

## **Shire Reports Positive Results from First of Three Phase III Trials of velaglucerase alfa for Type 1 Gaucher Disease and Provides Important Updates on Interactions with FDA**

Treatment Protocol Accepted and Rolling Submission of New Drug Application Initiated

**Lexington, Massachusetts, US – August 3, 2009** – Shire plc (LSE: SHP, NASDAQ: SHPGY), the global specialty biopharmaceutical company, today reported positive results from the first of three Phase III studies of velaglucerase alfa, its enzyme replacement therapy in development for the treatment of Type 1 Gaucher disease. The Company also announced that the U.S. Food and Drug Administration (FDA) has accepted its treatment protocol for velaglucerase alfa and that Shire has begun its rolling submission of the New Drug Application (NDA) for velaglucerase alfa allowed under the Fast Track process.

“We are very pleased with the progress of the velaglucerase alfa program from both a clinical and regulatory perspective,” said Sylvie Grégoire, President of Shire Human Genetic Therapies. “This data are consistent with those previously reported from the Phase I/II and extension studies. We will continue to work diligently with the FDA and other regulatory agencies to make velaglucerase alfa available as soon as possible to help meet the needs of the Gaucher community.”

Shire's velaglucerase alfa program is the largest and most comprehensive set of Phase III clinical trials conducted to date for Gaucher disease. Over 100 patients at 24 sites in 10 countries around the world have participated in the clinical studies.

Velaglucerase alfa is made using Shire's proprietary technology, in a human cell line. The enzyme produced has the exact human amino acid sequence and carries a human glycosylation pattern.

### **Phase III Study Overview and Results**

The first trial in the Phase III program to be completed was a multicenter, randomized, double-blind, two dose study of velaglucerase alfa in patients with Type 1 Gaucher disease. The primary goal of this study was to evaluate the safety and efficacy of velaglucerase alfa in 25 patients with Type 1 Gaucher disease.

Patients aged two years and older who were treatment naïve were eligible to participate in the study if they presented with disease-related anemia and had at least one of the following clinical manifestations of Gaucher disease: thrombocytopenia, moderate splenomegaly or a readily palpable enlarged liver. Patients were randomized to receive velaglucerase alfa at either 45 U/ kg or 60 U/ kg for a duration of 12 months.

In the trial, the primary endpoint was reached with patients benefiting from a clinically important and statistically significant ( $p < 0.0001$ ) increase in mean hemoglobin concentration compared with baseline after receiving velaglucerase alfa at 60 U/kg IV every other week for 12 months. Statistically significant improvements compared with baselines were also observed in platelet and spleen sizes, and nominally significant improvements were observed in liver size at this dose. Results were clinically important as defined by standard criteria and consistent with the previously published Phase I/II data.

At the 45 U/kg IV dose, statistically significant improvements in hemoglobin, platelet count, and spleen volume were also demonstrated. The magnitude of changes in the 45U/kg dose

was also clinically important, and a trend in liver volume reduction was observed. The 60U/kg dose performed numerically as well or better than 45U/kg across all measured clinical endpoints.

The specific data from this trial will be presented at a scientific meeting later this year.

Velaglucerase alfa was found to be generally well tolerated with no drug-related serious adverse events reported in the trial. No patients withdrew from the trial due to an adverse event.

Most of the drug-related adverse events were reported in association with velaglucerase alfa infusions, all of which were mild and resolved without sequelae.

“These findings are very encouraging. They illustrate important potential benefits that velaglucerase alfa may provide to patients who are affected by Type 1 Gaucher disease,” said Dr. Atul Mehta, Clinical Director of the Lysosomal Storage Disorders Unit, Royal Free Hospital, London. “Velaglucerase alfa appears to be an excellent choice for Type 1 Gaucher patients. The prospect of having another treatment option available to help patients achieve therapeutic goals is very important and is welcomed by both the physicians and patients.”

### **Regulatory Updates**

With regard to ongoing interactions with the FDA, Shire provided the following important updates:

- The FDA has accepted Shire’s treatment protocol for velaglucerase alfa. The acceptance of the treatment protocol by the FDA will enable physicians to treat Gaucher patients with velaglucerase alfa prior to commercialization. Shire will initially provide velaglucerase alfa free of charge to patients who are enrolled in the protocol.
- Shire has begun a rolling submission of a New Drug Application (NDA) to the FDA for velaglucerase alfa to treat patients with Type 1 Gaucher disease. The submission was initiated on July 30, 2009, three weeks after Shire received Fast Track designation. Fast Track designation allows a company to file the sections of the NDA as they become available and enables the agency to commence its review on a rolling basis. The company expects to complete the NDA submission by the end of this quarter.

### **Background on Gaucher disease**

Gaucher disease is an autosomal recessive disease and the most prevalent Lysosomal Storage Disorder (LSD), with an incidence of about 1 in 20,000 live births. Despite the fact that Gaucher Disease consists of a phenotype, with varying degrees of severity, it has been sub-divided in three subtypes according to the presence or absence of neurological involvement. It is also the most common genetic disease affecting Ashkenazi Jewish people (Eastern, Central and Northern European ancestry), with a carrier frequency of 1 in 10 (Dr. John Barranger and Dr. Ed Ginns 1989). This panethnic disease involves many organ systems, such as liver, spleen, lungs, brain, metabolism and bone marrow.

Gaucher Disease results from a specific enzyme deficiency in the body, caused by a genetic mutation received from both parents. The disease course is quite variable, ranging from no outward symptoms to severe disability and death. Carrier status can be detected through blood or saliva to identify potential carriers of the Gaucher gene. Gaucher Disease can be diagnosed early through a blood test.

Worldwide the diagnosed population of Gaucher Disease patients is approximately 7,000. Based on incidence, the estimated total world population is likely to be between 10,000 and 15,000 patients.

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**Notes to editors**

**SHIRE PLC**

Shire's strategic goal is to become the leading specialty biopharmaceutical company that focuses on meeting the needs of the specialist physician. Shire focuses its business on attention deficit hyperactivity disorder (ADHD), human genetic therapies (HGT) and gastrointestinal (GI) diseases as well as opportunities in other therapeutic areas to the extent they arise through acquisitions. Shire's in-licensing, merger and acquisition efforts are focused on products in specialist markets with strong intellectual property protection and global rights. Shire believes that a carefully selected and balanced portfolio of products with strategically aligned and relatively small-scale sales forces will deliver strong results.

For further information on Shire, please visit the Company's website: [www.shire.com](http://www.shire.com).

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