Better Health, Brighter Future

News Release

Takeda's QDENGA®▼ (Dengue Tetravalent Vaccine [Live, Attenuated]) Approved for Use in European Union

- ***The European Commission Approved QDENGA (TAK-003) for Use in Individuals Four Years of Age and Older***[i]
- ***QDENGA Becomes the Only Dengue Vaccine Approved in the EU for Use in Individuals Regardless of Previous Dengue Exposure***[i]

OSAKA, Japan, and CAMBRIDGE, Massachusetts, December 8, 2022 – Takeda **(TSE:4502/NYSE:TAK)** today announced that the European Commission (EC) granted marketing authorization for the company's dengue vaccine QDENGA® (Dengue Tetravalent Vaccine [Live, Attenuated]) (TAK-003) for the prevention of dengue disease in individuals from four years of age in the European Union (EU).[i] QDENGA should be used in accordance with official recommendations. The approval follows the positive recommendation from the European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP) in October 2022.

"With the increasing ease of travel today, our once expansive world has become that much smaller, increasing the risk of dengue disease for those living in dengue-endemic areas and for those traveling to these regions," said Gary Dubin, M.D., president of the Global Vaccine Business Unit at Takeda. "The European Commission's approval marks an important turning point for QDENGA as we are one step closer to achieving our aspiration to help reduce the global burden of dengue. We are proud to introduce QDENGA in many parts of the EU, offering healthcare providers a new tool in dengue prevention for their patients living in the EU and traveling to endemic regions around the world."

The worldwide incidence of dengue has risen eight-fold in the past 20 years, and it continues to rise, fueled by climate change and urbanization.[ii] Today, dengue threatens about half the world's population with a risk of infection in over 125 countries, and the disease is endemic in most of the European overseas countries, territories and departments located in tropical areas.[ii,iii] These factors have led to events of local transmission in non-endemic areas in continental Europe, including France, Italy, Germany and Spain.[iv] Dengue is a leading cause of fever in travelers returning to Europe from endemic countries, and the incidence of dengue among European travelers is generally underestimated.[v,vi] The threat of disease is present for more than 26 million people from Europe who typically travel to endemic regions each year for holidays and visiting friends and family.[vii]

"Effective dengue prevention requires a multi-faceted approach, and previous methods have been insufficient for a number of reasons. With the potential for dengue to cause local outbreaks as demonstrated in several European countries over recent years, and the threat for European travelers visiting dengue-endemic countries, gaps exist that may put some people at risk," said Dr. Tomas Jelinek, Medical Director of the Berlin Centre for Travel and Tropical Medicine and Scientific Director of the CRM Centrum für Reisemedizin Dusseldorf. "As a clinician, it is encouraging to have a new dengue vaccination tool available for a broad population of my patients."

Approval from the EC was supported by results across 19 Phase 1, 2 and 3 trials with more than 28,000 children and adults, including four and a half years of follow-up data from the global, pivotal Phase 3 Tetravalent Immunization against Dengue Efficacy Study (TIDES) trial. The TIDES trial met its primary endpoint of overall vaccine efficacy (VE) by preventing 80.2% of symptomatic dengue cases 12 months after vaccination.[viii] In addition, TAK-003 met its key

secondary endpoint by preventing 90.4% of hospitalizations 18 months after vaccination.[ix] Efficacy varied by serotype (DENV-1 – 4).[viii,ix] The TIDES exploratory analyses showed that throughout the 4.5-year 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.[x] TAK-003 has been generally well tolerated, with no evidence of disease enhancement in vaccine recipients, and no important safety risks have been identified, to date.[x]

QDENGA is also approved in Indonesia for the prevention of dengue disease by any serotype in individuals six years to 45 years of age. Takeda continues to progress regulatory filings in other dengue-endemic countries in Asia and Latin America.

The EC decision has no impact on the full year consolidated reported forecast for the fiscal year ending March 31, 2023 (Fiscal Year 2022).

About QDENGA
QDENGA (TAK-003) is a dengue vaccine that is based on a live-attenuated dengue serotype 2 virus, which provides the genetic "backbone" for all four dengue virus serotypes and is designed to protect against any of these serotypes.[xi]

In the European Union (EU) Member States, QDENGA is indicated for the prevention of dengue disease in individuals from four years of age and should be administered subcutaneously as a 0.5 mL dose at a two-dose (0 and 3 months) schedule pursuant to approved dosing regimen.[i] QDENGA should be used in accordance with official recommendations.

QDENGA was assessed across a clinical development program that included 19 Phase 1, Phase 2 and Phase 3 trials, and more than 28,000 participants, including Takeda's pivotal Tetravalent Immunization against Dengue Efficacy Study (TIDES) trial. The TIDES trial met its primary endpoint of overall vaccine efficacy (VE) against virologically-confirmed dengue (VCD) with 80.2% efficacy at 12-months follow-up.[viii] The trial also met all secondary endpoints for which there were a sufficient number of dengue cases at 18-months follow-up.[ix] The VE result in preventing hospitalization due to VCD fever was 90.4%.[ix] Through four and a half years (54 months after the second dose), QDENGA demonstrated continued overall protection, with sustained overall VE of 61.2% and 84.1% VE against hospitalized dengue.[x] Observations of VE varies by serotype and remained consistent with previously reported results.[x] QDENGA 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.[x]

Important Safety Information

Please consult the Summary of Product Characteristics (SmPC) before prescribing.

Guidance for use: QDENGA should be administered by subcutaneous injection preferably in the upper arm in the region of deltoid. QDENGA must not be injected intravascularly, intradermally or intramuscularly. Vaccination should be postponed in subjects suffering from an acute severe febrile illness. The presence of a minor infection, such as a cold, should not result in a deferral of vaccination. Vaccination should be preceded by a review of the individual's medical history (especially with regards to previous vaccination and possible hypersensitivity reactions which occurred after vaccination). Appropriate medical treatment and supervision must always be readily available in the event of a rare anaphylactic reaction following administration of the vaccine. Anxiety-related reactions, including vasovagal reactions (syncope), hyperventilation or stress-related reactions may occur in association with vaccination as a psychogenic response to the needle injection. It is important that precautions are in place to avoid injury from fainting. A protective immune response with Qdenga may not be elicited in all vaccinees against all serotypes of dengue virus and may decline over time. It is currently unknown whether a lack of protection could result in an increased severity of dengue. It is recommended to continue personal protection measures against mosquito bites after vaccination. Individuals should seek medical care if they develop dengue symptoms or dengue warning signs.

Contraindications: Hypersensitivity to the active substances or excipients listed, or to previous Qdenga dose. Individuals with congenital or acquired immune deficiency, including immunosuppressive therapies such as

chemotherapy or high doses of systemic corticosteroids (eg, 20 mg/day or 2 mg/kg body weight/day of prednisone for 2 weeks or more) within 4 weeks prior to vaccination. Individuals with symptomatic HIV infection or asymptomatic HIV infection with impaired immune function. Pregnant and breast-feeding women.

Adverse Reactions: Most frequently reported reactions in subjects 4 to 60 years of age were injection site pain (50%), headache (35%), myalgia (31%), injection site erythema (27%), malaise (24%), asthenia (20%), and fever (11%). Very common: (≥1/10 of subjects): upper respiratory tract infection[a], decreased appetite[c], irritability[c], headache, somnolence[c], myalgia, injection site pain, injection site erythema, malaise, asthenia, fever. Common (≥1/100 to <1/10): nasopharyngitis, pharyngotonsillitis[b], arthralgia, injection site swelling, injection site bruising[e], injection site pruritus[e], influenza like illness. [a]Includes upper respiratory tract infection and viral upper respiratory tract infection. [b]Includes pharyngotonsillitis and tonsillitis. [c]Collected in children below 6 years of age in clinical studies. [d]Includes rash, viral rash, rash maculopapular, and rash pruritic. [e]Reported in adults in clinical studies. **Refer to the SmPC for details on full side effect profile and interactions.**

▼ 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.

For full prescribing information, please see the Summary of Product Characteristics (SmPC) for QDENGA®▼.

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.

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.[ii,xii] Dengue is mainly spread by Aedes aegypti mosquitoes and, to a lesser extent, Aedes albopictus mosquitoes. It is caused by any of four dengue virus serotypes, each of which can cause dengue fever or severe dengue.[ii] The prevalence of individual serotypes varies across different geographies, countries, regions, seasons and over time.[xiii] 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.[ii]

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.[viii] 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.[viii] 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.[viii] 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.[viii] 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.[ix] 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.[xiv] 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.[xiv]

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.[xiv] 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.[xv] 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.

Medical information

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