DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 206229

NDA APPROVAL

Medicines360
Attention: Andrea Olariu, M.D., Ph.D.,
Vice President of Clinical Affairs, General Manager
353 Sacramento Street, Suite 900
San Francisco, CA 94111

Dear Dr. Olariu:

Please refer to your New Drug Application (NDA) dated April 29, 2014, received April 30, 2014, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for Liletta (levonorgestrel-releasing intrauterine system [IUS]), 52 mg.

We acknowledge receipt of your amendments dated May 16, 19, 20, and 29, June 25, July 29, August 27, September 9, October 2, November 18 and 25, December 12, 2014; January 22 and 30, February 13, 18, and 25, 2015.

This new drug application provides for the use of Liletta (levonorgestrel-releasing IUS) for prevention of pregnancy for up to 3 years.

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 text for the 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 carton and immediate container labels that are identical to the enclosed carton and immediate container labels as soon as they are available, but no more than 30 days after they are printed. Please submit these labels 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 Carton and Container Labels for approved NDA 206229**." Approval of this submission by FDA is not required before the labeling is used.

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

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 pre-menarcheal patients because premenarcheal patients are not at risk of becoming pregnant and the use of this product before menarche is not indicated. We note that you have fulfilled the pediatric study requirement for post-menarcheal pediatric patients by extrapolation of adult data.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitment:

2874-1: A descriptive observational cohort study to evaluate performance of the THI-002 inserter in women receiving Liletta. The study cohort will include a minimum of 1,000 women who receive Liletta using the THI-002 inserter in a variety of clinical settings. The study should enroll representative proportions of nulliparous users and obese women to reflect the overall user population for the labeled indication. The enrolled subjects should be followed for a minimum of three months after insertion to monitor for expulsion, perforation, and infection because these adverse events are more common during this time period and may be related to the inserter or the insertion process. In addition, for women who have the IUS inserted post-partum, data should be collected on time since delivery or pregnancy termination, and on whether they are lactating. IUS removal data are not of primary importance and do not need to be obtained unless the IUS was removed specifically due to an insertion-related adverse event.

Data collected in this study will include:

- characterizing ease of insertion, insertion difficulties, and failed insertions, including use of local anesthesia, rigid dilation, and ultrasound guidance

- adverse events (AEs) such as pain, vasovagal events, excessive bleeding and uterine perforation during insertion and before the subject leaves the healthcare facility after insertion
- subsequent AEs such as pain and bleeding in the 7-14 days after IUS placement
- expulsions, infections, and other more serious AEs that may be delayed but related to the insertion procedure or IUS

The timetable you submitted on February 13, 2015, states that you will conduct this study according to the following schedule:

Final Protocol Submission:	02/28/2016
Study Completion:	02/28/2018
Final Report Submission:	02/28/2019

Submit clinical protocols to your IND 105836 for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all postmarketing 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 the 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 number of patients entered into the study. All submissions, including supplements, relating to the 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 to:

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

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).

If you have any questions, call Charlene Williamson, Regulatory Project Manager, at (301) 796-1025.

Sincerely,

{See appended electronic signature page}

Audrey Gassman, M.D.
Deputy Director
Division of Bone, Reproductive and Urologic Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

Enclosures:
Content of Labeling
Carton and 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/

AUDREY L GASSMAN
02/26/2015