DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 022256/S-004 **SUPPLEMENT APPROVAL**

Cypress Bioscience, Inc.
c/o Forest Laboratories, Inc.
Harborside Financial Center
Plaza III, Suite 602
Jersey City, NJ 07311

Attention: Michael K. Olchaskey, PharmD
Director, Regulatory Affairs

Dear Dr. Olchaskey:

Please refer to your supplemental new drug application dated and received November 11, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Savella (milnacipran HCl) 12.5 mg, 25 mg, 50 mg, and 100 mg Tablets.

We also refer to your submissions dated October 9, 2008, and September 22, 2009, and February 1, 2010, and to the approval letter for NDA 022256 dated January 14, 2009.

This Prior Approval supplemental new drug application provides for a proposed modification to the approved Risk Evaluation and Mitigation Strategy (REMS), and a REMS assessment.

We have completed our review of this application, as amended. It is approved, effective on the date of this letter.

RISK EVALUATION AND MITIGATION STRATEGIES (REMS) REQUIREMENTS

The REMS for Savella (milnacipran HCl) was approved on January 14, 2009. The REMS consisted of a Medication Guide and a timetable for submission for assessments of the REMS. The proposed modified REMS for Savella (milnacipran HCl) includes a revised timetable for submission of assessments of the REMS specifying the appropriate dates the assessments are due, as calculated from the initial REMS approval date. The modified REMS also states that the assessments will be received by FDA on or before the due dates.

Your proposed modified REMS, submitted on February 1, 2010, and appended to this letter is approved. The REMS assessment plan will remain the same as that approved on January 14, 2009.

The requirements for assessments of an approved REMS under section 505-1(g)(3) include, in section 505-1(g)(3)(B) and (C), requirements for information on the status of any post-approval study or clinical trial required under section 505(o) or otherwise undertaken to investigate a safety issue. You can satisfy these requirements in your REMS assessments by referring to relevant information included in the most recent annual report required under section 506B and 21 CFR 601.70 and including any updates to the status information since the annual report was prepared. Failure to comply with the REMS assessment provisions in 505-1(g) could result in enforcement action.

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

Prominently identify submissions containing 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:

NDA 022256
REMS ASSESSMENT

NEW SUPPLEMENT FOR NDA 022256
PROPOSED REMS MODIFICATION
REMS ASSESSMENT

NEW SUPPLEMENT (NEW INDICATION FOR USE)
FOR NDA 22256
REMS ASSESSMENT
PROPOSED REMS MODIFICATION (if included)

If you do not submit electronically, please send 5 copies of REMS-related submissions.

LETTERS TO HEALTH CARE PROFESSIONALS

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

MedWatch
Food and Drug Administration
5600 Fishers Lane, Room 12B05
Rockville, MD 20857

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, contact Diana Walker, Ph.D., Regulatory Project Manager, at (301) 796-4029.

Sincerely,

{See appended electronic signature page}

Larissa Lapteva, M.D.
Deputy Division Director for Safety
Division of Anesthesia, Analgesia
and Rheumatology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosures:
REMS
Medication Guide

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22256	SUPPL-4	CYPRESS BIOSCIENCE INC	SAVELLA TABLETS

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

/s/

LARISSA LAPTEVA
02/02/2010