



ENGAGE Randomized Clinical Trial Evaluating Cerdelga® (eliglustat) for Treatment-Naïve Patients with Gaucher Disease Type 1 Published in *The Journal of the American Medical Association*

- Treatment with Genzyme's Cerdelga® (eliglustat) for nine months results in significant improvements in spleen volume, hemoglobin level, liver volume and platelet count compared to placebo -

Paris - February 17, 2015 - [Sanofi](#) and its subsidiary [Genzyme](#), today announced the publication of results from the ENGAGE registration study evaluating Cerdelga® (eliglustat) in treatment-naïve patients with Gaucher disease type 1 in the February 17, 2015 issue ([link to the article](#)) of *The Journal of the American Medical Association*.

The ENGAGE study is a Phase 3 randomized, double-blinded, placebo-controlled, multinational registration trial of 40 eligible treatment-naïve patients with Gaucher disease type 1 who had splenomegaly in addition to thrombocytopenia and/or anemia at study entry. Gaucher disease is a genetic disorder in which individuals fail to produce glucocerebrosidase, an important enzyme that breaks down the glycolipid glucocerebroside within lysosomes. In the absence of glucocerebrosidase, lipids accumulate in the bone marrow, lungs, spleen, liver and the brain – causing spleen and liver enlargement, red and white blood cell abnormalities and bone deterioration; therefore endpoints that specifically measured change in these symptoms were used in the study.

Patients were stratified by baseline spleen volume and randomized 1:1 to receive Cerdelga (50 or 100 mg twice daily) or placebo for nine months, following assessment for improvements in disease manifestations.

According to the lead author Pramod Mistry, MD, PhD, FRCP, Professor of Pediatrics & Internal Medicine at Yale University School of Medicine, *"We are very encouraged by these results as they ultimately point to a safe and effective oral treatment option for patients living with Gaucher disease."*

The primary efficacy endpoint of the study demonstrated:

- A statistically significant reduction from baseline in spleen size by a mean of 28 percent compared in Cerdelga patients with a mean increase of two percent in placebo patients, for an absolute difference of 30 percent (P less than 0.0001)

Secondary endpoints were also statistically significant:

- Hemoglobin levels increased from baseline by an absolute difference of 1.2 g/dL compared with placebo (P=0.006)
- Liver volume decreased from baseline by an absolute difference of 6.6 percent compared with placebo (P=0.0072)
- Platelet levels increased from baseline by an absolute difference of 41 percent compared with placebo (P less than 0.0001)



There were no serious adverse events associated with either treatment group. All adverse reactions reported in the primary analysis period of the ENGAGE study were mild or moderate and included arthralgia, headache, migraine, flatulence, nausea, and oropharyngeal pain (all occurring in greater than 10% of Cerdelga treated patients and more frequently than placebo). One patient withdrew from the trial for a reason not related to treatment. At the end of the nine months, patients who were on placebo were transitioned to Cerdelga.

Genzyme developed Cerdelga, a first-line oral small molecule, to provide a therapeutic alternative for individuals with Gaucher disease type 1 and expand the range of available treatment options for this rare genetic disease. Cerdelga is a ceramide analog that works by blocking the enzyme beta-glucosylceramide synthase, slowing the production of glucocerebroside, the substance that builds-up in patients' lysosomes. Patients with Gaucher disease type 1 retain some residual glucocerebroside enzyme activity and Cerdelga aims to slow the formation of the lipid to help balance the cell's ability to clear it.

"We pioneered the world's first therapy for Gaucher disease more than 20 years ago and have been dedicated ever since to advancing the science behind Gaucher disease treatments," said Genzyme's Acting Head of Rare Diseases, Richard Peters MD, Ph.D. *"We remain committed to exploring alternative and effective therapeutic approaches, like oral therapy, that translate into meaningful outcomes for patients with unmet needs."*

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, beta-glucosidase (glucocerebroside) 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, with approximately 400 patients treated in 30 countries.

On August 19, 2014, the U.S. Food and Drug Administration (FDA) approved Cerdelga® (eliglustat) capsules, the only first-line oral therapy for certain adult Gaucher disease type 1 patients. The FDA approval was based on efficacy data from two positive Phase 3 studies for Cerdelga®: one in patients new to therapy (ENGAGE), and the other in patients switching from approved enzyme replacement therapies (ENCORE). The filing also incorporated four years of efficacy data from the Cerdelga® Phase 2 study. On January 19, 2015, the European Commission (EC) also granted marketing authorization for Cerdelga.

IMPORTANT SAFETY INFORMATION

Indications and Usage

Cerdelga® (eliglustat) capsules are indicated for the long-term treatment of adults with Gaucher disease type 1 (GD1) who are CYP2D6 extensive metabolizers (EMs), intermediate metabolizers (IMs) or poor metabolizers (PMs) as detected by an FDA-cleared test. Patients who are CYP2D6 ultra-rapid metabolizers (URMs) may not achieve adequate concentrations of Cerdelga® to achieve a



therapeutic effect. A specific dose cannot be recommended for those patients whose CYP2D6 genotype cannot be determined (indeterminate metabolizers).

Important Safety Information

Cerdelga® is contraindicated in the following patients due to the risk of significantly increased Cerdelga® plasma concentrations which may result in prolongation of the PR, QTc and/or QRS cardiac intervals that could result in cardiac arrhythmias: EMs or IMs taking a strong or moderate CYP2D6 inhibitor concomitantly with a strong or moderate CYP3A inhibitor and IMs or PMs taking a strong CYP3A inhibitor.

Drugs that inhibit CYP2D6 and CYP3A may significantly increase the exposure to Cerdelga®; Cerdelga® dose adjustment may be needed, depending on metabolizer status. See section 7 of the full Prescribing Information for more details and other potentially significant drug interactions.

Because Cerdelga® is predicted to cause increases in ECG intervals at substantially elevated plasma concentrations, use is not recommended in patients with pre-existing cardiac disease, long QT syndrome, or in combination with Class IA and Class III antiarrhythmic medications.

The most common adverse reactions (greater than equal to 10%) for Cerdelga® are: fatigue, headache, nausea, diarrhea, back pain, pain in extremities and upper abdominal pain.

Only administer Cerdelga® during pregnancy if the potential benefit justifies the potential risk; based on animal data, Cerdelga® may cause fetal harm. Discontinue drug or nursing based on importance of drug to mother. Cerdelga® is not recommended in patients with moderate to severe renal impairment or in patients with hepatic impairment.

To report SUSPECTED ADVERSE REACTIONS, contact Genzyme Corporation at (1-800-745-4447) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see full Prescribing Information, including patient Medication Guide, for additional important safety information.

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.

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About Sanofi

Sanofi, a global and diversified 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](http://www.sanofi.com)) and in New York (NYSE: [SNY](http://www.sanofi.com)).



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 labeling 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, 2011. 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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