METHODS: Patients were randomized 1:1:1 to 6 weeks of once-daily, fixed-dose dasotraline 2 or 4 mg/day, or placebo. The primary efficacy endpoint was change from baseline (CFB) at Week 6 in ADHD Rating Scale Version IV – Home Version (ADHD RS-IV HV) total score, using a mixed model for repeated measures (MMRM) in the intent-to-treat (ITT) population. Secondary endpoints included Clinical Global Impression-Severity (CGI-S) score and safety endpoints.

RESULTS: The mean age of 342 randomized patients was 9.1 [SD: 1.9] years; 66.7% were male. Overall, 79% of patients completed the study. In the ITT population (N = 336), ADHD RS-IV HV total score improved significantly with dasotraline 4 mg/day vs placebo(least squares [LS] mean [SE] CFB at Week 6: −17.53 [± 1.31] vs −11.36 [± 1.29], respectively, $p < 0.001$; effect size [ES]: 0.48). Inattentiveness and hyperactivity/impulsivity subscale scores significantly improved with 4 mg/day vs placebo at Week 6 ($p = 0.001$, $p = 0.003$, respectively). Improvement in CGI-S score was statistically significant with dasotraline 4 mg/day vs placebo(LS mean [SE] CFB at Week 6: −1.39 [± 0.12] vs −1.04 [± 0.12], respectively, $p = 0.040$; ES: 0.29). No significant improvement was observed on the ADHD RS-IV HV total score and the CGI-S score for dasotraline 2 mg/day vs placebo. The most frequent treatment-emergent AEs (≥5% and higher than placebo) were (2 mg/day; 4 mg/day; placebo): insomnia (15.3%; 21.7%; 4.3%, all terms combined), decreased appetite (12.6%; 21.7%; 5.2%), weight loss (5.4%; 8.7%; 0%), irritability (3.6%; 7.0%; 6.0%), nasopharyngitis (0.9%; 5.2%; 0.9%), and nausea (0%; 5.2%; 2.6%).

CONCLUSIONS: Compared with placebo, dasotraline 4 mg/day significantly improved ADHD symptoms in children, as assessed by ADHD RS-IV HV total score and inattentiveness and hyperactivity/impulsivity subscale scores. Dasotraline was generally well tolerated; most common AEs were insomnia, decreased appetite, weight loss and irritability.

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Efficacy of Dasotraline in Children With Attention Deficit Hyperactivity Disorder in a Laboratory Classroom Setting

Robert Goldman, PhD[1]; Ann Childress, MD[2]; Sharon B Wigal, PhD[3]; Seth C Hopkins, PhD[1]; Kenneth S Koblan, PhD[1]; Kaushik Sarma, MD[1]; Jay Hsu, PhD[1]; and Antony Loebel, MD[1]

[1] Sunovion Pharmaceuticals Inc., Marlborough, MA
[2] Center for Psychiatry and Behavioral Medicine, Las Vegas, NV
[3] AVIDA Inc., Newport Beach, CA

ABSTRACT: Objectives: Once-daily dosing with dasotraline, a novel dopamine and norepinephrine reuptake inhibitor, achieves stable plasma concentrations over 24 hours. This phase 3 study evaluated the efficacy and safety of dasotraline in children with attention deficit-hyperactivity disorder (ADHD) throughout the day, in a laboratory classroom setting (NCT02734693).

METHODS: Children (6–12 years) meeting DSM-5 criteria for ADHD were randomized to 2 weeks of dasotraline or placebo (dosed daily at home at approximately 8 PM). Following an abbreviated practice day, laboratory classroom evaluations took place at baseline and on Day 15. The primary endpoint was mean change from baseline at Day 15 in ADHD symptoms, as measured by the Swanson, Kotkin, Agler, M-Flynn, and Pelham Combined Score (SKAMP-CS), obtained from the average of 7 assessments collected across the 12-hour laboratory classroom day (12–24 hours post-dose). Secondary endpoints included SKAMP scores obtained throughout the day at individual timepoints from 8 AM through 8 PM (12–24 hours post-dose), and measures of safety and tolerability.

RESULTS: The ITT population comprised 112 patients. Mean age was 9.5 years, 68.8% were male; 92% completed the study. Dasotraline 4 mg/day significantly improved mean SKAMP-CS versus placebo ($p < 0.0001$, effect size 0.85) with significant effects persisting throughout the day. Mean SKAMP subscores improved significantly versus placebo (Attention $p < 0.0001$, effect size 0.81; Deportment $p < 0.001$, effect size 0.70). Treatment-emergent adverse events were generally mild or moderate in severity; most frequent (with dasotraline 4 mg/day; placebo) included: insomnia (19.6%; 3.6%, all terms combined), decreased appetite (10.7%; 3.6%), headache (10.7%; 8.9%), affect lability (8.9%; 7.1%), irritability (5.4%; 3.6%), postural orthostatic tachycardia syndrome (5.4%; 0%), and perceptual disturbances (5.4%; 0%).

CONCLUSIONS: In this 2-week, randomized, double-blind, laboratory classroom study in children with ADHD, once-daily dasotraline significantly improved ADHD symptoms (including deportment and attention), compared with placebo, and demonstrated sustained efficacyup to 24 hours post-dose. The most common adverse events were insomnia, decreased appetite, and headache.

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