DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 205831

NDA APPROVAL

Rhodes Pharmaceuticals L.P.
Attention: Todd M. Delehant, PhD
Associate Director of Regulatory Affairs
498 Washington Street
Coventry, RI 02816

Dear Dr. Delehant:

Please refer to your New Drug Application (NDA) dated and received June 18, 2014, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Aptensio XR (methylphenidate hydrochloride extended-release) capsules, 10 mg, 15 mg, 20 mg, 30 mg, 40 mg, 50 mg, and 60 mg.

We acknowledge receipt of your amendments dated:

August 13, 2014	August 28, 2014	September 5, 2014	September 18, 2014
October 2, 2014	October 3, 2014	December 11, 2014	December 16, 2014
December 17, 2014	December 19, 2014	January 8, 2015	January 12, 2015
January 13, 2015	January 15, 2015	January 16, 2015	January 21, 2015
February 4, 2015	February 20, 2015	February 25, 2015	March 24, 2015
March 26, 2015	March 27, 2015	April 7, 2015	April 15, 2015

This new drug application provides for the use of Aptensio XR (methylphenidate hydrochloride) extended-release) capsules for the treatment of Attention Deficit Hyperactivity Disorder (ADHD).

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.

WAIVER OF PREGNANCY, LABOR AND DELIVERY, AND NURSING MOTHERS SUBSECTIONS

We are waiving the current requirements of 21 CFR 201.56(d)(1) and 201.57(c)(9)(i) through (iii), regarding the content and format of labeling for subsections 8.1 Pregnancy, 8.2 Labor and Delivery, and 8.3 Nursing Mothers of prescribing information. Your approved labeling for subsections 8.1, 8.2, and 8.3 reflects the content and format requirements of the Pregnancy and Lactation Labeling Rule (79 FR 72063, December 4, 2014) which implements on June 30, 2015.

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, Medication Guide). 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 submitted carton and immediate container labels, dated April 15, 2015, revised to include following text on the side panel: Each capsule contains xx mg of methylphenidate hydrochloride (equivalent to xx mg of methylphenidate free base), as agreed upon in an April 17, 2015 email from Todd Delehant, 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 205831**." 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 studies requirement for ages 0 to 3 years because necessary studies are impossible or highly impracticable. This is because the diagnostic criteria and assessment measures for determining efficacy for the treatment of ADHD in children less than 4 years old are not well defined, and pharmaceutical treatment in this age group is uncommon.

We are deferring submission of your pediatric studies for ages 4 to 5 years for this application because pediatric studies should be delayed until additional safety or effectiveness data have been collected. At the current time, the Division has limited experience with the study of ADHD in younger children (4 to less than 6 years old), so we will defer studies in this younger age group for drugs seeking a claim in ADHD.

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 FDCA. These required studies are listed below.

2899-1 A randomized, double-blind, placebo-controlled, flexible-dose titration study of methylphenidate hydrochloride extended-release capsules (Aptensio XR) in children ages 4 to 5 years diagnosed with ADHD

Final Protocol Submission:	December 2015
Study/Trial Completion:	March 2019
Final Report Submission:	December 2019

2899-2 A single-dose, open-label, randomized pharmacokinetic study of Aptensio XR capsules in male or female children (4 to less than 6 years of age) with ADHD in fed condition.

Final Protocol Submission:	March 2015
Study/Trial Completion:	December 2016
Final Report Submission:	June 2017

2899-3 A one year Pediatric Open-Label Safety Study for patients age 4 to 5 years (at the time of entry into Study 1 or Study 2 or at the time of enrollment if directly enrolled into Study 3) with ADHD.

Final Protocol Submission:	December 2015
Study/Trial Completion:	March 2019
Final Report Submission:	December 2019

Submit the protocol(s) to your IND 104624, with a cross-reference letter to this NDA.

Reports of this/these required pediatric postmarketing study(ies) must be submitted as a new drug application (NDA) or as a supplement to your approved NDA with the proposed labeling changes you believe are warranted based on the data derived from these studies. When submitting the reports, please clearly mark your submission "**SUBMISSION OF REQUIRED PEDIATRIC ASSESSMENTS**" in large font, bolded type at the beginning of the cover letter of the submission.

We note that you have fulfilled the pediatric study requirement for ages 6 to 17 years for this application.

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, contact Shin-Ye Sandy Chang, Regulatory Project Manager, at shinye.chang@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Mitchell V. Mathis, M.D
CAPT, USPHS
Director
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure(s): Content of Labeling

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

/s/

MITCHELL V Mathis
04/17/2015