particular need for treatments for inattentive symptoms, which are the most frequently endorsed ADHD symptoms in adults. AKL-T01 (EndeavorRx®) is an FDA-authorized digital therapeutic, currently approved for attention in children ages 8-12 with inattentive or combined-type ADHD and a demonstrated attention issue. This study evaluated the efficacy and safety of AKL-T01 in adults.

Methods. STARS-ADHD-Adults (NCT05183919) was a multicenter, single-arm trial at 14 US sites. Enrolled patients were 18 or older, had a diagnosis of ADHD (combined or inattentive), and demonstrated attentional impairment with a Test of Variables of Attention (TOVA) Attention Comparison Score (ACS) ≤ -1.8. Treatment involved using AKL-T01 at home 25 minutes/day, 5 days/week, for 6 weeks. The primary endpoint was change in TOVA-ACS. Secondary endpoints were changes in the ADHD Rating Scale-IV (ADHD-RS-IV) inattention subscale and total score, and Adult ADHD Quality of Life (AAQoL) total score. Safety, tolerability, and compliance were assessed.

Results. Of 440 participants screened, 221 were enrolled, and 153 (*M* age = 39.9, 70% female; 39% current stimulant use) had sufficient data for analysis. TOVA-ACS significantly improved from baseline to study day 42, *M* change = 6.46, *SD* = 6.95, $t(152) = 11.49$, $p < .0001$. There was significant improvement across all secondary endpoints (*p*s <.0001). In exploratory responder analyses, 36.6% moved into the normative range on TOVA (ACS>0), and 27.1% had ADHD-RS-IV improvement ≥ 30%. The treatment was well-tolerated (5% reported ADEs; none serious), and compliance was high (*M* = 81.1%).

Conclusions. Results support the efficacy of AKL-T01 in adults, and the magnitude of TOVA change in adults was nearly 7x the change reported in pediatric trials. Given the increasing rates of ADHD in adults, the barriers to accessing evidence-based treatments, and the centrality of inattentive symptoms as ADHD patients develop into adulthood, AKL-T01 holds promise as a scalable, targeted treatment for attention in adult ADHD with impacts to real-world symptoms.

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Evaluation of the Efficacy of Viloxazine ER in Children and Adolescents with ADHD Inattentive and Combined Presentations

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Introduction. Studies show stimulant medications are effective for different ADHD presentations (predominantly inattentive [IA], predominantly hyperactive-impulsive [HI] or combined [C]); however, few studies have evaluated nonstimulant efficacy in different ADHD presentations. Viloxazine ER [VLX ER] is a nonstimulant, FDA-approved medication for pediatric (≥6 yrs) and adult ADHD. This post-hoc analysis of 4 double-blind (DB), Phase 3, clinical trials (2 in adolescents [NCT03247517 and NCT03247556], 2 in children [NCT03247530 and NCT03247543]), evaluates VLX ER efficacy by ADHD presentation as derived from ADHD Rating Scale, 5th Edition (ADHD-RS-5) assessments at Baseline.

Methods. Children and adolescents with ADHD and an ADHD-RS-5 Total score ≥ 28 were eligible for enrollment. ADHD presentation was defined as a rating of ≥2 on at least 6 of 9 ADHD-RS-5 inattention items, or hyperactive-impulsive items or both. For each ADHD presentation, the change from Baseline (CFB) in ADHD-RS-5 Total score (primary outcome in each study) was assessed using mixed models for repeated measures (MMRM). Responder rate (secondary outcome), ≥50% reduction from baseline in ADHD-RS-5 Total score, was analyzed using generalized estimating equations (GEE).

Results. Of 1354 subjects [placebo N = 452, VLX ER N = 902], ADHD presentation was assigned as 288 (21.3%) [IA], 1010 (74.5%) [C], 40 (3.0%) [HI], 16 (1.2%) [none of these]. Due to the small sample size of [HI], only the [IA] and [C] results are presented. At Week 6 (pooled data endpoint), ADHD-RS-5 Total scores were significantly improved for VLX ER relative to placebo for both the [IA] and [C] ADHD presentations. LS mean (SE) treatment differences, p-values were: [IA] -3.1 (1.35), p = 0.0219, and [C] 5.8 (0.97), p < 0.0001. Responder rates were also significantly higher for VLX ER: 43.0% [IA] and 42.7% [C] relative to placebo 29.5% [IA] and 25.5 % [C] (p=.0311 and p<.0001).

Conclusions. Viloxazine ER significantly reduced ADHD symptoms in individuals meeting criteria for ADHD [IA] or [C] presentations at Baseline. Limitations include post-hoc methodology, smaller sample sizes of [IA] and [HI] groups, and the ADHD-RS-5 ≥ 28 eligibility requirement, that may favor enrollment of individuals with ADHD [C] over ADHD [IA] or [HI] presentations. Consistency of response during long-term use should be evaluated.

Funding. Supernus Pharmaceuticals, Inc.

Centanafadine Sustained Release Is Efficacious in the Treatment of Adult ADHD Across Disease Severities

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Introduction. Centanafadine (CTN) is a potential first-in-class norepinephrine/dopamine/serotonin triple reuptake inhibitor (NDSRI). The efficacy, safety, and tolerability of CTN sustained release (SR) for adults with ADHD was demonstrated in 2 pivotal phase 3 trials (Adler LA, et al. J Clin Psychopharmacol. 2022;42:429-39).
Methods. Adults (18–55 years) meeting DSM-5 criteria for ADHD enrolled in these double-blind, multicenter, placebo-controlled trials and randomized to treatment if ADHD Investigator Symptom Rating Scale (AISRS) score was ≥28 at screening (if not receiving pharmacologic treatment for ADHD) or ≥22 at screening and ≥28 at baseline (BL) (if receiving treatment). Having had no prior benefit from ≥2 ADHD therapies of 2 different classes, taking prohibited medications, and positive alcohol/drug screen were exclusionary. Trials had 4 periods: (1) screening and washout (≤28 days), (2) single-blind placebo run-in (1 week), (3) double-blind treatment (6 weeks), and (4) follow-up (10 days after last dose). Patients with ≥30% improvement in the Adult ADHD Self-report Scale (ASRS) from start to end of screening were screen failures; those with ≥30% ASRS improvement from start to end of placebo run-in were terminated early. Patients were randomized 1:1:1 to twice-daily CTN SR (200 or 400 mg total daily dose [TDD]) or matching placebo. The 200 mg/d group received CTN SR 200 mg TDD from days 1–42; the 400 mg/d group received 200 mg TDD on days 1–7, and increased to 400 mg TDD on day 8. This analysis assessed CTN SR effects based on median BL AISRS severity score (<38 or ≥38) using a mixed model for repeated measures analysis. Least squares mean (LSM) differences (95% CI) from BL at day 42 were compared between individual CTN SR dose groups and placebo, tested at a 2-sided significance level of 0.05.
Results. In total, 859 patients were randomized (200 mg TDD, n=287; 400 mg TDD, n=287; placebo, n=285). Significant LSM differences on the AISRS were observed vs placebo in the overall population (200 mg TDD and 400 mg TDD, $P<0.0001$ for each), in the low BL severity (200 mg TDD [$P=0.016$]; 400 mg TDD [$P=0.019$]), and in the high BL severity (200 mg TDD [$P=0.005$]; 400 mg TDD [$P=0.003$]) populations at day 42. Significant LSM differences vs placebo ($P<0.01$) began at day 7 (200 mg) and day 14 (400 mg) overall, remaining significant to day 42. Significant LSM differences were observed vs placebo ($P<0.05$) from day 14 (400 mg TDD) and day 21 (200 mg) in the low severity populations, and from day 21 (400 mg TDD) and day 7 (200 mg TDD) in the high severity population, remaining significant ($P<0.05$) to day 42.
Conclusions. CTN SR, a potential first-in-class NDSRI, is efficacious for patients with adult ADHD of low or high BL symptom severity, with significant improvements observed vs placebo within the first 3 weeks.
Study Registration: NCT03605680, NCT03605836
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Dosing, Patterns, Effectiveness, and Treatment Satisfaction with Deutetrabenazine When Initiated Using a 4-Week Patient Titration Kit: Interim Results of the START Study

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Introduction. Deutetrabenazine is a vesicular monoamine transporter type 2 inhibitor (VMAT2i) for treatment of adults with tardive dyskinesia (TD) and Huntington disease (HD)-related chorea. A 4-week patient titration kit was launched (July 2021) to assist patients in titrating to optimal deutetrabenazine dosages.
Methods. START is an ongoing, routine-care, 2-cohort (TD and HD) study evaluating deutetrabenazine dosing patterns, effectiveness, and treatment satisfaction when initiated using a 4-week patient titration kit, with further titration allowed based on effectiveness and tolerability. Patient satisfaction with the kit was assessed via questionnaire at week 8. Results from the first 50 patients enrolled in the TD cohort are presented in this interim analysis.
Results. 50 patients in the TD cohort were included (mean age, 58.7 years, 66% female, 74% White, mean baseline Abnormal Involuntary Movement Scale [AIMS] total motor score, 13.8). 39 of 50 (78%) patients successfully completed the titration kit (completed within 5 weeks or reached optimal dose [≥24 mg/day] within 4 weeks; mean [SE] days, 27.5 [0.32]). Mean (SE) time to reach optimal dosage for the 38 (76%) patients who reached it was 46.3 (5.48) days. Mean (SE) deutetrabenazine dosages were 27.7 (0.92) mg/day at week 4, 32.5 (1.00) mg/day at week 8, and 32.8 (1.18) mg/day at week 12. After completion of the kit, mean (SE) dosage was 31.8 (1.24) mg/day, and 95% of patients reaching week 12 had a maintenance dosage ≥24 mg/day. Mean (SE) adherence with the kit was 97.2% (1.39%). 22% of patients had an adverse event (AE); AEs led to dose reduction for 2%, drug interruption for 2%, and study discontinuation for 6% of patients. Serious and treatment-related adverse events were reported for 2% and 6% of patients. 24 of 49 (49%)23 of 49 patients achieved treatment success ("much"/"very much" improved) at week

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