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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Disclosure

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Potential conflict of interest with the following business, organization and individual

Name of business, organization or individual	Nature of conflict
Aadrvark, Attentive, and Sky	Consultant
Allergan, Adlon, Lilly, Sanofi, Suven, and Syndeio	Research Support
Akili and Cingulate	Advisory Board, Consultant, and Research Support
Bristol Myers Squibb	Advisory Board
Lumos and Zevra Therapeutics Inc (previously KemPharm, Inc)	Consultant and Research Support
Otsuka and Sunovion	Advisory Board, Consultant, Research Support and Writing Support
Supernus	Advisory Board, Consultant, Research Support, and Speakers Bureau
Noven and Corium	Advisory Board, Consultant, Speakers Bureau and Writing Support
Takeda	Research Support, Speakers Bureau and Writing Support
Tris Pharma and Collegium (previously Ironshore)	Advisory Board, Consultant, Research Support, Speakers Bureau and Writing Support

Background and Objectives

- **Inadequately managed ADHD** contributes to significant health, social, and economic burden in children and adolescents[1]
- Many patients treated with long-acting stimulants experience **inadequate symptom control during the day**[2]
- Strategies to **improve onset and duration of treatment** are hampered by the need to take multiple medication doses per day
- **CTx-1301 is a once-daily, trimodal extended-release dexmethylphenidate** (d-MPH) tablet designed to provide rapid onset and sustained symptom relief throughout the day using Precision Timed Release™ technology[3]

- **Primary objective:** Efficacy of three fixed doses of CTx-1301 (18.75, 25, and 37.5 mg) versus placebo based on changes in ADHD-rating scale, version 5 (ADHD-RS-5) total score
- **Secondary objectives:** Clinical Global Impressions-Severity & Improvement (CGI-S & CGI-I), safety, and tolerability

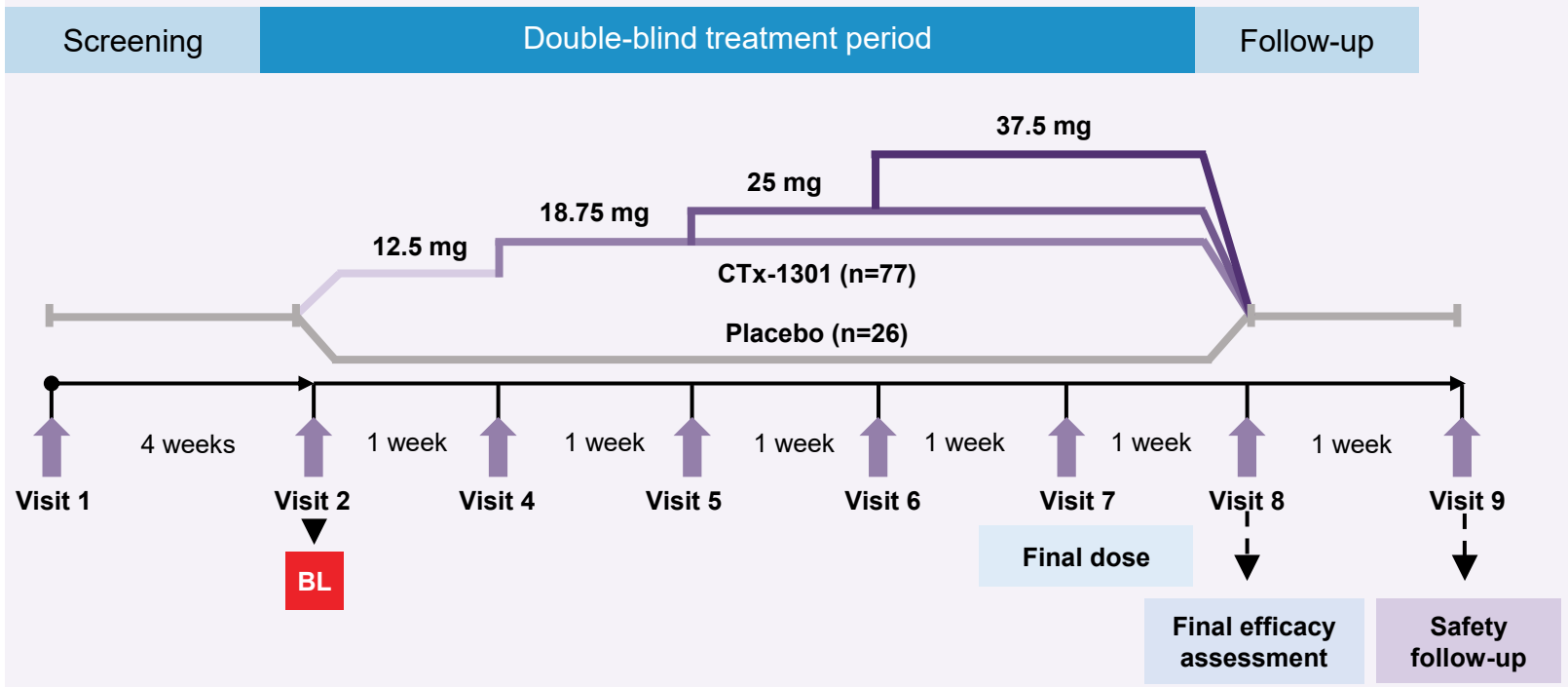
ADHD, attention-deficit/hyperactivity disorder; ADHD-RS-5, ADHD rating scale, version 5; CGI-I, Clinical Global Impression–Improvement; CGI-S, Clinical Global Impressions-Severity; d-MPH, dexmethylphenidate.

1. Schein J, et al. *J Med Econ*. 2022;25(1):193-205; 2. Sallee FR. *J Child Adolesc Psychopharmacol*. 2015;25(7):558-565; 3. Silva R, et al. [Poster]. APSARD 2018, Washington, DC.

Study Design and Endpoints

N=103

Phase 3, double-blind, randomized, placebo-controlled, fixed-dose, parallel-group study in patients aged 6–17 years with confirmed ADHD



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

ADHD, attention-deficit/hyperactivity ; ADHD-RS-5, ADHD rating scale, version 5; BL, baseline; CGI-I, Clinical Global Impression–Improvement; CGI-S, Clinical Global Impressions-Severity.

Patients

Key inclusion criteria

- Patients aged 6 to 17 years
- Confirmed ADHD by DSM-5 criteria or any of the three presentations (combined, inattentive, or hyperactive/impulsive) assessed by MINI-KID
- Baseline ADHD-RS-5 score ≥28 and CGI-S score ≥4
- Body weight between the 5th and 95th percentile for the respective age and sex

Key exclusion

- Any psychiatric diagnosis of bipolar I or II, major depressive, conduct, disruptive mood dysregulation, intellectual disability, obsessive compulsive, anxiety, or eating disorders; history of psychosis, autism spectrum disorder, Tourette's syndrome; intellectual disability; or genetic disorders with cognitive/behavioral disturbances or any other conditions deemed exclusionary by the investigator
- Evidence of any chronic CNS disease (such as tumors, inflammation, seizure disorder, vascular disorder, or other CNS-related disorders)

- 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

ADHD, attention-deficit/hyperactivity ; ADHD-RS-5, ADHD er rating scale, version 5; CGI-S, Clinical Global Impressions-Severity; CNS, central nervous system; DSM-5, Diagnostic and Statistical Manual of Mental Disorders - Fifth Edition; ITT, intent to treat; MINI-KID, MINI International Neuropsychiatric Interview of Children and Adolescents.

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

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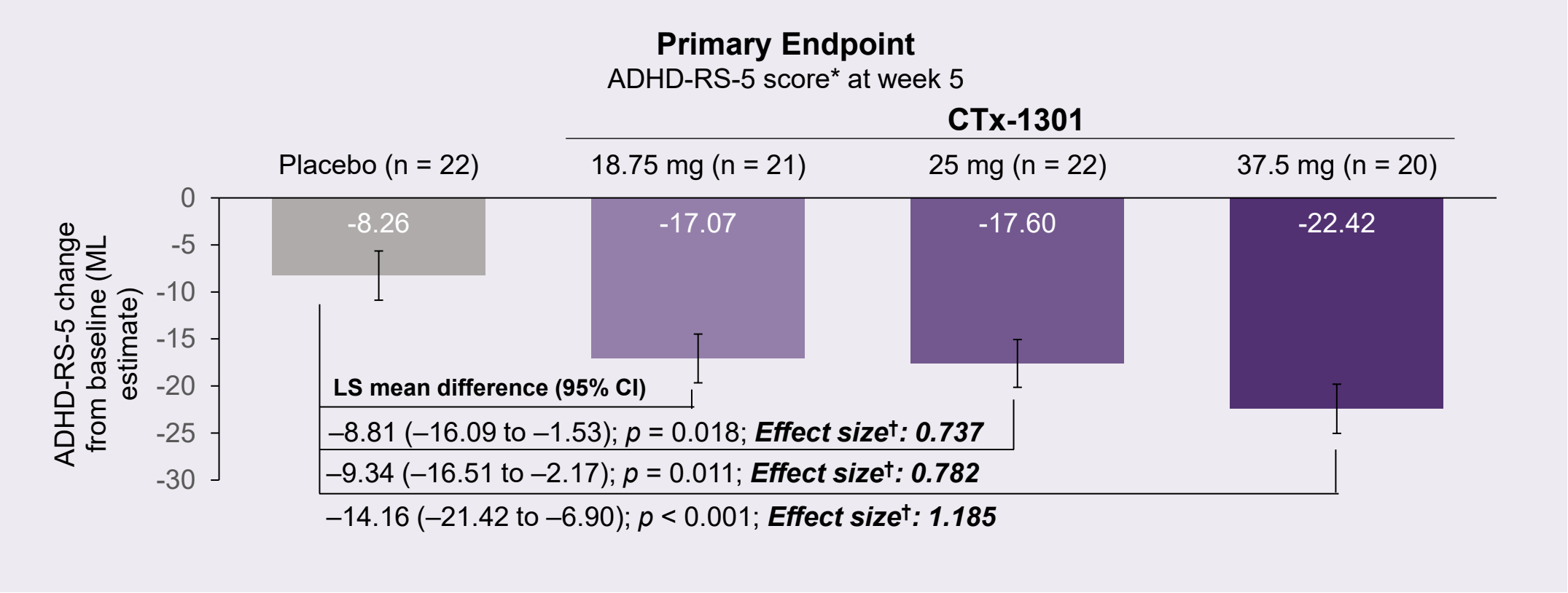
*Date of ADHD diagnosis recorded as start date in medical history, for incomplete diagnosis date: if day was missing, then the first of the month was used; if day and month were missing, then only year was considered.

ADHD, attention-deficit/hyperactivity; ADHD-RS-5, ADHD rating scale, version 5; BL, baseline; CGI-S, Clinical Global Impressions-Severity; d-MPH, dexmethylphenidate; HCL, hydrochloride; SD, standard deviation.

CTx-1301 Significantly Improved ADHD-RS-5 Score Compared With Placebo



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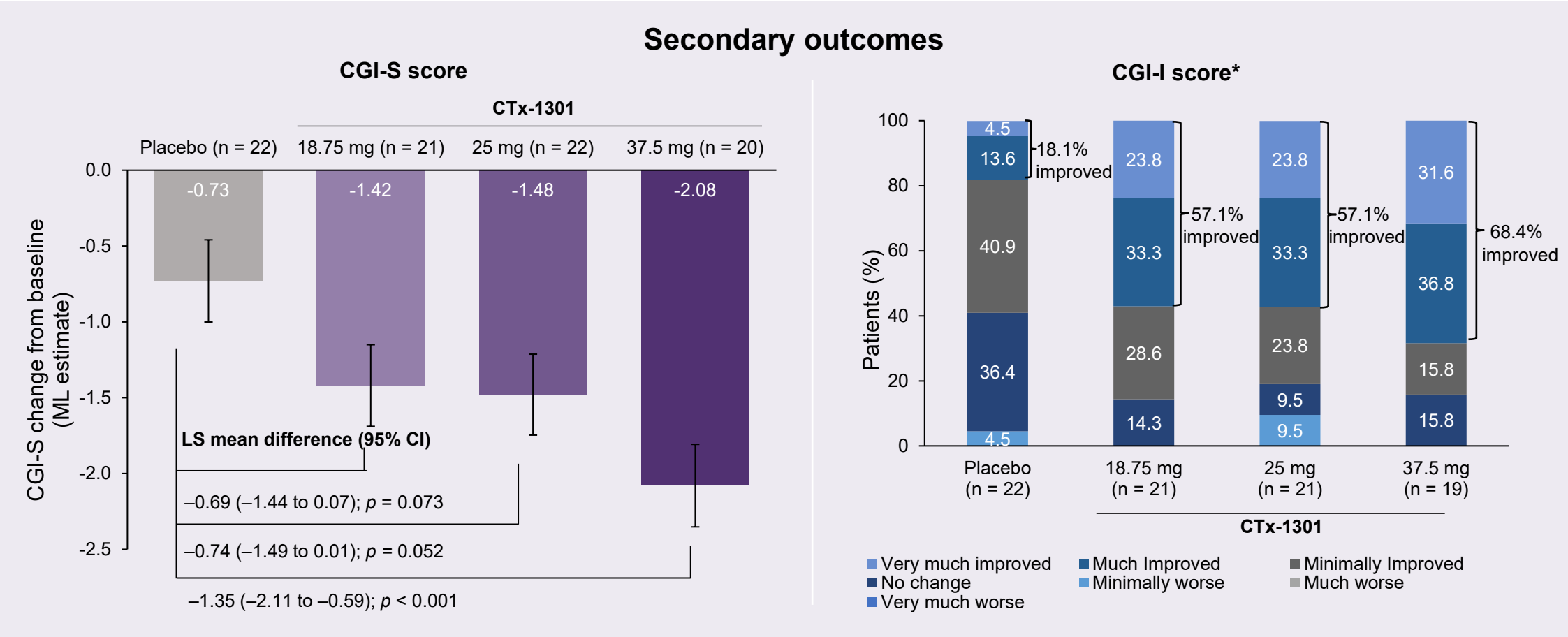
*Data were analyzed using a mixed-effect model for repeated measures in the ITT population. †Effect sizes for ADHD-RS-5 were derived from a post hoc analysis.

ADHD-RS-5, attention-deficit/hyperactivity rating scale, version 5; BL, baseline; CI, confidence interval; ITT, intent to treat; LS, least square; ML, maximum likelihood.

CTx-1301 Improved CGI-S and Greater Proportion of Patients Demonstrated Improvement Based on CGI-I Scores Compared to Placebo



*Of the 103 patients in the ITT population, 83 patients had clinician-rated CGI-I score data at week 5.

BL, baseline; CGI-I, Clinical Global Impressions-Improvement; CGI-S, Clinical Global Impressions-Severity; CI, confidence interval; ITT, intent to treat, LS, least square; ML, maximum likelihood.

Safety Profile

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 (%)				
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)

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

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*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.

BP, blood pressure; TEAEs, treatment-emergent adverse events; URTI, upper respiratory tract infection.

Summary

CTx-1301 demonstrated consistent **dose-dependent efficacy** in improving ADHD symptoms in children and adolescents

The 37.5-mg dose demonstrated the **largest effect size and symptom reduction;** effect sizes were substantial considering the fixed-dose study design

CTx-1301 showed **favorable safety profile** for all three dosage strengths

The study findings demonstrated the efficacy and safety of CTx-1301 for the treatment of ADHD in pediatric patients

ADHD, attention-deficit/hyperactivity disorder.