Press Release

Astellas Announces FDA Update on the FORTIS Clinical Trial of AT845 in Adults with Late-Onset Pompe Disease

TOKYO, June 27, 2022 - Astellas Pharma Inc. (TSE: 4503, President and CEO: Kenji Yasukawa, Ph.D., "Astellas") announced that the US Food and Drug Administration (FDA) has placed a clinical hold on the FORTIS Ph1/2 trial following the occurrence of a serious adverse event (SAE) of peripheral sensory neuropathy in one of the trial participants. FORTIS is a clinical trial evaluating AT845, an investigational adeno-associated virus (AAV) gene replacement therapy in adults with Late-Onset Pompe Disease.

The FDA informed Astellas that it did not have sufficient information to assess the risks to subjects and requires additional information about the recently reported SAE. To date, the SAE has been classified by the site investigator as Grade 1 (mild in severity) and deemed serious due to medical significance. A written explanation for the basis of the hold will be issued by the FDA and sent to Astellas within the next 30 days.

Astellas is working with the site investigator to closely follow the patient's clinical course and will continue to gather and review all relevant data. All currently enrolled participants will continue to be monitored closely per the study protocol.

"Patient safety is our top priority, and we are working closely with the FDA to determine appropriate next steps," explained Weston Miller, M.D., Senior Medical Director, Clinical Development at Astellas Gene Therapies. "We remain committed to the safe and effective development of AT845 and will keep the scientific and patient communities informed with updates as we learn more."

Astellas is focused on developing genetic medicines and working alongside its world-renowned partners to build a portfolio of potentially life-changing gene therapies. Astellas strives to identify, develop and deliver therapies for patients with genetic diseases who currently have few or no effective treatment options.

Astellas is reviewing potential financial impacts of this matter for the fiscal year ending March 31, 2023.

About Pompe Disease
Pompe disease is a rare, severe, autosomal recessive metabolic disease characterized by progressive muscular 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 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 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 I/II first-in-human clinical trial to determine if AT845 is safe and tolerable in adults with 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. Based on an innovative scientific approach and industry leading internal manufacturing capability and expertise, we are currently exploring three gene therapy modalities: gene replacement, exon skipping gene therapy, and vectorized RNA knockdown and will also advance additional Astellas gene therapy programs toward clinical investigation. We are based in San Francisco, with manufacturing and laboratory facilities in South San Francisco and Sanford, N.C.

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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References

[1] Kishnani, PS, et al. Pompe disease diagnosis and management guideline. Genetics in medicine: official journal of the American College of Medical Genetics, 2006. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3110959/

[2]Ausems MG, et al. Frequency of glycogen storage disease type II in The Netherlands: implications for diagnosis and genetic counselling. European Journal of Human Genetics, 1999. Available from:

https://www.nature.com/articles/5200367.pdf?origin=ppub; Lin CY, et al. Pompe's disease in Chinese and prenatal diagnosis by determination of alpha-glucosidase activity. Journal of Inherited Metabolic Disease, 1987. Available from: https://pubmed.ncbi.nlm.nih.gov/3106710/; Hirschhorn R, et al. Pediatric Research, 2004; Bashan N, et al. Glycogen storage disease type II in Israel. Israel Journal of Medical Sciences, 1988. Available from: https://europepmc.org/article/med/3132435; Meikle PJ, et al. Prevalence of Lysosomal Storage Disorders. JAMA, 1999. Available from: https://jamanetwork.com/journals/jama/article-abstract/188380