

New data demonstrate clinical safety, benefit and durability of Nexviazyme® across a wide-range of Pompe disease patient groups

Paris, February 5, 2024. New data suggest treatment with Nexviazyme® (avalglucosidase alfa) meaningfully improved ptosis, or drooping eyelid, in pediatric patients with infantile-onset Pompe disease (IOPD) over nearly three years. These findings, from the Phase 2 Mini-COMET study long-term extension, will be featured at the 20th annual *WORLDSymposium™*, along with debut data (positive safety results) from the Phase 3 Baby-COMET trial, the first study of avalglucosidase alfa in never-before-treated patients with IOPD, and the first study in over 20 years of any treatment in naïve IOPD patients. Ptosis (drooping eyelid) impacts ~50% of IOPD patients, potentially causing vision loss and decreased quality of life¹. Nexviazyme is a monotherapy approved in the US and other markets for juvenile and adult patients with LOPD. It is also approved for IOPD in certain markets outside of the US.

Priya S. Kishnani, MD

C.L. and Su Chen Professor of Pediatrics; Medical Director, YT and Alice Chen Pediatrics Genetics and Genomics Center; and Division Chief, Medical Genetics, Duke University Medical Center

“Infantile-onset Pompe disease, the most severe form, remains an area of great unmet need in many regions around the world, with limited treatment options available. These findings at this year’s WORLDSymposium showed meaningful improvements in ptosis in IOPD patients treated with avalglucosidase alfa.”

Also featured at *WORLDSymposium™* 2024 are presentations of key findings surrounding avalglucosidase alfa use in late-onset Pompe disease (LOPD). This includes positive long-term results from the NEO-EXT study up to eight years, as well as real-world findings from the international, voluntary Pompe Registry sponsored by Sanofi, of people who switched to avalglucosidase alfa from prior treatment with long-time standard of care, alglucosidase alfa.

Alaa Hamed, MD, MPH, MBA

Global Head of Medical Affairs, Rare Diseases, Sanofi

“The totality of data presented at WORLDSymposium build upon existing evidence that supports the value of avalglucosidase alfa in treating Pompe disease, showcasing the therapy’s long-term durability and favorable efficacy and safety profile across a wide-range of patient types and clinical circumstances – adults and children, those living with late-onset and infantile-onset Pompe disease, and newly diagnosed and previously-treated individuals. After decades of support for the Pompe community, our researchers continue to follow the science and outcomes so we can continue innovating and help address unmet needs.”

In the comparative COMET study, fewer LOPD patients in the avalglucosidase alfa group reported at least 1 IAR (13/51 [25.5%]) in comparison to the alglucosidase alfa group (16/49 [32.7%]). The most frequently reported treatment-emergent IARs (>2 patients) in the avalglucosidase alfa group were pruritus (7.8%) and urticaria (5.9%). Additionally, hypersensitivity reactions were observed in 12 (24%) participants in the avalglucosidase alfa group and 15 (31%) in the Myozyme group. The majority of IARs and hypersensitivity reactions were mild or moderate.

Nexviazyme Data in Infantile-Onset Pompe Disease

Ptosis findings from Mini-COMET

The Phase 2 Mini-COMET study evaluated the efficacy and safety of avalglucosidase alfa in patients under 18 years of age with IOPD who previously received alglucosidase alfa for six or

more months and showed either clinical decline (Cohorts 1 and 2) or suboptimal response (Cohort 3).

In the 25-week primary analysis period, Cohort 1 received 20 mg/kg of avalglucosidase alfa every two weeks (n=6), Cohort 2 received 40 mg/kg of avalglucosidase alfa every two weeks (n=5), and Cohort 3 was randomized to either avalglucosidase alfa 40 mg/kg every two weeks (3a; n=5) or alglucosidase alfa at their pre-enrollment stable dose (3b; within a range of 20mg/kg every two weeks to 40mg/kg weekly [n=6]). All 22 participants entered an extension period to receive up to 40 mg/kg of avalglucosidase alfa every two weeks for up to nearly three years (Week 145).

At predefined time points, ptosis, a secondary endpoint, was evaluated by an ophthalmologist through standard eyelid measurements. After nearly three years (Week 145), patients who received the higher dose of avalglucosidase alfa every two weeks (40 mg/kg; Cohorts 2 and 3a) had clinically meaningful improvements in ptosis compared to those on an initial bi-weekly 20 mg/kg dose of avalglucosidase alfa (Cohort 1) or those initially receiving alglucosidase alfa for the first 25 weeks (Cohort 3b).

Safety findings from Baby-COMET

Safety results from the Phase 3 Baby-COMET trial, the first study evaluating the safety and efficacy of avalglucosidase alfa for treatment-naïve patients with IOPD (≤ 6 months of age at enrollment) (n=11), showed no unexpected safety issues at data cut-off.

9/11 (82%) participants had a total of 59 treatment-emergent adverse events (TEAEs): none had severe TEAEs, four patients had a total of six serious TEAEs (two of COVID-19, and one each of bronchitis, urinary tract infection, hyperkalemia, febrile convulsion). No deaths were reported.

Nexviazyme Data in Late-Onset Pompe Disease

Real-world findings in patients switching from prior therapy

Real-world evidence from the international, voluntary Pompe Registry sponsored by Sanofi aimed to characterize the clinical characteristics of patients with LOPD who switched from long-time standard of care, alglucosidase alfa, to avalglucosidase alfa treatment. The analysis followed 161 patients with LOPD who had received avalglucosidase alfa for up to one-year post-switch, with 60.2% having received alglucosidase alfa for ≥ 5 years pre-switch. Results showed that patients who switched to avalglucosidase alfa had stabilized respiratory function and mobility, as measured by upright forced vital capacity and 6-minute walk test, respectively. Patients also had improvements in disease-associated biomarkers after switching to avalglucosidase alfa, as measured by urinary glucose tetrasaccharide/hexose tetrasaccharide levels as well as creatinine kinase (CK), a measure of muscle dysfunction.

Long-term follow-up data from NEO-EXT

Eight-year follow-up results from the NEO-EXT trial, a Phase 2/3 study investigating the long-term safety, tolerability, pharmacokinetics, pharmacodynamics, and exploratory efficacy of avalglucosidase alfa in patients with LOPD who participated in the Phase 1 NEO1 trial, were reported. Muscle quantitative magnetic resonance imaging (qMRI) showed a trend of stabilization over time, corroborating the clinical stability demonstrated through retained lung capacity and physical endurance.

Participants in the NEO-1 trial were treatment-naïve (n=10) or had received alglucosidase alfa for ≥ 9 months (Switch, n=14) at baseline and received avalglucosidase alfa (5, 10, or 20 mg/kg/every other week [qow]) for six months. Nineteen participants entered NEO-EXT receiving their NEO1 avalglucosidase alfa dose until 2016; thereafter all received avalglucosidase alfa 20 mg/kg/qow.

About Pompe disease

People living with Pompe disease have low levels of the enzyme acid alpha-glucosidase (GAA), which results in build-up of glycogen in muscle cells throughout the body, leading to potentially irreversible damage to skeletal and cardiac muscles.

Pompe disease can present as infantile-onset Pompe disease (IOPD), the most severe form of the disease with early onset of symptoms in infancy that rapidly progress, or late-onset Pompe disease (LOPD), which progressively damages muscles over time. If left untreated, IOPD can lead to heart failure and death within the first year of life, while people living with LOPD may require mechanical ventilation to help with breathing or a wheelchair to assist with mobility as the disease progresses.

About Nexviazyme (avalglucosidase alfa)

Nexviazyme (avalglucosidase alfa) is an enzyme replacement therapy (ERT) designed with high-binding affinity to target the mannose-6-phosphate (M6P) receptor, the key pathway for uptake and transport of ERT. Nexviazyme aims to help improve uptake and enhance glycogen clearance in target tissues with an approximately 15-fold higher level of M6P moieties as compared to alglucosidase alfa, the comparator therapy in the pivotal study.

Nexviazyme is approved in multiple markets around the world for the treatment of people living with Pompe disease, with specific indications varying by country. In the US, Nexviazyme is indicated for the treatment of late-onset Pompe Disease in patients one year of age and older. In Europe, the medicine is marketed under the brand name Nexviadyme and is indicated for the treatment of both late-onset and infantile-onset Pompe disease.

About Sanofi

We are an innovative global healthcare company, driven by one purpose: we chase the miracles of science to improve people's lives. Our team, across some 100 countries, is dedicated to transforming the practice of medicine by working to turn the impossible into the possible. We provide potentially life-changing treatment options and life-saving vaccine protection to millions of people globally, while putting sustainability and social responsibility at the center of our ambitions.

Sanofi is listed on Euronext: SAN and NASDAQ: SNY

Media Relations

Sally Bain | + 1 617 834 6026 | sally.bain@sanofi.com

Victor Rouault | + 33 6 70 93 71 40 | victor.rouault@sanofi.com

Timothy Gilbert | + 1 516 521 2929 | timothy.gilbert@sanofi.com

Sandrine Guendoul | + 33 6 25 09 14 25 | sandrine.quendoul@sanofi.com

Investor Relations

Eva Schaefer-Jansen | + 33 7 86 80 56 39 | eva.schaefer-jansen@sanofi.com

Arnaud Delépine | + 33 6 73 69 36 93 | arnaud.delepine@sanofi.com

Corentine Driancourt | + 33 6 40 56 92 21 | corentine.driancourt@sanofi.com

Felix Lauscher | + 1 908 612 7239 | felix.lauscher@sanofi.com

Tarik Elgoutni | + 1 617 710 3587 | tarik.elgoutni@sanofi.com

Nathalie Pham | + 33 7 85 93 30 17 | nathalie.pham@sanofi.com

Sanofi Forward-Looking Statements

This media update 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 pandemics or other global crises may 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. 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, 2022. Other than as required by applicable law, Sanofi does not undertake any obligation to update or revise any forward-looking information or statements.

ⁱ [Blepharoptosis in infantile onset Pompe disease: Histological findings and surgical outcomes - ScienceDirect](#)