Efficacy and Safety of CTx-1301 in Pediatric Subjects with ADHD: Results From a Phase 3, Randomized, Double-Blind, Placebo-Controlled Trial

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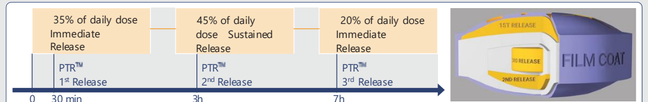
Background

- Attention-deficit/hyperactivity disorder (ADHD) is a neurodevelopmental disorder affecting ~11% of children and ~6% of adults in the US[1]
- Diagnosis and treatment of ADHD continue to increase, with stimulants comprising ~90% of prescriptions in the US[2]
- Despite use of long-acting stimulants, many patients experience inadequate symptom control across the day.[3,4] These gaps in symptom control may lead to crash/rebound effects, requiring the need for "booster" doses to ensure continued efficacy[5-7]
- Booster doses are immediate release (IR) stimulants, that bring an increased risk for non-compliance, missed doses, and abuse, misuse, and diversion[8,9]
- There remains a need for treatment approaches that provide consistent, full-day symptom control while minimizing reliance on booster medications
- CTx-1301 is a trimodal extended-release dexmethylphenidate (d-MPH) tablet using Precision Timed Release™ (PTR™) technology,[10] with a built-in booster dose
- PTR™ delivers three distinct pulses across the day:

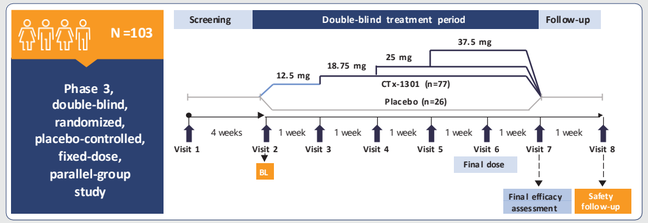


This unique pulsatile delivery profile is intended for active day coverage, reducing the need for afternoon booster dosing

Objective

To assess the efficacy and safety of CTx-1301 using a fixed-dose titration study in a pediatric population (6-17 y/o).

Methods



Key inclusion criteria

- Children and adolescents aged 6–17 years
- ADHD diagnosis confirmed according to DSM-5 criteria, including any of the three presentations (combined, inattentive, or hyperactive/impulsive), as assessed using MINI-KID
- Baseline ADHD-RS-5 score ≥28 and CGI-S score ≥4
- Body weight within the 5th–95th percentile for age and sex

Key exclusion criteria

- BPD, MDD, CD, DMDD, intellectual disability, OCD, eating disorder, anxiety disorder, or ASD; history of psychosis, motor or vocal tics, or Tourette's syndrome; genetic disorders with cognitive/behavioral disturbances; or any other psychiatric conditions deemed exclusionary by the investigator
- Evidence of any chronic CNS disease
- Sleep disorder or history of suicidality or seizures (excluding febrile seizures)
- Refractory to ADHD treatment or intolerant to stimulant therapy

Primary endpoint:
Change in ADHD-RS-5 total score from BL to week 5

Key secondary endpoint:
Change in CGI-S score from BL to week 5

Other secondary endpoints:
- CGI-I score at week 5
- Safety

All 103 patients were included in the ITT and safety populations

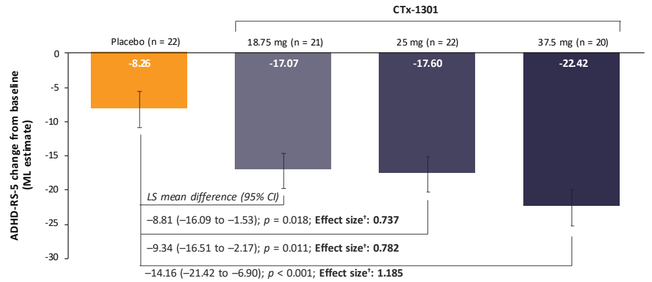
*Missing drug concentrations, sample date/time, or incomplete dosing information were excluded from the analysis

Results

CTx-1301 significantly improved the ADHD-RS-5 score compared with the placebo

Primary endpoint

ADHD-RS-5 score* at week 5

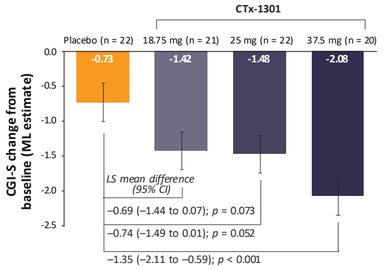


ADHD-RS-5, ADHD Rating Scale, Version 5; CI, confidence interval; LS, least squares; ML, maximum likelihood.
†Data were analyzed using a mixed-effect model for repeated measures in the ITT population. ‡Effect sizes for ADHD-RS-5 were derived from a post-hoc analysis.

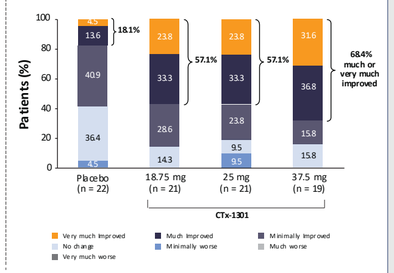
CTx-1301 improved CGI-S and a greater proportion of patients demonstrated improvement based on CGI-I scores compared to placebo

Secondary outcomes

CGI-S score



CGI-I score*



CGI-I, Clinical Global Impressions–Improvement; CGI-S, Clinical Global Impressions-Severity; CI, confidence interval; LS, least squares; ML, maximum likelihood.
*Of the 103 patients in the ITT population, 83 patients had clinician-rated CGI-I score data at week 5.

CTx-1301 demonstrated a favorable safety profile, with no serious TEAEs
No clinically relevant findings for clinical laboratory measurements, vital signs, or physical examinations

Category	Placebo	CTx-1301		
	(n = 26)	18.75 mg (n = 26)	25 mg (n = 26)	37.5 mg (n = 25)
Any TEAE, n (%)	10 (38.5)	13 (50.0)	9 (34.6)	17 (68.0)
Mild	5 (19.2)	11 (42.3)	5 (19.2)	11 (44.0)
Moderate	5 (19.2)	2 (7.7)	4 (15.4)	6 (24.0)
Severe	0	0	0	0
Serious TEAEs, n (%)	0	0	0	0
TEAEs leading to study drug withdrawal*, n (%)	1 (3.8)	1 (3.8)	0	1 (4.0)
Most common TEAEs†, n (%)				
Initial insomnia	0	1 (3.8)	1 (3.8)	0
Decreased appetite	0	3 (11.5)	5 (19.2)	7 (28.0)
Upper abdominal pain	2 (7.7)	1 (3.8)	1 (3.8)	4 (16.0)
Headache	3 (11.5)	3 (11.5)	0	1 (4.0)
BP increased	1 (3.8)	1 (3.8)	0	2 (8.0)
Tachycardia	0	1 (3.8)	2 (7.7)	1 (4.0)
Nasopharyngitis	2 (7.7)	0	0	1 (4.0)
URTI	0	1 (3.8)	1 (3.8)	1 (4.0)

BP, blood pressure; TEAE, treatment-emergent adverse event; URTI, upper respiratory tract infection.
*All TEAEs leading to study drug withdrawal were considered at least possibly related to study drug. †TEAEs that occurred in 3 or more patients in the overall study population.

Demographics and baseline characteristics were generally similar among treatment groups

Characteristics	Placebo	CTx-1301		
	(n = 26)	18.75 mg (n = 26)	25 mg (n = 26)	37.5 mg (n = 25)
Age, mean ± SD, years	11.5 ± 3.3	11.4 ± 3.6	11.3 ± 3.2	11.0 ± 3.2
Male sex, n (%)	17 (65.4)	13 (50.0)	16 (61.5)	16 (64.0)
Race, n (%)				
Black or African American	13 (50.0)	12 (46.2)	12 (46.2)	14 (56.0)
White	12 (46.2)	11 (42.3)	11 (42.3)	11 (44.0)
Multiple	1 (3.8)	3 (11.5)	2 (7.7)	0
Asian	0	0	1 (3.8)	0
Duration of ADHD, mean ± SD, years*	3.8 ± 3.3	4.6 ± 4.2	3.7 ± 3.6	3.9 ± 3.7
Prior stimulant use, n (%)				
Mixed amphetamine salts	7 (26.9)	7 (26.9)	4 (15.4)	3 (12.0)
Methylphenidate	3 (11.5)	3 (11.5)	4 (15.4)	2 (8.0)
Methylphenidate HCL	4 (15.4)	4 (15.4)	1 (3.8)	3 (12.0)
Lisdexamfetamine	6 (23.1)	3 (11.5)	0	2 (8.0)
d-MPH	0	1 (3.8)	2 (7.7)	1 (4.0)
Amphetamine	0	1 (3.8)	0	0
d-MPH/serdexmethylphenidate	0	1 (3.8)	0	0
BL ADHD-RS-5 total score, mean ± SD	40.0 ± 7.6	41.2 ± 7.7	40.7 ± 7.8	40.0 ± 8.3
BL CGI-S score, mean ± SD	4.7 ± 0.8	4.7 ± 1.0	4.7 ± 0.8	4.8 ± 0.9

ADHD, attention-deficit/hyperactivity disorder; ADHD-RS-5, ADHD Rating Scale, Version 5; BL, baseline; CGI-S, Clinical Global Impressions–Severity; d-MPH, dexmethylphenidate; HCL, hydrochloride; SD, standard deviation
*Date of ADHD diagnosis recorded as start date in medical history, for incomplete diagnosis date: if day was missing, then the first of the month was used; if day and month were missing, then only year was considered.

Conclusions

- CTx-1301 demonstrated statistically significant, dose-dependent improvement in core ADHD symptoms in children and adolescents
- Across the three doses, the 37.5 mg CTx-1301 dose significantly reduced ADHD symptoms versus placebo, with a clinically meaningful effect size, given the fixed-dose study design
- On a clinician-rated responder measure (CGI-I), over 60% of CTx-1301 patients were "much" or "very much" improved versus 18% with placebo
- In spite of small sample size, meaningful effect size and statistically significant findings were evident
- CTx-1301 was well tolerated with withdrawal rates similar to placebo; AEs were consistent with the known stimulant class profile
- No clinically meaningful increase was observed in insomnia or appetite-related AEs, associated with afternoon dosing. In addition, no clinically meaningful trends were observed in vital signs (including z-scores), growth parameters (length, weight, and BMI), physical examination, or ECG findings during treatment

Limitations

- Fixed-dose design does not reflect real-world practice, where treatment is typically titrated to optimize the balance of efficacy and safety/tolerability for individual patients
- Limited sample size within each treatment arm reduced power to detect statistical significance, underscoring the importance of effect size estimates when interpreting results
- Results may have limited generalizability to wider patient populations particularly those with differing demographic or geographic characteristics from the study sample

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Disclosures

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ADHD, attention-deficit/hyperactivity disorder; ADHD-RS-5, ADHD Rating Scale, Version 5; ASD, autism spectrum disorder; BPD, bipolar disorder; CD, conduct disorder; CGI-I, Clinical Global Impression-i-Improvement; CGI-S, Clinical Global Impression-s-Severity; CNS, central nervous system; DMDD, disruptive mood dysregulation disorder; DSM-5, Diagnostic and Statistical Manual of Mental Disorders–Fifth Edition; ITT, intent-to-treat; MDD, major depressive disorder; MINI-KID, MINI International Neuropsychiatric Interview of Children and Adolescents; OCD, obsessive-compulsive disorder; US, United States.