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Press Release

Source: Sanofi (EURONEXT: SAN) (NASDAQ: SNY)

FDA grants priority review for avalglucosidase alfa, a potential new therapy for Pompe disease

- The FDA decision date for avalglucosidase alfa, an investigational enzyme replacement therapy, is set for May 18, 2021
- Regulatory submission based on positive data from two trials in patients with late-onset and infantile-onset Pompe disease, respectively
- Avalglucosidase alfa received FDA Breakthrough Therapy and Fast Track designations for the treatment of people with Pompe Disease
- Pompe disease, a rare degenerative muscle disorder, affects approximately 3,500 people in the U.S.
- Milestone reinforces 20+year commitment to Pompe disease community

PARIS – November 18, 2020 - The U.S. Food and Drug Administration (FDA) has accepted for priority review the Biologics License Application (BLA) for avalglucosidase alfa for long-term enzyme replacement therapy for the treatment of patients with Pompe disease (acid α-glucosidase deficiency). The target action date for the FDA decision is May 18, 2021.

Avalglucosidase alfa is an investigational enzyme replacement therapy designed to improve the delivery of acid alpha-glucosidase (GAA) enzyme to muscle cells, and if approved, would offer a potential new standard of care for patients with Pompe disease.

In October, the European Medicines Agency accepted for review the Marketing Authorization Application for avalglucosidase alfa for long-term enzyme replacement therapy for the treatment of patients with Pompe disease. The Medicines and Healthcare Products Regulatory Agency in the UK has granted Promising Innovative Medicine designation for avalglucosidase alfa.

> *"The hallmarks of Pompe disease are the relentless and debilitating deterioration of the muscles, which causes decreased respiratory function and mobility," said Karin Knobe, Head of Development for Rare Diseases and Rare Blood Disorders at Sanofi. "Avalglucosidase alfa is specifically designed to deliver more GAA enzyme into the lysosomes of the muscle cells. We have been greatly encouraged by positive clinical trial results in patients with late-onset and infantile-onset Pompe disease."*

Pompe disease is a rare, degenerative muscle disorder that can impact an individual's ability to move and breathe. It affects an estimated 3,500 people in the U.S. and can manifest at any age from infancy to late adulthood.[i]

The BLA is based on positive data from two trials:

- Pivotal Phase 3, double-blind, global comparator-controlled trial (COMET), which evaluated the safety and efficacy of avalglucosidase alfa compared to alglucosidase alfa (standard of care) in patients with late-onset Pompe disease. Results from this trial were presented during a Sanofi-hosted virtual scientific session in June 2020 and in October 2020 at World Muscle Society and the American Association of Neuromuscular and Electrodiagnostic Medicine.
- The Phase 2 (mini-COMET) trial evaluated the safety and exploratory efficacy of avalglucosidase alfa in patients with infantile-onset Pompe disease previously treated with alglucosidase alfa. Results from this trial were presented at the WORLDSymposium, in February 2020.

Delivery of GAA to Clear Glycogen

Pompe disease is caused by a genetic deficiency or dysfunction of the lysosomal enzyme GAA, which results in build-up of complex sugars (glycogen) in muscle cells throughout the body. The accumulation of glycogen leads to irreversible damage to the muscles, including respiratory muscles and the diaphragm muscle supporting lung function, and other skeletal muscles that affect mobility.

To reduce the glycogen accumulation caused by Pompe disease, the GAA enzyme must be delivered into the lysosomes within muscle cells. Research led by Sanofi has focused on ways to enhance the delivery of GAA into the lysosomes of muscle cells by targeting the mannose-6-phosphate (M6P) receptor that plays a key role in the transport of GAA.

Avalglucosidase alfa is designed with approximately 15-fold increase in M6P content, compared to standard of care alglucosidase alfa, and aims to help improve cellular enzyme uptake and enhance glycogen clearance in target tissues.[ii] The clinical relevance of this difference has not been confirmed.

Avalglucosidase alfa is currently under clinical investigation and its safety and efficacy have not been evaluated by any regulatory authority worldwide.

About Sanofi

Sanofi is dedicated to supporting people through their health challenges. We are a global biopharmaceutical company focused on human health. We prevent illness with vaccines, provide innovative treatments to fight pain and ease suffering. We stand by the few who suffer from rare diseases and the millions with long-term chronic conditions.

With more than 100,000 people in 100 countries, Sanofi is transforming scientific innovation into healthcare solutions around the globe.

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Sanofi Forward-Looking Statements

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[i] https://rarediseases.org/rare-diseases/pompe-disease/

[ii] Zhou Q. Bioconjug Chem. 2011 Apr 20;22(4):741-51