Better Health, Brighter Future

News Release

Takeda Announces Favorable Phase 3 Safety and Efficacy Results of TAK-755 as Compared to Standard of Care in Congenital Thrombotic Thrombocytopenic Purpura (cTTP)

- ***Results are From First and Only Phase 3 Trial in cTTP, an Ultra-Rare Disease with Limited Treatment Options***
- ***cTTP is Caused by a Deficiency in ADAMTS13 Protease;[1] TAK-755 Is Designed to Replace Missing or Deficient ADAMTS13 Enzyme[2]***
- ***Takeda Plans to Seek Marketing Authorization for TAK-755 as the First ADAMTS13 Replacement Therapy for the Treatment of cTTP***

OSAKA, Japan, and CAMBRIDGE, Massachusetts, January 5, 2023 – Takeda (TSE:4502/NYSE:TAK) today announced that the totality of evidence from a pre-planned interim analysis of a pivotal Phase 3 study supports the efficacy and safety of TAK-755 as enzyme replacement therapy for congenital thrombotic thrombocytopenic purpura (cTTP). cTTP is an ultra-rare sub-type of thrombotic thrombocytopenic purpura (TTP), a rare, chronic and debilitating blood clotting disorder caused by a deficiency in ADAMTS13 protease.[1,3] Acute TTP has a mortality rate of >90%, if left untreated.[4]

The trial was designed to evaluate the clinical benefit of TAK-755 across multiple clinically relevant endpoints and based on the totality of the evidence provided by efficacy, pharmacokinetic, safety and tolerability data.[5] This approach was discussed with global regulatory agencies. The study evaluated TAK-755 compared to plasma-based therapies, which are the current standard of care (SoC), in a randomized cross-over study. The interim results 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 SoC. 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 that while receiving SoC therapy (47.7%).

Based on these data from the Phase 3 interim analysis, Takeda aims to seek marketing authorization for TAK-755 as the first recombinant ADAMTS13 (rADAMTS13) replacement therapy for cTTP, a disorder with considerable unmet patient need.

“We are committed to advancing treatment options for those living with cTTP, who currently have no therapies approved specifically to manage their condition,” said Daniel Curran, M.D., Head, Rare Genetics & Hematology Therapeutic Area Unit at Takeda. “The results of the trial are very

encouraging, and we look forward to continuing to engage with global regulatory bodies with the aim of bringing TAK-755 to patients as rapidly as possible."

Takeda plans to submit the results of this interim analysis for presentation at an upcoming scientific meeting.

In addition to announcing these results, Takeda indicated that the December 22, 2022, edition of the New England Journal of Medicine (NEJM) included two case reports written and submitted by two physicians who requested compassionate use of TAK-755 to treat patients who were facing critical health complications related to cTTP. The case reports are available on NEJM's website.

TAK-755 is also being investigated in a Phase 2 study to evaluate the pharmacokinetics, safety and efficacy of rADAMTS13 in immune-mediated TTP (iTTP).[6]

Results from the interim analysis of the Phase 3 study have no impact on the full year consolidated reported forecast for the fiscal year ending March 31, 2023 (Fiscal Year 2022).

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.[7]

The TAK-755 cTTP clinical development program includes one first-in-human, Phase 1 study, 281101 (NCT02216084),[8] and two Phase 3 studies: a pivotal Phase 3 study, Study 281102 (NCT03393975), and one Phase 3b continuation study, Study TAK-755-3002 (NCT04683003).[5,9] TAK-755 is also being investigated in immune-mediated TTP (iTTP) and sickle cell disease, with Phase 2 (NCT03922308) and Phase 1 (NCT03997760) trials ongoing, respectively, and due to provide data in 2023.[6,10]

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 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 blood clotting disorder associated with life-threatening acute episodes and debilitating chronic symptoms.[1,3] cTTP is a sub-type 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.[3,14] 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.[3,12,15,16] rADAMTS13 is a novel investigational therapeutic approach for cTTP.[17]

The current standard of care for cTTP is plasma therapy,[16] which is insufficient in restoring ADAMTS13, time-consuming, and costly.[7,18,19]

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.

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