A 12-Month Open Label Safety Study of Aptensio XR® in Children Ages 4-5 Years Diagnosed With ADHD (EF004)

This study is not yet open for participant recruitment. (see Contacts and Locations)

Verified February 2016 by Rhodes Pharmaceuticals, L.P.

Sponsor:
Rhodes Pharmaceuticals, L.P.

Information provided by (Responsible Party):
Rhodes Pharmaceuticals, L.P.

ClinicalTrials.gov Identifier:
NCT02677519

First received: February 4, 2016
Last updated: February 8, 2016
Last verified: February 2016

Purpose

The primary objective of this study is to evaluate the long-term safety and tolerability of methylphenidate hydrochloride extended-release capsules (Aptensio XR®) in children aged 4-5 years who have been diagnosed with attention-deficit/hyperactivity disorder (ADHD).

Safety and tolerability will be evaluated by assessing treatment-emergent adverse events (TEAEs) blood pressure, pulse, height, weight, electrocardiograms (ECGs), laboratory values and Columbia Suicide Severity Rating Scale (C-SSRS). Disturbances in sleep (quantity and quality) patterns will also be assessed using the Child Sleep Habits Questionnaire (CSHQ).

Secondary objectives include assessment of long-term efficacy of Aptensio XR®.

Secondary measures include:

- Investigator administered Attention-Deficit/Hyperactivity Disorder Rating Scale Preschool Version (ADHD-RS-IV Preschool Version)
- Clinical Global Impressions-Severity Scale (CGI-S)
- Connors Early Childhood Behavior-Parent Short form [Conners EC BEH-P(S)]
Study Type: Interventional

Study Design: Allocation: Non-Randomized
Endpoint Classification: Safety/Efficacy Study
Intervention Model: Single Group Assignment
Masking: Open Label
Primary Purpose: Treatment

Official Title: A 12-Month Open Label Safety Study of Methylphenidate Hydrochloride Extended-Release Capsules (Aptensio XR®) in Children Ages 4-5 Years Diagnosed With Attention-Deficit/Hyperactivity Disorder (ADHD)

Resource links provided by NLM:

MedlinePlus related topics: Attention Deficit Hyperactivity Disorder

Drug Information available for: Methylphenidate Methylphenidate hydrochloride

U.S. FDA Resources

Further study details as provided by Rhodes Pharmaceuticals, L.P.:

Primary Outcome Measures:
- Treatment-emergent adverse events (TEAEs) [Time Frame: 12 month maintenance phase] [Designated as safety issue: Yes]
  Incidence of TEAEs during maintenance phase

- Columbia Suicide Severity Rating Scale (C-SSRS) [Time Frame: 12 month maintenance phase] [Designated as safety issue: Yes]
  Standardized assessment of suicide risk

- Vital signs [Time Frame: 12 month maintenance phase] [Designated as safety issue: Yes]
  blood pressure, pulse, height, weight

- 12-lead electrocardiogram [Time Frame: 12 month maintenance phase] [Designated as safety issue: Yes]

Secondary Outcome Measures:

- ADHD-RS-IV Preschool Version [Time Frame: 12 month maintenance phase] [Designated as safety issue: No]
  Investigator administered Attention-Deficit/Hyperactivity Disorder Rating Scale Preschool Version (ADHD-RS-IV Preschool Version) to assess ADHD severity and functioning
- **Clinical Global Impressions-Severity Scale (CGI-S)** [Time Frame: 12 month maintenance phase] [Designated as safety issue: No]
  
  This scale provides a global rating of illness severity and improvement during the study. The subject is rated relative to the clinician's past experience with other patients who have the same diagnosis. The CGI-S is rated on a 7-point scale, with the severity of illness scale using a range of responses from 1 (normal) through to 7 (among the most severely ill patients).

- **Connors Early Childhood Behavior-Parent Short [ConnorsEC BEH-P(S)]** [Time Frame: 12 month maintenance phase] [Designated as safety issue: No]
  
  Assesses behavior of preschool-aged children 2 to 6

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**Estimated Enrollment:** 120

**Study Start Date:** February 2016

**Estimated Study Completion Date:** September 2017

**Estimated Primary Completion Date:** April 2017 (Final data collection date for primary outcome measure)

### Arms and Assigned Interventions

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<th>Arms</th>
<th>Assigned Interventions</th>
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| Experimental: 10 mg Aptensio XR  
10 mg methylphenidate, extended release | Drug: Aptensio XR  
Orally-administered extended release formulation of methylphenidate; once daily dosing  
Other Name: Methylphenidate Extended Release |
| Experimental: 15 mg Aptensio XR  
15 mg methylphenidate, extended release | Drug: Aptensio XR  
Orally-administered extended release formulation of methylphenidate; once daily dosing  
Other Name: Methylphenidate Extended Release |
| Experimental: 20 mg Aptensio XR  
20 mg methylphenidate, extended release once daily | Drug: Aptensio XR  
Orally-administered extended release formulation of methylphenidate; once daily dosing  
Other Name: Methylphenidate Extended Release |
| Experimental: 30 mg Aptensio XR  
30 mg methylphenidate, extended release | Drug: Aptensio XR  
Orally-administered extended release formulation of methylphenidate; once daily dosing  
Other Name: Methylphenidate Extended Release |
| Experimental: 40 mg Aptensio XR  
40 mg methylphenidate, extended release | Drug: Aptensio XR  
Orally-administered extended release formulation of methylphenidate; once daily dosing |
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<th>Other Name: Methylphenidate Extended Release</th>
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<td>Orally-administered extended release formula of methylphenidate; once daily dosing</td>
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**Detailed Description:**

There are several pathways by which subjects enter the 12-month Maintenance Phase of this long-term safety study:

- Subjects may have previously participated in one of two studies where: (i) an optimized dose of Aptensio XR® was directly determined (Study RP-BP-EF003) or (ii) an optimized dose of Aptensio XR® was inferred (Study RP-BP-PK003). Henceforth, these Studies and Subjects will be referred to as Prior Studies and Ongoing Subjects, respectively.

- Subjects may be naïve to Aptensio XR®, and will undergo a dose optimization phase in this study prior to beginning the long-term maintenance phase (New Subjects).

Male and female children with a diagnosis of ADHD (combined, inattentive or hyperactive/impulsive type) based on the Diagnostic and Statistical Manual of Mental Disorders Fifth Edition (DSM-5) criteria, who were 4 to less than 6 years of age at time of consent for Prior Studies, will be enrolled. New Subjects with a diagnosis of ADHD (based on the DSM-5) must be at least 4 and less than 6 years of age at the time of consent for this study. For new subjects, ADHD-RS IV ratings obtained at screening will include the 6-months immediately prior to screening.

There will be four phases in this study: (i) a screening phase, (ii) a dose optimization phase (New Subjects, only), (iii) a dose maintenance phase and (iv) a follow-up phase. Ongoing Subjects will complete the Screening/Baseline assessments the same day as the End of Study Visit from a Prior Study and begin Aptensio XR® at their previously determined optimal dose. New Subjects will complete the Screening/Baseline assessments and begin Aptensio XR® after all eligibility criteria have been met.

New Subjects will initially receive Aptensio XR® 10 mg capsules. The dose may be subsequently increased on a weekly basis to 15, 20, 30, 40, 50 or 60 mg based on responses measured by the ADHD-RS-IV Preschool Version and tolerability. The dose may be decreased if tolerability issues arise. Subjects who cannot tolerate Aptensio XR® 10 mg will be discontinued from the trial. Once an optimal dose is achieved and observed for 2 weeks, New Subjects will enter the dose maintenance phase.

Visits will occur every four weeks for 12 months during treatment with Aptensio XR®. At the investigator's discretion, Aptensio XR® dose may be titrated during this phase to sustain optimal clinical response.

Approximately two weeks after the final study visit or treatment discontinuation, a follow-up phone call will be made to assess for ongoing adverse events and concomitant medications.

Approximately 120 subjects will be enrolled in this trial.

#### Eligibility

**Ages Eligible for Study:** 4 Years to 6 Years  
**Genders Eligible for Study:** Both
Accepts Healthy Volunteers: No

Criteria

Inclusion Criteria:

- Male and female subjects aged 4 to less than 6 years inclusive at the time consent was given to participate in Prior Studies. New Subjects must be at least 4 years but less than 6 years of age when written consent is given to participate in this trial.
- Meets DSM-5 criteria for ADHD, combined, hyperactive/impulsive or inattentive presentation diagnosed during a clinical interview by an experienced clinician, and confirmed with Kiddie-Sads-Present and Lifetime Version (K-SADS-PL) during Prior Studies or at the screening visit for the current trial.
- Subjects who completed the pre-school pharmacokinetic study (RP-BP-PK003) must meet the following criteria (Note: these data are collected during methylphenidate washout for RP-BP-PK003): (i) Age- and sex-adjusted ratings of 90th percentile Total Score on the ADHD-RS-IV Pre-school version, (ii) A score of <65 on the Child Global Assessment (CGAS) and (iii) A score of ≥4 on the Clinical Global Impressions-severity (CGI-S) scale
- Subjects who have not participated in Prior Studies must also meet the following criteria: (i) ADHD symptoms must have been present for at least 6 months, (ii) Subject has undergone a course of behavior therapy for ADHD or ADHD symptoms are severe enough to warrant medication treatment without prior behavior treatment, (ii) Age- and sex-adjusted ratings of 90th percentile Total Score on the ADHD-RS-IV Preschool Version Score of <65 on the Child Global Assessment, (iii) Must have a score of ≥4 on the Clinical Global Impressions-Severity (CGI-S) at Visit T1, (iv) Estimated IQ ≥80 on the Kaufman Brief Intelligence Test (KBIT-2), (v) Laboratory values and ECG results that are normal or not clinically-significant at screening, (vi) Urine drug screen that is negative except for prescribed stimulant medication
- The subject has a parent or legal guardian who will give written informed consent for the subject to participate in the study
- Subject must give written assent to participate in the study (if applicable)
- Subject and parent/legal guardian must be able to speak and understand English
- Subject and parent/legal guardian must be willing to comply with all study requirements
- Systolic and diastolic blood pressure below the 95th percentile for age and gender
- Subject must have lived with same parent or guardian for at least six months

Exclusion Criteria:

- The subject has had a lack of response to a trial of adequate dose and duration of MPH or intolerance to previous (MPH) treatment
- The subject is using any other current psychotropic medication except stimulants or has taken an investigational drug (other than Aptensio XR® in an antecedent trial) in the 30 days prior to screening
- The subject has used monoamine oxidase inhibitors within 14 days of the screening visit
- The subject plans to use prohibited drugs or agents at any point between the screening visit and the end of the study
- Use of anticonvulsants, antidepressants or antipsychotics in the 30 days prior to screening
- The subject has a history of chronic vocal or motor tics or Tourette's syndrome
- The subject has any clinically-significant ECG abnormalities at screening
- The subject has any major medical conditions that would interfere with involvement in a study or could be affected negatively by methylphenidate
• The subject has chronic medical illnesses including a seizure disorder (excluding a history of febrile seizures), severe hypertension, untreated thyroid disease, known structural cardiac abnormalities, serious arrhythmias, cardiomyopathy, glaucoma, or a family history of sudden death

• History (in the preceding 12 months) or presence of clinically significant cardiovascular, cerebrovascular, renal, hepatic, gastrointestinal, pulmonary, immunological, hematological, endocrine, or neurological disease that in the opinion of the investigator could put the subject at risk if he/she participates in the trial or could confound study results

• Family history (parent or sibling) of structural cardiovascular disease

• Current or recent (past 12 months) history of drug abuse in someone living in the subject’s home

• Current symptoms or history of major psychiatric illness (for example schizophrenia, psychosis, bipolar disorder, post-traumatic stress disorder, depression, severe anxiety disorder, obsessive compulsive disorder or autistic spectrum disorder) in addition to ADHD that requires treatment with additional medication or, in the opinion of the PI, would contraindicate study participation

• History or presence of suicidal ideation or significant self-injurious behavior

• The subject shows evidence of current physical, sexual, or emotional abuse

• Both biological parents of the subject have a history of bipolar disorder

• Non-compliance during Prior Studies

Contacts and Locations

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the Contacts provided below. For general information, see Learn About Clinical Studies.

Please refer to this study by its ClinicalTrials.gov identifier: NCT02677519

Contacts

Contact: Akwete Adjei, PhD akwete.adjei@pharma.com

Locations

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Sponsors and Collaborators
Rhodes Pharmaceuticals, L.P.

Investigators

Principal Investigator: Ann Childress, MD Center for Psychiatry And Behavioral Medicine Inc.
Principal Investigator: Scott Kollins, Department of Psychiatry & Behavioral Sciences, Duke University,
Investigator: MD Durham, NC

No publications provided

Responsible Party: Rhodes Pharmaceuticals, L.P.
ClinicalTrials.gov Identifier: NCT02677519
Other Study ID Numbers: RP-BP-EF004
Study First Received: February 4, 2016
Last Updated: February 8, 2016
Health Authority: United States: Food and Drug Administration

Keywords provided by Rhodes Pharmaceuticals, L.P.: ADHD children methylphenidate

Additional relevant MeSH terms:
Attention Deficit Disorder with Hyperactivity Central Nervous System Agents
Hyperkinesis Central Nervous System Stimulants
Attention Deficit and Disruptive Behavior Disorders Dopamine Agents
Dyskinesias Dopamine Uptake Inhibitors
Mental Disorders Molecular Mechanisms of Pharmacological Action
Mental Disorders Diagnosed in Childhood Neurotransmitter Agents
Nervous System Diseases Neurotransmitter Uptake Inhibitors
Neurologic Manifestations Pharmacologic Actions
Signs and Symptoms Physiological Effects of Drugs
Methylphenidate Therapeutic Uses

ClinicalTrials.gov processed this record on February 08, 2016