



European Commission Grants Marketing Authorization for Cerdelga® (eliglustat), Genzyme's Oral Therapy for Gaucher Disease Type 1

Paris - January 22, 2015 - [Sanofi](#) and its subsidiary [Genzyme](#) announced today that the European Commission (EC) has granted marketing authorization for Cerdelga® (eliglustat) capsules, a first line oral therapy for certain adults living with Gaucher disease type 1. A small number of adult patients who metabolize Cerdelga more quickly or at an undetermined rate, as detected by an established genetic laboratory test, will not be eligible for Cerdelga treatment. Cerdelga was approved by the U.S. Food and Drug Administration in August 2014, and is under review by other regulatory authorities around the world. It is expected that Cerdelga will be available commercially in EU countries beginning in 2015 and over the next few years.

Cerdelga is a potent, highly specific ceramide analogue inhibitor of glucosylceramide synthase with broad tissue distribution including to bone marrow. It reduces the production of glucosylceramide, the substance that builds up in the cells and tissues of people with Gaucher disease type 1. Cerdelga is indicated in the European Union for the long-term treatment of adult patients with Gaucher disease type 1 (GD1), who are CYP2D6 poor metabolizers (PMs), intermediate metabolizers (IMs) or extensive metabolizers (EMs).

The majority of adverse reactions of Cerdelga are mild and transient. The most commonly reported adverse reaction with Cerdelga is diarrhea, in approximately 6% of the patients. The incidence of diarrhea was the same or higher with placebo than with Cerdelga in the placebo-controlled pivotal study. Less than 2% of patients receiving Cerdelga permanently discontinued treatment due to any adverse reaction.

The EC approval was based on data from the Cerdelga clinical development program, the largest clinical research program ever conducted in Gaucher disease type 1, with approximately 400 patients treated in 29 countries. The development program included two pivotal Phase 3 clinical trials. In a Phase 3 placebo-controlled trial (ENGAGE, a study in treatment-naïve patients with Gaucher disease type 1) improvements were seen across the following endpoints after 9 months on Cerdelga: spleen size, platelet levels, hemoglobin levels, and liver volume. The second Phase 3 trial was designed to assess disease stability in patients previously treated with enzyme replacement therapy (ENCORE). That trial met the pre-specified criteria for non-inferiority to an enzyme replacement therapy (imiglucerase), which was a composite endpoint of each of the following parameters: spleen volume, hemoglobin levels, platelet counts, and liver volume. Patients in the registration studies continued to receive Cerdelga in the extension periods, and the majority of patients are in their 4th or 5th year of treatment. In a Phase 2 clinical study in treatment-naïve patients, Cerdelga has shown a positive effect on bone parameters including Bone Marrow Burden (BMB) and Bone Mineral Density (BMD) which was sustained over a period of at least 4 years. The majority of phase 2 patients in the extension period are now in their 8th year of treatment.

About Gaucher Disease

Gaucher disease is an inherited condition affecting fewer than 10,000 people worldwide. People with Gaucher disease do not have enough of an enzyme, acid beta-glucosidase (glucocerebrosidase) that breaks down a certain type of fat molecule. As a result, lipid engorged cells (called Gaucher cells) amass in different parts of the body, primarily the spleen, liver and bone marrow. Accumulation of Gaucher cells may cause spleen and liver enlargement, anemia, excessive bleeding and bruising,



bone disease and a number of other signs and symptoms. The most common form of Gaucher disease, type 1, generally does not affect the brain.

About Cerdelga

Cerdelga (eliglustat), a novel glucosylceramide analog given orally, was designed to partially inhibit the enzyme glucosylceramide synthase, which results in reduced production of glucosylceramide. Glucosylceramide is the substance that builds up in the cells and tissues of people with Gaucher disease. The concept was initially developed by the late Norman Radin, PhD, from the University of Michigan. In pre-clinical studies, the molecule, developed with James A. Shayman, MD, also from the University of Michigan, showed specificity for glucosylceramide synthase. Following an extensive pre-clinical and early clinical research program, Cerdelga was studied in the largest Phase 3 clinical program ever conducted in Gaucher disease.

Cerdelga is registered as an orphan medicinal product for the treatment of Gaucher disease in the Community Register of Orphan Medicinal Products.

EU indication and Usage

Cerdelga is indicated for the long-term treatment of adult patients with Gaucher disease type 1 (GD1), who are CYP2D6 poor metabolisers (PMs), intermediate metabolisers (IMs) or extensive metabolisers (EMs).

Important Safety Information about Cerdelga for EU patients

Cerdelga is contraindicated in patients who are CYP2D6 intermediate metabolisers (IMs) or extensive metabolisers (EMs) taking a strong or moderate CYP2D6 inhibitor concomitantly with a strong or moderate CYP3A inhibitor, and in patients who are CYP2D6 poor metabolisers (PMs) taking a strong CYP3A inhibitor. Under these conditions both major metabolic pathways for eliglustat metabolism are impaired, with predicted substantially elevated eliglustat plasma concentrations. Although no significant QTc increases were seen in a thorough QT study in healthy volunteers, based on PK/PD modelling, eliglustat plasma concentrations 11-fold the predicted human C_{max} are predicted to cause mild increases in the PR, QRS, and QTc intervals.

Use of Cerdelga in patients with pre-existing cardiac conditions has not been studied during clinical trials. Because eliglustat is predicted to cause mild increases in ECG intervals at substantially elevated plasma concentrations, use of Cerdelga should be avoided in patients with cardiac disease (congestive heart failure, recent acute myocardial infarction, bradycardia, heart block, ventricular arrhythmia), long QT syndrome, and in combination with Class IA (e.g. quinidine) and Class III (e.g. amiodarone, sotalol) antiarrhythmic medicinal products.

Patients should be regularly monitored for clinical response.

The most common side effects of Cerdelga (greater than 2% of patients) are headache, nausea, diarrhoea, abdominal pain, flatulence, arthralgia, and fatigue. The most frequently reported serious adverse reaction in clinical studies was syncope (0.76%). All events were associated with predisposing risk factors and appeared to be vasovagal in nature. None of these events led to discontinuation from the study.

Prescribing information and more information about Cerdelga for EU patients will be available shortly at: http://ec.europa.eu/health/documents/community-register/html/index_en.htm.

For full prescribing information and more information about Cerdelga for U.S. patients, please visit: http://www.cerdelga.com/pdf/cerdelga_prescribing_information.pdf.

About Genzyme, a Sanofi Company

Genzyme has pioneered the development and delivery of transformative therapies for patients affected by rare and debilitating diseases for over 30 years. We accomplish our goals through world-class research and with the compassion and commitment of our employees. With a focus on rare diseases and multiple sclerosis, we are dedicated to making a positive impact on the lives of the patients and families we serve. That goal guides and inspires us every day. Genzyme's portfolio of transformative therapies, which are marketed in countries around the world, represents



groundbreaking and life-saving advances in medicine. As a Sanofi company, Genzyme benefits from the reach and resources of one of the world's largest pharmaceutical companies, with a shared commitment to improving the lives of patients. Learn more at www.genzyme.com.

Genzyme® and Cerdelga® are registered trademarks of Genzyme Corporation.

About Sanofi

Sanofi, a global healthcare leader, discovers, develops and distributes therapeutic solutions focused on patients' needs. Sanofi has core strengths in the field of healthcare with seven growth platforms: diabetes solutions, human vaccines, innovative drugs, consumer healthcare, emerging markets, animal health and the new Genzyme. Sanofi is listed in Paris (EURONEXT: [SAN](#)) and in New York (NYSE: [SNY](#)).

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 absence of guarantee that the product candidates if approved will be commercially successful, the future approval and commercial success of therapeutic alternatives, the Group's ability to benefit from external growth opportunities, trends in exchange rates and prevailing interest rates, the impact of cost containment policies and subsequent changes thereto, the average number of shares outstanding as well as those 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, 2013. 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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