such as the DVI (Dengue Vaccine Initiative) to raise awareness and move dengue vaccination higher 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

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

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