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News Release

U.S. Food & Drug Administration Grants Priority Review of TAK-755 for the Treatment of Congenital Thrombotic Thrombocytopenic Purpura (cTTP)

- ***Submission Based on Favorable Results from the First Phase 3 Randomized, Controlled Trial in Patients with cTTP***
- ***FDA has Granted TAK-755 Priority Review and Rare Pediatric Disease Designation, as well as Fast Track Designation and Orphan Drug Designation in cTTP***

OSAKA, Japan, and CAMBRIDGE, Massachusetts, May 16, 2023 – Takeda (TSE: 4502/NYSE:TAK) today announced that the U.S. Food and Drug Administration (FDA) has accepted Takeda's Biologics License Application (BLA) for TAK-755, an enzyme replacement therapy for the treatment of congenital thrombotic thrombocytopenic purpura (cTTP), an ADAMTS13 deficiency disorder. The TAK-755 application was accepted by the FDA on May 16th, and has been granted Priority Review.

FDA has also granted TAK-755 Rare Pediatric Disease (RPD) designation for cTTP. TAK-755 has previously received Fast Track Designation and Orphan Drug Designation in cTTP.

If approved, TAK-755 would be the first and only recombinant ADAMTS13 (rADAMTS13) replacement therapy for cTTP, a disorder with considerable unmet patient need.

cTTP is an ultra-rare inherited form of thrombotic thrombocytopenic purpura (TTP), a chronic and debilitating clotting disorder caused by a deficiency in ADAMTS13 protease.[1,2] Acute TTP has a mortality rate of >90%, if left untreated.[3]

"There is a critical need for treatment options for people living with cTTP, an ultra-rare, life-threatening disorder that has no therapies specifically approved for prophylactic treatment," said Daniel Curran, M.D., Head, Rare Genetics & Hematology Therapeutic Area Unit at Takeda. "TAK-755 is the first and only treatment in clinical development that provides targeted replacement of ADAMTS13, addressing the underlying cause of the disease. We continue to be encouraged by the data and are working closely with the U.S. FDA and other global regulatory bodies with the goal to bring this treatment to patients."

The BLA is supported by the totality of the evidence provided by efficacy, pharmacokinetic, safety and tolerability data from the first randomized, controlled trial in cTTP, and supported by long-term safety and efficacy data from a continuation study. The Phase 3 trial was designed to evaluate the clinical benefit of TAK-755 across multiple clinically relevant endpoints, compared to plasma-based therapies, in a randomized cross-over study. The interim results, announced by Takeda in January 2023, showed that TAK-755 reduced the incidence of thrombocytopenia events by 60% (95% Confidence Interval, 30%-70%), an important marker of disease activity in cTTP, as compared to plasma-based therapy. The proportion of subjects experiencing adverse events determined to be related to the treatment was substantially lower among subjects during treatment with TAK-755 (8.9%) compared to plasma-based therapies (47.7%). The interim analysis of the Phase 3 results will be presented at an upcoming scientific meeting.

Takeda is also investigating the safety, efficacy and pharmacokinetics of TAK-755 treatment in immune-mediated TTP (iTTP) in an ongoing Phase 2b study.[4]

BLA acceptance by the U.S. FDA has no impact on the full year consolidated reported forecast for the fiscal year ending March 31, 2024 (Fiscal Year 2023).

ABOUT TAK-755

TAK-755 is the first and only recombinant ADAMTS13 protein in development. It provides targeted therapy to address an unmet medical need in patients with thrombotic thrombocytopenic purpura (TTP), by replacing the missing or deficient ADAMTS13 enzyme.[5]

The TAK-755 cTTP clinical development program includes one first-in-human, Phase 1 study, 281101 (NCT02216084),[6] and two Phase 3 studies: a pivotal Phase 3 study, Study 281102 (NCT03393975), and one Phase 3b continuation study, Study TAK-755-3002 (NCT04683003)[7,8] TAK-755 is also being investigated in immune-mediated TTP (iTTP) and sickle cell disease, with Phase 2b (NCT05714969) and Phase 1 (NCT03997760) trials ongoing, respectively.[4,9]

TAK-755 was granted Orphan Drug Designation (ODD) by the U.S. Food and Drug Administration (FDA) for the treatment (ODA-08-2622) and prevention (ODA-08-2652) of TTP including its congenital, acquired idiopathic and secondary forms; and by the European Medicines Agency (EMA) and Japan's Ministry of Health, Labour and Welfare (MHLW) for the treatment of TTP (EU/3/08/588). The FDA has also granted TAK-755 Rare Pediatric Disease Designation for the treatment of cTTP, as well as Fast Track Designation (FTD) for the treatment, prevention, and routine prophylaxis of acute episodes of TTP in patients with hereditary (congenital) ADAMTS13 deficiency.

ABOUT cTTP

cTTP is an ultra-rare, chronic, and debilitating clotting disorder associated with life-threatening acute episodes and debilitating chronic symptoms.[1,10] cTTP is a inherited form of TTP that has an estimated prevalence of 2-6 cases/million,[11] with cTTP accounting for ≤5% of patients with TTP.[12,13] 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.[1] The accumulation of ultra-large VWF multimers leads to uncontrolled platelet aggregation and adhesion.[10,14] This can lead to abnormal clotting in the small blood vessels of the body and is associated with hemolytic anemia and low platelet levels (thrombocytopenia).[14]

cTTP has both acute and chronic manifestations (including stroke and cardiovascular disease) and is associated with a significant disease burden. Patients' quality of life and lifespan are significantly reduced compared to the general population, due to serious, ongoing widespread organ damage and other co-morbidities resulting from an ADAMTS13-deficient state.[10, 11,12,15] rADAMTS13 is a novel investigational therapeutic approach for cTTP.[16]

There are no medications specifically approved by regulatory authorities for routine prophylactic treatment of cTTP. Current treatment centers around plasma therapy, either by infusion or plasma exchange.[17] Plasma therapy is time consuming and can be associated with severe treatment complications[11,17,18]. These can include treatment-limiting volume overload and allergic reactions.[17,18]

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 disease, 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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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.

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