A randomized, single-dose, four-sequence, four-period, crossover study in adult ADHD subjects to establish comparative bioavailability of CTx-1301 (dexmethylphenidate) to the listed drug (Focalin® XR) under fasted conditions.

M. Brams[1], R. Silva[1], A. Straughn[1], H. Mitzel[1], B. Vince[2], D. Kelsh[2] , S. Schaffer[1]

[1]Cingulate Therapeutics 913-942-3200, cingulatetherapeutics.com; [2]Altasciences, 913-696-1601, altasciences.com

ABSTRACT

Objectives: This study compared the bioavailability and dose proportionality of a novel dexmethylphenidate (d-MPH) formulation, CTx-1301 (trimodal tablet), to the listed drug, Focalin XR (biphasic capsule). Additional objectives were to characterize the pharmacokinetics and evaluate safety and tolerability.

Methods: 45 adult ADHD subjects were randomized to four d-MPH dosage forms: CTx-1301 6.25mg, CTx-1301 50-mg, Focalin XR 5-mg, and Focalin XR 40-mg. 22 blood samples were obtained over each 28-hour treatment period; plasma profiles were evaluated using a validated bioanalytical method. Statistics were based on 39 subjects completing all four treatments.

Results: Data confirmed that CTx-1301 exhibited similar systemic d-MPH exposure to Focalin XR up to 8 hours after administration. Plasma concentrations of CTx-1301 at 15-16 hours were similar to Focalin XR at 12 hours, demonstrating the potential for extended duration of action, up to 16 hours. CTx-1301 demonstrated a statistically significant higher concentration ($p<0.05$) vs Focalin XR from 9 to 16 hours in both the low and high doses. CTx-1301 is expected to have a similar onset of action as Focalin XR (30 minutes). The C_{max} was 3.07 ng/mL vs 2.82 ng/mL and 23.1 ng/mL vs 24.3 ng/mL for Focalin XR and CTx-1301, low and high doses respectively. T_{max} was similar in all treatments (~6 hours). CTx-1301 subjects experienced a 28.6% fewer drug-related TEAE's than Focalin XR.

Conclusion: CTx-1301 tablets demonstrate a trimodal pharmacokinetic profile with fast onset, entire active-day duration, further potential to minimize crash and rebound and eliminate the need for booster doses. Phase 3 Trials are scheduled to evaluate the efficacy, safety, and pharmacodynamic benefits.

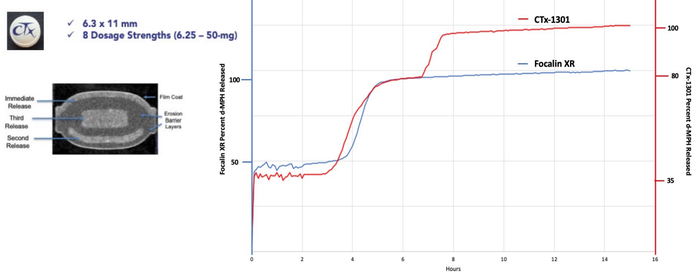
Clinical Trial Information: NCT04138498

BACKGROUND

Cingulate Therapeutics™ achieves optimal once-daily dosing using the company's innovative, proprietary, Precision Timed Release™ (PTR™) drug delivery platform technology which incorporates a patented Erosion Barrier Layer (EBL) providing control of drug release at precise, predefined times. It comprises an immediate release layer, a delayed extended-release layer, and a final immediate release core. This formulation is designed to provide a fast onset, therapeutically active levels of d-MPH lasting 14-16 hours and eliminate the need for booster dosing.

CTx-1301 is designed to deliver 25% more d-MPH versus Focalin XR. Cingulate's tri-modal tablet delivers a precisely timed, unique ratio, and style of drug delivery as opposed to the 50%/50% bi-phasic profile with drug release at time 0 and 4 hours. CTx-1301 formulation delivers 35% of the total daily dose at time 0 as an immediate-release, 45% at 3 hours post dose in a sustained release over 90 minutes, and a built-in-booster of 20% immediate release at 7 hours post dose.

A comparative in-vitro dissolution study was performed between CTx-1301 25-mg tablets and Focalin XR 20-mg capsules. The dissolution test was conducted in two phases: an acidic solution for 2 hours and a pH neutral phase for the remainder of the run.



SUMMARY

CTx-1301 Demonstrated Plasma Levels at 15-16 hours versus Focalin XR at 12 hours

- ✓ **CTx-1301 blood levels demonstrate the potential for a duration of action for the entire active-day, up to 16 hours, vs. Focalin XR 12-hour duration**
- ✓ **CTx-1301 performed as designed, with its precise 20% 'built-in-booster'**
- ✓ **Phase 3 Trials designed to confirm expected duration and additional potential benefits**

CTx-1301 Demonstrated Plasma Levels Equal to Focalin XR at 30 Minutes

- ✓ **CTx-1301 demonstrates rapid and equivalent blood levels of Focalin XR, indicative of a 30-minute onset of action**
- ✓ **Phase 3 Trials designed to confirm expected 30-minute onset of action**

CTx-1301 Demonstrated a Controlled Descent of Plasma Levels versus Focalin XR

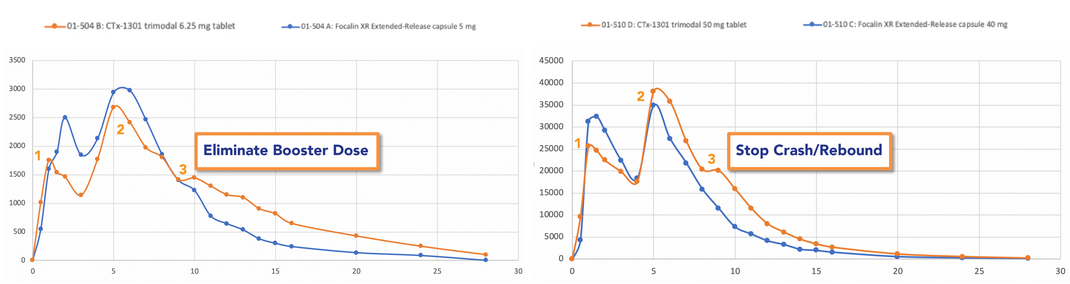
- ✓ **CTx-1301's precise, 20% 3rd delivery stopped the mid-afternoon plummeting of blood levels, controlling the decline until early evening**
- ✓ **Phase 3 Trials designed to further investigate the potential benefits of this controlled release to prevent 'wear-off', 'crash/rebound', and eliminate the need for a 'booster or recovery' dose**

CTx-1301 Demonstrated Significantly Lower Treatment Emergent Adverse Events at Higher Dose

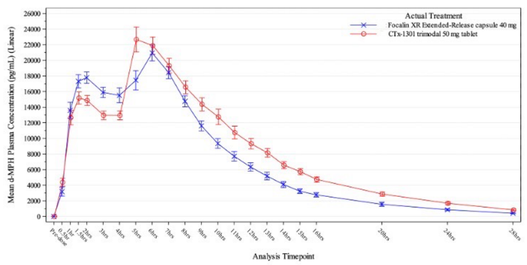
- ✓ **ADHD patients received 25% more d-MPH in CTx-1301 than Focalin XR via the PTR Platform in a precisely timed, unique ratio**
- ✓ **CTx-1301 patients experienced a 28.6% reduction of TEAE's related to study drug versus Focalin XR (14.3% difference)**

RESULTS

At the Individual Patient Level, Tri-modal Delivery is Clear



Precision Timed Release™ Technology Delivers Minimal Intersubject Variability



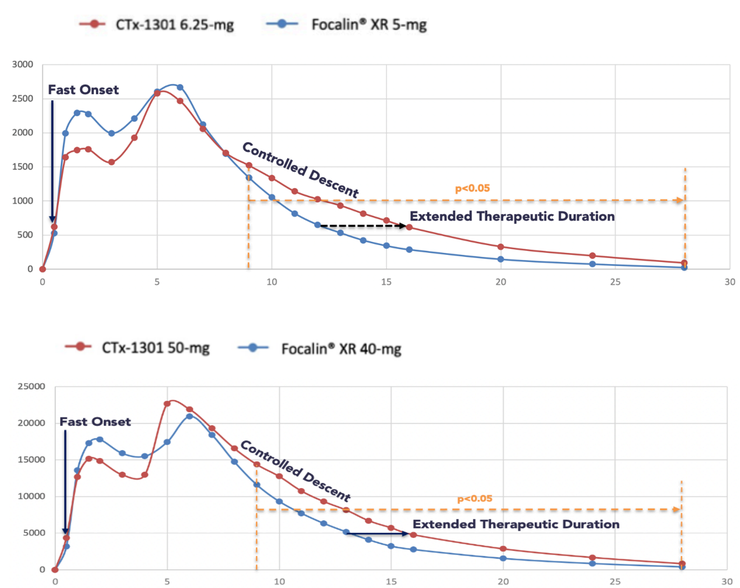
- ✓ **Designed to cover "Entire Active Day"**
- ✓ **Potential for duration of action up to 16 hours**
- ✓ **Ability to deliver fast onset of action**
- ✓ **Potential to minimize 'crash/rebound' effect**
- ✓ **Eliminate need for "booster" dose**

CTx-1301 Demonstrated Significantly Lower TEAE's

Category	Focalin XR 5-mg Treatment A (N=41)	CTx-1301 6.25-mg Treatment B (N=39)	Focalin XR 40-mg Treatment C (N=43)	CTx-1301 50-mg Treatment D (N=42)	All CTx-1301 (N=42)	All Focalin XR™ (N=44)
All Periods	41	39	43	42	42	44
Subjects with at least one Treatment Emergent Adverse Event (TEAE)	7 (17.1%)	4 (10.3%)	22 (51.2%)	14 (33.3%)	17 (40.5%)	25 (56.8%)
Mild	7 (17.1%)	4 (10.3%)	20 (46.5%)	14 (33.3%)	17 (40.5%)	23 (52.3%)
Moderate	0	0	2 (4.7%)	0	0	2 (4.5%)
Severe	0	0	0	0	0	0
TEAE Related to Study Drug	5 (12.2%)	3 (7.7%)	20 (46.5%)	13 (31.0%)	15 (35.7%)	22 (50.0%)
TEAE Related to Procedure	0	0	1 (2.3%)	0	0	1 (2.3%)
Serious Adverse Event (SAE)	0	0	0	0	0	0
SAE Related to Study Drug	0	0	0	0	0	0
SAE Related to Procedure	0	0	0	0	0	0
Adverse Event Leading to Study or Drug Withdrawal	1 (2.4%)	0	1 (2.3%)	0	0	2 (4.5%)
Adverse Event Leading to Death	0	0	0	0	0	0

Source: CSR CTx-1301-001 Listing 16.2.7.1

CTx-1301 Phase 1/2 Study Results



ACKNOWLEDGEMENTS

Contact Information:

Cingulate Therapeutics LLC:
1901 W. 47th Pl, Westwood, KS 66205
913-942-2300; info@cingulatetherapeutics.com

Study was funded by

CINGULATE® THERAPEUTICS

Poster Presented at The American Professional Society of ADHD and related Disorders (APSARD), 15-17 January 2021.