Tackling dengue's four-serotype challenge: Inside Takeda's science behind durable immunity

Dengue vaccine development has long been hindered by the virus's four-serotype complexity. In an exclusive interaction with ETPharma, Takeda's Dr Jill Livengood explains how the scientific focus on achieving tetravalent seroconversion has shaped the development of its dengue vaccine candidate, aiming for durable protection across all strains.

Dr. Jill Livengood, Global Head – Clinical Assays and Serology at Takeda.

New Delhi: After more than five decades of scientific effort, Takeda's live-attenuated tetravalent dengue vaccine, TAK-003 (marketed as Qdenga), is emerging as one of the most comprehensively studied dengue vaccines globally—demonstrating strong, durable immune responses across all four dengue serotypes in large, geographically diverse clinical trials.

"Dengue is not a single virus but a complex disease caused by four distinct viral serotypes," said Dr Jill Livengood, Global Head – Clinical Assays and Serology at Takeda, in an exclusive interaction with ETPharma's Rashmi Mabiyan Kaur. She underscored that this biological complexity has been one of the biggest challenges in dengue vaccine development. "Our goal was to achieve tetravalent seroconversion—ensuring that an individual mounts a robust immune response against all four dengue serotypes," she said.

TAK-003 is administered as a two-dose regimen given three months apart. In Takeda's pivotal Phase III clinical trial—involving around 21,000 participants across more than eight countries—the vaccine achieved 99 per cent tetravalent seroconversion following the second dose.

"That means individuals developed detectable antibodies to dengue serotypes 1, 2, 3 and 4," Livengood said. "Importantly, these immune responses are durable, and we've been very encouraged by how well the antibody titers hold up over time."

Long-term followup from the seven-year pivotal Phase 3 Tetravalent Immunization against Dengue Efficacy Study (TIDES) further strengthen the vaccine's profile. The data, which included an exploratory analysis of a booster dose, confirmed the favourable benefit–risk profile of

TAK-003 and showed that the two-dose regimen provides sustained protection against dengue.

A critical element of Takeda's vaccine development journey has been its focus on the ability to reliably measure immune responses to each dengue serotype independently.

"To understand whether a vaccine works, you must be able to measure seroconversion accurately," Livengood explained. "That requires very specific reagents, viruses and assays. We've built systems that can reliably detect dengue-specific antibodies and confirm immune responses to each individual serotype."

Beyond antibodies, Takeda has also explored cell-mediated immunity, including T-cell responses to dengue non-structural proteins—an area increasingly recognised as important for long-term protection.

“Some immune responses, particularly T-cell responses, may play a key role in durable protection,” she noted, adding that these exploratory immunogenicity findings have strengthened confidence in the vaccine’s long-term profile.

Long-term follow-up, real-world relevance

Participants in the phase three study were tracked for several years, allowing researchers to evaluate durability of protection in the context of fluctuating dengue epidemiology.

After 4.5 years, two doses of TAK-003 demonstrated 61.2 per cent vaccine efficacy in preventing virologically confirmed dengue. An exploratory booster dose administered at 4.5 years only marginally increased efficacy to 74.3 per cent after two additional years.

Importantly, TAK-003 showed 84.1 per cent efficacy in preventing dengue-related hospitalisations at 4.5 years, with protection remaining consistently high at 90.6 per cent following the booster dose.

The seven-year analysis also showed overall efficacy across all four dengue virus serotypes, with no new safety signals observed after booster administration.

“Although we don’t currently recommend a booster, the data helped us better understand protection against serotypes that are harder to study because of lower case numbers,” Livengood said, noting that vaccine efficacy against dengue 4 was demonstrated and signals for dengue 3 improved over time, though not conclusively.

TAK-003 is the most comprehensively studied dengue vaccine, with more than 60,000 participants globally in the clinical trial

Since its first approval in Indonesia in 2022, TAK-003 has been authorised in 41 countries, with 18.6 million doses distributed across 11 dengue-endemic countries as of September 2025, said the company in a November 2025 statement.

Dr Jill mentioned that Takeda has recently completed a phase three dengue vaccine trial in India. TAK-003’s application is currently under regulatory review in India.

“We plan to supply 50 million doses manufactured by Biological E,” Livengood said, highlighting the role India will play in global dengue vaccine access. In February 2024, the company announced a strategic partnership with Hyderabad-based Biological E. Limited to scale up manufacturing of TAK-003 multi-dose vials, strengthening sustainable vaccine supply and enabling broader access across dengue-endemic countries. BE will ramp up to a manufacturing capacity of up to 50 million doses a year, accelerating Takeda’s efforts to manufacture 100 million doses a year within the decade.

Climate change and the future of dengue control

As climate change reshapes mosquito habitats, dengue is expanding into new geographies, intensifying the need for scalable prevention tools.

“The epidemiology of dengue is changing,” Livengood warned. “Mosquitoes are moving into areas they didn’t previously inhabit. That makes long-term surveillance and real-world evidence even more critical.”

To address this, Takeda is currently conducting the DEN-401 real-world effectiveness study, enrolling more than 70,000 participants across Thailand, Indonesia and Malaysia. The study is designed to assess vaccine performance in routine settings, with baseline serostatus carefully documented prior to vaccination.

“There is still a lot to learn about dengue,” Livengood said. “But with the scale of data we now have—and the studies still underway—the next few years will be incredibly important for understanding how vaccines like TAK-003 can change the trajectory of this disease.”

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