QDENGA: TRANSFORMING DENGUE PREVENTION

Ramona Sequeira
President, Global Portfolio Division

Derek Wallace
Vice President, Head of Dengue Global Program

Guest Speaker:
Eng Eong Ooi
Professor, Programme in Emerging Infectious Diseases,
Duke-NUS Medical School

March 15, 2023 EST / March 16, 2023 JST
For the purposes of this notice, “presentation” means this document, any oral presentation, any question and answer session and any written or oral material discussed or distributed by Takeda Pharmaceutical Company Limited ("Takeda") regarding this presentation. This presentation (including any oral briefing and any question-and-answer in connection with it) is not intended to, and does not constitute, represent or form part of any offer, invitation or solicitation of any offer to purchase, otherwise acquire, subscribe for, exchange, sell or otherwise dispose of, any securities or the solicitation of any vote or approval in any jurisdiction. No shares or other securities are being offered to the public by means of this presentation. No offering of securities shall be made in the United States except pursuant to registration under the U.S. Securities Act of 1933, as amended, or an exemption therefrom. This presentation is being given (together with any further information which may be provided to the recipient) on the condition that it is for use by the recipient for information purposes only (and not for the evaluation of any investment, acquisition, disposal or any other transaction). Any failure to comply with these restrictions may constitute a violation of applicable securities laws.

The companies in which Takeda directly and indirectly owns investments are separate entities. In this presentation, "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.

The product names appearing in this document are trademarks or registered trademarks owned by Takeda, or their respective owners.

Forward-Looking Statements
This presentation and any materials distributed in connection with this presentation 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); the extent to which our internal energy conservation measures and future advancements in renewable energy or low carbon energy technology will enable us to reduce our greenhouse gas emissions; 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 presentation 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 presentation may not be indicative of, and are not an estimate, forecast, guarantee or projection of Takeda's future results.

Financial Information and Certain Non-IFRS Financial Measures
Takeda's financial statements are prepared in accordance with International Financial Reporting Standards ("IFRS").

This presentation and materials distributed in connection with this presentation include certain financial measures not presented in accordance with IFRS, such as Core Revenue, Core Operating Profit, Core Net Profit, Core EPS, Constant Exchange Rate ("CER") change, Net Debt, EBITDA, Adjusted EBITDA and Free Cash Flow. Takeda's management evaluates results and makes operating and investment decisions using both IFRS and non-IFRS measures included in this presentation. These non-IFRS measures exclude certain income, cost and cash flow items which are included in, or are calculated differently from, the IFRS financial measures, which are in the financial appendix appearing at the end of this presentation.

Exchange Rates
In this presentation, certain amounts presented in Japanese yen have been translated to US dollars solely for the convenience of the reader. Except where otherwise noted, these convenience translations have been made at an exchange rate of 1USD = 131.81 JPY, the Noon Buying Rate certified by the Federal Reserve Bank of New York on December 30, 2022. The rate and methodologies used for these convenience translations differ from the currency exchange rates and translation methodologies under IFRS used for the preparation of Takeda's consolidated financial statements. These translations should not be construed as a representation that the relevant Japanese yen amounts could be converted into U.S. dollars at this or any other rate.

Medical information
This presentation contains information about products that may not be available in all countries, or may be available under different trademarks, for different indications, in different dosages, or in different strengths. Nothing contained herein should be considered a solicitation, promotion or advertisement for any prescription drugs including the ones under development.
TODAY’S SPEAKERS

Presenting

Ramona Sequeira
President,
Global Portfolio Division

Derek Wallace
Vice President,
Head of Dengue Global Program

Gary Dubin
President,
Global Vaccines Business Unit

Renata Campos
President,
Growth and Emerging Markets Business Unit

Joining by Special Guest

Eng Eong Ooi
Professor,
Programme in Emerging Infectious Diseases,
Duke-NUS Medical School
DENGUE – TOP 10 THREAT TO GLOBAL PUBLIC HEALTH

Ramona Sequeira – President, Global Portfolio Division
DENGUE IS LISTED BY THE WORLD HEALTH ORGANIZATION AS ONE OF TEN THREATS TO GLOBAL HEALTH

>3.9 Billion
people are at risk of
dengue infection globally

Endemic in over
125 countries; 70% of the
burden in Asia

390M estimated infections and
500,000 hospitalizations each
year, with an estimated death
rate of 20-25,000 per year,
primarily in children

Growing prevalence

Global incidence rates have
increased 30-fold over the last
50 years due to urbanization,
travel and climate change

>125

Severe dengue is a leading cause of hospitalization and death in children and adults of all ages in endemic regions, resulting in a high burden on healthcare systems

Significant economic burden of disease; families in endemic regions may spend 15-23% of monthly household income for hospitalizations

Urgent need for a safe and effective vaccine for endemic and travel markets

Dengue is a leading cause of fever among travelers returning from Latin America, the Caribbean & Southeast Asia

More than 90 million arrivals from the United States, Canada and Europe to dengue endemic countries in 2018

QDENG A STRATEGIC LAUNCH IMPERATIVES

Create awareness of the health and economic risks associated with dengue for consumers living or traveling to endemic regions

Build confidence with regulators, recommending bodies, HCPs and consumers by leveraging strong clinical profile

Establish rapid and broad access at an individual- and population-level

Ensure launch preparedness through increased manufacturing capacity, established supply network and proven global commercial capabilities
TODAY’S AGENDA

Dengue Burden and Control – Eng Eong Ooi BMBS, PhD, FRCPath Professor Programme in Emerging Infectious Diseases, Duke NUS Medical School. Singapore

QDENGA Program and Clinical Results – Derek Wallace

QDENGA Commercial Outlook – Ramona Sequeira

Q&A – Ramona Sequeira, Derek Wallace, Gary Dubin, Renata Campos and Eng Eong Ooi
Dengue burden and control
Why the world needs a vaccine

Eng Eong Ooi BMBS, PhD, FRCPath
Professor
Programme in Emerging Infectious Diseases
THE GLOBAL BURDEN OF DENGUE

- More than 4 billion people are at risk and estimated 390 million infections per year\(^1\)

- 30 times increase in disease over the past 50 years\(^2\)

Driven by

- Urbanization
- Global warming
- Increased global travel

More mosquitos
More mosquito / people contact

- By 2080, more than 6 billion people are estimated to be at risk\(^3\)

---

DENGUE SYMPTOMS AND PRESENTATION VARIES

Most dengue infections are asymptomatic or lead to mild illness with flu-like symptoms. Severe dengue is present in 5% of cases. High plasma viral load and NS1 levels have been associated with plasma leakage, a hallmark of severe dengue.

3. Wilder-Smith A. Current Infectious Disease Reports. 2018;20:50
4. Clinical Infectious Diseases, Volume 72, Issue 12, 15 June 2021, Pages e1074-e1083, https://doi.org/10.1093/cid/ciaa1840
RISK OF SEVERE DENGUE PEAKS WITHIN A NARROW RANGE OF PRE-INFECTION ANTIBODY LEVELS

1. Salje et al, Nature 2018
DENGUE TYPES 1 AND 2 CAUSE MAJORITY OF OUTBREAKS

Four strains of the dengue virus (DENV) 1-4 are spread by the *Aedes aegypti* and *Aedes albopictus* mosquitoes worldwide.

In recent years, **DENV-1 and DENV-2 have emerged as the most prominent strains associated with known outbreaks**¹

- According to empirical data, the highest pooled mortality rate has been reported during DENV-2 outbreaks¹

- Studies have also shown that DENV-2 causes more severe secondary infections than other serotypes¹

---

Dengue outbreaks occur every few years\textsuperscript{1}

Hospitals can become overwhelmed with the spike in cases\textsuperscript{2}

Current efforts for dengue control are directed at reducing infection rate through vector control methods.

In the medium to long term, this could cause lower population immunity and make them more susceptible to dengue outbreaks.

Elevating immunity levels with vaccination is the missing link in integrated dengue control.

1. Data from Ministry of Health, Singapore
   Adapted from Ooi et al, Emerg Infect Dis 2006
DEVELOPING SAFE AND EFFECTIVE VACCINE FOR A BROAD POPULATION

Derek Wallace, MBBS – Head of Dengue Global Program
DENGUE VIRUS INFECTIONS HAVE A DISTINCT PATHOPHYSIOLOGY

Severe disease, although rare, is unpredictable and typically affects children¹,²

Severe dengue infections are characterized by vascular leakage associated with a high risk of hospitalization and mortality²

- Dengue virus non-structural (NS) protein 1 can trigger vascular leakage
- NS1 protein is highly conserved across the four dengue serotypes
- No specific treatment options exist to manage vascular leakage

Potential for disease enhancement²

- After an initial infection, a subsequent infection with a different serotype can lead to more severe outcomes
- There is no method of predicting or preventing disease enhancement in patients

¹ An estimated 1 in 4 dengue virus infections are symptomatic. Symptomatic dengue virus infection most commonly presents as a mild to moderate, nonspecific, acute febrile illness. Approximately 1 in 20 patients with dengue virus disease progress to develop severe, life-threatening disease called severe dengue.

QDENGGA: ENGINEERED TO ELICIT A BROAD AND LASTING IMMUNE RESPONSE AGAINST ALL DENGUE SEROTYPES

Tetravalent QDENGGA was engineered:

1. To contain the structural genes of serotypes 1 to 4

2. Built on a dengue virus serotype 2 backbone containing dengue virus non-structural genes, including NS-1 protein

QDENGGA VACCINATION HYPOTHESIS

Activation of....

With the objective of....

Antibodies against structural proteins for serotypes 1-4

Efficiently blocking infection with wildtype virus of all serotypes

Antibodies against NS proteins cross-reactive against all NS serotypes

Reducing risk for severe dengue by preventing vascular leakage induced by NS1 protein

T- and B-cells reactive against dengue antigens

Support long-term immunity against dengue infections with different serotypes

WITH THE GOAL TO DEMONSTRATE....

Reduction in Symptomatic Dengue

Reduction in Hospitalizations

Sustained Protection Against All Serotypes

Reduction in symptomatic dengue

Reduction in hospitalizations

Sustained protection against all serotypes
PHASE 3 TIDES TRIAL DESIGNED TO ASSESS THE SAFETY AND EFFICACY OF TAK-003 IN BROAD POPULATION

Trial design met WHO recommendations for a second-generation dengue vaccine – 3-5 years of follow-up prior to licensure

Participants stratified by serostatus

Primary endpoint – prevention of symptomatic dengue cases @ 12mo

Key secondary endpoint – reduction in hospitalizations @ 18mo

Exploratory endpoint – sustained preventions of symptomatic dengue and reduction in hospitalization @ 4.5yrs

1. Serostatus – is whether a patient has had a prior infection or not.
2. Sero-positive (earlier exposure to dengue) and sero-negative (not exposed before)
SUSTAINED PROTECTION AGAINST ALL DENGUE SEROTYPES & LOWER RISK OF HOSPITALIZATION REGARDLESS OF PREVIOUS EXPOSURE

Strong efficacy across all endpoints

Reduction in symptomatic VCD & hospitalizations regardless of previous exposure

- 80.2% reduction in symptomatic VCD @ 12mo (primary endpoint)
- 90.4% reduction in hospitalizations @ 18mos (secondary endpoint)

No important identified safety risks

- No evidence of disease enhancement
- Well tolerated
- Most frequently reported reactions were common to vaccines, including injection site pain, headache, myalgia, injection site erythema, malaise, asthenia and fever

Durable Reduction in Hospitalizations @ 4.5 yrs (exploratory endpoint)

- 84% reduction in hospitalizations @ 4.5 yrs

Cumulative incidence of participants with hospitalised VCD, %

Time Since First Vaccination, Months

Placebo, seropositive
Placebo, seronegative
TAK-003, seropositive
TAK-003, seronegative

3 Tricou, V. Efficacy and Safety of Takeda's Tetravalent Dengue Vaccine Candidate (TAK-003) After 4.5 Years of Follow-Up. Presented at the 8th Northern European Conference of Travel Medicine; June 2022.

VCD – Virologically confirmed dengue
SIGNIFICANT REGULATORY MOMENTUM: QDENGA APPROVED WITH BROAD LABEL REGARDLESS OF SEROSTATUS

Approved in Indonesia¹ for ages 6-45

August 2022

EU-M4all application receives Positive CHMP opinion

October 2022

US FDA accepts filing

November 2022

Approved in EU² for ages 4 and up

December 2022

Approved in Brazil for ages 4 - 60³

2023

Ongoing regulatory reviews in several endemic countries & travel markets

---


QDENGA is approved in Indonesia, EU, UK, Norway, Iceland, Lichtenstein, Brazil

**QDENG A STRATEGIC LAUNCH IMPERATIVES**

- **Create awareness** of the health and economic risks associated with dengue for consumers living or traveling to endemic regions

- **Build confidence** with regulators, recommending bodies, HCPs and consumers by leveraging strong clinical profile

- **Establish rapid and broad access** at an individual- and population-level

- **Ensure launch preparedness** through increased manufacturing capacity, established supply network and proven global commercial capabilities
COUNTRY-LEVEL ACTIVATION OF STRATEGIC IMPERATIVES INITIATED AHEAD OF EXPECTED APPROVALS

Driving consumer awareness of dengue risk and prevalence in THAILAND

- 70M+ people in country

Public Education Partnerships
- Partnering with 11 entities to raise public awareness
- Ing-Ma virtual human video campaign launched: >35 million views
- Partnership with Kao Thailand, top consumer brand

Establishing trust in dengue prevention in BRAZIL

- 200M+ people in country

Consumer Engagement Initiatives
- UNICEF partnership to educate 90,000 people to reduce the transmission of water and vector borne infectious diseases
- Dengue prevention social media campaign

Building a dengue travel business in NON-ENDEMIC COUNTRIES

- 90M+ arrivals from the US, CA & EU*

Critical External Engagements
- Partnership with leading travel immunization clinics and HCPs
- Ongoing engagements with CDC ACIP dengue working group

ESTABLISH RAPID AND BROAD ACCESS AT AN INDIVIDUAL- AND POPULATION-LEVEL - BRAZIL

Steps to broaden access happen in parallel, volume increases with each step as we work towards launch of NIP

- Initially available to consumers paying out-of-pocket
- Partnering with large corporations to vaccinate their employees
- Engaging at a state and municipal level to implement decentralized government programs prior to NIP launch
- Initiation of National Immunization programs (NIP)

Time to program implementation

# of people vaccinated
## VARIABLE PRICING APPROACH TO MEET THE NEEDS OF INDIVIDUAL COUNTRIES & MARKET SEGMENTS

We aim to make **QDENGA available to all who are eligible for vaccination** in the countries where approved.

### PRIVATE ENDEMIC
- Pricing at or below the average price for other innovative vaccines
- Tiered pricing corridors based on factors such as GDP & sophistication of healthcare system.

Maximum retail price for Indonesia is $40 USD\(^6\) per dose\(^1\), $26 USD\(^6\) ex-factory

Average price for innovative vaccines in Indonesia is $73 USD\(^6\) per dose\(^2,3\)

### PUBLIC ENDEMIC
- Aim to price lower than average for innovative vaccines.
- One pricing corridor and a discount matrix.

Ensures affordability for all.

### TRAVEL
- Pricing similar to other innovative travel vaccines in their respective countries.

Retail price in Germany $115 USD\(^7\) per dose\(^1\), $80 USD\(^7\) ex-factory

Average price for innovative vaccines in Germany is $119 USD\(^7\) per dose\(^2,4\)

---

Implementation of QDENGA has the potential to create **significant cost savings** for individuals and governments taking into account economic factors such as: cost of care, missed work, lost tourism, etc\(^5\)

---

1. Two-dose series
2. Dosing regimens vary by vaccine
3. The average retail price obtained based on market survey (printed price on the box) and validated with IQVIA/IPMA data
4. Basket of licensed innovative vaccines in travel markets (unweighted average used for comparison)
6. 15117.87 IDR/USD
7. 1.0199 EUR/USD
LAUNCH READY: ESTABLISHED MANUFACTURING & SUPPLY CHAIN AND LEVERAGING BROAD GLOBAL FOOTPRINT

Manufacturing capacity in place for launch and investing to expand for growth

- Early investments to established in-house manufacturing for launch
- Aim to achieve **100 mill doses per year** through in-house and strategic CMO partnerships

Well-established distribution network

- Cold chain distribution partner has broad global network.
- Existing distribution networks and commercial infrastructure in the initial launch markets

Proven track record in Growth & Emerging Markets (GEM)

- **150 successful commercial launches** since 2019
- **14.5% FY2022 Q3YTD revenue growth YoY at CER**
GLOBAL EXPANSION THROUGH THE END OF THE DECADE

Target launches in >20 countries by 2025, representing 55% of eligible at-risk population

Leveraging EU-M4all review process to potentially accelerate approvals in participating endemic markets

Indonesia, Malaysia, Thailand, Colombia, Brazil, Mexico, Singapore, Sri Lanka, Argentina, US, EU

China, India, Cuba, Honduras, Venezuela, additional PAHO countries, GAVI**

NEAR-TERM

FY22-FY24

Significant regulatory progress
Initiating launches where approved

FY25-FY27*

Canada, Israel, Ecuador, Guatemala, Paraguay, Peru, Costa Rica, El Salvador, Panama, Nicaragua, Dom. Rep., Philippines, Hong Kong, Australia, Vietnam

MID-TERM

FY28-FY30

LONG TERM

FY30+

*Anticipated access via PAHO
**assuming dengue is incorporated in Gavi Vaccine Investment Strategy
STEADY REVENUE GROWTH THROUGH THE END OF THE DECADE

$1.6 - 2.0B
Peak sales

Strong Clinical Profile - 4.5-yr data demonstrating durable reduction in hospitalization and no important safety signals consistent with 1° & 2° endpoints

Momentum with regulators – Brazil, Indonesia & EU approvals with broad labels, regardless of serostatus

Expanding manufacturing capacity with aim to achieve annual output 100M+ doses
  • Continuing to add to in-house capacity and manufacturing efficiencies
  • Contracting for additional capacity with CMOs; actively exploring potential partners in India and other large endemic markets

Previous peak sales estimate of $700M - $1.6B was based on:

- 24-month data – prior to the 4.5-year data readout
- Manufacturing assumptions of 50M+ doses annually
SUMMARY OF QDENGTA COMMERCIAL OUTLOOK

Near-term: Drive Early Adoption

- Launch into key endemic and travel markets – leveraging strong clinical profile
- Establish rapid access – Private segment/local partnerships
- Ensure affordability through variable pricing approach

Mid-term: Accelerate Volume Growth

- Initiation of national vaccination programs will drive volume
- Recognize economies of scale to reduce CoGS as volume grows

Long-term: Durable Sales Post Peak

- Continued global expansion into the next decade
- Ensure new generations are being vaccinated
- Durable sales post peak – Vaccines face limited generic threats due to high barriers to entry
Significant, Growing Global Burden

• >3.9 billion people at risk of infection¹
• Growing prevalence – increasing 30-fold over the last 50yrs²
• Significant economic burden of disease both at the government, healthcare systems and patient level³⁴

Differentiated Clinical Profile₅

• Demonstrated strong safety and efficacy against all dengue serotypes regardless of previous exposure
• Durable reduction in hospitalizations – 84% reduction @ 4.5yrs
• No important safety risks identified

Delivering Steady Revenue Growth Through the End of the Decade

• Peak sales expected to grow to $1.6 - 2.0B USD
• Innovative access strategy to drive rapid and broad access
• Established manufacturing, supply chain and global footprint to ensure launch readiness

5. 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. The trial also met all secondary endpoints for which there was sufficient number of dengue cases at 18 months follow-up. The VE result in preventing hospitalization due to VCD fever was 90.4%. Through year 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. Observations of VE varied by serotype and remained consistent with previously reported results. 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.
THANK YOU