Better Health, Brighter Future

News Release

Takeda Receives Positive CHMP Opinion Recommending Approval of Dengue Vaccine Candidate in EU and Dengue-Endemic Countries

- ***TAK-003 Recommended for the Prevention of Dengue Disease Caused by Any Dengue Virus Serotype in Individuals Four Years of Age and Older in the EU and in Dengue-Endemic Countries Participating in the EU-M4all Procedure***
- ***Positive Opinion for TAK-003 Based on 4.5 Years of Safety and Efficacy Data from Pivotal Phase 3 Trial of Over 20,000 Children and Adolescents Across Eight Dengue-Endemic Countries***
- ***Marketing Authorization Expected in Coming Months in Europe Followed by Regulatory Decisions in Latin America and Asia***

OSAKA, Japan, and CAMBRIDGE, Massachusetts, October 14, 2022 – Takeda **(TSE:4502/NYSE:TAK)** today announced that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) recommended the approval of Takeda's dengue vaccine candidate, TAK-003, for the prevention of dengue disease caused by any serotype in individuals four years of age and older in Europe and in dengue-endemic countries participating in the parallel EU-M4all procedure. The final step in the path to approval in Europe is Marketing Authorization from the EMA, which is expected in the coming months. Regulatory reviews will also progress in dengue-endemic countries in Latin America and Asia.

"We are one step closer towards the approval of a dengue vaccine that could benefit many of the millions of individuals around the world exposed to dengue. This is a major moment for the global health community, European countries and the dengue-endemic countries that participated in the EU-M4all procedure," said Gary Dubin, M.D., president of the Global Vaccine Business Unit at Takeda. "We have been working for many years to help improve the way dengue can be prevented. Our efforts to provide a new option for dengue prevention support Takeda's overall goal to provide long-term societal value to the people we serve."

The incidence of dengue has grown dramatically around the world in recent decades, causing an estimated 390 million infections and 500,000 hospitalizations annually.[1,2] The rise in cases can be attributed to factors such as urbanization, globalization and climate change.[1] Severe dengue accounts for about 5% of dengue cases and is a leading cause of serious illness and death among children and adults in Latin America and Asia.[3,4] Dengue is the second most diagnosed cause of fever in travelers returning to Europe from endemic countries.[5] Its presence is far-reaching in endemic countries across the Americas, South-East Asia and Western Pacific regions and is growing in non-endemic areas in continental Europe, including France, Italy, Germany, Spain and the United States.[6]

"The global health community has been eager for a dengue vaccine that is accessible without the barrier of pre-vaccination testing," said Dr. Ooi Eng Eong, Professor of Emerging Infectious Diseases at Duke-NUS Medical School in Singapore. "The robust clinical data provided by Takeda shows that its dengue vaccine has the potential to help prevent dengue cases and hospitalizations. Today, we are closer to helping improve dengue prevention and reducing the burden of disease on countries, communities and health systems."

The Committee's positive opinion was supported by results across five Phase 1, 2 and 3 trials with more than 28,000 children and adults. This includes four and a half years of follow-up data from the global, pivotal Phase 3 Tetravalent Immunization against Dengue Efficacy Study (TIDES) trial, consistent with the World Health Organization's (WHO) recommendation to obtain three to five years of follow-up data after the completion of a primary dengue vaccination in order to most accurately assess safety and efficacy.[7] TIDES exploratory analyses showed that throughout the four and a half years of study follow-up, TAK-003 prevented 84% of hospitalized dengue cases and 61% of symptomatic dengue cases in the overall population, including both seropositive and seronegative individuals. TAK-003 has been generally well tolerated, with no evidence of disease enhancement in vaccine recipients, and no important safety risks have been identified in the TIDES trial, to date.

In August 2022, Takeda's dengue vaccine, known as QDENGA® ▼ (Dengue Tetravalent Vaccine [Live, Attenuated]) (TAK-003), was approved by the Indonesia National Agency for Drug and Food Control, BADAN POM, for the prevention of dengue disease by any serotype in individuals six years to 45 years of age. TAK-003 has not yet been approved anywhere else in the world and Takeda will continue to initiate and progress regulatory filings in other dengue-endemic and non-endemic countries. Regulatory approval and use of the vaccine is dependent on evaluation by relevant local authorities and for the indication they deem appropriate.

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See Section 4.8 of the SmPC for how to report adverse reactions.

Please consult with your local regulatory agency for any approved labeling in your country.
The drug information contained herein is intended to disclose corporate information. Nothing contained in this document should be considered a solicitation, promotion, or indication for any prescription drug, including those currently under development.

The CHMP's positive recommendation has no impact on the full year consolidated reported forecast for the fiscal year ending March 31, 2023 (Fiscal Year 2022).

Takeda will hold a TAK-003 Investor Event in December 2022 to provide more detail on commercial planning and updates on regulatory progress.

About Dengue
Dengue is a mosquito-borne viral disease that spreads rapidly around the world and was one of the WHO's top 10 threats to global health in 2019.[8] Dengue is mainly spread by Aedes aegypti mosquitoes and, to a lesser extent, Aedes albopictus mosquitoes.[1] It is caused by any of four dengue virus serotypes, each of which can cause dengue fever or severe dengue. The prevalence of individual serotypes varies across different geographies, countries, regions, seasons and over time.[2] Recovery from infection by one serotype provides lifelong immunity against only that serotype, and later exposure to any of the remaining serotypes is associated with an increased risk of severe disease.[1]

About TAK-003
Takeda's tetravalent dengue vaccine candidate (TAK-003) is based on a live-attenuated dengue serotype 2 virus, which provides the genetic "backbone" for all four vaccine viruses.[9] Clinical Phase 2 data in children and adolescents showed that TAK-003 induced immune responses against all four dengue serotypes, in both seropositive and seronegative participants, which persisted through 48 months after vaccination, and the vaccine was found to be generally safe and well tolerated.[10] The pivotal Phase 3 Tetravalent Immunization against Dengue Efficacy Study (TIDES) trial met its primary endpoint of overall vaccine efficacy (VE) against virologically-confirmed dengue (VCD) at 12-months follow-up and all secondary endpoints at 18-months follow-up for which there were a sufficient number of dengue cases, including VE against hospitalized dengue and VE in baseline seropositive and baseline seronegative individuals.[11,12] Efficacy varied by serotype. The results demonstrated TAK-003 was generally well tolerated, and there have been no important safety risks observed to date.

About EU-M4all[13]
EU-M4all (or EU-Medicines for all) is a procedure designed to facilitate patient access to essential medicines or vaccines intended to help prevent or treat diseases of major public health interest. Through the EU-M4all procedure (previously known as the Article 58 procedure), the EMA, in cooperation with the World Health Organization (WHO), can provide scientific opinion on medicines and vaccines for public health priority diseases that are intended for markets outside of the EU that have registered in the procedure.

About the Phase 3 TIDES (DEN-301) Trial
The double-blind, randomized, placebo-controlled Phase 3 Tetravalent Immunization against Dengue Efficacy Study (TIDES) trial is evaluating the safety and efficacy of two doses of TAK-003 in the prevention of laboratory-confirmed symptomatic dengue fever of any severity and due to any of the four dengue virus serotypes in children and adolescents. The TIDES trial is Takeda's largest interventional clinical trial to date and enrolled over 20,000 healthy children and adolescents ages four to 16 years living in dengue-endemic areas.[11] Study participants were randomized 2:1 to receive two doses of TAK-003 0.5 mL or placebo on Months 0 and 3, administered subcutaneously.[11] The study is comprised of five parts. Part 1 and the primary endpoint analysis evaluated vaccine efficacy (VE) and safety through 12 months after the second dose.[11] Part 2 continued for an additional six months to complete the assessment of the secondary endpoints of VE by serotype, baseline serostatus and disease severity, including VE against hospitalized dengue.[11] Part 3 evaluated VE and long-term safety by following participants for an additional two and a half to three years, as per WHO recommendations.[14] Part 4 will evaluate efficacy and safety for 13 months following booster vaccination and Part 5 will evaluate long-term efficacy and safety for one year after completion of Part 4.[14]

The trial is taking place at sites in dengue-endemic areas in Latin America (Brazil, Colombia, Panama, the Dominican Republic and Nicaragua) and Asia (Philippines, Thailand and Sri Lanka) where there are unmet needs in dengue prevention and where severe dengue is a leading cause of serious illness and death among children.[14] Baseline blood samples were collected from all individuals participating in the trial to allow for evaluation of safety and efficacy based on serostatus. Takeda and an independent Data Monitoring Committee of experts are actively monitoring safety on an ongoing basis.

Takeda's Commitment to Vaccines
Vaccines prevent 3.5 to 5 million deaths each year and have transformed global public health.[15] For more than 70 years, Takeda has supplied vaccines to protect the health of people in Japan. Today, Takeda's global vaccine business is applying innovation to tackle some of the world's most challenging infectious diseases, such as dengue, COVID-19, pandemic flu and Zika. Takeda's team brings an outstanding track record and a wealth of knowledge in vaccine development and manufacturing to advance a pipeline of vaccines to address some of the world's most pressing public health needs. For more information, visit www.Takeda.com/what-we-do/areas-of-focus/vaccines/.

About Takeda
Takeda is a global, values-based, R&D-driven biopharmaceutical leader headquartered in Japan, committed to discover and deliver life-transforming treatments, guided by our commitment to patients, our people and the planet. Takeda focuses its R&D efforts on four therapeutic areas: Oncology, Rare Genetics and Hematology, Neuroscience, and Gastroenterology (GI). We also make targeted R&D investments in Plasma-Derived Therapies and Vaccines. We are focusing on developing highly innovative medicines that contribute to making a difference in people's lives by advancing the frontier of new treatment options and leveraging our enhanced collaborative R&D engine and capabilities to create a robust, modality-diverse pipeline. Our employees are committed to improving quality of life for patients and to working with our partners in health care in approximately 80 countries and regions. For more information, visit https://www.takeda.com.

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The companies in which Takeda directly and indirectly owns investments are separate entities. In this press release, "Takeda" is sometimes used for convenience where references are made to Takeda and its subsidiaries in general. Likewise, the words "we", "us" and "our" are also used to refer to subsidiaries in general or to those who work for them. These expressions are also used where no useful purpose is served by identifying the particular company or companies.

Forward-Looking Statements
This press release and any materials distributed in connection with this press release may contain forward-looking statements, beliefs or opinions regarding Takeda's future business, future position and results of operations, including estimates, forecasts, targets and plans for Takeda. Without limitation, forward-looking statements often include words such as "targets", "plans", "believes", "hopes", "continues", "expects", "aims", "intends", "ensures", "will", "may", "should", "would", "could" "anticipates", "estimates", "projects" or similar expressions or the negative thereof. These forward-looking statements are based on assumptions about many important factors, including the following, which could cause actual results to differ materially from those expressed or implied by the forward-looking statements: the economic circumstances surrounding Takeda's global business, including general economic conditions in Japan and the United States; competitive pressures and developments; changes to applicable laws and regulations, including global health care reforms; challenges inherent in new product development, including uncertainty of clinical success and decisions of regulatory authorities and the timing thereof; uncertainty of commercial success for new and existing products; manufacturing difficulties or delays; fluctuations in interest and currency exchange rates; claims or concerns regarding the safety or efficacy of marketed products or product candidates; the impact of health crises, like the novel coronavirus pandemic, on Takeda and its customers and suppliers, including foreign governments in countries in which Takeda operates, or on other facets of its business; the timing and impact of post-merger integration efforts with acquired companies; the ability to divest assets that are not core to Takeda's operations and the timing of any such divestment(s); and other factors identified in Takeda's most recent Annual Report on Form 20-F and Takeda's other reports filed with the U.S. Securities and Exchange Commission, available on Takeda's website at: https://www.takeda.com/investors/sec-filings/ or at www.sec.gov. Takeda does not undertake to update any of the forward-looking statements contained in this press release or any other forward-looking statements it may make, except as required by law or stock exchange rule. Past performance is not an indicator of future results and the results or statements of Takeda in this press release may not be indicative of, and are not an estimate, forecast, guarantee or projection of Takeda's future results.

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