genzyme

# MYOZYME® (2000 L) SUPPLY UPDATE – US VERSION – JANUARY 2009

We would like to take this opportunity to provide an important update to the Pompe Community.

## Background

In the early stages of development of Myozyme® (alglucosidase alfa), Genzyme initiated manufacturing at the 160 liter (L) scale, and has since scaled-up the process to produce larger quantities of product for commercial use worldwide. The bioreactors in which alglucosidase alfa has been produced over the course of time have steadily grown in size to the 2000 L scale that currently produces product for worldwide use including US patients enrolled in the Myozyme Temporary Access Program (MTAP). In the US, patients under 18 years of age continue to receive Myozyme produced at the 160 L scale. This incremental scale-up is standard manufacturing practice for any biological drug development process. In the US, the FDA determined that alglucosidase alfa produced at the 160 L scale and alglucosidase alfa produced at the 2000 L scale should be classified as two different products. A new Biologics License Application (BLA) was submitted to the FDA for the 2000 L product and a response is expected on or before February 28, 2009.

Due to the rapidly growing number of patients with Pompe disease receiving treatment, worldwide demand for Myozyme has continuously increased since it was launched in April 2006. Anticipating a higher long-term demand, Genzyme started to develop an even larger production facility of 4000 L bioreactors approximately five years ago at a manufacturing facility located in Belgium. Genzyme has submitted an application to the European Medicines Evaluation Agency (EMEA), the regulatory authority that assesses whether a drug is efficacious and safe in the European Union. Under the standard 60-day review process we would expect approval in April 2009 at the earliest. Genzyme has requested an expedited review of its application from the EMEA Committee for Medicinal Products for Human Use (CHMP). Ultimately, Genzyme plans to apply for 4000 L approval with regulatory agencies throughout the world, including the US, to be the main supply source of alglucosidase alfa in its effort to assure a sustainable supply for the Pompe Community.

## Update

As Genzyme previously stated in July 2008 and again in October 2008, due to greater than expected adoption and rapidly increasing global demand, Myozyme (2000 L) supply will be particularly tight until 4000 L production is approved in the European Union. Beginning in January inventory levels are expected to be so tight that there is a risk of delays in order fulfillment that could result in potential interruptions to therapy. To responsibly manage through this temporary supply constraint and best support those currently receiving Myozyme produced at the 2000 L scale, and in particular to safeguard supply for infants and children

worldwide, the company has taken a number of steps to ensure optimal management of the existing supply until the 4000 L manufacturing scale is approved by the European Medicines Evaluation Agency (EMEA). Genzyme will continue to work collaboratively with the EMEA to expedite the review of the 4000 L process. Also, Genzyme is exploring the potential for providing Pompe patients with access to Myozyme produced at the 4000 L scale prior to approval in the European Union, should this become necessary.

In addition, Genzyme has also collaborated with a group of stakeholders from the global Pompe Community, the Myozyme Stakeholders Working Group (MSWG) composed of leading physicians from several countries, including the US, and patient community representatives from the International Pompe Association, to develop a guidance document to help with clinical decision making during this temporary period of supply constraint. In the US, this guidance will affect patients currently enrolled in MTAP. These measures will NOT impact patients receiving treatment with commercial Myozyme produced at the 160 L scale.

**The following recommended guidelines will be in effect as of January 13, 2009:**

- In the US, infants and children should continue to receive their prescribed treatment (Myozyme produced at the 160 L scale) without any interruptions, and all newly diagnosed infants and children should start therapy as recommended by their physicians.

- In the US, patients enrolled in the Myozyme Temporary Access Program (MTAP) should immediately cancel their infusion between January 15th and January 31st and one infusion each subsequent month until further information becomes available from Genzyme.

- Outside the US, all adults (ages 19 and older) receiving Myozyme (2000 L) through commercial, charitable, or temporary access channels should receive monthly infusions beginning in January until Myozyme inventory levels return to normal. This means adults should immediately cancel their infusion between January 15th and January 31st and cancel one infusion each month until further information becomes available from Genzyme.

- No new adult patients should initiate therapy until Myozyme (2000 L) inventory levels return to normal. In the US, the 2000 L product is not yet approved for commercial use and is still under review at the FDA. A response from the FDA is expected by February 28, 2009. Enrollment in MTAP remains closed at this time. Any physician who feels their patient is in urgent need of therapy may contact Genzyme Medical Information at (800) 745-4447, option 2.

Genzyme will continue to provide frequent updates to the community as new information becomes available. Anyone requiring immediate assistance and who cannot reach their local Genzyme representative is encouraged to contact Genzyme Medical Information at 800-745-4447 option 2. In the meantime, we fully appreciate the impact of this situation on both families and physicians. Please know that we remain committed to resolving the supply constraints as quickly as possible.