DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-348

Actelion Pharmaceuticals US, Inc.
Attention: Thomas Lategan, Ph.D.
Vice President, Regulatory Affairs
56 Huckleberry Lane
North Andover, MA 01845

Dear Dr. Lategan:

Please refer to your new drug application (NDA) dated April 20, 2001, received April 23, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Zavesca (miglustat) 100 mg Capsules.

We acknowledge receipt of your submissions dated June 27 and October 14 and 16, 2002, and February 7, March 6 and 31, April 2, 8, and 9, May 27 and 28, June 10 and 13, and July 31, 2003.

The February 7, 2003, submission constituted a complete response to our June 20, 2002, action letter.

This new drug application provides for the use of Zavesca (miglustat) 100 mg Capsules for the treatment of mild to moderate Type I Gaucher disease in adults for whom enzyme replacement therapy is not a therapeutic option (e.g., due to constraints such as allergy, hypersensitivity, or poor venous access).

We completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text and with the minor editorial revisions listed below:

1. On the **Blister** and **Carton labels**, the word "Capsules" should be moved to immediately follow "(miglustat)".

2. On the **Carton label**, the storage statement should be changed to read, "Store at 20^{o} to 25^{o} C (68^{o} to 77^{o}F). Brief exposure to 15^{o} to 30^{o} C (59^{o} to 86^{o} F) permitted (see USP Controlled Room Temperature)".

3. On the **Carton label**, the statement (b)(4)---------- (b)(4)-------- should be changed to "Rx only".

The final printed labeling (FPL) must be identical to the enclosed labeling (text for package insert and patient package insert, submitted July 31, 2003). The final printed labeling FPL must be identical to the enclosed labeling (the blister and carton label, submitted April 9, 2003) except for inclusion of the revisions listed above. These revisions are terms of the NDA approval.

Marketing the product before making the revisions, exactly as stated, in the product's labeling may render the product misbranded and an unapproved new drug.

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA.* Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate this submission "**FPL for approved NDA 21-348**." Approval of this submission by FDA is not required before the labeling is used.

We acknowledge your May 28, 2003, voluntary agreement to limit the distribution of Zavesca to qualified physicians.

We remind you of your postmarketing study commitments in your submissions dated July 17 and 24, 2003. These commitments are listed below.

1. To conduct a two-year carcinogenicity study in mice.

Protocol Submission:	January 13, 2003
Study Start:	April 2003
Final Report Submission:	March 2006

2. To conduct a two-year carcinogenicity study in rats.

Protocol Submission:	November 5, 2001
Study Start:	March 2002
Final Report Submission:	January 2005

Submit study final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, and any changes in plans since the last annual report. All submissions, including supplements, relating to these postmarketing study commitments should be prominently labeled "**Postmarketing Study Protocol", "Postmarketing Study Final Report", or "Postmarketing Study Correspondence."**

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to the Division of Metabolic and Endocrine Drug Products and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising,
and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

We have not completed validation of the regulatory methods. However, we expect your continued cooperation to resolve any problems that may be identified.

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

The MedWatch-to-Manufacturer Program provides manufacturers with copies of serious adverse event reports that are received directly by the FDA. New molecular entities and important new biologics qualify for inclusion for three years after approval. Your firm is eligible to receive copies of reports for this product. To participate in the program, please see the enrollment instructions and program description details at www.fda.gov/medwatch/report/mmp.htm.

If you have any questions, call Pat Madara, Regulatory Project Manager, at (301) 827-6416.

Sincerely,

{See appended electronic signature page}

Robert J. Meyer, M.D.
Director
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosures: Package Insert
Patient Package Insert
Blister Label
Carton Label

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

/s/

Robert Meyer

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