Genzyme Presents Phase 3 Clinical Trial Extension Results for Cerdelga® (eliglustat) at Lysosomal Disease Network’s WORLD Symposium 2015

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Trials Demonstrate Long-term Efficacy, Safety and Tolerability of Oral Therapy to Treat Certain Adults with Gaucher Disease Type 1

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Genzyme, a Sanofi company, today reported extension study data from its Phase 3 ENGAGE and ENCORE studies of Cerdelga®, (eliglustat), a first-line oral therapy approved by the FDA and the European Commission for the treatment of certain adults with Gaucher disease type 1. The results from the studies were presented today at the 11th Annual Lysosomal Disease Network WORLD Symposium in Orlando, Fla. Both extension studies demonstrated continued stability and/or improvements across established end points and published therapeutic treatment goals.

Genzyme developed Cerdelga, a capsule taken orally, to provide a treatment alternative for certain adult patients with Gaucher disease type 1 and to provide a broader range of treatment options for patients and physicians. Genzyme’s clinical development program for Cerdelga represents the largest clinical program ever focused on Gaucher disease, with approximately 400 patients treated in 29 countries.

The oral presentations on these Phase 3 studies were:

- **ENGAGE** — A Phase 3, Randomized, Double-Blind, Placebo-Controlled, Multi-Center Study to Investigate the Efficacy and Safety of Eliglustat in Adults with Gaucher Disease Type 1: Results after 18 Months, Pramod Mistry, MBBS, PhD, F.R.C.P, Director of Yale Lysosomal Disease Center and Gaucher Disease Treatment Center Yale School of Medicine: In the primary analysis period, improvements were seen across the following endpoints after 9 months on Cerdelga: spleen size, platelet count, hemoglobin concentration, and liver volume. In the 9 month extension phase, patients who switched from placebo to eliglustat showed improvements similar to the eliglustat-treated patients during the primary analysis while the eliglustat-treated patients continued to show improvements during the 9 month extension period. There were no treatment-related discontinuations.

- **ENCORE**— a Phase 3, Randomized, Controlled, Open-Label Non-Inferiority Study Comparing Eliglustat to Imiglucerase in Gaucher Disease Type 1 Patients Stabilized on Enzyme Replacement Therapy: 24-Month Results, Timothy M. Cox, MD, FRCP, Research Director and Professor of Medicine, Addenbrooke’s Hospital, Cambridge, UK. The study, which met the primary analysis criteria for non-inferiority to imiglucerase (Cerezyme®), had a composite endpoint of each of the following parameters: spleen volume, hemoglobin concentration, platelet counts, and liver volume at 12 months. During the 12-month extension period, the patients who crossed over to eliglustat treatment from imiglucerase remained stable. Patients treated with eliglustat for 24 months also maintained stability of clinical parameters during the extension period.

The most common adverse reactions (≥10%) in the primary analysis periods of ENGAGE and ENCORE were fatigue, headache, nausea, diarrhea, back pain, pain in extremities, and upper abdominal pain. In both extension studies the majority of adverse reactions with Cerdelga were mild and transient, and consistent with those in the primary analysis periods.

Most patients in both of the Phase 3 studies continue to receive Cerdelga in longer term extension periods. The majority of patients are now in their 4th or 5th year of treatment.

“The continued work within Genzyme’s Gaucher program and the approval of Cerdelga represent are important to both the company and this patient community,” said Genzyme’s Acting Head of Rare Diseases, Richard Peters, M.D., Ph.D. “The results of the extension studies in which the majority of patients stayed on therapy support the use of Cerdelga as a first-line treatment option for the long-term management of Gaucher disease type 1.”

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 the enzyme, β-glucosidase (glucocerebrosidase) leading to the accumulation of its substrate, glucosylceramide. 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.

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 (≥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.

Cerezyme Important Safety Information

Approximately 15% of patients have developed IgG antibodies to Cerezyme during the first year of therapy. Approximately 46% of patients with detectable IgG antibodies experienced symptoms of hypersensitivity, and these patients have a higher risk of hypersensitivity. It is suggested that patients be monitored periodically for IgG antibody formation during the first year of treatment.

Hypersensitivity has also been observed in patients without detectable IgG antibodies. Symptoms suggestive of hypersensitivity have been noted in approximately 6.6% of all patients, and anaphylactoid reactions in less than 1%. Treatment with Cerezyme should be approached with caution in patients who have exhibited hypersensitivity symptoms such as pruritus, flushing, urticaria, angioedema, chest discomfort, dyspnea, coughing, cyanosis, and hypotension. Pre-treatment with antihistamines and/or corticosteroids and a reduced rate of infusion may allow continued treatment in most patients.

In less than 1% of patients, pulmonary hypertension and pneumonia have been observed during treatment with Cerezyme. These are known complications of Gaucher disease regardless of treatment. Patients with respiratory symptoms in the absence of fever should be evaluated for the presence of pulmonary hypertension.

Approximately 13.8% of patients have experienced adverse events related to treatment with Cerezyme. Some of these are injection site reactions such as discomfort, pruritus, burning, swelling or sterile abscess at the site of injection. Additional adverse reactions that have been reported include nausea, abdominal pain, vomiting, diarrhea, rash, fatigue, headache, fever, dizziness, chills, backache, and tachycardia. Transient peripheral edema has also been reported for this therapeutic class of drug.

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 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 Genzyme. Sanofi is listed in Paris (EURONEXT: SAN) and in New York (NYSE: SNY).

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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