SANOFI

Media Update

Data presented at WORLD*Symposium*™ reinforces robust rare disease pipeline and highlights additional clinical data for investigational avalglucosidase alfa in Pompe disease

February 2, 2021

Data with investigational enzyme replacement therapy avalglucosidase alfa in late-onset Pompe disease (LOPD) and infantile-onset Pompe disease (IOPD) will be featured as platform and poster presentations at the 17th annual WORLD*Symposium*™, to be held February 8-12, 2021. These results will be presented along with data highlighting other Sanofi investigational therapies, including olipudase alfa and venglustat, underscoring Sanofi's pledge to develop meaningful solutions for the rare disease community.

"Our pipeline of investigational therapies across a range of rare diseases is unmatched within the industry and continues to grow as a result of our persistent, decades-long scientific pursuit of potential therapeutic solutions for patients in need," said Karin Knobe, Head of Development of Rare Diseases and Rare Blood Disorders at Sanofi. "As trailblazers in rare diseases, we persevere to discover therapies where no other treatment options exist. We uncover potential new options for difficult-to-treat diseases and our research in Pompe disease exemplifies this, as avalglucosidase alfa is designed to improve the delivery of a deficient enzyme into the muscle cells of patients."

Pompe disease is caused by a genetic deficiency or dysfunction of the lysosomal enzyme acid α-glucosidase deficiency (GAA), which results in build-up of complex sugars (glycogen) in muscle cells throughout the body. This accumulation of glycogen leads to irreversible damage to the muscles, including the diaphragm muscle supporting lung function and breathing, and other skeletal muscles that affect mobility.

To reduce the glycogen accumulation, Sanofi research 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 an approximately 15-fold increase in M6P content, compared to standard of care alglucosidase alfa, and aims to help improve cellular enzyme uptake and enhance glycogen clearance in target tissues.[1] The clinical relevance of this difference has not been confirmed.[2]

Data at WORLD*Symposium* on avalglucosidase alfa, some of which were previously presented in a virtual scientific session hosted by Sanofi, support the growing body of clinical evidence for avalglucosidase alfa:

Pompe	Efficacy and safety results of the avalglucosidase alfa phase 3 COMET trial in late-onset Pompe disease patients	P121;Platform Presentation February 12; 11:12 a.m. ET Priya Kishnani
Pompe	Mini-COMET study: Effects of repeat avalglucosidase alfa dosing on ptosis in participants with infantile-onset Pompe disease (IOPD) who were previously treated with alglucosidase alfa	P52; Poster Session February 10; 2:30-3:30 p.m. ET James Davison
Pompe	Mini-COMET study: Individual participant-level responses to treatment in patients with infantile-onset Pompe disease receiving repeated dose regimens of avalglucosidase alfa or alglucosidase alfa who were previously treated with alglucosidase alfa	P122; Poster Session February 10; 2:30-3:30 p.m. ET Priya Kishnani
Pompe	NEO1/NEO-EXT studies: Safety and exploratory efficacy of repeat avalglucosidase alfa dosing after up to 6 years in participant with late-onset Pompe disease (LOPD)	P58; Poster Session February 10; 2:30-3:30 p.m. ET Mazen Dimachkie
Pompe	NEO1/NEO-EXT studies: Muscle MRI results in patients with Pompe disease after long-term avalglucosidase alfa treatment	P LB-06; Poster Session February 12; 2:30-3:30 p.m. ET Pierre G. Carlier
Pompe	The Qualitative Development of the Pompe Disease Symptom Scale and Pompe Disease Impact Scale	P15; Poster Session February 11; 2:30-3:30 p.m. ET Eileen Baranowski
Pompe	Miglustat does not enhance alglucosidase alfa or avalglucosidase alfa efficacy in Pompe mice	P6; Poster Session February 11; 2:30-3:30 p.m. ET Allyson Anding

Data at WORLD*Symposium* that feature other investigational therapies from Sanofi's robust rare disease pipeline, as well as historical, real-world evidence gathered in disease registries:

Acid Sphingomyelinase Deficiency (ASMD)	Children treated with olipudase alfa for chronic acid sphingomyelinase deficiency show meaningful improvement on clinically relevant outcomes and an overall favorable safety profile: 1-year results of the ASCEND-Peds trial	Platform Presentation February 10; 11:00 a.m. ET George Diaz
ASMD	Adults with chronic sphingomyelinase deficiency show significant visceral, pulmonary, and hematologic improvements after enzyme replacement therapy with olipudase alfa: 1-year results of the ASCEND placebo-controlled trial	P265; Platform Presentation February 10; 1:12 p.m. ET Melissa Wasserstein
Gaucher	Hematologic Malignancies and Monoclonal Gammopathy of Undetermined Significance (MGUS) in Gaucher Disease (Registry data; Encore)	P214; Poster Session February 10; 2:30-3:30 p.m. ET Barry Rosenbloom
Gaucher disease type 3 (GD3)	Venglustat Combined with imiglucerase positively affects neurological features and brain connectivity in adult with Gaucher disease type 3 (Encore)	P223; Platform Presentation February 10; 1:36 p.m. ET Raphael Schiffman
Gaucher disease type 3 (GD3)	A qualitative study of the experience of venglustat for patients with Gaucher disease type 3 (GD3) in LEAP: a phase II open-label, multicenter, multinational study	P213; Poster Session February 11; 2:30-3:30 p.m. ET Camille Rochmann

Parkinson's disease GBA mutation (GBA PD)	Oral venglustat in Parkinson's disease patients with a GBA mutation: study design of part 2 of the MOVES-PD trial and patient characteristics	P196; Poster Session February 11; 2:30-3:30 p.m. ET Judith Peterschmitt
Fabry	Burden of Illness of Fabry Disease: A Retrospective Claims Analysis of a German Sickness Fund Database	P100; Poster Session February 11; 2:30-3:30 p.m. ET Max Hilz
Fabry	Stabilization of kidney function decline and cardiomyopathy in male patients with classic Fabry disease: a pre- vs. post-agalsidase beta treatment Fabry Registry analysis	P LB-37; Poster Session February 12; 2:30-3:30 p.m. ET Alberto Ortiz
Fabry	Reduced delays in diagnosis of patients with Fabry disease over time: a Fabry Registry analysis of data (1985-2020) stratified by gender and phenotype	P LB-51; Poster Session February 12; 2:30-3:30 p.m. ET Christoph Wanner
Fabry	Pregnancy outcomes in agalsidase beta-treated and untreated females with Fabry disease and their offspring: A Fabry Pregnancy Sub-Registry and Pharmacovigilance database 15-year retrospective study	P LB-27; Poster Session February 12; 2:30-3:30 p.m. ET Dawn A. Laney

Avalglucosidase alfa has not been approved by any regulatory authority and its safety and efficacy are still being evaluated. Olipudase alfa and venglustat are currently under clinical investigation and their safety and efficacy have not been evaluated by any regulatory authority worldwide.

Editor's Note:

About Avalglucosidase Alfa

In November 2020, the U.S. Food and Drug Administration (FDA) accepted for Priority Review the Biologics License Application (BLA) for avalglucosidase alfa for long-term enzyme replacement therapy for the treatment of patients with Pompe disease. A decision by the FDA is anticipated in May 2021. The FDA also granted Breakthrough Therapy and Fast Track designations to avalglucosidase alfa.

In October 2020, the European Medicines Agency accepted for review the Marketing Authorization Application for avalglucosidase alfa for long-term enzyme replacement therapy for the treatment of patients with 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.[3]

About Olipudase Alfa

Olipudase alfa is an investigational enzyme replacement therapy designed to replace deficient or defective enzyme acid sphingomyelinase, an enzyme which is found in special compartments within cells called lysosomes and is required to break down lipids called sphingomyelin. Olipudase alfa is currently being investigated to treat non-CNS manifestations of ASMD.

ASMD, historically known as Niemann-Pick Disease type A and type B, is a rare, lysosomal storage disease. ASMD represents a spectrum of disease caused by the same enzymatic deficiency, with two types that may represent opposite ends of a continuum, sometimes referred to as ASMD type A and ASMD type B. ASMD type A is a rapidly progressive neurological form of the disease resulting in death in early childhood due to CNS complications. ASMD type B, is a serious and potentially life-threatening disease that predominantly, but not only, impacts the lungs, liver, spleen and heart. ASMD type A/B represents an intermediate form that includes varying degrees of neurologic involvement. Olipudase alfa has not been studied in ASMD type A patients.

Olipudase alfa has been granted Breakthrough Therapy designation by the FDA, PRIority Medicines, also known as PRIME, designation by the European Medicines Agency and SAKIGAKE designation in Japan.

About Venglustat

Venglustat is an investigational oral glucosylceramide synthase inhibitor in development for multiple diseases with disruptions in the GSL metabolic pathway. These diseases include three lysosomal storage disorders: Gaucher disease type 3, Fabry disease and GM2 gangliosidosis as well as autosomal dominant polycystic kidney (ADPKD) disease and GBA-associated Parkinson's disease.

The GSL pathway is a metabolic hub within the body where critical cellular building blocks called glycosphingolipids (GSLs) are made and metabolized. These GSLs are fatty substances essential for maintaining the cell membranes. GSLs are routinely metabolized in healthy cells; however, malfunctions in the GSL pathway can occur in people with certain gene mutations causing the build up of GSLs in the cells and ultimately cause disease.[4]

The FDA has granted Fast Track designation for the development of venglustat as an investigational therapy for the treatment of Gaucher disease type 3, Fabry disease and GM2 gangliosidosis.

Sanofi has been granted Orphan Drug Designation for venglustat in Europe and the U.S. for treatment of patients with Fabry disease, ADPKD, Gaucher disease and GM2 gangliosidosis.

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

[2] Sanofi's investigational enzyme replacement therapy shows clinically meaningful improvement in critical manifestations of late-onset Pompe disease. https://www.sanofi.com/en/media-room/press-releases/2020/2020-06-16-14-00-00. June 16, 2020.

[3] 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 January 11, 2021.

[4] Merscher, S and Fornoni, A. Podocyte pathology and nephropathy - sphingolipids in glomerular diseases. Front Endocrinol. 2014; 5:127. 10.3389/fendo.2014.00127