DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 21-304

Roche Global Development-Palo Alto
Syntex (U.S.A.) LLC
Attention: Hermine Mante, PharmD.
Regulatory Program Manager
3401 Hillview Avenue
Palo Alto, California 94304-1397

Dear Dr. Mante:

Please refer to your new drug application (NDA) dated September 28, 2000, received September 29, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Valcyte (valganciclovir hydrochloride) 450 mg tablets.

We acknowledge receipt of your submissions dated:

October 9, 2000
November 16, 2000
November 27, 2000
December 1, 2000
January 9, 2001
January 16, 2001 (3)
January 19, 2001 (2)
January 26, 2001 (3)
January 30, 2001 (2)
January 31, 2001
February 2, 2001 (2)
February 5, 2001
February 6, 2001
February 7, 2001 (2)
February 13, 2001 (2)
February 15, 2001
February 16, 2001 (2)
February 19, 2001
February 20, 2001 (2)
February 22, 2001
March 6, 2001
March 8, 2001
March 13, 2001 (2)
March 14, 2001 (2)
March 15, 2001 (2)
March 16, 2001
March 20, 2001
March 22. 2001 (3)
March 23, 2001
March 26, 2001
March 27, 2001
March 28, 2001
March 29, 2001

This new drug application provides for the use of Valcyte (valganciclovir hydrochloride) 450 mg tablets for the treatment of cytomegalovirus (CMV) retinitis in patients with acquired immunodeficiency syndrome (AIDS).

We have completed the review of this application. We have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon labeling text. Accordingly, the application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the draft labeling submitted on March 29, 2001 and draft immediate container and carton labels in your submission dated March 14, 2001. Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit the FPL electronically according to the guidance for industry titled, *Providing Regulatory Submissions in Electronic Format - NDAs* (January 1999). For administrative purposes, this submission should be designated "FPL for approved NDA 21-304." In addition, please provide a clean text MS Word version of the label as a desk copy. Approval of this submission by FDA is not required before the labeling is used.

Alternatively, you may submit 20 paper copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material.

In addition, we note the following postmarketing commitments in your submission dated March 23, 2001. These commitments include:

1. The applicant will commit to the timely completion and submission of study results from study PV 16000, "A Randomized, Double-Blind, Double-Dummy, Active-Comparator Controlled Multi-Center Study of the Efficacy and Safety of Valganciclovir Vs. Oral Ganciclovir for Prevention of Cytomegalovirus Disease in High-Risk Heart, Liver, and Kidney Allograft Recipients". The timing of this submission is estimated to be during the fourth quarter of 2002.

2. At the time that the efficacy supplement outlined above is submitted, the applicant will commit to submission of all available safety data collected in studies WV15376 and WV15705. The timing of this submission is estimated to be during the fourth quarter of 2002.

3. (b)(4)

Submit clinical protocols to your IND for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all 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, any changes in plans since the last annual report, and, for clinical studies, number of patients entered into each study. All submissions, including supplements, relating to these postmarketing study commitments must be prominently labeled "**Postmarketing Study Protocol", "Postmarketing Study Final Report", or "Postmarketing Study Correspondence."**

Validation of the regulatory methods has not been completed. At the present time, it is the policy of the Center not to withhold approval because the methods are being validated. Nevertheless, we expect your continued cooperation to resolve any problems that may be identified.

Be advised that, as of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 *FR* 66632). At this time, there are an insufficient number of pediatric AIDS patients with CMV retinitis to perform an adequate study to establish safety and efficacy in the pediatric population. Therefore, we are waiving the pediatric study requirement for this action on the indication in this application.

In addition, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit one copy to this Division 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, Maryland 20857

Please submit one market package of the drug product when it is available.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Leslie Stephens, Regulatory Project Manager, at (301) 827-2335.

Sincerely,

Debra B. Birnkrant, M.D.
Acting Director
Division of Antiviral Drug Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research