SANOFI

Press Release

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

EMA accepts regulatory submission for avalglucosidase alfa, a potentially new standard of care enzyme replacement therapy for Pompe disease

- Avalglucosidase alfa, an investigational enzyme replacement therapy for patients with Pompe disease, reaches its first important regulatory milestone
- Pompe disease affects an estimated 50,000 people worldwide
- Submission based on positive data from two trials including both infantile-onset and late-onset Pompe disease patients
- Regulatory approval in Europe anticipated in the second half of 2021
- Milestone builds on company's 20+ year commitment to the Pompe disease community
- Avalglucosidase alfa receives Promising Innovative Medicine designation in UK, adding to U.S. Breakthrough Therapy designation received earlier this year

PARIS – October 2, 2020 –The European Medicines Agency (EMA) has accepted for review the Marketing Authorization Application (MAA) for avalglucosidase alfa, for long-term enzyme replacement therapy for the treatment of patients with Pompe disease (acid α-glucosidase deficiency). Avalglucosidase alfa is an investigational enzyme replacement therapy, which, if approved, would offer a potential new standard of care for patients with 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 50,000 people worldwide and can manifest at any age from infancy to late adulthood.

The MAA is based on positive data from two trials:

- Phase 3, double-blind, comparator-controlled, pivotal COMET trial, 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.
- Phase 2 mini-COMET trial, which 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 WORLD*Symposium*, in February 2020.

Pompe disease is caused by a genetic deficiency or dysfunction of the lysosomal enzyme acid alpha-glucosidase (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, such as the diaphragm muscle that supports the lungs, and other skeletal muscles that affect mobility. Avalglucosidase alfa is designed to improve the delivery of GAA enzyme into the lysosomes of muscle cells to breakdown glycogen and help address respiratory impairment, as well as decreased muscle strength and function (i.e. mobility), which are critical manifestations of Pompe disease.

The Medicines and Healthcare Products Regulatory Agency in the UK has granted Promising Innovative Medicine designation for avalglucosidase alfa, an early indication that the investigational therapy is a promising candidate for the Early Access to Medicines Scheme in the UK.[i]

The U.S. Food and Drug Administration has granted Breakthrough Therapy and Fast Track designations to avalglucosidase alfa.

Delivery of GAA to Clear Glycogen

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 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.

Media Relations Contact
Sally Bain
Tel.: +1 781 264 1091
sally.bain@sanofi.com

Sanofi Investor Relations Contacts Paris
Eva Schaefer-Jansen
Arnaud Delepine
Yvonne Naughton

Sanofi Investor Relations Contacts North America
Felix Lauscher
Fara Berkowitz
Suzanne Greco

IR main line:
Tel.: +33 (0)1 53 77 45 45
ir@sanofi.com

Sanofi Forward-Looking Statements

This press release contains forward-looking statements as defined in the Private Securities Litigation Reform Act of 1995, as amended. Forward-looking statements are statements that are not historical facts. These statements include projections and estimates and their underlying assumptions, statements regarding plans, objectives, intentions and expectations with respect to future financial results, events, operations, services, product development and potential, and statements regarding future performance. Forward-looking statements are generally identified by the words "expects", "anticipates", "believes", "intends", "estimates", "plans" and similar expressions. Although Sanofi's management believes that the expectations reflected in such forward-looking statements are reasonable, investors are cautioned that forward-looking information and statements are subject to various risks and uncertainties, many of which are difficult to predict and generally beyond the control of Sanofi, that could cause actual results and developments to differ materially from those expressed in, or implied or projected by, the forward-looking information and statements. These risks and uncertainties include among other things, the uncertainties inherent in research and development, future clinical data and analysis, including post marketing, decisions by regulatory authorities, such as the FDA or the EMA, regarding whether and when to approve any drug, device or biological application that may be filed for any such product candidates as well as their decisions regarding labelling and other matters that could affect the availability or commercial potential of such product candidates, the fact that product candidates if approved may not be commercially successful, the future approval and commercial success of therapeutic alternatives, Sanofi's ability to benefit from external growth opportunities, to complete related transactions and/or obtain regulatory clearances, risks associated with intellectual property and any related pending or future litigation and the ultimate outcome of such litigation, trends in exchange rates and prevailing interest rates, volatile economic and market conditions, cost containment initiatives and subsequent changes thereto, and the impact that COVID-19 will have on us, our customers, suppliers, vendors, and other business partners, and the financial condition of any one of them, as well as on our employees and on the global economy as a whole. Any material effect of COVID-19 on any of the foregoing could also adversely impact us. This situation is changing rapidly and additional impacts may arise of which we are not currently aware and may exacerbate other previously identified risks. The risks and uncertainties also include the uncertainties discussed or identified in the public filings with the SEC and the AMF made by Sanofi, including those listed under "Risk Factors" and "Cautionary Statement Regarding Forward-Looking Statements" in Sanofi's annual report on Form 20-F for the year ended December 31, 2019. Other than as required by applicable law, Sanofi does not undertake any obligation to update or revise any forward-looking information or statements.

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[i] Medicines and Healthcare Products Regulatory Agency. Promising Innovative Medicine (PIM) Designation - Step I of Early Access to Medicines Scheme (EAMS). Gov.UK. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/375327/PIM_designation_guidance.pdf. Published April 2014. Accessed September 24, 2020.

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