Request for Copy of Published Material

Please note, this is an investigational product and is not approved by the US Food and Drug Administration (FDA).

Enclosure:

- POSTER: Oberdhan D, Childress AC, Ward CL, et al. Presented at: The Neuroscience Education Institute (NEI) Fall Congress 2025; November 6-9, 2025, Colorado Springs, CO, USA

Impact of Centanafadine on Learning Problems in Pediatric Patients With ADHD: Analysis of Conners 3 and Exit Survey Responses

Dorothee Oberdhan[1], Ann C. Childress[2], Caroline L. Ward[1], Judy van Stralen[3], Timothy E. Wilens[4]

[1]Otsuka Pharmaceutical Development & Commercialization, Inc., Rockville, MD, United States; [2]Center for Psychiatry and Behavioral Medicine, Inc., Las Vegas, NV, United States; [3]Center for Pediatric Excellence, Ottawa, ON, Canada; [4]Division of Child and Adolescent Psychiatry, Massachusetts General Hospital, Boston, MA, United States

Scan the QR code to receive a PDF of the poster

INTRODUCTION

- Attention-deficit/hyperactivity disorder (ADHD) is one of the most common pediatric neurodevelopmental disorders, characterized by symptoms of inattention, hyperactivity, and impulsivity—all of which can disrupt focus, organization, and task completion, hindering effective learning[1,2]
- The Conners 3–Parent Short (PS) measures some aspects of learning as well as symptoms of inattention, hyperactivity, and impulsivity[3]
- Extended-release centanafadine, a norepinephrine, dopamine, serotonin reuptake inhibitor (NDSRI),[4,5] was shown to be efficacious in treating core symptoms and associated features of ADHD in two phase 3 trials for the treatment of ADHD in children aged 6–12 years[6] and adolescents aged 13–17 years[7]

OBJECTIVE

- To assess if treatment with centanafadine improved learning problems in children and adolescents with ADHD

METHODS

- **Studies:** Two phase 3, multicenter, randomized, double-blind, placebo-controlled trials conducted in the United States and Canada (children[6]: NCT05428033; adolescents[7]: NCT05257265)
- **Eligible participants:** Children (6–12 years) or adolescents (13–17 years) with a primary diagnosis of ADHD (of any presentation) according to *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition (DSM-5) criteria, as confirmed by the Mini International Neuropsychiatric Interview for Children and Adolescents (MINI-KID)
- **Treatment:** Participants were randomized (1:1:1) to receive once-daily extended-release high-dose centanafadine, low-dose centanafadine, or placebo for 6 weeks without titration
- **Dosing:**
  - Children: Weight-based, with participants divided into the following categories: <20, ≥20–<35, 35–50, or >50 kg and receiving 41.1, 82.2, 123.3, or 164.4 mg, respectively, if they were randomized to low-dose centanafadine, or 82.2, 164.4, 246.6, or 328.8 mg, respectively, if they were randomized to high-dose centanafadine. Weight categories were combined for the data analyses
  - Adolescents: High-dose (328.8 mg) centanafadine, low-dose (164.4 mg) centanafadine, or placebo
  - Only data from high-dose centanafadine will be presented here
- **Efficacy outcomes:**
  - Change from baseline in the Conners 3–PS Learning Problems Content Scale (containing 5 individual line items: cannot grasp arithmetic, need extra explanation, trouble with reading, spelling is poor, does not understand what's read) T-score at Week 6 (key secondary endpoint) (**Figure 1**)
  - The percentage of participants with clinically meaningful change in Conners 3–PS Learning Problems T-scores (≥9-point improvement from baseline)
    - From an anchor-based analysis using the Clinical Global Impressions of Severity modified for ADHD (CGI-S-ADHD), a ≥9-point change in Conners 3–PS Learning Problems T-scores was used because at the population level this would correspond to a 2-point, clinically meaningful change in CGI-S-ADHD score (data on file)
- **Exit survey:** The exit survey was administered to parents/caregivers and adolescents at Baseline and Week 6
- **Analyses:**
  - Key secondary efficacy outcomes were analyzed using a mixed-effect model for repeated measures
  - The meaningful change over time in Conners 3–PS Learning Problems T-Scores was analyzed via a Cochran-Mantel-Haenszel test
  - Low-dose centanafadine did not meet the primary endpoint; thus, low-dose centanafadine has been excluded from this presentation of secondary and/or exploratory endpoints and presented *P*-values were not controlled for multiplicity
- **Other outcomes:** Safety

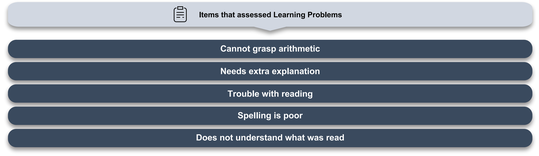
RESULTS

- Overall, 76.5% (367/480) of children (for total population: mean age 9.2 years, 58.3% male; **Figure 2A**) and 80.8% (371/459) of adolescents (for total population: mean age 14.7 years, 59.3% male; **Figure 2B**) completed their respective studies
- In participants treated with centanafadine, a greater improvement than placebo in the mean change from baseline at Week 6 in Conner 3–PS Learning Problems T-score was observed for both children (mean change [SE]: centanafadine, −8.2 [0.95]; placebo, −2.8 [0.93], *P*<0.0001; **Figure 3A**) and adolescents (centanafadine, −8.0 [0.92]; placebo, −3.1 [0.90], *P*<0.0001; **Figure 3B**). Similar improvements were observed when adolescents self-reported (**Figure 3B**)
- In participants treated with centanafadine, a greater proportion of children (38.8% vs 21.5%; *P*=0.0011) and adolescents (40.4% vs 24.1%; *P*=0.0015) had a clinically meaningful change from baseline (≥9-point reduction) in Conners 3–PS Learning Problems Content Scale T-scores when compared to placebo (**Figure 4**)
- Per the caregiver-reported exit survey, of those treated with centanafadine, 52.3% (vs 37.7% placebo) of children and 68.6% (vs 45.3% placebo) of adolescents saw improvement in completing tasks at home (**Figure 5A, B**). A similar improvement was self-reported by adolescents (70.8% vs 43.0%, respectively) (**Figure 5C**)
- Similarly, per the caregiver-reported exit survey, 50.5% (vs 37.7% placebo) of children and 63.7% (vs 44.2% placebo) of adolescents saw improvement in completing work at school (**Figure 5A, B**). Per adolescent self-report, 65.1% (vs 49.0% placebo) of adolescents saw improvement (**Figure 5C**)
- Likewise, per the caregiver-reported exit survey, 50.5% (vs 36.8% placebo) of children and 58.8% (vs 42.1% placebo) of adolescents saw improvement in their ability to learn (**Figure 5A, B**). Per adolescent self-report, 61.3% (vs 47.0% placebo) of adolescents saw improvement (**Figure 5C**)

Safety

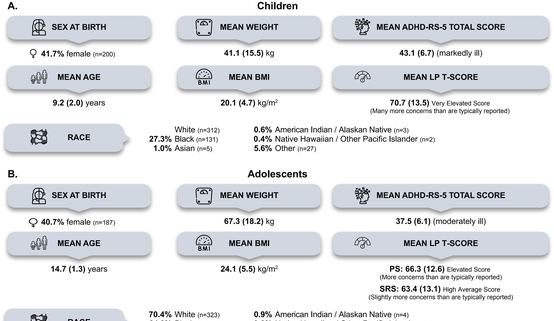
- Most treatment-emergent adverse events were mild to moderate, with the most common (≥5% in the centanafadine group and greater than placebo) being decreased appetite (7.6%) and rash (5.7%) for children, and decreased appetite (15.2%), nausea (9.9%), headache (6.0%), and rash (6.0%) for adolescents

Figure 1. Conners 3–PS line items to assess Learning Problems



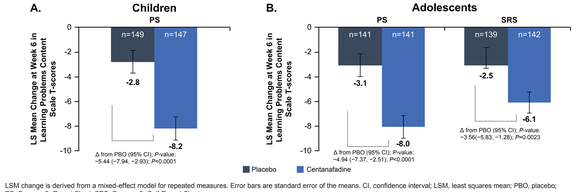
Conners 3–PS, Conners 3–Parent Short.

Figure 2. Baseline demographics and clinical characteristics of all randomized (A) children (N=480) and (B) adolescents (N=459)



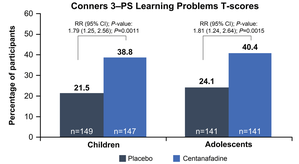
Means are presented with standard deviations. ADHD, attention-deficit/hyperactivity disorder; ADHD-RS-5, ADHD Rating Scale-5; BMI, body mass index; LP, Learning Problems; PS, Conners 3–Parent Short; SRS, Conners 3–Self-Report Short.

Figure 3. Change from baseline in Conners 3–Learning Problems Content Scale T-scores in (A) children and (B) adolescents



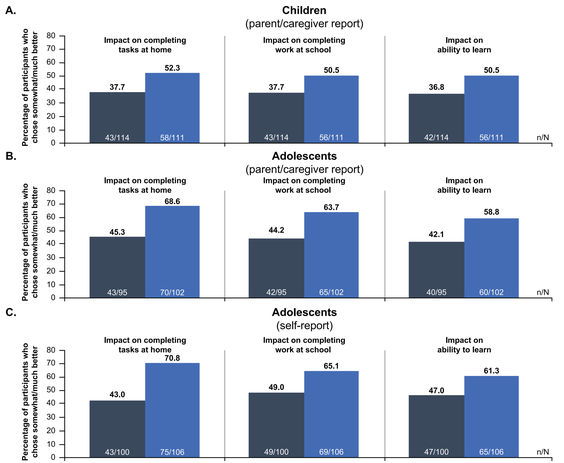
LSM change is derived from a mixed-effect model for repeated measures. Error bars are standard error of the means. CI, confidence interval; LSM, least squares mean; PBO, placebo; PS, Conners 3–Parent Short; SRS, Conners 3–Self-Report Short.

Figure 4. Proportion of participants meeting clinically meaningful within-patient change thresholds for Conners 3-PS Learning Problems T-scores



Data represent the last observation carried forward analysis set, which was analyzed via Cochran-Mantel-Haenszel general association test controlling for trial site. Conners 3–PS, Conners 3–Parent Short; RR, relative risk.

Figure 5. Impact of centanafadine on completing tasks at home, completing work at school, and ability to learn in (A) children (parent/caregiver report), (B) adolescents (parent/caregiver report), and (C) adolescents (self-report)



Survey Question: How did the study medication affect each of the following areas of your child's life? (Please select one response for each row.) Responses included: much worse, somewhat worse, no change, somewhat better, much better. Values reflect those who selected either "somewhat better" or "much better." Impact on completing tasks at home: children: ≤4.2% of any treatment arm were "somewhat" or "much worse" and the remainder were "no change" (44.5–57.0%); adolescents caregiver report: ≤4.2% of any treatment arm were "somewhat" or "much worse" and the remainder were "no change" (31.4–48.4%); adolescents self-report: ≤3.0% of any treatment arm were "somewhat" or "much worse" and the remainder were "no change" (25.5–50.0%). Impact on completing work at school: children: ≤3.5% of any treatment arm were "somewhat" or "much worse" and the remainder were "no change" (40.5–51.8%); adolescents caregiver report: impact on completing work at school: ≤2.1% of any treatment arm were "somewhat" or "much worse" and the remainder were "no change" (28.4–42.1%); adolescents self-report: ≤2.0% of any treatment arm were "somewhat" or "much worse" and the remainder were "no change" (25.5–43.0%). Impact on ability to learn: children: ≤3.5% of any treatment arm were "somewhat" or "much worse" and the remainder were "no change" (45.9–57.0%); adolescents caregiver report: impact on ability to learn: ≤2.0% of any treatment arm were "somewhat" or "much worse" and the remainder were "no change" (32.4–50.5%); adolescents self-report: ≤2.0% of any treatment arm were "somewhat" or "much worse" and the remainder were "no change" (31.1–48.0%).

CONCLUSIONS

- Centanafadine was efficacious with a favorable safety profile and improved the ability to learn as assessed by the Conners 3–Learning Problems Content Scale in children and adolescents
- With centanafadine treatment, clinically meaningful change in learning problems was observed, as well as caregiver- and self-reported (for adolescent participants) improvement of completing tasks at home and school and ability to learn

References

1. Drechsler R, et al. *Neuropediatrics*. 2020;51(5):315-35.
2. Sharma A, et al. *Ann Pharmacother*. 2014;48(2):209-25.
3. Conners CK. Conners CBRS: Conners Comprehensive Behavior Rating Scales. Assessment of behaviors, emotions, academic, and social problems in youth aged 6 to 18 years. Multi-Health Systems Assessment. https://storefront.mhs.com/collections/conners-cbrs.
4. Bymaster FP, et al. *Synapse*. 2012;66(6):522-32.
5. Matuskey D, et al. *J Psychopharmacol*. 2023;37(2):164-71.
6. Ward CL, et al. *Pediatrics Open Sci*. In press. 2025;1(3):1-11.
7. Ward CL, et al. *J Am Acad Child Adolesc Psychiatry*. Published online July 4, 2025.

Acknowledgements

Medical writing and poster development support were provided by The Medicine Group, LLC (New Hope, PA, United States) in accordance with Good Publication Practice guidelines.

At Otsuka, we hold a deep respect for the value of every mind. We will not rest until mental illnesses and brain diseases are approached with the same priority and urgency as our physical health and recognized as chronic diseases that warrant early, equitable, and accessible intervention for patients and caregivers everywhere.

Funding

The study and poster development support were sponsored by Otsuka Pharmaceutical Development & Commercialization, Inc., Princeton, NJ, United States.

Disclosures

DO and **CLW** are full-time employees of Otsuka Pharmaceutical Development & Commercialization, Inc. **ACC** has been a consultant for Aardvark, Arbor, Attentiv, Aytu, Corium, Ironshore, Jazz, Lumos, Neos Therapeutics, Neurocentria, Noven, Otsuka, Purdue, Rhodes, Sky, Sunovion, Supernus, Tris, and Zevra Therapeutics (previously KemPharm); participated on speakers' bureaus for Arbor, Ironshore, Neos Therapeutics, Supernus, Takeda, and Tris; has received research support from Adlon, Akili, Allergan, Arbor, Emalex, Ironshore, Lumos, Neos Therapeutics, Otsuka, Purdue, Rhodes, Servier, Sunovion, Supernus, Takeda, Tris, US Food and Drug Administration, and Zevra Therapeutics (previously KemPharm); and has received writing support from Arbor, Ironshore, Neos Therapeutics, Takeda, Purdue, Rhodes, Sunovion, and Tris; and participated on advisory boards for Adlon, Akili, Arbor, Cingulate, Corium, Ironshore, Neos Therapeutics, Neurovance, NLS, Otsuka, Purdue, Rhodes, Sunovion, Supernus, Takeda, and Tris. **JvS** has received consulting fees from Janssen, Otsuka, Purdue, and Takeda. She has received advisory board fees, educational grants, and speaker fees from Janssen, Purdue, and Takeda; owns Johnson & Johnson stock and has received research grants from Biohaven, Emalex, GW Research Ltd., Janssen, Nuvelution, Otsuka, and Teva; and has received funding for multi-center trials as a primary investigator from Elvium, Purdue, and Takeda. **TEW** has received grant/research support from Ironshore and NIH (NIDA) as a principal investigator; receives royalties and owns intellectual property with Cambridge University Press Guilford Press, and Ironshore; is a consultant for Bay Cove Human Services, Gavin Foundation, US Minor/Major League Baseball, US National Football League (ERM Associates), and White Rhone/3D; and is a coeditor for Elsevier Psychiatric Clinics of North America (ADHD).

Previously presented at WPA 2025; October 5–8, 2025; Prague, Czech Republic.

Poster presented at NEI Global 2025; November 6–9, 2025; Colorado Springs, CO, USA.