DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-976/S-007

Tibotec, Incorporated
Attention: Susan Fiordeliso
Manager, Global Regulatory Affairs
1020 Stony Hill Road, Suite 300
Yardley, PA 19067

Dear Ms. Fiordeliso:

Please refer to your supplemental new drug application dated December 20, 2007, received December 21, 2007, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for PREZISTA (darunavir) 400 mg tablets.

We acknowledge receipt of your submissions dated February 28, 2008, March 28, 2008, April 30, 2008, May 14, 2008, June 13, 2008, July 2, 2008, July 21, 2008, July 31, 2008 and October 15, 2008.

This supplemental new drug application was submitted to expand the indication to include the treatment of human immunodeficiency virus (HIV) in antiretroviral treatment-naïve adults and to include a new dosing regimen, two 400 mg tablets of PREZISTA once a day, co-administered with 100 mg of ritonavir.

We completed our review of this application, as amended. This application is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text and patient labeling. Approval of this supplement and NDA 21-976, supplement 006 fulfills the commitment made under 21 CFR 314.510, listed as PMC 2 in the June 23, 2006, approval letter:

2. By December 31, 2007, submit the final study reports and datasets of the 48 week data for the ongoing Phase 3 studies TMC114-C211 and TMC114-C214.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for ages 0 to below 3 years because of evidence strongly suggesting the drug would be unsafe in this pediatric age group. This decision was based on the results of juvenile rat toxicology studies that provide evidence of a potential safety risk as a result of the drug-brain accumulation.

We are deferring submission of your pediatric studies for antiretroviral treatment-naïve pediatric subjects 3 to less than 18 years of age for this application because this product is ready for approval for use in adults and the pediatric studies have not been completed.

Your deferred pediatric studies required by section 505B(2) of the Federal Food and Drug and Cosmetic Act are required postmarketing studies. The status of these postmarketing studies must be reported annually according to 21 CFR 314.81 and section 505B(a)(3)(B) of the Federal Food and Drug, and Cosmetic Act. These required studies are listed below.

1. Deferred pediatric study under PREA for the treatment of HIV-1 infection in treatment-naïve pediatric subjects from 12 to <18 years of age. Conduct a pediatric safety and activity study of darunavir, in combination with ritonavir, in the treatment-naïve population with activity based on the results of virologic response over at least 24 weeks of dosing and safety monitored over 48 weeks.

Submission of final protocol:	June, 2009
Submission of final study report:	July, 2012

2. Deferred pediatric study under PREA for the treatment of HIV-1 infection in treatment-naïve pediatric subjects from 3 to <12 years of age. Conduct a pediatric safety and activity study of darunavir, in combination with ritonavir, in the treatment-naïve population with activity based on the results of virologic response over at least 24 weeks of dosing and safety over 48 weeks.

Submission of final protocol:	March, 2011
Submission of final study report:	March, 2015

Submit final study reports to this NDA. For administrative purposes, all submissions related to these required pediatric postmarketing studies must be clearly designated "**Required Pediatric Assessments**".

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, please submit the content of labeling [21 CFR 314.50(1)] in structured product labeling (SPL) format as described at http://www.fda.gov/oc/datacouncil/spl/html that is identical to the enclosed labeling (text for the package insert and text for the patient package insert). Upon receipt, we will transmit that version to the National Library of Medicine for public dissemination**. For administrative purposes, please designate this submission "SPL for approved NDA 21-976/S-007."**

In addition, within 21 days of the date of this letter, amend any pending applications for this NDA with content of labeling in structures product labeling (SPL) format to include the changes approved in this application.

Marketing the product with FPL that is not identical to the approved labeling text and in the required format may render the product misbranded and an unapproved new drug.

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 Antiviral Products and two copies of both the promotional materials and the package insert directly to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

LETTERS TO HEALTH CARE PROFESSIONALS

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH
Food and Drug Administration
Suite 12B05
5600 Fishers Lane
Rockville, MD 20857

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

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

If you have any questions, call Stacy Newalu, Regulatory Project Manager, at (301) 796-3978.

Sincerely,

{See appended electronic signature page}

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

Enclosure (clean copy of approved labels)

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

/s/

Jeffrey Murray

10/21/2008 06:29:52 PM