DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 022081/S-032

SUPPLEMENT APPROVAL

Gilead Sciences, Inc.
Attention: Saima Malik, M.Sc.
Senior Associate, Regulatory Affairs
333 Lakeside Drive
Foster City, CA 94404

Dear Ms. Malik:

Please refer to your Supplemental New Drug Application (sNDA) dated and March 31, 2014, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Letairis (ambrisentan) 5 mg and 10 mg Tablets.

We acknowledge receipt of your amendments dated August 19, 2014 and September 25, 2014.

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

The REMS for Letairis (ambrisentan) was originally approved on May 29, 2009, and the most recent modification was approved on January 31, 2014. The REMS consists of a Medication Guide, elements to assure safe use, implementation system, and a timetable for submission of assessments of the REMS. Your proposed modifications to the REMS consist of the following:

- Revisions to the *Reproductive Potential Status Form* to change the name to the *Change in Reproductive Potential Status and Pre-pubertal Annual Verification Form* and to clarify the change in classification categories.
- Revisions to the REMS Document and changes to the *Reproductive Potential Status and Pre-pubertal Annual Verification Form, Prescriber Guide for the Letairis REMS Program,* and the *Letairis REMS Program Guide for Females Who Can Get Pregnant* and REMS website to include changes to the definition of females of non-reproductive potential (FNRP).
- Revisions to the *Patient Enrollment and Consent Form* to communicate that Gilead is paying pharmacies for health information in order to conduct the REMS program.

Your proposed modified REMS, submitted on March 31, 2014, amended on August 19 and September 25, 2014 and appended to this letter, is approved.

There are no changes to the REMS assessment plan described in our August 17, 2013 letter.

In addition to the assessments submitted according to the timetable included in the approved REMS, you must submit a REMS assessment when you submit a supplemental application for a new indication for use as described in section 505-1(g)(2)(A) of the FDCA.

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:

NDA022081 REMS CORRESPONDENCE
(insert concise description of content in bold capital letters, e.g.,
UPDATE TO REMS SUPPORTING DOCUMENT - ASSESSMENT METHODOLOGY)

An authorized generic drug under this NDA must have an approved REMS prior to marketing. Should you decide to market, sell, or distribute an authorized generic drug under this NDA, contact us to discuss what will be required in the authorized generic drug REMS submission.

We remind you that section 505-1(f)(8) of FDCA prohibits holders of an approved covered application with elements to assure safe use from using any element to block or delay approval of an application under section 505(b)(2) or (j). A violation of this provision in 505-1(f) could result in enforcement action.

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:

NDA022081 REMS ASSESSMENT

NEW SUPPLEMENT FOR NDA022081
PROPOSED REMS MODIFICATION

NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR NDA022081
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 NDA (21 CFR 314.80 and 314.81).

If you have any questions, please call:

Lori Anne Wachter, RN, BSN, RAC,
Regulatory Project Manager for Safety
(301) 796-3975.

Sincerely,

{See appended electronic signature page}

Mary Ross Southworth, PharmD.
Deputy Director for Safety
Office of Drug Evaluation I
Center for Drug Evaluation and Research

ENCLOSURE(S):
REMS

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

/s/

MARY R SOUTHWORTH
10/29/2014