

## FDA approves Nexviazyme® (avalglucosidase alfa-ngpt), an important new treatment option for late-onset Pompe disease

- \* Approval is based on positive Phase 3 data demonstrating improvements in key disease burden measures and establishing its safety profile
- \* Nexviazyme specifically targets the M6P receptor, the key pathway for enzyme replacement therapy, to effectively clear glycogen build-up in muscle cells

**PARIS – August 6, 2021** - The U.S. Food and Drug Administration (FDA) has approved Nexviazyme® (avalglucosidase alfa-ngpt) for the treatment of patients one year of age and older with late-onset Pompe disease, a progressive and debilitating muscle disorder that impairs a person’s ability to move and breathe. Nexviazyme is an enzyme replacement therapy (ERT) designed to specifically target the mannose-6-phosphate (M6P) receptor, the key pathway for cellular uptake of enzyme replacement therapy in Pompe disease. Nexviazyme has been shown in clinical trials to provide patients with improvements in respiratory function and walking distance.

*“Pompe disease is a debilitating and progressive condition that significantly inhibits mobility and breathing,”* said Bill Sibold, Executive Vice President of Sanofi Genzyme. *“For decades, we’ve made it our responsibility to research how to target the M6P receptor, the key pathway for cellular uptake of enzyme replacement therapy. Nexviazyme is a potential new standard of care for people living with late-onset Pompe disease and delivers on our promise to pursue medicines for patients living with rare diseases.”*

Pompe disease affects an estimated 3,500 people in the United States and can present as infantile-onset Pompe disease (IOPD), the most severe form of Pompe disease with rapid onset in infancy, and late-onset Pompe disease (LOPD), which progressively damages muscles over time. LOPD symptoms may present at any age. However, due to the wide spectrum of clinical presentations and progressive nature of the disease, it can take seven to nine years before patients receive an accurate diagnosis. As the disease progresses, people with LOPD may require mechanical ventilation to help with breathing or a wheelchair to assist with mobility.

### Targeted delivery to clear glycogen in muscle cells

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 the diaphragm that supports respiratory function and skeletal muscles that affect mobility, functional endurance and breathing.

The key pathway to transport GAA enzyme into the lysosomes in the cell is through the M6P receptor. Nexvazyme is specifically designed to target M6P to improve cellular enzyme uptake and enhance glycogen clearance in target tissues with an approximate 15-fold increase in M6P content compared to alglucosidase alfa, the comparator arm in the pivotal study.

### **Nexvazyme demonstrated improvements in pivotal study**

Nexvazyme has demonstrated improvements for people living with late-onset Pompe disease. In the pivotal Phase 3 trial (COMET), Nexvazyme showed improvements in respiratory function and walking distance measures in people with LOPD and established its safety profile.

*“Nexvazyme is a new and exciting therapeutic option for people with late-onset Pompe disease,”* said Mazen M. Dimachkie, MD, FAAN, FANA, Professor of Neurology, Chief of the Neuromuscular Division and Executive Vice Chair of the Department of Neurology at the University of Kansas Medical Center. *“The Phase 3 study results showed meaningful improvements in respiratory function and walking distance, which are impactful in this serious condition.”*

Results from the COMET study comparing Nexvazyme to alglucosidase alfa in LOPD included:

- When compared to baseline, patients treated with Nexvazyme had a 2.9-point improvement (SE=0.9) in forced vital capacity (FVC) percent-predicted at Week 49, the study’s primary endpoint. Patients treated with Nexvazyme had a 2.4-point greater improvement in FVC percent-predicted compared to patients treated with alglucosidase alfa at Week 49 meeting the measurement of non-inferiority (p=0.0074; 95% CI, -0.13, 4.99). Statistical superiority of Nexvazyme over alglucosidase alfa was not achieved (p=0.06).
- A key secondary endpoint in the trial measured functional endurance with the 6-minute walk test (6MWT). When compared to baseline, patients treated with Nexvazyme walked 32.2 meters farther (SE=9.9) at Week 49. Patients treated with Nexvazyme walked 30 meters farther (95% CI, 1.33, 58.69) than patients treated with alglucosidase alfa at Week 49. Per the hierarchy of the study protocol, formal statistical testing for all secondary endpoints was not conducted.
- During the double-blind active-controlled period of 49 weeks, serious adverse reactions were reported in two (2%) patients treated with Nexvazyme and in three (6%) patients treated with alglucosidase alfa. The most frequently reported adverse reactions (>5%) in Nexvazyme-treated patients were headache, pruritus (itching sensation), nausea, hives and fatigue.
- Infusion associated reactions were reported in 13 (25%) of the Nexvazyme-treated patients and in 16 (33%) of patients treated with alglucosidase alfa. Infusion

associated reactions reported in more than one patient on Nexviazyme were mild to moderate and included headache, diarrhea, itching, hives, and rash. None of the infusion associated reactions were severe.

## **Nexviazyme, a new ERT for late-onset Pompe disease**

Nexviazyme is administered as a monotherapy ERT every two weeks. The recommended dose is based on body weight (20 mg/kg for LOPD patients  $\geq 30$  kg or 40 mg/kg for LOPD patients  $< 30$  kg) and is administered incrementally via intravenous infusion. Nexviazyme is expected to be available in the U.S. in the coming weeks.

As part of [our commitment to ensure treatment access and affordability](#) for innovative therapies, Sanofi has decided to price Nexviazyme the same as alglucosidase alfa, the only other FDA-approved therapy for the treatment of Pompe disease and the comparator arm in the pivotal study. Sanofi's [CareConnectPSS Patient Support Services](#) (1-800-745-4447, Opt. 3) provides personalized support for people and their families impacted by Pompe disease, including patients transitioning to Nexviazyme.

The FDA approval follows a priority review by the FDA, which is reserved for medicines that, if approved, would represent significant improvements in safety or efficacy in treating serious conditions. Previously, Nexviazyme received FDA Breakthrough Therapy and Fast Track designations for the treatment of people with Pompe Disease. The European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) has adopted a positive opinion for avalglucosidase alfa. While Sanofi is pleased with the CHMP's recognition of the clinically meaningful improvements demonstrated in the avalglucosidase alfa development program, the CHMP has also rendered an opinion that avalglucosidase alfa does not qualify as a New Active Substance (NAS). As a result, Sanofi has requested a re-examination of the CHMP opinion in relation to the NAS conclusion. Sanofi also filed avalglucosidase alfa in Japan in January 2021. The safety and efficacy of avalglucosidase alfa has not been fully evaluated by any regulatory authority outside of the U.S.

### **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**

*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 regarding the marketing and other potential of the product, or regarding potential future revenues from the product. 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, unexpected regulatory actions or delays, or government regulation generally, that could affect the availability or commercial potential of the product, the fact that product may not be commercially successful, the uncertainties inherent in research and development, including future clinical data and analysis of existing clinical data relating to the product, including post marketing, unexpected safety, quality or manufacturing issues, competition in general, risks associated with intellectual property and any related future litigation and the ultimate outcome of such litigation, and volatile economic and market conditions, 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, 2020. Other than as required by applicable law, Sanofi does not undertake any obligation to update or revise any forward-looking information or statements.*