DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 207561

NDA APPROVAL

Gilead Sciences, Inc.
Attention: Erik Berglund, M.D., Ph.D., RAC
Associate Director, Regulatory Affairs
333 Lakeside Drive
Foster City, CA 94404

Dear Dr. Berglund:

Please refer to your New Drug Application (NDA) dated and received November 5, 2014, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for GENVOYA® (elvitegravir, cobicistat, emtricitabine, and tenofovir alafenamide), 150/150/200/10 mg fixed-dose combination tablet.

We acknowledge receipt of your amendments dated:

November 10, 2014	April 6, 2015	June 8, 2015	August 14, 2015
November 25, 2014	April 13, 2015	June 12, 2015	September 3, 2015
December 5, 2014	April 17, 2015	June 17, 2015	September 17, 2015
January 26, 2015	April 27, 2015	July 2, 2015	September 30, 2015
February 6, 2015	May 7, 2015	July 7, 2015	October 7, 2015
February 17, 2015	May 12, 2015	July 8, 2015	October 9, 2015
February 19, 2015	May 20, 2015	July 22, 2015	October 16, 2015
February 24, 2015	May 22, 2015	August 4, 2015	October 19, 2015
March 10, 2015	May 29, 2015	August 7, 2015	October 23, 2015
March 13, 2015	June 5, 2015	August 12, 2015	November 2, 2015 (x3)

We also acknowledge receipt of information related to GENVOYA® (elvitegravir, cobicistat, emtricitabine, and tenofovir alafenamide), 150/150/200/10 mg fixed-dose combination tablet for your Gilead Access Program that was reviewed as part of this application.

This new drug application provides for the use of GENVOYA® (elvitegravir, cobicistat, emtricitabine, and tenofovir alafenamide), 150/150/200/10 mg fixed-dose combination tablet for treatment of HIV-1 infection in adults and pediatric patients 12 years of age or older who have no antiretroviral treatment history or to replace the current antiretroviral regimen in those who are virologically-suppressed (HIV-1 RNA less than 50 copies per mL) on a stable antiretroviral regimen for at least 6 months with no history of treatment failure and no known substitutions associated with resistance to the individual components of GENVOYA®.

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling (text for the package insert and patient package insert). Information on submitting SPL files using eLIST may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*, available at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed immediate container label that is identical to the enclosed immediate container label, as soon as they are available, but no more than 30 days after they are printed. Please submit this label electronically according to the guidance for industry *Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (June 2008)*. Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission "**Final Printed Container Label for approved NDA 207561**." Approval of this submission by FDA is not required before the labeling is used.

Marketing the product(s) with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

ADVISORY COMMITTEE

Your application for GENVOYA was not referred to an FDA advisory committee because during the review process no substantive issues were encountered that would benefit from Advisory Committee discussion; three of the component drugs were previously approved and tenofovir alafenamide (the only New Molecular Entity) represents a second prodrug of a well-characterized antiretroviral.

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 less than 6 years of age because:

- In patients from birth up to 28 days of age, necessary studies are impossible or highly impracticable because the number of patients in this age group is too small and geographically dispersed to allow studies.

- In patients 29 days up to 6 years of age, the product fails to represent a meaningful therapeutic benefit over existing therapies for pediatric patients **and** is unlikely to be used in a substantial number of pediatric patients in this age group. In this age group, use of the individual component drugs or other antiretroviral formulations allows more accurate dosing across weights of rapidly growing children.

We are deferring submission of your pediatric study for ages 6 to less than 12 years for this application because this product is ready for approval for use in adults and the pediatric study has not been completed.

Your deferred pediatric study required by section 505B(a) of the FDCA are required postmarketing study. The status of this postmarketing study must be reported annually according to 21 CFR 314.81 and section 505B(a)(3)(B) of the FDCA. This required study is listed below.

2971-1 Conduct your deferred pediatric study in HIV-infected patients 6 years to less than 12 years to assess the pharmacokinetics, safety and tolerability, and antiviral activity of age-appropriate doses of elvitegravir, cobicistat, emtricitabine, and tenofovir alafenamide given in combination. At least some of the safety data must be derived from dosing as the GENVOYA® fixed dose combination (duration and number of subjects on GENVOYA® to be agreed upon with the Agency).

Protocol Submission:	January 15, 2015 (completed)
Study Completion:	September 2017
Final Report Submission:	March 2018

Reports of this required pediatric postmarketing study must be submitted as a new drug application (NDA) or as a supplement to your approved NDA with the proposed labeling changes you believe are warranted based on the data derived from this study. When submitting the reports, please clearly mark your submission "**SUBMISSION OF REQUIRED PEDIATRIC ASSESSMENTS**" in large font, bolded type at the beginning of the cover letter of the submission.

This product is appropriately labeled for use in ages 12 to less than 18 years for this indication. Therefore, no additional studies are needed in this pediatric age group for PREA purposes.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitment:

2971-2 Submit the long-term safety and antiviral activity data for Study GS-US-292-0106. Include data and analyses for the entire study population through Week 48 and for all subjects enrolled in the extension phase through 96 weeks of GENVOYA® dosing.

The timetable you submitted on October 16, 2015, states that you will conduct this study according to the following schedule:

Final Protocol Submission:	February 2013 (completed)
Study Completion:	September 2018
Final Report Submission:	March 2019

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 study 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 this postmarketing commitment should be prominently labeled **"Postmarketing Commitment Protocol," "Postmarketing Commitment Final Report," or "Postmarketing Commitment Correspondence."**

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert, and patient PI (as applicable) to:

OPDP Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion
5901-B Ammendale Road
Beltsville, MD 20705-1266

Alternatively, you may submit a request for advisory comments electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft Guidance for Industry (available at:

http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf).

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf. Information and Instructions for completing the form can be found at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

REPORTING REQUIREMENTS

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

MEDWATCH-TO-MANUFACTURER PROGRAM

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 http://www.fda.gov/Safety/MedWatch/HowToReport/ucm166910.htm.

POST APPROVAL FEEDBACK MEETING

New molecular entities and new biologics qualify for a post approval feedback meeting. Such meetings are used to discuss the quality of the application and to evaluate the communication process during drug development and marketing application review. The purpose is to learn from successful aspects of the review process and to identify areas that could benefit from improvement. If you would like to have such a meeting with us, call the Regulatory Project Manager for this application.

PDUFA V APPLICANT INTERVIEW

FDA has contracted with Eastern Research Group, Inc. (ERG) to conduct an independent interim and final assessment of the Program for Enhanced Review Transparency and Communication for NME NDAs and Original BLAs under PDUFA V ('the Program'). The PDUFA V Commitment Letter states that these assessments will include interviews with applicants following FDA action on applications reviewed in the Program. For this purpose, first-cycle actions include approvals, complete responses, and withdrawals after filing. The purpose of the interview is to better understand applicant experiences with the Program and its ability to improve transparency and communication during FDA review.

ERG will contact you to schedule a PDUFA V applicant interview and provide specifics about the interview process. Your responses during the interview will be confidential with respect to the FDA review team. ERG has signed a non-disclosure agreement and will not disclose any identifying information to anyone outside their project team. They will report only anonymized results and findings in the interim and final assessments. Members of the FDA review team will be interviewed by ERG separately. While your participation in the interview is voluntary, your feedback will be helpful to these assessments.

If you have any questions, call Myung-Joo Patricia Hong, M.S., Senior Regulatory Project Manager, at (301) 796-0806.

Sincerely,

{See appended electronic signature page}

John Farley, M.D., M.P.H.
Deputy Director
Office of Antimicrobial Products
Center for Drug Evaluation and Research

Enclosures:
Content of Labeling
Container Labeling

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

/s/

JOHN J FARLEY
11/05/2015