DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

BLA 125291/79

SUPPLEMENT APPROVAL

Genzyme Corporation
Attention: Jennifer Eaddy, RAC
Manager, Regulatory Affairs
500 Kendall Street
Cambridge, MA 02142

Dear Ms. Eaddy:

Please refer to your Supplemental Biologics License Application (sBLA), dated December 22, 2011, received December 22, 2011, submitted under section 351 of the Public Health Service Act for Lumizyme (alglucosidase alfa).

We acknowledge receipt of your amendment dated June 1, 2012, and your risk evaluation and mitigation strategy (REMS) assessment dated May 24, 2011. This supplement is in response to our communication dated August 1, 2011, based upon our review of your May 24, 2011, REMS assessment.

This supplemental new drug application provides for proposed modifications to the approved REMS.

We have completed our review of this supplemental application. It is approved effective on the date of this letter.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

The REMS for Lumizyme (alglucosidase alfa) was originally approved on May 24, 2010, and a REMS modification was approved on September 12, 2011. The REMS consists of a communication plan, elements to assure safe use, an implementation system, and a timetable for submission of assessments of the REMS. Your proposed modifications to the REMS consist of changes to the following:

1. Lumizyme ACE Program online training and certification program (slide deck):
    a. Addition of YES/NO options for completion of the program
    b. Addition of a slide with a link to print enrollment forms
    c. Inclusion of the following text to slide #13:
        i. "Lumizyme is individually bagged and shipped on a named-patient basis. Vials may be used only for the

intended patient and should not be substituted for another patient."

d. Addition of the following text to Slide # 19: "for materials to facilitate training at your site, click here."

2. Patient Enrollment and Acknowledgement Form: Revision of this form to make it user-friendly and to include the following text:

"late-onset patients with evidence of cardiac hypertrophy unrelated to their Pompe disease may still receive Lumizyme."

3. The REMS Document as follows:
   a. Editorial revisions to Section A, Communication Plan, to be consistent with current REMS documents. No programmatic changes were made to the REMS program.
   b. Addition of the following text to Section B 2 a ii, second bullet:
   "In rare events such as vial breakage, patient weight change impacting the current dose, or a rescheduled infusion where Lumizyme vials cannot be shipped to the facility in time, vials designated for a patient enrolled in the Lumizyme ACE Program can be used for another patient also enrolled in the Lumizyme ACE Program at the same healthcare facility. Prior to using these vials, the healthcare facility must contact Genzyme to review the details of the event and to order replacement vials."
   c. Modification of the timetable for submission of assessments to include the date of the REMS approval.

4. The REMS Materials as follows:
   a. Incorporate the following new safety information consistent with the label approved on July 9, 2012, into the Slide Deck, the Lumizyme ACE Training and Certification Program:
   "Nephrotic syndrome secondary to membranous glomerulonephritis was observed in a few Pompe disease patients treated with alglucosidase alfa who had persistently positive anti-rhGAA IgG antibody titers. In these patients renal biopsy was consistent with immune complex deposition. Patients improved following treatment interruption. It is therefore recommended to perform periodic urinalysis."
   b. Addition of the following forms in order to implement an electronic option for the prescriber and healthcare facility enrollment and reenrollment:
      - On-Line Healthcare Facility Enrollment and Attestation Form
      - On-Line Prescriber Enrollment and Attestation Form

5. Minor visual updates to the Patient Enrollment and Acknowledgement Form

6. Clarification of the REMS Program and process with the intent on improving customer use and understanding as reflected in the following materials:
   • Lumizyme ACE Program Training and Certification Program

- Healthcare Facility Enrollment and Acknowledgement Form
- Prescriber Enrollment and Attestation Form
- Lumizyme Infusion confirmation Form
- Lumizyme ACE Program: Information for healthcare professional brochure

7. The Lumizyme ACE Program: Information for healthcare professional brochure, the Dear Healthcare Provider Letter, and the Prescriber Introductory letter were modified as follows to be consistent with the Boxed Warning heading in the label:
   "WARNING: ANAPHYLAXIS and Restricted Distribution Program"

Your proposed modified REMS, submitted on December 22, 2011, and appended to this letter, is approved.

The timetable for submission of assessments of the REMS will remain the same as that approved on May 24, 2010.

There are no changes to the REMS assessment plan described in our May 24, 2010 letter.

In addition to the assessments submitted according to the timetable included in the approved REMS, you must submit a REMS assessment and may propose a modification to the approved REMS when you submit a supplemental application for a new indication for use.

If the assessment instruments and methodology for your REMS assessments are not included in the REMS supporting document, or if you propose changes to the submitted assessment instruments or methodology, you should update the REMS supporting document to include specific assessment instrument and methodology information at least 90 days before the assessments will be conducted. Updates to the REMS supporting document may be included in a new document that references previous REMS supporting document submission(s) for unchanged portions. Alternatively, updates may be made by modifying the complete previous REMS supporting document, with all changes marked and highlighted. Prominently identify the submission containing the assessment instruments and methodology with the following wording in bold capital letters at the top of the first page of the submission:

BLA 125291 REMS CORRESPONDENCE
(insert concise description of content in bold capital letters, e.g.,
UPDATE TO REMS SUPPORTING DOCUMENT - ASSESSMENT METHODOLOGY)

Prominently identify the submission containing the REMS assessments or proposed modifications of the REMS with the following wording in bold capital letters at the top of the first page of the submission as appropriate:

BLA 125291 REMS ASSESSMENT

NEW SUPPLEMENT FOR BLA 125291
PROPOSED REMS MODIFICATION

REMS ASSESSMENT

NEW SUPPLEMENT (NEW INDICATION FOR USE)
FORBLA 125291
REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)

If you do not submit electronically, please send 5 copies of REMS-related submissions.

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved BLA (in 21 CFR 600.80 and in 21 CFR 600.81).

If you have any questions, call Elizabeth Ford, Regulatory Project Manager, at (301) 796-0193.

Sincerely,

{See appended electronic signature page}

Joyce Korvick, M.D., M.P.H.
Deputy Director for Safety
Division of Gastroenterology and Inborn Errors Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

ENCLOSURE:
REMS

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

JOYCE A KORVICK
07/16/2012