Corium

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Corium Protocol KP415.P02 Statistical Analysis Plan and Note To File

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Note to File

To: Corium KP415.P02 Study File

From: [redacted], Biostatistician, PROMETRIKA

Study: Corium KP415.P02

Date: 30Sep2025

Issue: Final approved version of SAP incorrectly labeled as a draft

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The final approved Version 1.0 of the Statistical Analysis Plan (SAP), dated 27Feb2025, incorrectly identifies the version as a draft on the cover page and on the footer of the document. This was an oversight when the document was being finalized. Those signing this note to file attest that the SAP they signed on 27Feb2025 is the final version of the Corium P02 SAP and not a draft.

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STATISTICAL ANALYSIS PLAN

A Multicenter, Dose-Optimized, Open-Label, Safety/Tolerability and Pharmacokinetic Study with Azstarys® in Children 4 and 5 Years of Age with Attention-Deficit/Hyperactivity Disorder

KP415.P02

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LIST OF ABBREVIATIONS

Abbreviation	Full Term
AAP	American Academy of Pediatrics
ADHD	Attention-Deficit/Hyperactivity Disorder
ADHD-RS	ADHD Rating Scale
AE	Adverse Event
ANCOVA	Analysis of Covariance
ATC	Anatomic Therapeutic Class
BMI	Body Mass Index
CGI-I	Clinical Global Impressions–Improvement
CGI-S	Clinical Global Impressions–Severity
CI	Confidence Interval
CRF	Case Report Form
CSHQ	Children's Sleep Habits Questionnaire
C-SSRS	Columbia-Suicide Severity Rating Scale
d-MPH	d-methylphenidate
ECG	Electrocardiogram
EDC	Electronic Data Capture
ET	Early Termination
MMRM	Mixed Model Repeated Measures
PKAP	Pharmacokinetic Analysis Plan
PT	Preferred Term
SAE	Serious Adverse Event
SD	Standard Deviation
SDX	Serdexmethylphenidate
SOC	System Organ Class
Q1	25th Percentile (1st Quartile)
Q3	75th Percentile (3rd Quartile)
QT	Time between the start of the Q wave and end of the T wave (QT interval) in the heart's electrical cycle

1. INTRODUCTION

This is a multicenter, dose-optimized, open-label, safety/tolerability and pharmacokinetic (PK) study with Azstarys® in children 4 and 5 years of age with attention-deficit/hyperactivity disorder (ADHD). The goal of this study is to evaluate the safety, tolerability, efficacy, and population PK of Azstarys® in treating subjects with ADHD for up to 12 months.

This statistical analysis plan (SAP) contains a detailed description of the data presentations and statistical analyses for Protocol KP415.P02. The statistical analyses described here are based on Version 2 of the protocol dated 16 November 2022.

2. STUDY SUMMARY

2.1. Study Objectives

The primary objective is:

- To determine the safety and tolerability of treating children 4- and 5-years-of-age with ADHD with Azstarys® for up to 12 months. The safety objective includes changes in weight, height, and sleep behavior.

The secondary objective is:

- To determine efficacy with respect to the 12-month maintenance of ADHD symptom control through investigator ratings on the ADHD-RS-IV.

The pharmacokinetic objective is:

- To assess the population PK of Azstarys® in children 4 and 5 years old with ADHD.

2.2. Study Design

This is a multicenter, dose-optimized, open-label safety/tolerability and PK study with Azstarys® (SDX/dMPH) in children 4 and 5 years of age with ADHD. The study consists of 4 phases: up to 30 days in Screening Phase (New Subjects only), 3 weeks in Dose Optimization Phase, 360 $\pm$20 days in Treatment Phase, and a Follow-up Phone Call 5-9 days after administration of the last dose in the Treatment Phase.

Subjects rolled over from Study KP415.P01 will be enrolled in the Dose Optimization Phase immediately after receiving the last dose of study drug in Study KP415.P01, bypassing the Screening Phase of KP415.P02. Roll-over Subjects are subjects who successfully completed Study KP415.P01 and continued to meet eligibility criteria for Study KP415.P02. New Subjects are subjects who did not participate in Study KP415.P01 or were ineligible to enter KP415.P02 as Roll-over Subjects but are eligible as New Subjects (re-entry).

During the Dose Optimization Phase, subjects will start at 13.1 mg/2.6 mg, and may be titrated to doses of 26.1 mg/5.2 mg or 39.2 mg/7.8 mg Azstarys® (SDX/dMPH) capsules. The optimized dose for all subjects is their dose level achieved on Day 21 which represents the end of the Dose Optimization Phase (Visit 5). The starting dose of Azstarys® in the Treatment Phase (Visit 6) will

be the same as the optimized dose of Azstarys® (SDX/dMPH) at the end of the Dose Optimization Phase (Visit 5), although the daily dose may be changed at any time during the Treatment Phase to any of the allowed dose levels (13.1 mg/2.6 mg, 26.1/5.2 mg, or 39.2 mg/7.8 mg per day), per the Investigator' discretion, based on individual tolerability and dose response.

2.2.1. Number of Subjects

Approximately 100 subjects will be enrolled in the study. An appropriate number of new subjects will enter the screening period in addition to subjects rolling over from Study KP415.P01 to ensure approximately 100 subjects are enrolled. Approximately 20 sites will participate in this study.

2.2.2. Randomization and Blinding Procedures

This is an open-label study. Study subjects will not be randomized and study treatments will not be blinded.

2.2.3. Efficacy Assessments

2.2.3.1. ADHD Diagnosis

For New Subjects at Screening, eligible subjects must meet the inclusion criteria for a primary diagnosis of ADHD (Combined Presentation, Predominantly Inattentive Presentation, Predominantly Hyperactive/Impulsive Presentation) by Mini-International Neuropsychiatric Interview for Children and Adolescents (MINI Kid) per clinical evaluation. Roll-over Subjects from Study KP415.P01 had their ADHD diagnosis and diagnosis confirmation completed in KP415.P01, therefore the same diagnosis will be used for KP415.P02.

2.2.3.2. Mini-International Neuropsychiatric Interview for Children and Adolescents (MINI Kid)

The Mini-International Neuropsychiatric Interview for Children and Adolescents (MINI Kid) will be used to confirm the diagnosis of ADHD and identify comorbid psychiatric conditions at the Screening Visit only (in New Subjects).

2.2.3.3. ADHD-RS-IV

The Preschool Version of the ADHD-Rating Scale-IV (ADHD-RS-IV) is an 18-item scale based on the Diagnostic and Statistical Manual of Mental Disorders (American Psychiatric Association 2013) criteria of ADHD that rates symptoms on a 4-point scale. Each item is scored using a combination of severity and frequency ratings from a range of 0 (reflecting no symptoms or a frequency of never or rarely) to 3 (reflecting severe symptoms or a frequency of very often). The total ADHD-RS scores range from 0 to 54. The 18 items can be divided into two 9-item subscales: One for hyperactivity/impulsivity and the other for inattention. Scores will be obtained during a clinician-directed interview with the parent/guardian/caregiver at each visit. ADHD-RS scores should be collected using an ePRO device; for instances when the ePRO device is not available, ADHD-RS scores may be collected on paper CRFs.

2.2.3.4. Clinical Global Impressions—Severity (CGI-S)

The CGI-S is a clinician-rated scale that evaluates the severity of psychopathology (ADHD symptoms in the study) on a scale from 1 (not at all ill) to 7 (among the most severely ill). The CGI-S will be performed at Screening and at Visits 2 through 17. The CGI-S rating will be collected using an ePRO device.

2.2.3.5. Clinical Global Impressions—Improvement (CGI-I)

The CGI-I is a clinician-rated scale that evaluates the improvement of psychopathology (ADHD symptoms in the study) on a scale from 1 (very much improved) to 7 (very much worse). The CGI-I will be performed at Visits 3, 4 and 5. Since the CGI-I is an assessment of improvement versus baseline, there will be no CGI-I assessment at Screening or Visit 2. The CGI-I rating will be collected using an ePRO device.

2.2.3.6. ADHD Severity Over Time

During the Dose Optimization Phase, all subjects will need to meet additional efficacy-related eligibility criteria in order to enter into the Treatment Phase, meeting minimal treatment response thresholds based on the ADHD-RS-IV, CGI-I and CGI-S scale assessments (in conjunction with tolerability and safety) to guide dose optimization. The minimal treatment response thresholds are as follows: 1) A reduction of ≥30% in ADHD-RS-IV from baseline during the Dose Optimization Phase. The baseline is the ADHD-RD-IV score before the first dose of study drug (for Roll-over Subjects, from Study KP415.P01); 2) A CGI-I score of 1 or 2 points (“Very Much Improved” or “Much Improved”) at the end of the Dose Optimization Phase. The improvement will be judged from a baseline before the first dose of study drug (for Roll-over Subjects, from Study KP415.P01).

During the Treatment Phase, the ADHD-RS-IV and CGI-S scale assessments are the efficacy variables to evaluate the changes in ADHD severity over time and may be used (in conjunction with tolerability and safety) to further adjust the dose of study drug.

2.2.4. Safety Assessments

Safety assessments include medical history, adverse events (AEs), clinical laboratory tests, vital signs, physical examinations, electrocardiograms (ECGs), Children’s Sleep Habits Questionnaire (CSHQ) and Columbia-Suicide Severity Rating Scale (C-SSRS).

2.2.4.1. Medical History

For New Subjects, a complete medical history will be obtained at the Screening Visit including the recording of demographic data (date of birth, sex, age, race, ethnicity), collection of previous surgeries, medications and chronic conditions, past or present illnesses or dysfunctions, substance/drug abuse, and history of allergies or idiosyncratic responses to drugs. Medical history (changes from screening) will be updated at subsequent visits after the Screening Period.

For Roll-over Subjects, medical conditions that occurred during their participation in Study KP415.P01 will be transferred into the adverse event data for KP415.P02. However, these events will be considered medical history for KP415.P02 as they started prior to administration

of the first dose of open-label drug on Day 1 and will be summarized as adverse events from KP415.P01. Medical history recorded in KP415.P01 for Roll-over Subjects will also be included in medical history for KP415.P02. At Visit 2, only New Subjects will be reassessed for medical history.

2.2.4.2. Treatment-Emergent Adverse Events

Adverse events will be assessed and recorded from the first day of study drug administration in this study (after administration of the first dose of open-label drug on Day 1 for both New Subjects and Roll-over Subjects) through either Follow-up Phone Call or ET; these adverse events will be considered treatment-emergent for KP415.P02. AEs originating in Study KP415.P01 that were resolved in KP415.P01 or are on-going in KP415.P02 will be considered treatment-emergent only for Study KP415.P01 and will be considered as medical history for Study KP415.P02 (as described in Section 2.2.4.1). During at-home dosing, the subject's parent/guardian will be instructed to contact the study site for the reporting of AEs. In addition, at each study visit, study staff will interview the parent/guardian regarding AEs during the preceding at-home period. In cases in which the occurrence of an AE is unclear or for safety-related medical questions, the Medical Monitor should be consulted. All AEs, including serious adverse events (SAEs), will be followed to resolution when possible. For SAEs that occur during the study, follow up shall be performed and recorded for up to 30 days after last dose or until resolved or clinically stable for events considered definitely, probably, or possibly related to study drug.

2.2.4.3. Vital Signs, Body Weight, and Height

Vital sign measurements will be obtained at each visit after the subject has been seated for 3 minutes and will include sitting blood pressure (systolic and diastolic measurements), pulse rate (beats per minute), respiratory rate (breaths per minute), and oral temperature. Three blood pressure measurements will be collected 2 to 5 minutes apart, and the average of the three measurements will be recorded in the eCRF. Body weight (kg) and height (cm) will also be measured and recorded at each visit.

2.2.4.4. Physical Examination

A complete physical examination will be completed at Screening (New Subjects only), after approximately 6 months of treatment in the Treatment Phase (Visit 11), after the last dose of study drug in the Treatment Phase (Visit 17), or at ET (if possible).

The complete physical examination will be completed, consisting of a review of the subject's general appearance, skin, head and neck, musculoskeletal/extremities, heart, lungs, abdomen and a brief examination of the neurological system.

2.2.4.5. Electrocardiogram (ECG)

A 12-lead ECG will be obtained after the subject has been in a supine position for a minimum of 3 minutes. Abnormal ECGs may be repeated for confirmation in which case only the repeated ECG will be recorded. The following ECG parameters will be recorded: heart rate (bpm), QT

Interval (msec), RR Interval (msec), ECG evaluation (normal; abnormal, not clinically significant; abnormal, clinically significant).

2.2.4.6. Children's Sleep Habits Questionnaire (CSHQ)

Ratings from the modified, abbreviated CSHQ will be collected to assess changes in sleep behavior throughout the study. The CSHQ is a retrospective, 33-item parent questionnaire to examine sleep behavior in small children. Items are rated on a 3-point scale of "Usually", "Sometimes" and "Rarely" for occurrences in a number of key sleep domains (bedtime resistance, sleep onset delay, sleep duration, sleep anxiety, night wakings, parasomnias, sleep disordered breathing, and daytime sleepiness). The total Sleep Disturbance Score is a sum of the frequency ratings of the 33 items, accounting for reverse scoring of selected items.

CSHQ scores will be obtained during a clinician-directed interview with the parent/guardian/caregiver during all visits through the end of the Treatment Phase. For New Subjects, the Visit 2 CSHQ score will be used as baseline; for Roll-over Subjects the CSHQ score from Visit 2 in Study KP415.P01 will be used as baseline.

2.2.4.7. Columbia-Suicide Severity Rating Scale (C-SSRS)

Suicidal ideation will be assessed by the C-SSRS, Pediatric Version. The "Children's Baseline/Screening" version will be used at Screening (New Subjects only), and the "Children's Since Last Visit" version will be used at all visits through the Treatment Phase or ET. For subjects too young to comprehend the concept of suicidal ideation, the C-SSRS questionnaire will be filled in by the parent/guardian/caregiver.

2.2.4.8. Clinical Laboratory Measures

Clinical laboratory measures will be collected at the time points in Table 1. Clinical laboratory evaluations will consist of the following:

- Total hematology with differential: red blood cell count, white blood cell count with differential (neutrophils, lymphocytes, monocytes, eosinophils, basophils), hemoglobin, hematocrit, and platelets.
- Serum chemistry: aspartate aminotransferase (AST), alanine aminotransferase (ALT), albumin, alkaline phosphatase, bicarbonate, total bilirubin, blood urea nitrogen, phosphorus (inorganic) calcium, chloride, creatine phosphokinase, creatinine, gamma glutamyl transferase, glucose, lactate dehydrogenase, potassium, sodium, total protein, and TSH. TSH will be measured at Screening only (New Subjects only) to evaluate the exclusion criterion for uncontrolled thyroid disease.
- Urinalysis: bilirubin, blood, glucose, ketones, leukocytes, nitrite, pH, protein, and urobilinogen. At Screening, New Subjects will be tested for amphetamines, methamphetamines, methylphenidate, benzodiazepines, barbiturates, cannabinoids, cocaine, and opioids including oxycodone.

2.2.5. Pharmacokinetic Assessments

During Visits 6 and/or 7, a total of three (3) blood samples (3 mL each) for PK analyses will be collected at specified times relative to the time of oral administration of open-label study drug on the day of PK sample collection.

Table 1. Schedule of Events

Screening and Dose Optimization Phase

ASSESSMENTS[21]	**SCREENING PHASE (NEW SUBJECTS)**[1]	**OPEN-LABEL DOSE OPTIMIZATION PHASE**[20] **(All Subjects)** Days 0-21 ± 3 days (including at-home dosing)			
Study Day	-30 to -1	0		7 (±3 days)	14 (±3 days)
Visit Number	1	2 (New Subjects)	2 (Roll-over Subjects)	3	4
Parental Permission/Written	X		X		
ADHD Diagnosis and Confirmation [2]	X				
Inclusion/Exclusion [3]	X	X	X	X	X
Demographics	X				
Medical History [4]	X	X			
Physical Examination	X		X		
Body Weight and Height [5]	X	X	X	X	X
Vital Signs [6]	X	X	X	X	X
12-Lead ECG [7]	X		X		
Chemistry/Hematology/Urinalysis	X		X		
Urine Drug Screen [8]	X				
C-SSRS [9]	X	X	X	X	X
Washout ADHD Meds [10]	X	X			
Dispensing of unblinded Azstarys® capsules until next visit		X	X	X	X
Azstarys® Dosing [11]				X	X
Drug Accountability & Compliance Assessment [12]				X	X
ADHD-RS-IV [13]	X	X	X	X	X
MINI Kid [14]	X				
CGI-S [15]	X	X	X	X	X
CGI-I [16]			X	X	X
CSHQ [17]	X	X	X	X	X
Adverse Events [18]				X	X
Concomitant Medications [19]	X	X	X	X	X

ECG = electrocardiogram; MPH = methylphenidate; see footnotes for other abbreviations.

1. Screening Visit: For New Subjects only.
2. ADHD Diagnosis based on the Statistical Manual of Mental Disorders - Fifth Edition (DSM-5) criteria for a primary diagnosis of ADHD (combined, inattentive, or hyperactive/impulsive presentation) and by the Mini-International Neuropsychiatric Interview for Children and Adolescents (MINI Kid).

3. Study inclusion/exclusion criteria (different for New Subjects and Roll-over Subjects) will be evaluated at Screening (New Subjects) and Visit 2 (all subjects). Inclusion/exclusion criteria to be adhered to throughout the study (e.g., use of prohibited medications, suicidal ideation) will also be evaluated at Visits 3, 4, and 5.
4. Medical History: At Screening, a complete medical history including chronic conditions, relevant surgical procedures (with start date), and history of drug use will be obtained for New Subjects. For Roll-over Subjects, new medical conditions that occurred during their participation in Study KP415.P01 will be recorded at Visit 6 (P01)/Visit 2 (P02) as medical history for this study. At Visit 2, only New Subjects will be reassessed for medical history.
5. Height will be recorded in centimeters (cm) using a stadiometer with the subject's shoes removed. Body weight will be measured in kilograms (kg) using a calibrated scale; subjects will remain in their normal clothing with shoes and jacket (and/or outer clothing) removed.
6. Vital sign measurements will be obtained at each visit after the subject has been seated for at least 3 minutes. Vital signs will include sitting blood pressure (systolic and diastolic measurements), pulse rate (beats per minute), respiratory rate (breaths per minute), and oral temperature. Three (3) blood pressure measurements will be taken 2-5 minutes apart. Only the average of the 3 blood pressure measurements will be entered into the eCRF.
7. Electrocardiogram (ECG): A 12-lead ECG will be obtained after the subject has been in the supine position for at least 3 minutes. Abnormal ECGs may be repeated for confirmation in which case only the repeated ECG will be recorded.
8. Urine Screen for Drugs of Abuse: Urine samples will be tested for drugs of abuse (amphetamines, methamphetamines, methylphenidate, benzodiazepines, barbiturates, cannabinoids, cocaine, opioids including oxycodone) at the Screening visit for New Subjects. If the urine test is positive for any of the analytes at Screening, the subject will be excluded from study participation, with the exception of the following: Depending on a subject's current ADHD medication at Screening, the urine screen at Screening may test positive for methylphenidate for treatment of their ADHD. All ADHD medications must be washed out per New Subject Inclusion Criterion #7.
9. Columbia Suicide Severity Rating Scale (C-SSRS): The "Children's Baseline/Screening" version will be assessed at Screening, and the "Children's Since Last Visit" version will be assessed at all other visits. Subjects who have, in the opinion of the Investigator, clinically significant suicidal ideation/behavior, based on history of attempted suicide and the C-SSRS assessment at Screening or at any time before the last dose of study drug, will be excluded from further participation in the study.
10. New Subjects must wash out ADHD medications prior to Visit 2. Stimulant ADHD medications (with the exception of study drug), including herbal medications, are prohibited from 5 days prior to Visit 2 to the end of the Treatment Phase (Visit 17) or Early Termination (ET) Visit. Non-Stimulant ADHD medications are prohibited from 14 days prior to the start of the Dose Optimization Phase (Visit 2) to the end of the Treatment Phase (Visit 17) or ET Visit. Before or on the day during the screening period that subjects will need to start the washout of their ADHD medications (for example, 5 days before Visit 2 for stimulants), study site staff will contact the subject's parent/guardian by phone to remind them of the washout ("Washout Phone Call"). Other prohibited medications and the windows of prohibition are listed in the protocol.
11. Dose Optimization: Subjects will begin taking Azstarys® at home the morning following Visit 2. The starting dose will be 13.1 mg/2.6 mg day. Azstarys® dose adjustments, if needed, will be performed at approximately weekly intervals between visits. Actual visit dates may deviate from exactly being spaced 7 days apart such that the total duration of the Dose Optimization Phase is 3 weeks (21 ±3 days). The daily doses of Azstarys® used in the Dose Optimization Phase will be 13.1 mg/2.6 mg, 26.1 mg/5.2 mg, or 39.2 mg/7.8 mg. At Visits 3, 4, and 5 based on the CGI scores, interview with the parent/guardian/caregiver, and safety data, the Investigator will evaluate the subject's therapeutic responses and tolerability to treatment and decide whether the current Azstarys® dose should be increased, decreased, or remain the same for the next week of

dosing. If subjects experience symptoms of intolerance during the at-home treatment, they must contact the clinical site, and, at the discretion of the Investigator, their dose may be adjusted before the next scheduled visit. Unscheduled visits between Visits 2, 3, 4, and 5 are allowed as needed, at the discretion of the Investigator.

12. Drug Accountability & Compliance Assessment: Study drug receipt, dispensing, and return will be recorded by each site's pharmacy staff or Investigator-delegated employee. A record of the study drug accountability will be prepared and kept by the clinical site.
13. ADHD-Rating Scale-IV (ADHD-RS-IV) assessment: 1 assessment at the indicated visits.
14. Mini-International Neuropsychiatric Interview for Children and Adolescents (MINI Kid).
15. Clinical Global Impressions–Severity (CGI-S) scale assessment: 1 assessment at the indicated visits.
16. Clinical Global Impressions–Improvement (CGI-I) scale assessment: 1 assessment at the indicated visits.
17. Children's Sleep Habits Questionnaire (CSHQ) assessment: 1 assessment at the indicated visits.
18. Adverse Events: To be assessed and recorded in the electronic case report form (eCRF) following the first dose of open-label drug, on Day 1, through either the Follow-up Phone Call or ET. Subject's parent/guardian will be instructed to contact the study site for the reporting of AEs during the dosing periods at home.
19. Concomitant Medications: new and/or changed medications and dose, medical treatments and/or therapies will be recorded at Screening through the Follow-up Phone Call or ET.
20. Actual visit dates in the Dose Optimization Phase may deviate from being spaced exactly 7 days apart such that the total duration of the Dose Optimization Phase is 3 weeks (21 ±3 days). Any allowed deviation (up to 3 days in total) of the targeted 21-day Dose Optimization Phase will be carried over into the actual days for the subsequent visits.
21. Assessment changes due to COVID-19: If a subject is not able to attend the site for a scheduled visit due to COVID-19 restrictions, sites will be instructed to collect data for select safety assessments (vital signs, labs, ECG, physical exam) when the subject is next able to safely return to an on-site visit, even if those assessments would not normally be done at that visit. These assessments will be mapped to the nearest scheduled visit. Changes in scheduled visits and corresponding assessments due to COVID-19 restrictions will be captured in the eCRF. Assessments that do not require the subject's presence at the site (e.g., AEs, C-SSRS, ADHD-RS-IV, CGI-S, CGI-I, CSHQ) will be collected by phone at the scheduled visit times. If needed, alternate measures to dispense study drug to the subject during their COVID-19 isolation period will be implemented (e.g., study drug directly delivered to the subject's residence or dispensed to another family member).

Treatment Phase (First 6 Months; All Subjects)

ASSESSMENTS[17]	OPEN-LABEL TREATMENT PHASE (All Subjects)						
Study Day	(Day 21 of Dose Optimization Phase)	30 (±5 days)	60 (±5 days)	90 (±5 days)	120 (±5 days)	150 (±5 days)	180 (±5 days)
Visit Number	5	6	7	8	9	10	11
Inclusion/Exclusion	X						
Physical Examination [1]							X
Body Weight, Height [2]	X	X	X	X	X	X	X
Vital Signs [3]	X	X	X	X	X	X	X
12-Lead ECG [4]							X
C-SSRS [5]	X	X	X	X	X	X	X
Chemistry/Hematology/ Urinalysis							X
Eligibility Criteria for Treatment Phase / Enrollment in Treatment Phase	X						
Dispensing of unblinded Azstarys® capsules until next visit	X	X	X	X	X	X	X
Azstarys® Dosing [6]	X	X	X	X	X	X	X
Drug Accountability & Compliance Assessment [7]	X	X	X	X	X	X	X
ADHD-RS-IV [8]	X	X	X	X	X	X	X
CGI-S [9]	X	X	X	X	X	X	X
CGI-I [10]	X						
CSHQ [11]	X	X	X	X	X	X	X
Adverse Events [12]	X	X	X	X	X	X	X
Concomitant Medications [13]	X	X	X	X	X	X	X
Interim Safety Analysis[14]							X
Dosing Diary dispensing (for PK Subjects)	X	X					
PK Sampling (Randomized)/Dosing Diary collection/review[18]		X	X				

EOS = End of Study; ET = Early Termination; ECG = Electrocardiogram; see Treatment Phase (Second 6 Months), Early Termination and Follow-up Phone Call for all footnotes.

Treatment Phase (Second 6 Months), Early Termination and Follow-up Phone Call

ASSESSMENTS[17]	OPEN-LABEL TREATMENT PHASE (All Subjects)					END OF TREATMENT[15]	EARLY TERMINATION[16]	FOLLOW-UP PHONE CALL (EOS)
Study Day	210 (±5 days)	240 (±5 days)	270 (±5 days)	300 (±5 days)	330 (±5 days)	360 (±5 days)	-	365 (5-9 days after EOT)
Visit Number	12	13	14	15	16	17	-	18
Physical Examination [1]						X	X	
Body Weight, Height [2]	X	X	X	X	X	X	X	
Vital Signs [3]	X	X	X	X	X	X	X	
12-Lead ECG [4]						X	X	
Chemistry/Hematology/ Urinalysis						X	X	
Dispensing of unblinded Azstarys® capsules for use until the next visit	X	X	X	X	X			
Azstarys® Dosing [6]	X	X	X	X	X	X	X	
Drug Accountability & Compliance Assessment[7]	X	X	X	X	X	X	X	
C-SSRS[5]	X	X	X	X	X	X	X	
ADHD-RS-IV [8]	X	X	X	X	X	X	X	
CGI-S [9]	X	X	X	X	X	X	X	
CSHQ [11]	X	X	X	X	X	X	X	
Adverse Events [12]	X	X	X	X	X	X	X	X
Concomitant Medications [13]	X	X	X	X	X	X	X	X

EOS = End of Study; EOT = End of Treatment; ET = Early Termination; FU = Follow-up; ECG = Electrocardiogram; see footnotes for other abbreviations.

1. Physical examination at Visit 11, and at Visit 17 (EOT) or ET (if possible).
2. Body weight and height at each visit. Height will be recorded in centimeters (cm) using a stadiometer with the subject's shoes removed. Body weight will be measured in kilograms (kg) using a calibrated scale; subjects will remain in their normal clothing with shoes and jacket (and/or outer clothing) removed.
3. Vital sign measurements will be obtained after the subject has been seated for at least 3 minutes. Vital signs will include sitting blood pressure (systolic and diastolic measurements), pulse rate (beats per minute), respiratory rate (breaths per minute), and oral temperature. Three (3) blood pressure measurements will be taken 2-5 minutes apart at each visit. Only the average of the 3 blood pressure measurements will be entered into the eCRF.
4. Electrocardiogram (ECG): A 12-lead ECG will be obtained after the subject has been in the supine position for at least 3 minutes. Abnormal ECGs may be repeated for confirmation in which case only the repeated ECG will be recorded.
5. Columbia Suicide Severity Rating Scale (C-SSRS): The "Children's Since Last Visit" version will be assessed at all visits in the Treatment Phase and at ET (if applicable). The C-SSRS questionnaire will

be filled in by the parent/guardian/caregiver. Subjects who have, in the opinion of the Investigator, clinically significant suicidal ideation/behavior, based on history of attempted suicide and the
C-SSRS assessment from Screening to at any time before the last dose of study drug, will be excluded from further participation in the study.

6. Azstarys® Dosing: At Visit 5, the Investigator will evaluate the eligibility criteria based on assessments in the Dose Optimization Phase for continuation into the subsequent Treatment Phase. At Visit 5, All Subjects will be dosed with the last dose of the Dose Optimization Phase.
   For subjects eligible for the Treatment Phase, the optimal daily dose will be used as the daily dose in the Treatment Phase. Details on doses and dosing methods are found in Section 9.5 and Section 8.3.1 of Protocol.
7. Drug Accountability & Compliance Assessment: All study drug will be recorded by each site's pharmacy staff or Investigator-delegated employee. A record of the study drug accountability will be prepared and kept by the clinical site.
8. ADHD-Rating Scale-IV (ADHD-RS-IV) assessment: 1 assessment at the indicated visits.
9. Clinical Global Impressions–Severity (CGI-S) scale assessment: 1 assessment at the indicated visits.
10. Clinical Global Impressions–Improvement (CGI-I) scale assessment: 1 assessment at Visit 5.
11. Children's Sleep Habits Questionnaire (CSHQ) assessment: 1 assessment at the indicated visits.
12. Adverse Events: To be assessed and recorded in the eCRF following the first dose of Azstarys®, through either ET or Follow-up Phone Call. Subject's parent/guardian will be instructed to contact the study site for the reporting of AEs while away from the study site.
13. Concomitant Medications: new and/or changed medications and dose, medical treatments and/or therapies will be recorded at Visit 4 through either Follow-up Phone Call or ET. The investigator or designee will also review for prohibited medications (see Section 10 of Protocol).
14. Interim Safety Analysis: An interim analysis of the safety data will be conducted after approximately all subjects remaining in the study have completed approximately 180 days (Visit 11) in the Treatment Phase. After completion of the interim analysis, based on the safety profile of the treatment, the study may be stopped. Treatment in the current study will continue as planned while the interim analysis is conducted. If the decision is made to stop the study, all subjects remaining in the study will undergo the EOT Visit (with safety evaluations including fasting safety labs and ECGs) and a Follow Up Phone Call.
15. End-of-Treatment (EOT): Subjects will receive their last dose of study drug in the study.
16. Early Termination (ET): Subjects who meet withdrawal criteria post-dose during the Treatment Phase (after at least one dose of study drug is administered) will complete ET procedures. At the discretion of the Investigator, ensuring the safety of the subjects, any ET procedures that were performed on the same day as part of the procedures of the Treatment Phase, do not need to be repeated. Subjects who withdraw early from the study and complete the ET procedures will not have a Follow-up Phone Call. Therefore, the ET Visit is the EOS.
17. Assessment Changes due to COVID-19: If a subject is not able to attend the site for a scheduled visit due to COVID-19 restrictions, then sites will be instructed to collect data for select safety assessments (vital signs, labs, ECG, physical exam) when the subject is next able to safely return to an on-site visit, even if those assessments would not normally be done at that visit. These assessments will be mapped to the nearest

scheduled visit. Changes in scheduled visits and corresponding assessments due to COVID-19 restrictions will be captured in the eCRF. Assessments that do not require the subject's presence at the site (e.g., AEs, C-SSRS, ADHD-RS-IV, CGI-S, CGI-I, CSHQ) will be collected by phone at the scheduled visit times (remote visit). If needed, alternate measures to dispense study drug to the subjects during their COVID-19 isolation period will be implemented (e.g., study drug directly delivered to the subject's residence or dispensed to another family member).

18. At visits on which PK samples will be collected (Visit 6 and/or Visit 7), PK Subjects will come to the site in the morning of the scheduled visit and they will receive study drug at the study site after the pre-dose PK sample is collected. The PK Dosing Diary will be reviewed with the parent/caregiver. See Section 14.2 of Protocol for additional details.

3. STATISTICAL METHODS

3.1. General Methods

3.1.1. Computing Environment

All statistical analyses will be performed using SAS® Version 9.4 or higher for Windows.

3.1.2. Reporting of Numerical Values

All clinical study data will be presented in subject data listings. Relevant descriptive statistics (n, mean, standard deviation, median, minimum, and maximum) will be calculated for continuous variables. Additional percentile statistics may be reported as appropriate. Frequencies and percentages will be presented for categorical and ordinal variables. Percentages will be based on the number of non-missing values. If there are missing values, the number missing will be presented, but without a percentage. All confidence intervals (CIs) will be two-sided 95% CIs. All analyses will be descriptive. No inferential testing will be performed.

Means, medians, and CIs will be reported to one decimal place more than the data reported on the case report form (CRF) or by the laboratory/vendor up to a maximum of two decimal places. Standard deviations will be reported to one additional decimal place. A maximum of three decimal places will apply to all summary statistics.

3.1.3. Baseline Value and Change from Baseline

Baseline will be defined as the last non-missing value prior to the first administration of study drug in KP415.P01 for Roll-over Subjects and in KP415.P02 for New Subjects. Unless otherwise specified, post-baseline assessments will include only assessments collected during Study KP415.P02 for both Roll-over Subjects and New Subjects.

If an assessment is obtained on the same day as first dose of study drug and times are not available for both assessment and dosing, it will be assumed that the assessment is prior to dosing. Change from baseline will be calculated by subtracting the baseline value from the post-dose assessment for each subject (i.e., post-dose – baseline). Percent change from baseline will be calculated by dividing change from baseline by the baseline value given it is not missing or zero, and then multiplying by 100 for each subject (i.e., [change from baseline/baseline] x 100).

3.1.4. Handling of Missing/Incomplete Values

No substitutions will be made for missing/incomplete data points, except for adverse event and medication dates, as described below.

3.1.4.1. Adverse Events or Medication Missing Dates

Adverse events will only be assessed and recorded in this study following the first dose of open-label drug on Day 1, hence all events captured in Study KP415.P02 will be treatment-emergent to Study KP415.P02. On-going adverse events from Study KP415.P01 for the Roll-over Subjects will be treatment-emergent to Study KP415.P01 only.

New and/or changed medications will be recorded starting at Screening for New Subjects and Visit 2 for Roll-over Subjects. Partial dates for AEs and medications will be imputed for the ease of determining which study phase AEs were treatment-emergent to and whether medications were concomitant to study drug.

Missing or partial dates for AEs and medications will be handled as follows in the safety analysis:

Start Date	Missing day: If month and year are equal to the month and year of first dose date, set start date to the first dose date. Otherwise, set the day to the first of the month. Missing month and day: If year is equal to the year of first dose date, set start date to the first dose date. Otherwise, set the month and day to Jan 1. Missing year, month, and day: Set start date to the first dose date.
End Date	Missing day: set end date to the last day of the month. Missing month and day: set to Dec 31. Missing year, month, and day: no imputation

If imputation of a start date (and end date if both were imputed) results in a start date occurring after the end date, the imputed start date will be reset to equal the end date. If an imputed start or end date occurs after the database lock date, the imputed date will be reset to the database lock date. Imputed partial dates will only be used for identifying to which study phase an AE was treatment-emergent or whether a medication was concomitant to study drug. If it cannot be determined conclusively from the partial AE dates whether an AE was treatment-emergent to the Dose Optimization Phase or the Treatment Phase, then the AE will be classified as treatment-emergent to both. Listings will display the partial dates as recorded on the electronic CRF.

3.1.4.2. Handling of Missing Scores in ADHD-RS

Electronic Patient Reported Outcome (ePRO) data are entered in the Patient Cloud using the Apple iPad device provided by Medidata Rave Electronic Data Capture (EDC). Paper PRO eCRFs are available only in the rare event the device is not working.

Missing items for the ADHD-RS scales will be handled as follows:

1. If more than 3 items have missing data, the total score will be set to missing. If the total score is missing, then both subscales (inattention and hyperactivity/impulsivity) will be set to missing.

2. If 3 items or fewer have missing or invalid data, the values for the missing items will be imputed using the mean of the non-missing items rounded to the nearest integer for the purpose

of calculating the total score and subscale scores.

The change from baseline in ADHD Rating Score (ADHD-RS) total score will be analyzed using a Mixed Model Repeated Measures (MMRM) analysis of covariance (ANCOVA) model in which the missing data are handled implicitly under the assumption of Missing-At-Random (MAR).

3.1.5. Visit Windows

Visit windows will be used to determine analysis visits for all efficacy and safety endpoints except for ECGs and clinical laboratory assessments, which will use nominal visits. If a subject has multiple assessments (including unscheduled visits) within a visit window, the value closest to the target day for that visit will be selected for analysis. If more than 1 assessment is equidistant to the target day, the latest value will be selected. Any additional collected values that are not used in the analysis will be included in listings.

Analysis Visit	Relative Target Study Day	Study Days
Baseline	NA	See Section 3.1.3
Visit 3	7	1 - 10
Visit 4	14	11 - 17
Visit 5	21	18 - 24
Visit 6	30	25 - 45
Visit 7	60	46 - 75
Visit 8	90	76 - 105
Visit 9	120	106 - 135
Visit 10	150	136 - 165
Visit 11	180	166 - 195
Visit 12	210	196 - 225
Visit 13	240	226 - 255
Visit 14	270	256 - 285
Visit 15	300	286 - 315
Visit 16	330	316 - Day before EOT
Visit 17	360	EOT
Visit 18	365	Follow-up Phone Call

NA = Not Applicable.

3.1.6. Standard Calculations

Durations associated with ADHD Diagnosis and onset will be calculated as follows:

- Time since ADHD Diagnosis (months) = (date of informed consent for KP415.P02 – date of ADHD diagnosis + 1)/30.4375
- Time since ADHD Symptoms Onset (months) = (date of informed consent for KP415.P02 – date of ADHD symptoms + 1)/30.4375

At each visit, a bottle will be dispensed to the subject's parent or guardian with sufficient study drug until the next visit, and any unused study drug from the previous visit will be returned for drug accountability and compliance. Treatment compliance during the Treatment Phase will utilize the following calculation:

Treatment Compliance (%) = 100*(number of capsules dispensed – number of capsules returned) / number of capsules expected to be taken.

The calculation will only include the medication bottles that were both dispensed and returned. The number of capsules expected to be taken will be adjusted accordingly.

Weight and height z-scores will be calculated as follows:

z-score = (observed value - mean of the reference population) / standard deviation of the reference population.

The calculation of the weight and height z-scores (and percentiles) is based on a SAS® program from the CDC[1] which utilizes the United States 2000 CDC Growth Charts (ages 2 to <20 years; updated in the year 2000) as the reference population, developed with data from five national health examination surveys.[2]

The calculation of blood pressure percentiles is based on the SAS® program used in the 2017 American Academy of Pediatrics (AAP) guidelines for high blood pressure in children ages 1 to 17 years.[3] Blood pressure percentiles are derived from a quantile regression on the basis of normal-weight children (BMI <85th percentile) and account for sex, age, and height percentile.[4] Percentiles will be converted to z-scores under a standard normal distribution.

3.2. Sample Size Determination

No formal sample size calculations were conducted for the assessment of the primary objective. It was determined that approximately 50 subjects would be adequate to satisfy the primary objective of the study, which is to determine the safety and tolerability of Azstarys® in treating children with ADHD for approximately 12 months. Assuming a dropout rate of up to 50% over 12 months, approximately 100 subjects will be enrolled and approximately 50 subjects are expected to complete the 12-month Treatment Phase.

For the assessment of the population PK objective, a minimum of 40 subjects was required to achieve at least 80% power to target a 95% confidence interval within 60% and 140% of the geometric mean estimates of clearance and volume of distribution for d-MPH after Azstarys® administration in this pediatric group based on power calculations. Therefore, complete PK sample sets (pre-dose and 2 post-dose samples) will be collected from at least 40 subjects. In accordance with a male-to female distribution ratio of 3:1 of children diagnosed with ADHD in clinical practice, full PK sample sets will be collected from approximately 30 males and 10 females.

3.3. Analysis Populations and Subgroups

3.3.1. Definition of Analysis Populations

3.3.1.1. Treatment Phase Safety Population

The Treatment Phase Safety Population will consist of all enrolled subjects in the Treatment Phase who received at least one dose of study medication in the Treatment Phase. All baseline and safety data during the Treatment Phase will be analyzed using this population.

3.3.1.2. Efficacy Population

The Efficacy Population will consist of all enrolled subjects who received at least 30 days of study medication in the Treatment Phase, who had a baseline assessment and at least one post-baseline assessment of efficacy parameters (ADHD-RS-IV, CGI-I) and who had no protocol deviations that could affect the efficacy parameters. All efficacy analyses across the Treatment Phase will be analyzed using this population.

3.3.1.3. Dose Optimization Population

The Dose Optimization Population will consist of all enrolled subjects in the Dose Optimization Phase who received at least one dose of study medication in the Dose Optimization Phase. All data from the Dose Optimization Phase will be analyzed using this population.

3.3.1.4. Pharmacokinetic (PK) Population

The PK Population will consist of all subjects who received the daily treatment for at least 3 days before the blood samples for PK were collected, without any major protocol deviations potentially affecting PK, and who provided the plasma concentrations for d-methylphenidate (d-MPH) required to calculate the population PK parameters of d-MPH. Demographics and baseline characteristics will be summarized for the PK Population overall and by optimized dose received.

3.3.2. Definition of Subgroups

For inclusion in the study, subjects must have a body weight at Screening within the 5th and 95th percentiles of the gender-specific weight-for-age percentile charts from the Centers for Disease Control and Prevention (CDC). Subgroups will be defined as: 5th to 25th percentile, >25th to 50th percentile, >50th to 75th percentile, and >75th to 95th percentile. Adverse event incidences across these subgroups will be compared.

3.4. Analysis Variables

3.4.1. Safety Variables

Safety variables will include:

- Incidence of TEAEs
- Incidence of SAEs

- Incidence of drug-related TEAEs
- Incidence of abuse-related TEAEs
- Incidence of TEAEs leading to treatment discontinuation
- Change from baseline in clinical laboratory values (hematology, chemistry, urinalysis)
- Change from baseline in vital signs (systolic blood pressure, pulse, respiratory rate, and temperature)
- Incidence of clinically notable vital signs
- Change and percent change from baseline in body weight, height, and weight and height percentiles
- Change from baseline in ECG parameters
- Change and percent change from baseline in CSHQ scores
- Incidence of Columbia-Suicide Severity Rating Scale (C-SSRS) measured suicidal ideation and/or behavior

3.4.2. Efficacy Variables

Efficacy variables will include:

- Change from baseline in ADHD-RS total score
- Change from baseline in ADHD-RS hyperactivity/impulsivity score
- Change from baseline in ADHD-RS inattention score
- Change from baseline in CGI-S score
- CGI-I score (during Dose Optimization Phase only)

3.5. Subject Disposition and Evaluability

3.5.1. Subject Disposition

Subject disposition will be summarized for all subjects by optimized dose level and overall. The number of subjects screened in KP415.P02 and reasons for screen failure, Roll-over Subjects who participated in KP415.P01, and subjects enrolled in each Phase will be summarized. The number and percentage of subjects included in each analysis population, completing each visit, completing the treatment, and completing the study will be summarized. For subjects who discontinue treatment or from the study, the primary reason for discontinuation will be summarized by treatment phase, dose level and overall.

A listing of subject disposition will also be presented.

3.5.2. Protocol Deviations

Important protocol deviations will be summarized for all subjects in the Treatment Phase Safety Population by optimized dose level and overall and in the Dose Optimization Population overall.

All protocol deviations will be presented in a listing.

3.6. Demographics and Baseline Characteristics

3.6.1. Demographics and Baseline Characteristics

Subject demographics and baseline characteristics will be summarized descriptively for all subjects in the Treatment Phase Safety Population, Efficacy Population, and Pharmacokinetic Population by optimized dose level and overall and in the Dose Optimization Population overall. Frequencies and percentages will be presented for sex, race and ethnicity. Subjects of multiple races will be counted under "Other". Descriptive statistics will be presented for age, height, weight, and body mass index (BMI).

All demographics and baseline characteristics will be presented in a subject listing.

3.6.2. ADHD Diagnosis

ADHD diagnosis subtype will be summarized for the Treatment Phase Safety Population by optimized dose level and overall and for the Dose Optimization Population overall. Descriptive statistics will be provided for time since ADHD diagnosis (months) and time since onset of ADHD symptoms (months), if recorded. Frequencies and percentages will be presented for the attention-deficit/hyperactivity disorder, conduct disorder, and oppositional defiant disorder from the MINI Kid diagnostic modules. Refer to Section 3.1.6 for the calculation of time since ADHD diagnosis/symptoms onset.

All ADHD baseline characteristics will be presented in a subject listing.

3.6.3. Medical History

All relevant medical history will be coded using Medical Dictionary of Regulatory Activities (MedDRA) Version 25.1 and will be classified by system organ class (SOC) and preferred term (PT). Medical History will be summarized for all subjects in the Treatment Phase Safety Population by optimized dose level and overall and in the Dose Optimization Population overall. The number and percentage of subjects having a medical condition by SOC and PT will be presented. Each subject will be counted once under each SOC and PT within SOC. The summary will be sorted alphabetically by SOC, and within SOC, by decreasing frequency of PT for all subjects.

Medical history will be presented in a subject listing.

3.7. Prior and Concomitant Medications

Concomitant medications will be coded using the World Health Organization (WHO) Drug Dictionary Version B3 September 2022.

Concomitant medications are defined as medications that are being taken while on study drug.

Concomitant medications will be summarized for the Dose Optimization Population overall and the Treatment Phase Safety Population by optimized dose level and overall, and will include all concomitant medications taken starting from the first dose of study drug in the Dose Optimization Phase. The number and percentage of subjects who took at least one concomitant medication as well as the number and percentage of subjects who took each type of medication

will be presented by Anatomic Therapeutic Class (ATC) level 4 term and PT. Each subject will be counted once under each ATC level 4 term and PT within ATC level 4 term. The summary will be sorted alphabetically by ATC level 4 term, and within ATC level 4 term, by decreasing frequency of PT for all subjects.

All prior and concomitant medications will be presented in a subject listing.

3.8. Treatment Compliance and Exposure

3.8.1. Compliance to Study Treatment

Treatment compliance (%) of the Treatment Phase Safety Population during the Treatment Phase will be classified into the following categories: < 80%, 80-100%, >100 to 120%, and > 120%. The number and percentage of subjects within each of these compliance categories will be presented by optimized dose level and overall. Refer to Section 3.1.6 for the calculation of the treatment compliance.

3.8.2. Exposure to Study Treatment

Descriptive statistics will be provided for the total number of doses (capsules) received, total number of missed doses and duration of treatment (days) for subjects in the Treatment Phase Safety Population. Number and percentage of subjects at each optimized dose level administered in the Treatment Phase (13.1 mg/2.6 mg, 26.1 mg/5.2 mg, or 39.2 mg/7.8 mg per day) will be presented. The average dose received during the study (Dose Optimization Phase plus Treatment Phase) by each subject in the Treatment Phase Safety Population will be analyzed descriptively. The number and percentage of subjects that ended the study on a different dose level than their optimized dose level (i.e., the dose level they achieved at the end of the Dose Optimization Phase at Visit 5) will also be presented. Reasons for missed doses will also be summarized.

3.9. Safety Analysis

The safety analyses will be performed for the safety data collected during the Treatment Phase based on the Treatment Phase Safety Population by optimized dose level and overall. The safety analyses will be performed for the safety data collected during the Dose Optimization Phase based on the Dose Optimization Population.

For Roll-over Subjects, the number and percentage of subjects with any treatment-emergent adverse events in Study KP415.P01 will be summarized by MedDRA SOC and PT. The SOCs will be sorted by decreasing frequency, and within SOC, the PTs will be presented by decreasing frequency. All TEAEs for Roll-over Subjects in KP415.P01 will be presented in a subject listing.

3.9.1. Treatment Phase

The safety analyses described in this subsection will be performed for the safety data collected during the Treatment Phase based on the Treatment Phase Safety Population. All safety analyses will be performed by optimized dose level and overall.

3.9.1.1. Adverse Events

Adverse events will be mapped to SOC and PT using MedDRA Version 25.1.

TEAEs for the Treatment Phase are AEs that begin in the time period following the first administration of study medication in the Treatment Phase through 5 days after the last dose of study medication, or existing AEs that worsen in the time period following the first dose of study medication in the Treatment Phase through 5 days after the last dose of study medication. Investigator assessed causality to study drug will be categorized as "probably related", "possibly related" or "unrelated". Drug-related AEs will be considered those at least "possibly related" to study medication based on the Investigator's assessment. For summary purposes, "probably related" and "possibly related" will be considered "related". Any missing relationships will be considered "related" as well.

An overall summary of AEs will include the total number and percentage of subjects who experienced any TEAEs, SAEs, study drug-related TEAEs or SAEs, TEAEs leading to study drug discontinuation, and TEAEs leading to death. In addition, the greatest severity experienced by each subject will be summarized. Severity will be graded as mild, moderate, or severe.

A summary of TEAEs will include the number and percent of subjects who experience at least one TEAE, as well as the number and percent of subjects who experience at least one TEAE within each specific SOC and PT. A summary of PT only will also be presented. SAEs, drug-related TEAEs, TEAEs leading to study drug discontinuation, and TEAEs in Study KP415.P01 will be summarized similarly. TEAE incidences will also be summarized by maximum severity grade.

Abuse-related TEAEs will be analyzed in accordance with the 2017 FDA Guidance for Industry, Assessment of Abuse Potential of Drugs.

The following PTs from the guidance will be used to identify abuse-related TEAEs:

- Euphoria-related terms: Euphoric mood; Elevated mood; Feeling abnormal; Feeling drunk; Feeling of relaxation; Dizziness; Thinking abnormal; Hallucination; Inappropriate affect
- Terms indicative of impaired attention, cognition, and mood: Somnolence; Mood disorders and disturbances
- Dissociative/psychotic terms: Psychosis; Aggression; Confusion and disorientation
- Related terms not captured elsewhere: Drug tolerance; Habituation; Drug withdrawal syndrome; Substance-related disorders

The number and percentage of subjects with Abuse-related AEs will be summarized by MedDRA SOC and PT.

TEAE incidences will also be summarized by SOC and PT across gender-specific weight-for-age percentile subgroups: 5^{th} to 25^{th} percentile, $>25^{th}$ to 50^{th} percentile, $>50^{th}$ to 75^{th} percentile, and $>75^{th}$ to 95^{th} percentile.

For Roll-over Subjects only, subjects were randomized to either active or placebo treatment groups in Study KP415.P01. Roll-over subjects will be split into Placebo/Active, Active/Active, and Overall by their P01/P02 treatment groups for additional overall summaries of AEs and

TEAE incidences by SOC and PT. For presentation of AE incidences, the SOCs will be sorted by decreasing frequency, and within SOC, the PTs will be presented by decreasing frequency.

All AEs and SAEs will be listed for all subjects. A listing of AEs leading to treatment discontinuation and AEs leading to death will be provided as well.

3.9.1.2. Clinical Laboratory Evaluation

Clinical laboratory tests will be evaluated at Screening (New Subjects) or Visit 2 (Roll-over Subjects), at Visit 11, and at the end of the Treatment Phase or ET. All laboratory results will be summarized using standard units and presented in subject listings. Continuous laboratory data will be examined using descriptive statistics of actual values and changes from baseline over time. Values outside of normal ranges and clinically significant laboratory values will be listed.

All drug abuse test results will be presented in a subject listing.

3.9.1.3. Vital Signs

Vital signs will be assessed at each analysis visit. Vital signs will be summarized using descriptive statistics of actual values and changes from baseline over time. The incidence of clinically notable vital signs will be summarized by analysis visit. These will be defined as systolic blood pressure ≥130 mmHg, diastolic blood pressure ≥90 mmHg, pulse rate ≥130 beats/min, and respiratory rate ≥30 breaths/min. A summary of systolic blood pressure percentiles will also be presented by analysis visit.

Blood pressure data will be analyzed using the 2017 AAP guidelines[3] based on the average of 3 blood pressure measurements 2 to 5 minutes apart at each visit. Descriptive statistics will be presented by analysis visit for observed systolic and diastolic blood pressure (in mmHg) and the corresponding change and percent change from baseline, as well as blood pressure z-scores, and blood pressure percentiles.

Change from baseline in systolic and diastolic blood pressure will be analyzed using a mixed model repeated measures (MMRM) analysis of covariance (ANCOVA) model fitted using all observed data for the Treatment Phase. The dependent variable will be change from baseline to the post-baseline assessments of the systolic and diastolic blood pressure measurements for each subject. The model will include fixed effects for optimized dose, baseline blood pressure, analysis visit, and analysis visit-by-dose interaction as well as a random effect for the subject. The mixed model will utilize restricted maximum likelihood estimation with the Kenward-Roger method used to compute the denominator degrees of freedom for tests of fixed effects. The model will assume an unstructured covariance matrix. If the model does not converge under the unstructured covariance matrix when using the SAS PROC MIXED default Newton-Raphson algorithm, other numerical methods such as the Fisher scoring algorithm will be tried. Refer to Section 6 for sample SAS code for the model.

If the model using the unstructured covariance matrix still fails to converge, the following structures will be executed sequentially until convergence is attained: heterogeneous Toeplitz, heterogeneous Compound Symmetry, heterogeneous first-order autoregressive, Toeplitz, Compound Symmetry, and first-order autoregressive. If a structured covariance is used, then a

robust sandwich estimator will be utilized for estimating the variance of the treatment effect estimate.

The least-squares (LS) mean and 95% CIs for the change from baseline in blood pressure will be extracted from the model for each post-baseline visit and presented by optimized dose level. The analysis will be based on comparisons of optimized dose levels. From the MRMM model, the difference between LS means of Azstarys® optimized dose levels will be presented along with the corresponding 95% CIs for each pairwise comparison.

All vital sign results, including blood pressure z-scores and percentiles, will be presented in a subject listing.

3.9.1.4. Body Weight and Height

Body weight and height will be assessed at each analysis visit. Descriptive statistics will be presented by analysis visit for body weight (in kg), change and percent change from baseline in body weight, height (in cm), and change and percent change from baseline in height at each analysis visit. Additionally, weight and height percentiles will be summarized. Descriptive statistics for observed and change from baseline in weight-for-age percentiles and height-for-age percentiles will also be presented by P01/P02 treatment assignment (Placebo/Active, Active/Active) and Overall for Roll-over Subjects. The z-score system expresses the anthropometric value as a number of standard deviations (SDs) below or above the mean of a reference population. Z-scores normalize for the natural growth of children and adolescents by comparisons to age and sex-matched population standards. A positive z-score indicates that a child's weight/height is above average while a negative z-score indicates that it is below average. Since z-scores are standardized values of a normal distribution with mean 0 and SD of 1, there is a direct correlation to percentiles. A percentile indicates that the percentage of observations that fall below a certain value of the reference population. A z-score of 0 corresponds to the 50^{th} percentile in the reference population; a z-score of ±1 corresponds to approximately the 16^{th} and 84^{th} percentiles, respectively; and a z-score of ±2 corresponds to approximately the 2^{nd} and 98^{th} percentiles, respectively. Refer to Section 3.1.6 for the calculation of z-scores and percentiles.

The descriptive statistics will include n, mean, standard deviation, median, 1^{st} and 3^{rd} quartile (Q1, Q3), and range (minimum and maximum). The number and percentage of subjects with clinically notable weight loss (a weight decrease from baseline >5%) will be presented. In addition, descriptive statistics will be tabulated by sex and optimized dose.

All body weight and height results, including z-scores and percentiles, will be presented in a subject listing.

3.9.1.5. Physical Examinations

All physical examination findings at Screening (New Subjects) or Visit 2 (Roll-over Subjects), at Visit 11, and at the end of the Treatment Phase or ET will be presented in subject listings.

3.9.1.6. ECG

ECG parameters will be assessed at Screening (New Subjects) or Visit 2 (Roll-over Subjects), at Visit 11, and at the end of the Treatment Phase or ET. Heart rate (bpm), QT Interval (msec), RR Interval (msec) will be summarized using descriptive statistics of actual values and changes from

baseline over time. Frequencies and percentages will also be provided for overall ECG interpretation categories (normal; abnormal; not clinically significant; abnormal; clinically significant).

All ECG results will be presented in a subject listing.

3.9.1.7. CSHQ

CSHQ will be assessed at each analysis visit. The CSHQ Total Sleep Disturbance Score and the change and percent change from baseline in CSHQ Total Sleep Disturbance score will be analyzed descriptively by optimized dose level and overall. An MMRM ANCOVA model will be fitted using all data as observed. The dependent variable will be change from baseline to all post-baseline assessments of the CSHQ score for each subject during the Treatment Phase. The model will include fixed effects for optimized dose, baseline CSHQ score, analysis visit, and analysis visit-by-dose interaction as well as a random effect for the subject. The mixed model will be fitted in the same manner as described above for the Vital Signs endpoint analysis.

The least-squares (LS) mean and 95% CIs for the change from baseline in CSHQ score will be extracted from the model for each post-baseline visit and presented by optimized dose level. The analysis will be based on pairwise comparisons of Azstarys® optimized dose levels. From the MMRM model, the difference between least square (LS) means of Azstarys ® optimized dose levels will be presented along with the corresponding 95% CIs for each pairwise comparison.

Descriptive statistics will also be presented by analysis visit for the change and percent change from baseline in scores for Bedtime Resistance, Sleep Onset Delay, Sleep Duration, Sleep Anxiety, Night Wakings, Parasomnias, Sleep Disordered Breathing, and Daytime Sleepiness by optimized dose level and overall.

All CSHQ results will be presented in a subject listing.

3.9.1.8. C-SSRS

C-SSRS outcomes at each analysis visit will be summarized by the number and percentage of subjects in each optimized dose level and overall with the following: suicidal ideation, suicidal behavior, and suicidal ideation or behavior (ideation and behavior combined).

All C-SSRS results will be presented in a subject listing.

3.9.2. Dose Optimization Phase

The safety analyses described in this subsection will be performed for the safety data collected during the Dose Optimization Phase based on the Dose Optimization Population.

3.9.2.1. Adverse Events

The occurrence of adverse events will be assessed starting from the first dose of the study drug. Adverse events will be mapped to SOC and PT using the MedDRA.

TEAEs for the Dose Optimization Phase are AEs that begin in the time period following the first administration of study medication in the Dose Optimization Phase until the first dose of study medication in the Treatment Phase or existing AEs that worsen in that time period. Investigator

assessed causality to study drug will be categorized as “probably related”, “possibly related” or “unrelated”. Drug-related AEs will be considered those at least “possibly related” to study medication based on the Investigator’s assessment. For summary purposes, “probably related” and “possibly related” will be considered “related”. Any missing relationships will be considered “related” as well.

The number and percentage of subjects reporting TEAEs will be summarized by MedDRA SOC and PT, by severity, and by relationship to study treatment. The number and percentage of subjects with SAEs, and the number and percentage of subjects with AEs leading to treatment discontinuation will also be summarized by MedDRA SOC and PT.

TEAE incidences will also be summarized by SOC and PT across gender-specific weight-for-age percentile subgroups: 5^{th} to 25^{th} percentile, $>25^{th}$ to 50^{th} percentile, $>50^{th}$ to 75^{th} percentile, and $>75^{th}$ to 95^{th} percentile.

For presentation of AE incidences, the SOCs will be sorted by decreasing frequency, and within SOC, the PTs will be presented by decreasing frequency.

All AEs and SAEs will be listed for all subjects. A listing of AEs leading to treatment discontinuation and AEs leading to death will be provided as well.

3.9.2.2. Clinical Laboratory Evaluation

Clinical laboratory tests will be evaluated at Screening (New Subjects) or Visit 2 (Roll-over Subjects) during the Dose Optimization Phase. All laboratory results will be presented in subject listings. Values outside of normal ranges and clinically significant laboratory values will be listed. All drug abuse test results will be presented in a subject listing.

3.9.2.3. Vital Signs

Vital signs will be assessed at each analysis visit. Vital signs will be summarized using descriptive statistics of actual values and changes from baseline over time. The incidence of clinically notable vital signs will be summarized. These will be defined as systolic blood pressure ≥130 mmHg, diastolic blood pressure ≥90 mmHg, pulse rate ≥130 beats/min, and respiratory rate ≥30 breaths/min.

All vital sign results, including blood pressure z-scores and percentiles, will be presented in a subject listing.

3.9.2.4. Body Weight and Height

Body weight and height will be assessed at each analysis visit. Descriptive statistics will be presented by analysis visit for body weight (in kg), change and percent change from baseline in body weight, height (in cm), and change and percent change from baseline in height at each analysis visit.

All body weight and height results, including z-scores and percentiles, will be presented in a subject listing.

3.9.2.5. Physical Examinations

All physical examination findings will be presented in subject listings at Screening (New Subjects) or Visit 2 (Roll-over Subjects).

3.9.2.6. ECG

ECG parameters will be assessed at Screening (New Subjects) or Visit 2 (Roll-over Subjects). All ECG results will be presented in a subject listing.

3.9.2.7. CSHQ

CSHQ will be assessed at each analysis visit. The CSHQ Total Sleep Disturbance Score and the change and percent change from baseline CSHQ score will be analyzed descriptively. Descriptive statistics will also be presented by analysis visit for the change and percent change from baseline in scores for Bedtime Resistance, Sleep Onset Delay, Sleep Duration, Sleep Anxiety, Night Wakings, Parasomnias, Sleep Disordered Breathing, and Daytime Sleepiness.

All CSHQ results will be presented in a subject listing.

3.9.2.8. C-SSRS

C-SSRS outcomes at each analysis visit will be summarized by the number and percentage of subjects with the following: suicidal ideation, suicidal behavior, and suicidal ideation or behavior (ideation and behavior combined).

All C-SSRS results will be presented in a subject listing.

3.10. Efficacy Analysis

3.10.1. Treatment Phase

All efficacy analyses described in this subsection will be performed for the efficacy data collected during the Treatment Phase based on the Efficacy Population.

3.10.1.1. Primary Efficacy Endpoint

3.10.1.1.1. Change from Baseline in ADHD Rating Scale (ADHD-RS) Total Score

Descriptive statistics will be provided for baseline, all post baseline measurements, and changes from baseline to all post-baseline measurements of ADHD-RS-IV Total Score by optimized dose level and overall. In cases when ADHD-RS-IV scores were not collected using an ePRO device, but were instead collected on a paper CRF, data from both modalities will be used in the analysis.

Change from baseline in ADHD-RS-IV total score will be analyzed using a MMRM ANCOVA model fitted using all observed data for the Treatment Phase. The dependent variable will be change from baseline in the ADHD Rating Scale-IV total score for all post-baseline assessments for each subject. The model will include fixed effects for optimized dose, baseline ADHD-RS-IV total score, analysis visit, and analysis visit-by-dose interaction as well as a random effect for the subject. The mixed model will be fitted in the same manner as described above for the Vital

Signs endpoint analysis.

The least-squares (LS) mean and 95% CIs for the change from baseline in ADHD-RS total score will be extracted from the model for each post-baseline visit and presented by optimized dose level. The analysis will be based on comparisons of optimized dose levels. From the MRMM model, the difference between LS means of Azstarys® optimized dose levels will be presented along with the corresponding 95% CIs for each pairwise comparison. There will be no adjustments made for the use of prohibited therapies or other intercurrent events.

For Roll-over Subjects only, additional descriptive statistics will be provided for baseline, all post-baseline, and changes from baseline to all post-baseline measurements of ADHD-RS IV by P01/P02 treatment groups: Placebo/Active, Active/Active, and Overall.

LS mean changes from baseline over time with 95% CI from the analysis model will be plotted by optimized dose level.

All ADHD-RS total scores will be presented in a subject listing.

3.10.1.2. Secondary Efficacy Endpoints

3.10.1.2.1. Change from Baseline in ADHD-RS for Hyperactivity/Impulsivity and Inattention

Change from baseline in ADHD-RS for hyperactivity/impulsivity and ADHD-RS for inattention will be summarized using an MMRM ANCOVA model analogous to the primary efficacy endpoint, change from baseline in ADHD-RS-IV Total Score, except that the dependent variables will be change from baseline in ADHD-RS score for hyperactivity/impulsivity and change from baseline in ADHD-RS score for inattention. Additionally, instead of including a fixed effect for baseline ADHD-RS-IV total score, these models will include fixed effects for baseline ADHD-RS hyperactivity/impulsivity score and baseline ADHD-RS inattention score, respectively.

Descriptive statistics will be presented for baseline, all post baseline measurements, and changes from baseline to all post-baseline measurements of ADHD-RS for hyperactivity/impulsivity and ADHD-RS for inattention by optimized dose level and overall.

All ADHD-RS hyperactivity/impulsivity and inattention scores will be presented in a subject listing.

3.10.1.2.2. Change from Baseline in CGI-S

A MMRM ANCOVA model will be fitted using all data as observed during the Treatment Phase. The dependent variable will be change from baseline in CGI-S post-baseline assessments for each subject. The model will include fixed effects for optimized dose, baseline CGI-S, analysis visit, and analysis visit-by dose interaction as well as a random effect for the subject. The mixed model will be fitted in the same manner as described above for the Vital Signs endpoint analysis. The least-squares (LS) mean and 95% CIs for the change from baseline in CGI-S will be extracted from the model for each post-baseline visit and presented by optimized dose level. The analysis will be based on comparisons of optimized dose levels. From the MMRM model, the

difference between LS means of Azstarys® optimized dose levels will be presented along with the corresponding 95% CI.

Descriptive statistics will be presented for baseline, all post baseline measurements, and changes from baseline to all post-baseline measurements of CGI-S by optimized dose level and overall.

All CGI-S results will be presented in a subject listing.

3.10.2. Dose Optimization Phase

All efficacy analyses will be performed for the efficacy data collected during the Dose Optimization Phase based on the Dose Optimization Population. Descriptive statistics will be presented for baseline, all post baseline measurements, and changes from baseline to all post-baseline measurements, where applicable, for ADHD-RS total score, ADHD-RS hyperactivity/impulsivity score, ADHD-RS inattention score, CGI-S, and CGI-I. CGI-I will be assessed at Visits 2-5 in Roll-over Subjects and Visits 3-5 in New Subjects. All other endpoints will be assessed at each analysis visit (Visits 1-5).

All ADHD-RS scores and CGI results will be presented in subject listings.

3.11. Pharmacokinetic Analyses

Pharmacokinetic analyses are planned to assess the population PK of Azstarys® in children 4 and 5 years old with ADHD. All PK data will be analyzed using the Pharmacokinetic Population.

A population PK analysis will be performed for d-MPH based on the plasma concentrations of d-MPH based on the plasma concentrations of d-MPH measured in 3 samples per subject (sparse sampling approach) during the Treatment Phase. Three (3) blood samples will be drawn as indicated:

Sample **1**:

- Pre-dose sample: within 30 minutes pre-dose

Samples **2** and **3**, taken at two of the following times. A randomization scheme will be used to determine the 2 post-dosing times for the collection of the PK samples in each PK subject:

- 15-minute sample: 15 to 40 minutes post-dose
- 2-hour-sample: 1.5 to 2.5 hours post-dose
- 4-hour sample: 4 to 6 hours post-dose

Detailed descriptions of the population PK analyses will be provided in the pharmacokinetic analysis plan (PKAP).

3.12. Interim Analysis

3.12.1. Analysis Objective

An interim analysis of the safety data will be conducted once all of the subjects remaining in the study complete approximately 180 days (Visit 11) in the Treatment Phase to determine whether the study should be stopped. The interim analysis will primarily focus on the safety assessments (including changes in weight, and height) and include only subjects who have completed Visit

11. The safety data will be analyzed with the same statistical methods as described above for the main analysis after completion of the study. The study will be stopped early for any of the following reasons:

a. A clinically significant growth reduction in >40% of subjects. A clinically significant growth reduction is defined by meeting both criteria as follows:
    1. A decrease in weight or height percentile versus baseline crossing two percentile lines on a growth chart showing the 5^{th}, 10^{th}, 25^{th}, 50^{th}, 75^{th}, 90^{th}, and 95^{th} percentiles at Visit 11.
    2. For those subjects crossing two percentile lines in weight or height at Visit 11 (#1 above), subjects with a decrease in height or weight percentile below the 50^{th} percentile on the growth chart. This criterion excludes overweight subjects at baseline who progress towards a normal weight during treatment as this is not considered a safety risk.
b. An increase in systolic blood pressure >20 mmHg and systolic blood pressure percentile above the 95^{th} percentile for age and gender according to the 2017 AAP guidelines[3] after 180 days of treatment (Visit 11) in >25% of subjects who had baseline systolic blood pressure below the 95^{th} percentile for age and gender at baseline.
c. Subjects experienced AEs, laboratory parameters, electrocardiograms, or suicidal ideation, considering type, incidence and severity, such that further treatment is not in the best interest of the study participants.

The interim safety evaluation for stopping the study early will be judged by the Principal Investigator in collaboration with the Medical Monitor and Sponsor. If the decision is made to stop the study, all subjects remaining in the study will undergo the EOT Visit and a Follow-up Phone Call.

3.12.2. Analysis Methods

Refer to Section 3.1.6 for the calculation of z-scores and percentiles for body weight and height and blood pressure. All displays for the Interim Analysis will be across both study phases with all subjects combined.

3.12.2.1. Adverse Events

TEAEs for the Interim Analysis are AEs that begin in the time period following the first administration of study medication in the Dose Optimization Phase through 5 days after the Visit 11 dose of study medication, or existing AEs that worsen in that time period. Clinically significant changes in sleep (CSHQ) and laboratory parameters should be reported as AEs. An overall summary of AEs will include the total number and percentage of subjects who experienced any TEAEs, SAEs, study drug-related TEAEs or SAEs, TEAEs leading to study drug discontinuation, TEAEs leading to death, and TEAEs by maximum severity.

A summary of TEAEs will include the number and percent of subjects who experience at least one TEAE, as well as the number and percent of subjects who experience at least one TEAE within each specific SOC and PT. TEAEs leading to study drug discontinuation and SAEs will be summarized similarly. TEAE incidences will also be summarized by maximum severity grade.

3.12.2.2. Vital Signs

Vital signs will be summarized using descriptive statistics of actual values and changes from baseline to each post-baseline timepoint up until Visit 11. The incidence of clinically notable vital signs will be summarized by analysis visit.

Frequencies and percentages of subjects with an increase in systolic blood pressure >20 mmHg above the 95th percentile for age and gender from baseline at Visit 11 for those below the 95th percentile at baseline will be presented. Increases in systolic blood pressure from baseline will also be presented in a subject listing.

3.12.2.3. Body Weight and Height

Frequencies and percentages of subjects with a decrease in height or weight percentile from baseline to Visit 11 that crosses 0, 1, and 2+ percentile lines on a growth chart showing the 5th, 10th, 25th, 50th, 75th, 90th, and 95th percentiles will be presented.

For example, if a subject is in the 55th percentile at baseline and the 20th percentile at Visit 11, they crossed the 50th and 25th percentile lines and this would be considered a clinically significant growth reduction. If a subject is in the 50th percentile at baseline and the 20th percentile at Visit 11, they have only crossed one percentile line on the growth chart and the change would not be considered clinically significant.

For those subjects who cross 2+ percentile lines in height or weight from baseline, their height and weight percentiles will be plotted by analysis visit. Additionally, for subjects crossing 2+ percentile lines, the frequency and percentage of subjects with a height or weight z-score below the 50th percentile on the growth chart will be tabulated.

Weight and height, including weight and height percentiles, will also be presented in a subject listing.

3.12.2.4. ECG

Heart rate (bpm), QT Interval (msec), RR Interval (msec) will be summarized using descriptive statistics of actual values and changes from baseline at Visit 11. Frequencies and percentages will also be provided for overall ECG interpretation categories (normal; abnormal; not clinically significant; abnormal; clinically significant) at baseline and Visit 11.

3.12.2.5. C-SSRS

C-SSRS outcomes at each analysis visit through Visit 11 will be summarized by the number and percentage of subjects with the following: suicidal ideation, suicidal behavior, and suicidal ideation or behavior (ideation and behavior combined).

All C-SSRS results in subjects with any suicidal ideation or behavior will be presented in a subject listing.

4. CHANGES FROM PROTOCOL IN PLANNED ANALYSES

- Update from protocol in how new medical conditions that occurred during Study P01 will

be recorded and presented for P02. Please see change in Section 2.2.4.1. P01 AEs at Visit 6 (P01)/Visit 2 (P02) are not recorded as medical history, but as AEs treatment-emergent to P01.

- For the Treatment Phase Safety Population definition, require only that subjects receive at least one dose of study medication in the Treatment Phase, and removed the requirement of having at least one post-dose safety assessment in the Treatment Phase.
- Renamed Dose Optimization Safety Population to Dose Optimization Population. For the Dose Optimization Population definition, require only that subjects receive at least one dose of study medication in the Dose Optimization Phase, and removed the requirement of having at least one post-dose safety assessment in the Dose Optimization Phase.
- Shifts from normal range (low, normal, high) in laboratory values from baseline to post-baseline assessments will not be analyzed.
- Removed descriptive statistics and MMRM model for C-SSRS, as it is not captured as a score.
- For the Treatment Phase Safety Population, added analysis for subjects that switch to a different dose than their optimized dose level.
- Removed summary of TEAEs leading to study withdrawal – not collected in CRF.
- Updated language for stopping rules to 1) only use percentile instead of z-score and 2) exclude subjects enrolled with a baseline systolic blood pressure >95th percentile from the IA analyses for increase in systolic blood pressure because they were enrolled in the study despite not meeting this inclusion criteria.
- Removed CSHQ analyses from the IA since they are not considered an AE and sleep-related AEs are already captured in the AE IA analyses.

5. REFERENCES

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2. Kuczmarski RJ, Ogden CL, Guo SS, et al. 2000 CDC growth charts for the United States: Methods and development. National Center for Health Statistics. Vital Health Stat 11(246). 2002.

3. Flynn JT, Kaelber DC, Baker-Smith CM, et al. Clinical Practice Guideline for Screening and Management of High Blood Pressure in Children and Adolescents [published correction appears in Pediatrics. 2017 Nov 30:] [published correction appears in Pediatrics. 2018 Sep;142(3):].Pediatrics. 2017;140(3):e20171904. doi:10.1542/peds.2017-1904.

4. Rosner B, Cook N, Portman R, Daniels S, Falkner B. Determination of blood pressure percentiles in normal-weight children: some methodological issues. *Am J Epidemiol*. 2008;167(6):653–666

6. SAMPLE SAS CODE

MMRM