CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-866

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville, MD 20857

NDA 20-866

NDA APPROVAL

VeroScience, LLC
Attention: Anthony H. Cincotta, Ph.D.
President and Chief Scientific Officer
1334 Main Road
Tiverton, RI 02878

Dear Dr. Cincotta:

Please refer to your new drug application (NDA) dated August 22, 1997, received August 22, 1997, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Cycloset (bromocriptine mesylate) tablets, 0.8 mg.

We acknowledge receipt of your submissions dated April 9 and July 12, 2002, April 2 and November 24, 2003, March 4, 5, and 19, May 27 and July 12, 2004, May 16 (2) and December 21, 2006, January 11, March 9, June 1, and December 12, 2007, March 7, April 13, June 25 (2), August 4, September 4, 19, and 24, October 6, 8 (2), and 9 (2), November 12 and 24, and December 26, 2008, and January 5 and 21, February 16, March 3 and 10, April 13, and May 1, 2009.

The April 13, 2008, submission constituted a complete response to our October 15, 1999, action letter.

This new drug application provides for the use of Cycloset as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

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 (text for the package insert and patient counseling information submitted May 4, 2009, and carton and container labels submitted December 26, 2008).

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 the enclosed labeling (text for the package insert and patient counseling information). 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 20-866."**

CARTON AND IMMEDIATE CONTAINER LABELS

We acknowledge your December 26, 2008, submission containing printed carton and container labels. Submit final printed carton and 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 titled *Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (October 2005).* For administrative purposes, designate this submission **"Final Printed Carton and Container Labels for approved NDA 20-866."** 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.

PEDIATRIC RESEARCH EQUITY ACT (PREA)

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 in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for ages 0 to 9 years (inclusive) because necessary studies are impossible or highly impractical (there are too few children in this age range with type 2 diabetes mellitus to study).

We are deferring pediatric studies for ages 10 to 16 years (inclusive) for this application because this product is ready for approval for use in adults and the pediatric studies have not been completed.

Your deferred pediatric studies required by section 505B(a) of the Federal Food, Drug, and Cosmetic Act are required postmarketing studies. The status of these postmarketing studies must be reported annually according to 21 CFR 314.81 and section 505B(a)(3)(B) of the Federal Food, Drug, and Cosmetic Act. These required studies are listed below.

1. Deferred pediatric bioavailability study: To Assess the Safety, Tolerability and Pharmacokinetics of Cycloset in 10 to 16 year old Type 2 Diabetic Subjects

   Final Protocol Submission Date: No later than **December 31, 2009**
   Study Completion Date: No later than **August 31, 2010**
   Final Study Report Submission Date: No later than **October 31, 2010**

2. Deferred pediatric feasibility study: A Randomized, Double-Blind, Controlled Study To Assess the Use and Effectiveness of Cycloset in Children Aged 10 to 16 With a Diagnosis of Type 2 Diabetes Mellitus

   Final Protocol Submission Date: No later than **November 30, 2010**
   Study Completion Date: No later than **October 31, 2012**
   Final Study Report Submission Date: No later than **March 31, 2013**

3. Deferred clinical efficacy and safety study: A Pivotal, Randomized, Double-Blind, Controlled, Efficacy and Safety Study of the Use of Cycloset for the Treatment of Type 2 Diabetes Mellitus in Children Aged 10 – 16 years with a Diagnosis of Type 2 Diabetes Mellitus

   Final Protocol Submission Date: No later than **August 31, 2013**
   Study Completion Date: No later than **February 28, 2015**
   Final Study Report Submission Date: No later than **July 31, 2015**

Submit final study reports to this NDA. For administrative purposes, all submissions related to these pediatric postmarketing requirements must be clearly designated **"Required Pediatric Assessments."**

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
Division of Drug Marketing, Advertising, and Communications
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. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see www.fda.gov/cder/ddmac.

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
Suite 12B05
5600 Fishers Lane
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, please call Ms. Jena Weber, Regulatory Project Manager, at 301-796-1306.

Sincerely,

{See appended electronic signature page}

Mary H. Parks, MD
Director
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosures: Package Insert, Patient Counseling Information, Carton Labels, Container Labels

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

/s/

Mary Parks
5/5/2009 02:45:59 PM