Press Release

Astellas Announces Positive Safety Data from the FORTIS Study of AT845 in Adults with Late-Onset Pompe Disease

- Data presented at the 18th Annual WORLDSymposium™ 2022 -

TOKYO, Feb. 7, 2022 - Astellas Pharma Inc. (TSE: 4503, President and CEO: Kenji Yasukawa, Ph.D., "Astellas") today announced positive interim safety data from FORTIS, the Phase I/II clinical trial evaluating AT845, an investigational adeno-associated virus (AAV) gene replacement therapy to deliver a functional alpha-glucosidase (*GAA)* gene to express acid alpha-glucosidase (GAA) directly in muscle cells in adults with Late-Onset Pompe Disease (LOPD) (Presentation & Poster: 206).

Pompe disease, a rare, severe, autosomal recessive metabolic disease characterized by progressive muscular degeneration, results from a mutation in the *GAA* gene that interferes with the production or function of the GAA protein. GAA is responsible for metabolizing glycogen, and dysfunction or absence of this protein results in the accumulation of glycogen, primarily in the skeletal and cardiac muscles, where it causes damage to tissue structure and function. Currently, the only approved treatment for Pompe disease is enzyme replacement therapy (ERT), which is delivered via chronic intravenous infusions every two weeks and relies solely on tissue uptake of GAA from plasma.

"There is significant unmet need for patients with Pompe disease due to the short half-life, inefficient uptake in the key tissues affected by the disease and the immunogenicity of ERT," said Tahseen Mozaffar, M.D., Professor of Neurology at UC Irvine. "AT845 has the potential to be a best-in-class approach as a muscle-directed gene therapy using an AAV8 capsid serotype. It 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."

FORTIS is an ongoing 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. Enrolled participants receive a one-time peripheral intravenous infusion of AT845, followed by one year of frequent monitoring of safety, clinical and biochemical endpoints including GAA activity and protein level in muscle and four additional years of long-term safety monitoring. 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.

As of the December 3, 2021 data cut-off date, four participants have been enrolled in FORTIS, with two participants dosed at 3×10^{13} vg/kg (Cohort 1) and two participants dosed at 6×10^{13} vg/kg (Cohort 2). The reported data includes interim safety and tolerability assessments, as well as up to 24 weeks of follow-up for the two participants in Cohort 1 and preliminary data from the two participants in Cohort 2.

"We are pleased that AT845 has been well-tolerated so far in the four adults with LOPD who have received treatment," said Weston Miller, M.D., Senior Medical Director, Clinical Development at Astellas Gene Therapies. "In the two participants in Cohort 1 with follow-up

duration through week 24 after dosing, AT845 demonstrated an encouraging safety profile. Importantly, there have been no serious adverse events reported following dosing in any of the four participants as of the time of the data cut. One participant experienced elevated transaminases, which is considered a common immune-mediated treatment response based on the time of onset after dosing, its presentation during steroid taper initiation and its reversal with steroid re-initiation. These safety data are encouraging, and the program continues to enroll participants."

With the establishment of the Astellas Gene Therapies Center of Excellence following the 2020 acquisition of Audentes Therapeutics Inc., Astellas is a leader in genetic medicines, working alongside its world-renowned partners to build a portfolio of potentially life-changing gene therapies. Astellas strives to identify, develop and deliver transformative therapies for patients with genetic diseases who currently have few or no effective treatment options.

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,[i] although frequency and disease progression varies with age of onset, ethnicity and geography.[ii] 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 cardiac- and skeletal muscle-specific promotor, to deliver a functional copy of the *GAA* gene, for the treatment of Late-Onset Pompe Disease (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 is an ongoing multicenter, open-label, ascending dose Phase I/II 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 integrated its wholly owned subsidiary, Audentes Therapeutics, Inc., as of April 1, 2021 and established "Astellas Gene Therapies" within the organization as an Astellas Center of Excellence to develop 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 hope to 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, North Carolina.

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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