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Press Release

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

Sanofi's investigational enzyme replacement therapy shows clinically meaningful improvement in critical manifestations of late-onset Pompe disease

- Avalglucosidase alfa showed a 2.4-point improvement in percent-predicted forced vital capacity, an important measure of respiratory function in Pompe disease, compared to alglucosidase alfa (standard of care)
- Patients treated with avalglucosidase alfa walked 30 meters farther than those treated with standard of care, as measured by the 6-minute walk test
- Global regulatory submissions anticipated in the second half of 2020

PARIS – June 16, 2020 – Sanofi's investigational enzyme replacement therapy (ERT), avalglucosidase alfa, showed clinically meaningful improvement in critical manifestations (respiratory impairment and decreased mobility) of late-onset Pompe disease (LOPD) according to results from the Phase 3 trial presented today at a Sanofi-hosted scientific session. Avalglucosidase alfa met the primary endpoint demonstrating non-inferiority in improving respiratory function compared to alglucosidase alfa (standard of care) in patients with LOPD. These data will form the basis for global regulatory submissions anticipated in the second half of this year. The U.S. Food and Drug Administration (FDA) has granted Breakthrough Therapy and Fast Track designations to avalglucosidase alfa for the treatment of patients with Pompe disease.

The trial primary endpoint evaluated the change in respiratory muscle function using percent-predicted forced vital capacity (FVC) in the upright position. Patients treated with avalglucosidase alfa had a 2.4-point greater improvement in percent-predicted FVC compared to patients treated with standard of care (95% CI, -0.13 / 4.99), a numerical improvement in respiratory function that surpassed the study-designed measure of non-inferiority (p=0.0074).

The primary endpoint was also measured for superiority. Superiority statistical significance was not achieved for the avalglucosidase alfa arm (p=0.0626). As a result, per the hierarchy of the study protocol, formal statistical testing for all secondary endpoints was not conducted.

A key secondary endpoint in the trial measured mobility with the 6-minute walk test (6MWT). Patients treated with avalglucosidase alfa walked 30 meters farther (95% CI, 1.33 / 58.69) than patients treated with standard of care. Other secondary endpoints assessed respiratory muscle strength, motor function, and quality of life.

Trial Endpoints	Avalglucosidase Alfa* N = 51	Alglucosidase Alfa* N = 49	Least Square Mean Difference (95%CI) N = 100
Primary Endpoint			
FVC (% predicted)	2.89 (0.88)	0.46 (0.93)	2.43 (-0.13, 4.99)
Secondary Endpoints			
6MWT	32.21 (9.93)	2.19 (10.40)	30.01 (1.33, 58.69)
Maximum Inspiratory Pressure (% predicted)	-0.29 (3.84)	-2.87 (4.04)	2.58 (-8.54, 13.71)
Maximum Expiratory Pressure (% predicted)	2.39 (4.00)	5.00 (4.20)	-2.61 (-14.22, 9.00)
Hand-held dynamometry Composite Score	260.69 (46.07)	153.72 (48.54)	106.97 (-26.56, 240.50)
Quick Motor Function Test Total Score	3.98 (0.63)	1.89 (0.69)	2.08 (0.22, 3.95)
Health-related survey on quality of life (SF-12) Physical Component Summary Score Mental Component Summary Score	 2.37 (0.99) 2.88 (1.22)	 1.60 (1.07) 0.76 (1.32)	 0.77 (-2.13, 3.67) 2.12 (-1.46, 5.69)

* **Least square mean changes (standard error) from baseline at week 49**

> *"Pompe disease can be debilitating as it progressively deteriorates the muscles. It's important that potential new treatment options offer patients clinically meaningful improvement across multiple measures of respiratory and motor function,"* said Jordi Diaz-Manera, M.D., Ph.D., Professor of Neuromuscular Disorders, Translational Medicine and Genetics at the John Walton Muscular Dystrophy Research Center, Newcastle University, UK. *"The findings from the Phase 3 trial are very encouraging and add to the growing body of clinical evidence demonstrating the potential of avalglucosidase alfa to offer a new treatment option in addressing the hallmark symptoms of this disease."*

Also presented were results from a pre-specified preliminary analysis evaluating percent-predicted FVC and 6MWT in those patients who switched (switch patients) at 49 weeks from standard of care to avalglucosidase alfa for the open-label extension period of the trial. Due to sequential enrollment, preliminary analysis results at the time of data presentation were available at 97 weeks for 20 out of 49 switch patients for percent-predicted FVC, and 21 out of 49 switch patients for 6MWT. In these switch patients, avalglucosidase alfa demonstrated a 0.15-point improvement in FVC (95% CI, -1.95 / 2.25) and a 23.32-meter improvement in 6MWT (95% CI, -3.87 / 50.51).

> "*We're pleased that avalglucosidase alfa showed clinically meaningful improvement both in respiratory function and mobility, as measured by well-established standard Pompe disease outcome measures,"* said John Reed, M.D., Ph.D., Global Head of Research and Development at Sanofi. *"These results underscore our ambition to establish avalglucosidase alfa as a new standard of care treatment for Pompe disease."*

The safety profile of avalglucosidase alfa was found to be comparable to standard of care. Over the double-blinded 49-week period, 44 patients in the avalglucosidase alfa arm and 45 patients in the standard of care arm experienced an adverse event(s) (AEs). There were 6 patients with severe AEs in the avalglucosidase alfa arm and 7 patients in the standard of care arm. Fewer patients presented with serious adverse events (SAEs) in the avalglucosidase alfa arm (8 patients, including 1 patient with potentially treatment-related SAEs) compared to the standard of care arm (12 patients, including 3 patients with potentially treatment-related SAEs). In the standard of care arm of the trial, 4 patients had AEs leading to study withdrawal and 1 patient died due to an SAE of acute myocardial infarction (unrelated to treatment). In the avalglucosidase alfa arm, there were no patient discontinuations or deaths. Fewer patients in the avalglucosidase alfa arm (25.5%) experienced at least one protocol-defined infusion-associated reaction compared to the alglucosidase alfa arm (32.7%). Immunogenicity data is being analysed and will be presented at a future medical congress or publication.

Trial design

The randomized, double-blind, Phase 3, head-to-head COMET trial enrolled 100 previously untreated pediatric and adult patients with LOPD across 56 centers in 20 countries. Patients were randomized to receive either avalglucosidase alfa 20 mg/kg or alglucosidase alfa (standard of care) 20 mg/kg intravenous infusion every two weeks for 49 weeks. After 49 weeks, patients previously receiving standard of care switched to avalglucosidase alfa 20 mg/kg for the ongoing open-label treatment portion of the study.[i]

About Pompe disease

Pompe disease is caused by a genetic deficiency or dysfunction of the lysosomal enzyme acid alpha-glucosidase (GAA), resulting in build-up of glycogen in muscles, including the proximal muscles and the diaphragm, and eventually causing progressive and irreversible muscle damage. This rare disease affects an estimated 50,000 people worldwide and can manifest at any age from infancy to late adulthood. Pompe disease is often classified as late-onset Pompe disease (LOPD) or infantile-onset Pompe disease (IOPD). Patients with LOPD typically present any time after the first year of life to late adulthood. The hallmark symptoms of LOPD are impaired respiratory function and skeletal muscle weakness, which often leads to impaired mobility. Patients often require wheelchairs to assist with mobility and may require mechanical ventilation to help with breathing. Respiratory failure is the most common cause of death in patients with Pompe disease. Pompe disease is classified as IOPD when symptoms begin prior to one year of age. In addition to skeletal muscle weakness, heart function is also commonly impacted.

About Avalglucosidase alfa

The goal of ERT for Pompe disease is to deliver enzyme into the lysosomes within muscle cells to replace the missing or deficient GAA that is needed to prevent build-up of glycogen in the muscles. Avalglucosidase alfa is an investigational ERT for Pompe disease designed to improve the delivery of enzyme to the cells in the muscles, most notably into

skeletal muscle. With approximately 15-fold increase in mannose-6-phosphate content compared to standard of care alglucosidase alfa, avalglucosidase alfa 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.

Beyond the Phase 3 COMET trial, the avalglucosidase alfa clinical development program includes the ongoing Phase 2 NEO-EXT trial[iii] investigating the long-term safety, tolerability, pharmacokinetics, pharmacodynamics, and exploratory efficacy of avalglucosidase alfa in patients with LOPD for a duration of up to approximately 8 years in participants from the Phase 1 / 2 NEO1 trial. Also, the ongoing Phase 2 mini-COMET trial[iv] is investigating the safety and efficacy of treatment with avalglucosidase alfa in patients who have infantile-onset Pompe disease (IOPD) and were previously treated with alglucosidase alfa. For more information about the avalglucosidase alfa clinical development program, please visit https://www.clinicaltrials.gov.

Avalglucosidase alfa has not been approved by the U.S. FDA or any other regulatory agency worldwide for the uses under investigation.

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.

Sanofi, Empowering Life

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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] www.clinicaltrials.gov ClinicalTrials.gov Identifier: NCT02782741
[ii] Zhou Q. Bioconjug Chem. 2011 Apr 20;22(4):741-51
[iii] www.clinicaltrials.gov ClinicalTrials.gov Identifier: NCT02032524
[iv] www.clinicaltrials.gov ClinicalTrials.gov Identifier: NCT03019406