Press Release

Astellas Announces Update on Preliminary Safety and Efficacy Data from FORTIS Study of Investigational AT845 in Adults with Late-Onset Pompe Disease

Data presented at the 19th Annual WORLDSymposium™ 2023

TOKYO, February 22, 2023 – Astellas Pharma Inc. (TSE: 4503, President and CEO: Kenji Yasukawa, Ph.D., "Astellas") today announced an update on preliminary safety and efficacy data from its ongoing FORTIS Phase1/2 clinical trial evaluating the safety, tolerability and exploratory efficacy of investigational AT845 in adults with late-onset Pompe disease (LOPD). The data will be presented during a platform presentation at the 19th Annual WORLD*Symposium* in Orlando, FL (Poster: #95). AT845 is an investigational adeno-associated virus (AAV) gene replacement therapy designed to deliver a functional human acid alpha-glucosidase (*GAA*) gene directly in muscle cells in adults with LOPD.

“There is tremendous need for new treatment approaches in progressive, debilitating, genetic diseases like LOPD that move beyond standard of care enzyme replacement therapy (ERT),” said Jordi Díaz-Manera, MD, PhD, Professor of Neuromuscular Disorders and Honorary Consultant Clinical Geneticist for the Newcastle Hospitals NHS Foundation Trust at Newcastle University, UK. *“*AAV gene therapies have the potential to be a safe and effective approach to delivering a functional *GAA* gene directly to the muscle tissues in patients with LOPD."

FORTIS is an ongoing multicenter, open-label, ascending dose Phase 1/2 first-in-human clinical trial to determine the safety, tolerability and exploratory efficacy of AT845 in adults with LOPD. As of the September 15th, 2022, data cut-off, four participants received a one-time intravenous infusion of AT845, with two dosed at the $3x10^{13}$ vg/kg dose level and two dosed at the $6x10^{13}$ vg/kg dose level, with up to 78 weeks of safety follow-up in the clinical trial. Three of the four participants have discontinued ERT following administration of AT845, and their measured functional outcomes have been stable while off ERT for 19, 44, and 51 weeks, respectively. The ongoing evaluation of the dosed participants, including those who discontinued ERT, showed continued stability of disease functional endpoints, including forced vital capacity and the 6-minute walk test. Patient-reported outcomes for fatigue and daily activities (Pompe-specific) also appeared stable.

Each participant’s infusion of AT845 was generally well-tolerated, and most treatment-emergent adverse effects were mild (grade 1) and considered to be unrelated to study treatment. A possible infusion-related reaction occurred in one participant and resolved with oral diphenhydramine and acetaminophen. Three participants developed transient transaminitis and deemed possibly related to AT845. In all cases, the event resolved with modifications to immune suppression. A grade 2 peripheral sensory polyneuropathy event was reported in one participant in the

6x10^{13} vg/kg cohort, which led to an FDA clinical hold in June 2022. The FDA lifted this clinical hold in January 2023.

“We are excited to share these new findings from the ongoing FORTIS clinical study of AT845. These data, along with our recent announcement of the clinical hold lift of the FORTIS clinical trial, are very positive developments for the program,” said Ha Tran, Executive Medical Director for Astellas. “The preliminary data presented are encouraging. We look forward to continuing the FORTIS clinical trial as we advance towards our goal of developing innovative gene therapies and bringing new potential treatments to patients with high unmet need.”

About Pompe Disease
Pompe disease is a rare, severe, autosomal recessive metabolic disease characterized by progressive neuromuscular degeneration. The overall incidence is estimated to be approximately 1 in 40,000 births[1], although frequency and disease progression varies with age of onset, ethnicity and geography[2]. The disease is caused by mutations in the *acid alpha-glucosidase (GAA)* gene that prevent the production and function of a protein called acid alpha-glucosidase (GAA). GAA is responsible for metabolizing glycogen, and dysfunction or absence of this protein results in the accumulation of glycogen in tissues, primarily in the skeletal and cardiac muscles, where it causes damage to tissue structure and function. Currently, the only approved treatment for Pompe is enzyme replacement therapy (ERT), which is a chronic treatment delivered in bi-weekly infusions and relies solely on tissue uptake of GAA from plasma.

About AT845 for the treatment of Late-Onset Pompe Disease (LOPD)
Astellas is developing AT845, a novel gene replacement therapy using an AAV8 vector under a muscle-specific promotor to deliver a functional copy of the *GAA* gene, for the treatment of adult LOPD. AT845 is being investigated to determine whether it can deliver a functional *GAA* gene that is efficiently transduced to express GAA directly in tissues affected by the disease, including skeletal and cardiac muscle.

About FORTIS
FORTIS (NCT04174105) is a multicenter, open-label, ascending dose Phase 1/2 first-in-human clinical trial to determine if AT845 is safe and tolerable in adults with Late-Onset Pompe Disease (LOPD). The primary endpoints of the trial are safety and tolerability, as well as efficacy measures, including change in muscle GAA protein expression and enzyme activity from baseline. Secondary endpoints evaluate improvements in respiratory, endurance and quality of life measures.

About Astellas
Astellas Pharma Inc. is a pharmaceutical company conducting business in more than 70 countries around the world. We are promoting the Focus Area Approach that is designed to identify opportunities for the continuous creation of new drugs to address diseases with high unmet medical needs by focusing on Biology and Modality. Furthermore, we are also looking beyond our foundational Rx focus to create Rx+® healthcare solutions that combine our expertise and knowledge with cutting-edge technology in different fields of external partners. Through these efforts, Astellas stands on the forefront of healthcare change to turn innovative science into VALUE for patients. For more information, please visit our website at https://www.astellas.com/en.

About Astellas Gene Therapies
Astellas Gene Therapies is an Astellas Center of Excellence developing genetic medicines with the potential to deliver transformative value for patients. Our gene therapy drug discovery engine is built around innovative science, a validated AAV platform, and industry leading internal manufacturing capability with a particular focus on rare diseases of the eye, CNS and neuromuscular system. Astellas Gene Therapies will also be advancing additional Astellas gene therapy programs toward clinical investigation. Astellas Gene Therapies is based in San Francisco, with manufacturing and laboratory facilities in South San Francisco, Calif., Sanford, N.C. and Tsukuba, Japan.

Astellas Cautionary Notes
In this press release, statements made with respect to current plans, estimates, strategies and beliefs and other statements that are not historical facts are forward-looking statements about the future performance of Astellas. These statements are based on management's current assumptions and beliefs in light of the information currently available to it and involve known and unknown risks and uncertainties. A number of factors could cause actual results to differ materially from those discussed in the forward-looking statements. Such factors include, but are not limited to: (i) changes in general economic conditions and in laws and regulations, relating to pharmaceutical markets, (ii) currency exchange rate fluctuations, (iii) delays in new product launches, (iv) the inability of Astellas to market existing and new products effectively, (v) the inability of Astellas to continue to effectively research and develop products accepted by customers in highly competitive markets, and (vi) infringements of Astellas' intellectual property rights by third parties. Information about pharmaceutical products (including products currently in development) which is included in this press release is not intended to constitute an advertisement or medical advice.

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