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News Release

Takeda's ADZYNMA (ADAMTS13, recombinant-krhn) Approved by U.S. FDA as the First and Only Recombinant ADAMTS13 Enzyme Replacement Therapy for the Treatment of Congenital Thrombotic Thrombocytopenic Purpura (cTTP)

- ***cTTP is an Ultra-rare Blood Clotting Disorder Associated with Life-Threatening Acute Events and Debilitating Chronic Symptoms***
- ***Takeda Continues 70-plus Year Legacy of Driving Innovation for the Rare Hematology Community***

OSAKA, Japan, and CAMBRIDGE, Massachusetts, November 9, 2023 – Takeda ***(*****TSE:4502/NYSE:TAK)** today announced that the U.S. Food and Drug Administration (FDA) has approved ADZYNMA (ADAMTS13, recombinant-krhn) for the prophylactic and on-demand treatment of adult and pediatric patients with congenital thrombotic thrombocytopenic purpura (cTTP). ADZYNMA is the first and only FDA-approved recombinant ADAMTS13 (rADAMTS13) protein designed to address an unmet medical need in people with cTTP by replacing the deficient ADAMTS13 enzyme.[1,2]

"People living with cTTP face serious, life-threatening health challenges, and until today, were without any approved treatment specifically indicated for their disease," said Julie Kim, president, U.S. Business Unit and U.S. country head at Takeda. "As we strive to help patients with limited or no treatment options, developing innovative treatments in rare diseases is an inspiring challenge and one we have taken on for 70-plus years as a leader in hematology. Today, we are proud to further support the rare disease community by delivering ADZYNMA as the first FDA-approved therapeutic option for people with cTTP."

cTTP is an ultra-rare, chronic blood clotting disorder caused by a deficiency in the ADAMTS13 enzyme.[3] It is associated with acute events and debilitating chronic symptoms or thrombotic thrombocytopenic purpura (TTP) manifestations, which can include thrombocytopenia, microangiopathic hemolytic anemia, headache and abdominal pain.[3,4,5] When left untreated, acute TTP events have a mortality rate of >90%.[3,5]

"In recent decades, significant progress has been made to better understand the link between ADAMTS13 deficiency and cTTP, ultimately leading to this moment where we finally have an FDA-approved treatment option for patients living with this rare disease," said Spero R. Cataland, M.D., professor of internal medicine at the Wexner Medical Center at The Ohio State University, co-director at the U.S. Thrombotic Microangiopathy Alliance (USTMA) and ADZYNMA clinical trial investigator. "ADZYNMA provides patients with a treatment option that replaces their deficient ADAMTS13 enzyme and offers a favorable efficacy and safety profile and reduced administration time and volume compared to current plasma-based therapies. Today marks a significant achievement, providing new possibilities for the cTTP patient community."

The FDA approval of ADZYNMA was supported by the totality of the evidence provided by the analysis of efficacy, pharmacokinetic, safety and tolerability data from the first randomized, controlled, open-label, crossover Phase 3 trial in cTTP as well as by data from the continuation trial. In the Phase 3 trial, patients received 40 IU/kg ADZYNMA IV or plasma-based therapy every other week or weekly based on regimen at enrollment for months 1-6 (period 1), crossing over to the alternate treatment for months 7-12 (period 2), and all patients received ADZYNMA for months 13-18 (period 3).[1]

No patient experienced an acute TTP event while receiving ADZYNMA prophylactic treatment (n=37), while there was one acute TTP event in a patient receiving plasma-based therapies (n=38).[1] No subacute TTP events were reported in patients receiving ADZYNMA during the Phase 3 study-controlled comparison periods 1 and 2, compared to five subacute TTP events in four patients receiving plasma-based therapies. In the continuation period (period 3), two patients receiving ADZYNMA prophylaxis had two subacute events.[1]

The mean annualized event rate (SD) of thrombocytopenia manifestations was 2.0 (4.706) for patients receiving ADZYNMA (9/37 patients experienced a manifestation) compared to 4.44 (6.312) in patients receiving plasma-based therapies (19/38 patients experienced a manifestation).[1] While the clinical significance of the comparison is unknown, thrombocytopenia is a manifestation of TTP, and as such is an important biomarker of disease activity.

ADZYNMA is a recombinant form of the ADAMTS13 protein. In a pharmacokinetic assessment, patients receiving 40 IU/kg ADZYNMA IV (n=23) achieved a four- to five-fold increase in ADAMTS13 activity following a single infusion compared to plasma-based therapies.[1]

ADZYNMA demonstrated a favorable safety profile compared to plasma-based therapies. The most common adverse reactions (incidence >5%) were headache, diarrhea, migraine, abdominal pain, nausea, upper respiratory tract infection, dizziness and vomiting.[1] [1]No patients receiving ADZYNMA developed neutralizing antibodies.[1]

This approval does not result in any changes to Takeda's consolidated forecast for the fiscal year ending March 31, 2024 (FY2023).

ABOUT ADZYNMA

ADZYNMA (ADAMTS13, recombinant-krhn) is a human recombinant "A disintegrin and metalloproteinase with thrombospondin motifs 13" ADAMTS13 (rADAMTS13) indicated for prophylactic or on-demand enzyme replacement therapy (ERT) in adult and pediatric patients with congenital thrombotic thrombocytopenic purpura (cTTP).[1]

ADZYNMA was previously granted Orphan Drug Designation (ODD) by the U.S. FDA for the treatment and prevention of TTP, including its acquired idiopathic and secondary forms, as well as Fast Track and Rare Pediatric Disease Designation. The U.S. FDA granted Takeda a Rare Pediatric Disease Voucher for the approval of ADZYNMA. ADZYNMA has also been granted ODD by the European Medicines Agency (EMA) and Japan's Ministry of Health, Labour and Welfare (MHLW) for the treatment of TTP.

Important Safety Information

ADZYNMA is contraindicated in patients who have experienced life-threatening hypersensitivity reactions to ADZYNMA or its components.

Hypersensitivity Reactions: Allergic-type hypersensitivity, including anaphylactic reactions, may occur with ADZYNMA. Patients should be educated about early signs of hypersensitivity such as tachycardia, chest tightness, wheezing and/or acute respiratory distress, hypotension, generalized urticaria, pruritus, rhinoconjunctivitis, angioedema, lethargy, nausea, vomiting, paresthesia, and restlessness. If signs and symptoms of severe allergic reactions occur, immediately discontinue administration of ADZYNMA and provide appropriate supportive care.

Immunogenicity: There is a potential for immunogenicity with ADZYNMA. Patients may develop neutralizing antibodies to ADAMTS13, which could potentially result in a decreased or lack of response to ADAMTS13. Patients may develop antibodies to host cell proteins which could potentially result in adverse reactions. There are no data on immunogenicity with ADZYNMA or to host cell proteins in previously untreated patients (subjects naïve to plasma-based products).

Adverse Reactions: The most commonly observed adverse reactions (>5% of subjects) associated with ADZYNMA are headache, diarrhea, migraine, abdominal pain, nausea, upper respiratory tract infection, dizziness and vomiting.

Use in Specific Populations: The safety of ADZYNMA for use during pregnancy has not been established in controlled clinical trials. Limited data are insufficient to inform a drug associated risk of adverse developmental outcomes. There is no information regarding the presence of ADZYNMA in human milk, its effects on milk production, or the breastfed infant.

To report SUSPECTED ADVERSE REACTIONS, contact Takeda Pharmaceuticals U.S.A, Inc. at 1-877-TAKEDA-7 (1-877-825-3327) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see full Prescribing Information, including information for patients.

ABOUT cTTP

cTTP is an ultra-rare, chronic and debilitating clotting disorder associated with life-threatening acute events and debilitating chronic symptoms, or TTP manifestations.[6,7] TTP has an estimated prevalence of 2-6 cases/million. The inherited form of the disease, cTTP, accounts for ≤5% of TTP patients.[7,8,9] It develops due to deficiency in ADAMTS13, a von Willebrand factor (VWF) cleaving protease, which results in the accumulation of ultra-large VWF multimers in the blood.[6] The accumulation of ultra-large VWF multimers leads to uncontrolled platelet aggregation and adhesion.[4,7] This can lead to abnormal clotting in the small blood vessels of the body and is associated with microangiopathic hemolytic anemia and low platelet levels (thrombocytopenia).[4]

cTTP has both acute and chronic manifestations (including stroke and cardiovascular disease) and when left untreated, acute TTP events have a mortality rate of >90%.[3,10] cTTP can also cause ongoing widespread organ damage and other co-morbidities resulting from an ADAMTS13-deficient state.[5,7,10,11]

About Takeda

Takeda is focused on creating better health for people and a brighter future for the world. We aim to discover and deliver life-transforming treatments in our core therapeutic and business areas, including gastrointestinal and inflammation, rare diseases, plasma-derived therapies, oncology, neuroscience and vaccines. Together with our partners, we aim to improve the patient experience and advance a new frontier of treatment options through our dynamic and diverse pipeline. As a leading values-based, R&D-driven biopharmaceutical company headquartered in Japan, we are guided by our commitment to patients, our people and the planet. Our employees in approximately 80 countries and regions are driven by our purpose and are grounded in the values that have defined us for more than two centuries. For more information, visit www.takeda.com.

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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

This press release 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.

ADZYNMA is a trademark of Takeda Pharmaceuticals International AG.

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