DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

NDA 22-256/S-001

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 January 16, 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 acknowledge receipt of your submissions dated February 24 and March 11, 2009.

This supplemental new drug application provides for a new color scheme for 12.5 mg, 50 mg, and 100 mg tablets as a result of the removal of FD&C Blue #1 and FD&C Yellow #5 from Film Coats of 50 mg tablets and removal of FD&C Blue #1 from Film Coats of 100 mg tablets; a change in **(b) (4)** bottle size; the addition of an alternate bottle packaging site; removal of the FD&C Yellow #5 labeling precaution section; and revising the labeling and packaging to reflect the change in tablet color.

We have 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 with the minor editorial revisions/comments listed below.

1. Although your labels and labeling contain the required statement alerting the dispenser to provide the Medication Guide with the product for all strengths and formulations, we recommend the following language, dependent upon whether the Medication Guide accompanies the product or is enclosed in the carton (unit of use):

    a. “Dispense the enclosed Medication Guide to each patient.” or

    b. “Dispense the accompanying Medication Guide to each patient.”

2. Sufficient numbers of Medication Guides should be provided with the product such that a dispenser can provide one Medication Guide with each new or refilled prescription. We recommend that each packaging configuration contain enough Medication Guides so that one is provided for each “usual” or average dose. For example:

a. A minimum of four Medication Guides would be provided with a bottle of 100 for a product where the usual or average dose is 1 capsule/tablet daily, thus a monthly supply is 30 tablets.

b. A minimum of one Medication Guide would be provided with unit of use where it is expected that all tablets/capsules would be supplied to the patient.

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(l)] in structured product labeling (SPL) format as described at http://www.fda.gov/oc/datacouncil/spl.html that is identical to, except with the revisions listed above, the submitted labeling (package insert and Medication Guide submitted January 16, 2009). These revisions are terms of the NDA approval. 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 22-256/S-001."

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and container labels that are identical to the carton and immediate container labels submitted January 16, 2009, except with the revisions listed above, 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 titled *Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (October 2005).* 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 22-256**." 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.

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
WO 22, Room 4447
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

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 www.fda.gov/medwatch/report/mmp.htm.

ADDITIONAL COMMENTS

We remind you of your commitment, submitted April 3, 2009, to carry out studies for at least three lots under accelerated and long term stability conditions through the shelf life of the product. The data obtained should be included in the annual reports.

If you have any questions, contact Diana Walker, Ph.D., Regulatory Project Manager, at (301) 796-4029.

Sincerely,

{See appended electronic signature page}

Bob A. Rappaport, M.D.
Director
Division of Anesthesia, Analgesia
and Rheumatology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosure

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

/s/

Sharon Hertz
4/16/2009 03:58:45 PM
Signing for Bob Rappaport, M.D.