

# Serdexmethylphenidate/d-Methylphenidate Capsules for Children With ADHD: Effects on SKAMP-C and WREMB-R as Evaluated in a Randomized, Double-blind, Placebo-controlled Laboratory Classroom Study

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## BACKGROUND

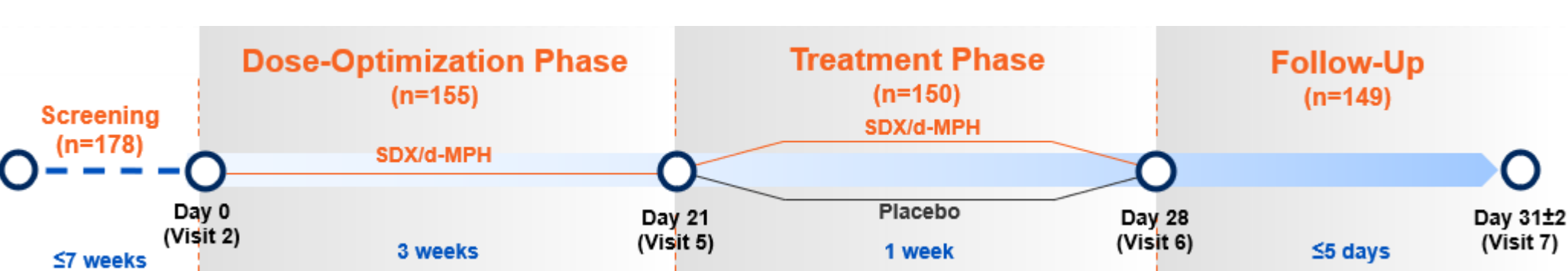
- Serdexmethylphenidate (SDX)/dexamethylphenidate (d-MPH) is a central nervous system (CNS) stimulant indicated for the treatment of ADHD in patients 6 years of age and older<sup>1</sup>
- SDX/d-MPH capsules contain a fixed molar ratio of 70% SDX, a novel prodrug of d-MPH<sup>1</sup>, and 30% d-MPH
- SDX/d-MPH is a once-daily capsule offering both rapid onset and extended duration of efficacy for the treatment of ADHD
- Children with ADHD may experience severe symptoms of ADHD, especially during the early morning routine and evening homework times of the day<sup>2</sup>
- Weekly Rating of Evening and Morning Behavior - Revised (WREMB-R) scale is an instrument that allows for the assessment of ADHD-related difficulties over the day<sup>3</sup>
- The objective of this study was to evaluate the efficacy, safety, and tolerability of SDX/d-MPH capsules in children 6 to 12 years of age with ADHD

## METHODS

### Study Design and Subjects

- This was a multicenter, randomized, double-blind, placebo-controlled, parallel, efficacy laboratory classroom study
- The study was comprised of a Screening Period, a 3-week open-label Dose-Optimization Phase, and a 1-week double-blind Treatment Phase (Figure 1)
- Eligible subjects were children 6 to 12 years of age in good health who met DSM-5 criteria for a primary diagnosis of ADHD<sup>4</sup> per clinical evaluation and confirmed by the Mini International Neuropsychiatric Interview for Children and Adolescents (MINI-KID)
- Eligible subjects must have had scores of  $\geq 3$  (mildly ill) on the Clinician-administered Global Impressions–Severity (CGI-S) scale, as well as scores of  $\geq 25$  on the ADHD-Rating Scale-5 total score on Visit 2 (Day 0)<sup>5</sup>
- Subjects must have washed out ADHD medications 5 days prior to Visit 2, the start of the Dose-Optimization Phase (Day 0)

Figure 1. Study Design



- Following open-label dose optimization, subjects were randomized on a 1:1 basis to receive single daily doses of their optimized dose of SDX/d-MPH (Table 1) or placebo for 7 days

Table 1. SDX/d-MPH Dosage Strengths

SDX/d-MPH dosage strength	Total d-MPH HCl equivalence
26.1/5.2 mg	20 mg
39.2/7.8 mg	30 mg
52.3/10.4 mg	40 mg

- Safety assessments were conducted at each visit, which included monitoring of treatment-emergent adverse events (TEAEs), physical exams, vital signs, ECG parameters, clinical laboratory tests, and Columbia-Suicide Severity Rating Scale (C-SSRS)

### Statistical Analyses

- The primary efficacy endpoint was the mean change from predose SKAMP-C scores collected at Visit 5, the baseline measurement, to SKAMP-C scores collected postdose over the classroom day during Visit 6, with assessments conducted at 0.5, 1, 2, 4, 8, 10, 12, and 13 hours postdose
- Though the SKAMP questionnaire uses the Likert scale, the SKAMP-C, which aggregates the scores from all the domains, was treated as a continuous measure
- A repeated measures analysis using the Mixed-Effect Model Repeated Measure (MMRM) model was performed to estimate the difference between SDX/d-MPH and placebo
- An additional secondary endpoint included mean change from baseline (Visit 2) in WREMB-R scores (total score, and morning and evening subscores) at Visit 5 and Visit 6
- WREMB-R Scale is an 11-item, parent-rated questionnaire that was developed to assess behaviors for their severity during the morning hours and evening hours<sup>6</sup>
- WREMB-R scores were analyzed as continuous measures using paired and 2-sample t-tests during the Dose Optimization and Treatment Phases, respectively

## RESULTS

### Subject Disposition and Demographics

- A total of 155 subjects were enrolled in the Dose-Optimization Phase, of which 150 were randomized into the Treatment Phase: 74 and 76 subjects in the SDX/d-MPH and Placebo groups, respectively
- All subjects completed the study through the follow-up visit except for one subject in the placebo group who was lost to follow-up
- In the intention-to-treat (ITT) population (N=150), the mean age was 9.6 years, and a majority of subjects were white (50.7%) and male (61.3%)

### Efficacy Assessments

- The mean change from baseline (Visit 5) in the SKAMP-C scores,

averaged across the test day (Visit 6), was statistically significantly lower (indicating improvement) with SDX/d-MPH compared to placebo ( $P < 0.001$ ; Table 2)<sup>1</sup>

Table 2. Primary Efficacy Measure: SKAMP-C Scores Averaged Over Classroom Day in Subjects 6–12 Years With ADHD (Visit 5 as Baseline)

Treatment Group	N	Mean Baseline Score† (SD)	LS Mean Change From Baseline‡ (SE)	Placebo-Subtracted Difference§ (95% CI)
SDX/d-MPH (26.1/5.2, 39.2/7.8, 52.3/10.4 mg/day)	74	17.9 (9.2)	-4.87 (0.62)	-5.4 (-7.1, -3.7)
Placebo	76	17.9 (10.4)	0.54 (0.70)	

† Baseline score assessed predose on the practice classroom day/randomization visit after 2 days of active drug washout (Visit 5).

‡ Classroom day least-squares mean change from baseline over hours 0.5, 1, 2, 4, 8, 10, 12, and 13.

§ Difference (active drug minus placebo) in least-squares mean change from baseline.

- During the Treatment Phase, the mean evening score at Visit 6 significantly improved in the SDX/d-MPH group from Baseline (Visit 2) compared with the placebo group (Table 3)
- No treatment-related improvement was observed in the morning score

Table 3. Mean WREMB-R Scores in Subjects Treated With SDX/d-MPH or Placebo During the Treatment Phase

WREMB-R Scores	SDX/d-MPH			Placebo			Treatment Difference P-value
	N	Mean (SD)	Mean Difference From Baseline (SD)	N	Mean (SD)	Mean Difference From Baseline (SD)	
Overall Baseline (visit 2; day 0)	74	22.6 (5.3)	-11.7 (9.2)	75	23.6 (6.5)	-7.2 (9.1)	0.003
Visit 6 (day 28)	74	10.9 (8.2)		76	16.4 (7.9)		
Morning Baseline (visit 2; day 0)	74	5.2 (3.0)	-2.5 (3.4)	75	5.9 (2.7)	-2.2 (3.2)	0.595
Visit 6 (day 28)	74	2.7 (2.9)		76	3.7 (2.8)		
Evening Baseline (visit 2; day 0)	74	17.4 (3.9)	-9.2 (6.7)	75	17.7 (4.9)	-5.0 (6.6)	<0.001
Visit 6 (day 28)	74	8.2 (6.1)		76	12.7 (5.8)		

### Safety and Tolerability

- No serious AEs, deaths, or overdoses were reported
- During the Dose-Optimization Phase, 2 subjects experienced an AE of severe insomnia leading to discontinuation
- The most common TEAEs reported during the double-blind Treatment Phase are shown in Table 4

- The majority of TEAEs were graded as mild or moderate in severity
- The TEAEs were similar to those reported for approved MPH products

Table 4. TEAEs Reported in >2% of Subjects During the Treatment Phase

TEAE, n (%)	SDX/d-MPH (n=74)	Placebo (n=76)
<b>Any TEAE</b>	<b>23 (31.1%)</b>	<b>11 (14.5%)</b>
Upper respiratory tract infection	2 (2.7%)	4 (5.3%)
Headache	4 (5.4%)	1 (1.3%)
Abdominal pain upper	3 (4.1%)	1 (1.3%)
Insomnia	2 (2.7%)	1 (1.3%)
Pharyngitis	2 (2.7%)	0 (0%)

- Changes in vital signs, ECGs, laboratory measurements, and physical examinations were minimal and comparable between the SDX/d-MPH and Placebo groups

## CONCLUSIONS

- SDX/d-MPH showed efficacy relative to placebo for treating ADHD in children 6–12 years of age
- SDX/d-MPH showed improvement in ADHD symptoms overall and in the evening hours as assessed by WREMB-R
- SDX/d-MPH was generally well-tolerated, no notable safety signals were identified, and adverse events were similar to those reported for approved MPH products

**DISCLOSURES:** ACB is an employee and shareholder of KemPharm, Inc. CO and MC are employees and shareholders of Corium, Inc. This study was funded by KemPharm, Inc., Celebration, FL. Poster design support was provided by Simpson Healthcare.

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