Media Update

Nexviazyme® (avalglucosidase alfa) shows sustained improvements in respiratory function and mobility in patients with Pompe disease

- Long-term data from the pivotal Phase 3 COMET trial in late-onset Pompe disease presented at WORLDSymposium™ 2022
- Additional data featured included long-term safety and efficacy results from the Phase 2 Mini-COMET study of Nexviazyme in infantile-onset Pompe disease
- Baby-COMET trial design also featured representing the first study of Nexviazyme in treatment-naive patients with infantile-onset Pompe disease

Paris, February 8, 2022. New data demonstrate people living with late-onset Pompe disease (LOPD), a rare muscle disorder, maintained improvements in respiratory function and mobility following nearly two years of treatment with Nexviazyme® (avalglucosidase alfa). This analysis of an open-label, long-term extension of the randomized, double-blind, Phase 3 COMET trial, will be presented at the 18th annual WORLD*Symposium*™.

Long-term efficacy and safety outcomes were assessed in patients who had received continuous treatment with Nexviazyme. In addition, patients treated with Nexviazyme, for at least 48 weeks, after switching from prior treatment with alglucosidase alfa (previously the only available treatment option for Pompe disease and standard of care) were included in the analysis. Over the 97 weeks, there was sustained treatment effect with Nexviazyme along with stabilization of treatment effect in patients switching from alglucosidase alfa in respiratory function (measured by forced vital capacity [FVC] percent-predicted) and walking distance (measured by the six-minute walk test [6MWT]).

> ***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
> *"This analysis builds on the positive 49-week results from the Phase 3 COMET trial, evaluating the treatment effect of avalglucosidase alfa over approximately two years in patients with late-onset Pompe disease. In addition, the results support the potential of avalglucosidase alfa to stabilize treatment effect after switching from standard-of-care treatment."*

Nexviazyme is an enzyme replacement therapy (ERT) designed to specifically target the mannose-6-phosphate receptor, the key pathway for cellular uptake of ERT in Pompe disease.

Phase 3 COMET study long-term extension results

The COMET study enrolled 100 previously untreated patients with LOPD across 55 centers in 20 countries. The primary endpoint evaluated the change in FVC percent-predicted in the upright position compared to baseline, and a key secondary endpoint measured mobility with the 6MWT compared to baseline. Patients were randomized to receive either Nexviazyme 20 mg/kg or alglucosidase alfa 20 mg/kg intravenous infusion every two weeks for 49 weeks.

During the extension period of COMET, patients who had initially received Nexviazyme continued their treatment, while patients who were previously treated with alglucosidase alfa switched to Nexviazyme 20 mg/kg. Of the 95 participants who entered the extension period, 86 (91%) remained on treatment up to last follow-up.

After nearly two years, changes (LS mean [SE]) from baseline at week 97 showed:

- Treatment with Nexviazyme in both the primary analysis and extension periods led to a 2.65 (1.05) point improvement in FVC percent-predicted compared to baseline. Patients who were treated with Nexviazyme only during the extension period showed a 0.36 (1.12) point improvement compared to baseline.
- Patients who were treated with Nexviazyme during both the primary analysis and extension periods experienced an average increase of 18.6 (12.01) meters in walking distance as measured by the 6MWT compared with the distance walked at baseline. Patients who were treated with Nexviazyme only during the extension period showed an average increase of 4.56 (12.44) meters from baseline.

The safety profile was comparable between both treatment arms (those treated with Nexviazyme throughout the study and those switching to treatment with Nexviazyme) during treatment with Nexviazyme. No new safety signals were observed in patients who switched from alglucosidase alfa to Nexviazyme during the extension period. Across both groups, five individuals discontinued treatment during the extension period due to adverse events (AEs) (ocular hyperemia, erythema, urticaria, respiratory distress, acute myocardial infarction, pancreatic adenocarcinoma). Six participants experienced serious treatment-emergent adverse reactions potentially related to therapy.

Phase 2 Mini-COMET study long-term extension results

Also for presentation at the WORLD*Symposium* are results from the extension period of the Phase 2 Mini-COMET trial. This open-label, ascending-dose, three-cohort study evaluated the safety and efficacy of Nexviazyme in patients under 18 years of age with infantile-onset Pompe disease (IOPD), a use that remains under investigation in the United States, who previously received alglucosidase alfa for six or more months and showed either a suboptimal response or a clinical decline. Patients were enrolled into one of three cohorts: (1) 20 mg/kg of Nexviazyme every two weeks (n=6), (2) 40 mg/kg of Nexviazyme every two weeks (n=5), and (3) randomized to Nexviazyme 40 mg/kg every two weeks (n=5) or alglucosidase alfa at their pre-enrollment stable dose (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 Nexviazyme every two weeks.

During the extension period:

- The most commonly reported treatment-emergent AEs were mild to moderate in severity and included rashes (8 participants), falls, pneumonia, pyrexia (7 participants each), headache, upper respiratory tract infections (6 participants each) and vomiting (5 participants). There were no serious or severe treatment-related AEs or deaths.
- The higher Nexviazyme dose (40 mg/kg every two weeks) had no increased safety risk seen in participants who switched from alglucosidase alfa to Nexviazyme.

After two years (at week 97), results showed that patients treated with Nexviazyme showed stable or improved motor function as measured by gross motor function measure (GMFM-88), quick motor function test (QMFT) total percent score, and Pompe-PEDI (Pediatric Evaluation of Disability Index) Functional Skills Scale. Additionally, all participants had a left ventricle mass z-score (LVMZ) score within normal range.

Alaa Hamed, M.D., MPH, MBA
Global Head of Medical Affairs, Rare Diseases, Sanofi
"These new data demonstrate the impact of Nexviazyme to provide sustained effect in key disease measures for both late-onset and infantile-onset Pompe disease. The research also adds to a growing body of evidence supporting this treatment's use as a new standard of care for this debilitating, life-long disease."

Phase 3 Baby-COMET trial methodology

The trial design of Baby-COMET, a Phase 3, single group, open-label, multinational, multi-center study will also be presented at the congress. Baby-COMET is the first study of Nexviazyme to include participants with IOPD who have never been treated. This study will determine the effects of Nexviazyme, externally compared with alglucosidase alfa, on overall and ventilator-free survival in participants with IOPD ≤6 months of age at enrollment.

About Pompe disease

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 muscle that supports lung function and skeletal muscles that affect mobility, as well as cardiac muscles in infantile-onset Pompe disease.

Pompe disease 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.

About Nexviazyme® (avalglucosidase alfa)

Nexviazyme® (avalglucosidase alfa) is an enzyme replacement therapy designed to target the mannose-6-phosphate (M6P) receptor. Nexviazyme is approved in the U.S. for patients with late-onset Pompe disease who are one year of age or older. Use of Nexviazyme for infantile-onset Pompe disease in the U.S. is investigational. Nexviazyme is also approved for the treatment of patients with late-onset Pompe disease and/or infantile-onset Pompe disease in several markets across the world including Japan, Canada, Switzerland, Australia and Brazil. In all other countries, use of Nexviazyme is investigational and its efficacy and safety have not been confirmed by the respective health authority.

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.

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Media Relations

Sandrine Guendoul | + 33 6 25 09 14 25 | sandrine.guendoul@sanofi.com
Sally Bain | + 1 617 834 6026 | sally.bain@sanofi.com
Chrystel Baude | + 33 6 70 98 70 59 | chrystel.baude@sanofi.com
Nicolas Obrist | + 33 6 77 21 27 55 | nicolas.obrist@sanofi.com
Victor Rouault | + 33 6 70 93 71 40 | victor.rouault@sanofi.com
Lisa Zobel | + 1 908 967 4605 | lisa.zobel@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
Priya Nanduri | +1 908 981 5560 | priya.nanduri@sanofi.com
Nathalie Pham | + 33 7 85 93 30 17 | nathalie.pham@sanofi.com

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