CTD Holdings (CTDH)

Poster Presentation Highlights Potential of Trappsol Cyclo for Niemann-Pick Type C

On February 15th, CTD Holdings (OTC: CTDH) presented a poster at the 13th Annual WORLD *Symposium*, a medical conference dedicated to research on lysosomal storage disorders. The poster was focused on results from a compassionate use program with *Trappsol Cyclo*, a proprietary, intravenous (IV) formulation of hydroxypropyl-b-cyclodextrin (HPbCD), that CTD is developing for the treatment of Niemann-Pick Type C (NPC) disease. Data were presented by Dr. Sharon Hrynkow, Senior Vice President of Medical Affairs at CTD, and Dr. Caroline Hastings of the UCSF Benioff Children's Hospital Oakland, who is the Principal Investigator (PI) of the Company's US clinical trial. Results indicate that *Trappsol Cyclo* was safe and well tolerated, and certain patients experienced benefits related to neurological function, motor skills, and quality of life. These data provide the rationale to pursue further clinical studies with *Trappsol Cyclo*, and CTD Holdings plans to begin US and EU studies in early 2017.

- **Compassionate Use Data Highlight Potential of Trappsol Cyclo.** CTD Holdings' poster focused on results from patients with NPC being treated with IV HPbCD through a compassionate use program. Investigators noted that patients with moderate NPC demonstrated disease stabilization, while those with severe NPC experienced alternating periods of stability and progression. This is exemplified by the improvements in NPC Clinical Severity Score (NCSS) observed in certain patients, presented in **Figure 1**. Treating physicians also reported neurologic improvements during IV HPbCD therapy, and upon initiation of intrathecal (IT) treatment (while maintaining IV HPbCD), there was not further improvement. We discuss the results in greater detail below.
- **Trappsol Cyclo Recently Received Fast Track Designation.** On January 17, 2017, CTD Holdings announced that *Trappsol Cyclo* received Fast Track designation from the FDA. This program intends to facilitate the development and expedite the review of drugs being developed for serious conditions that would fill an unmet need. Fast Track designation enables more frequent FDA meetings to discuss the drugs' development plan and ensure collection of appropriate data for approval, and may also lead to Accelerated Approval and Priority Review. *Trappsol Cyclo* also has Orphan Drug designation in the US and EU.

Expected Upcoming Milestones

- Q1 2017 – Initiate a Phase I trial in the US with *Trappsol Cyclo* for NPC.
- Q1 2017 – Initiate a Phase I/II trial in the EU with *Trappsol Cyclo* for NPC.
- H2 2017 – Pursue listing on national exchange.

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Market Data

Price	$0.48
Market Cap (M)	$32
EV (M)	$31
Shares Outstanding (M)	67.0
Fully Diluted Shares (M)	76.5
Avg Daily Vol	9,340
52-week Range:	$0.34 - $0.70
Cash (M)	$1.3
Net Cash/Share	$0.02
Annualized Cash Burn (M)	$5.5
Years of Cash Left	0.2
Debt (M)	$0.0

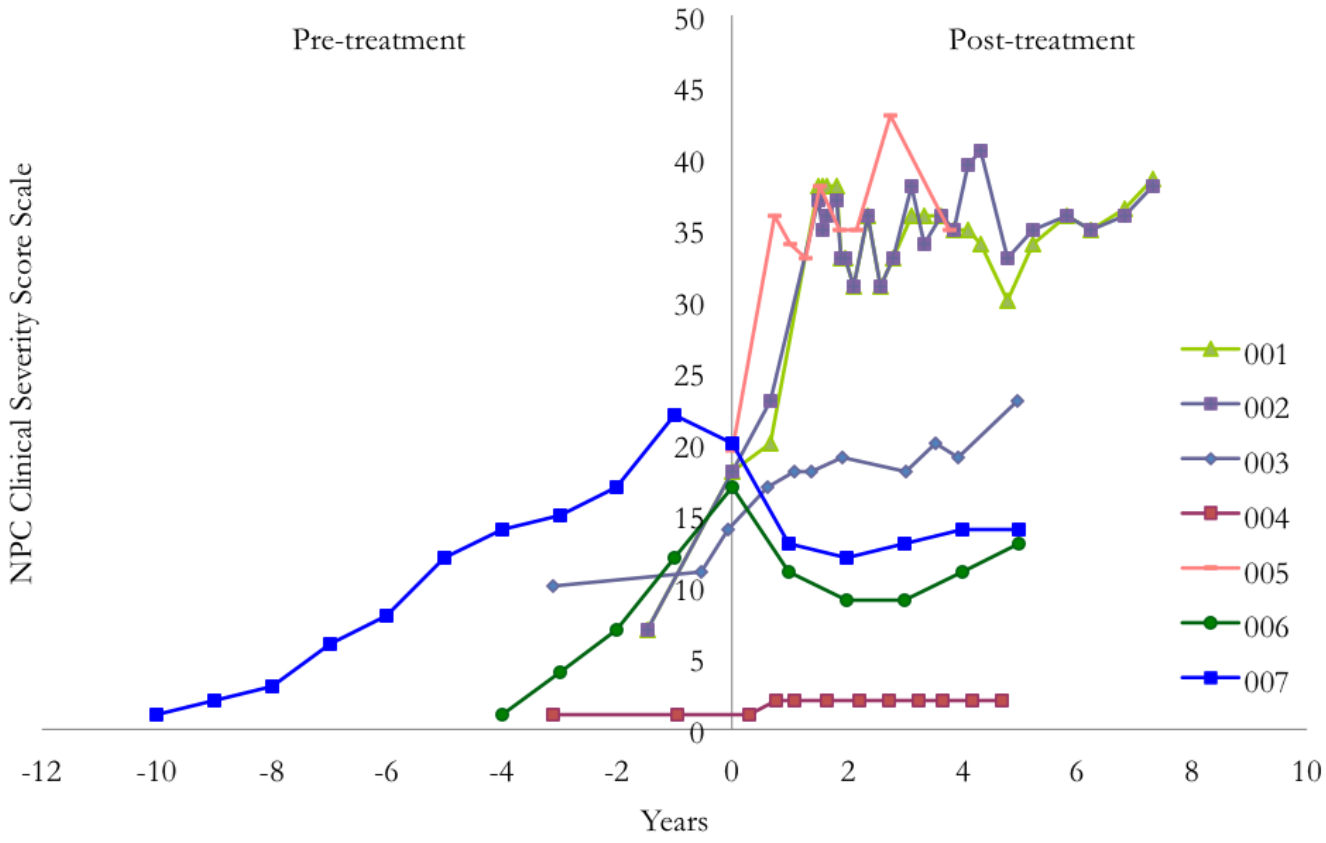
Financials

FY Dec		2014A	2015A	2016A
EPS	Q1	0.00A	(0.01)A	(0.01)A
	Q2	0.00A	(0.01)A	(0.02)A
	Q3	0.00A	(0.01)A	(0.02)A
	Q4	(0.01)A	(0.02)A	NA
	FY	(0.01)A	(0.05)A	NA

For analyst certification and disclosures please see page 4

- **Findings From a Compassionate Use Program with Trappsol Cyclo for NPC.** At this year's WORLD*Symposium*, CTD Holdings presented a meta-analysis of patients treated with *Trappsol Cyclo* through a compassionate use program, and findings are supportive of the development of this agent for the treatment of NPC. We note that these data were previously presented at the 2016 Parseghian Scientific Conference for Niemann-Pick Type C Research. Results indicate improvements in NPC Clinical Severity Score (NCSS), which is a severity scale that serves as a tool to quantify disease progression.[ref] NCSS utilizes the following nine major domains, which are scored 0-5: ambulation, cognition, eye movement, fine motor, hearing, memory, seizures, speech, and swallowing. It also incorporates the following eight minor domains, which are scored 0-2: auditory brainstem response, behavior, gelastic cataplexy, hyperreflexia, incontinence, narcolepsy, psychiatric, and respiratory problems. Major and minor domain scores are added together for a score that ranges from 0-61, with 0 representing no disease and 61 representing most severe disease. The NCSSs for each patient over time are presented in **Figure 1**. NCSS before the initiation of treatment are on the left side of the graph, while NCSS after the initiation of IV HPβCD treatment are on the right side of the graph.

Figure 1. NPC Severity Scores (NCSS) with *Trappsol Cyclo*



Source: Poster Presentation

Patients 006 and 007 demonstrated decreases in NCSS following the initiation of treatment, while patients 001, 002, 003, 004, and 005 appear to show moderate stabilizations in NCSS after 1 year of therapy. Although these data are from a small number of patients and have not yet been published, the reductions in NCSS score occurring in patients 006 and 007 and disease stabilization in a number of patients represent potentially meaningful trends. Other improvements were observed in individual patients as well, including reduction in liver size, improvements in transaminase levels, resolution of interstitial lung disease, subjective changes such as return of language and motor skills, and behavioral and cognitive improvements, among other quality of life enhancements.

Regarding safety, AEs associated with drug administration included rash, flu-like symptoms, headache, and nausea, though these were managed adequately. An infection was also reported at a site of venous device implantation, though such a device is not required protocol for drug administration. In light of the severe nature of NPC this AE profile should be acceptable if *Trappsol Cyclo* is able to demonstrate a clinically meaningful benefit.

- **Protocol for the Compassionate Use of Trappsol Cyclo for NPC.** The data presented are a compilation of case reports from 11 patients that received IV *Trappsol Cyclo* for an average of 9-12 months followed by combination IV and IT HPβCD treatment. Patients received infusions of 2,000-2,500 mg/kg *Trappsol Cyclo*, which was administered weekly or bi-weekly for up to 7 years. Patients receiving IT HPβCD were administered doses of 175-350 mg bi-weekly. Clinicians assessed patients with the NCSS. Safety and adverse events were also monitored during the compassionate use program.
- **Phase I US Trial Design**. This randomized, double-blind, Phase I trial will examine the safety and tolerability of *Trappsol Cyclo* for the treatment of NPC1. 12 patients are expected to be randomized 1:1 to receive 1,500 or 2,500 mg/kg IV *Trappsol Cyclo* via 8-hour slow infusion every 2 weeks for up to 14 weeks of treatment. Primary outcome measures of this study are based on pharmacokinetics and include maximum plasma concentration (C_{max}), time to maximum concentration (T_{max}), volume of distribution, and elimination half-life of *Trappsol Cyclo*. Secondary outcome measures include levels of *Trappsol Cyclo* in cerebral spinal fluid (CSF), blood biomarkers of NPC1, potential CSF biomarkers of NPC1, serum cholesterol precursors and metabolites, hepatic cholesterol, and adverse events. The Company expects that the first patient will be enrolled in this study in the first quarter of 2017, with data in the fourth quarter of 2017.
- **Phase I/II EU Trial Design**. This randomized, double-blind Phase I/II trial will examine the safety and pharmacokinetics of *Trappsol Cyclo* for the treatment of NPC1. 12 patients are expected to be randomized 1:1:1 to receive 1,500, 2,000, or 2,500 mg/kg IV *Trappsol Cyclo* via 8-hour slow infusion every 2 weeks for up to 48 weeks of treatment. Primary outcome measures of this study are maximum plasma concentration (C_{max}), time to maximum concentration (T_{max}), volume of distribution, and elimination half-life of *Trappsol Cyclo*. Secondary outcome measures include change in NIH NPC severity scale, markers of cholesterol metabolism, levels of CSF *Trappsol Cyclo*, and adverse events. CTD Holdings expects that the first patient will be enrolled in this study in the first quarter of 2017, with data in the third quarter of 2018.

Risk to Invesment

We consider an investment in CTD Holdings to be a high-risk investment. CTD Holdings is a clinical stage biotechnology company focused on the development of cyclodextrin-based therapies for the treatment of rare diseases and other indications. CTD Holdings has generated limited clinical data to date, and early signs of safety and efficacy may not necessarily translate into late-stage success. There are clinical and commercialization risks associated with each program. As with any company, CTD Holdings may be unable to obtain sufficient capital to fund planned development programs. There are regulatory risks associated with the development of any drug, and CTD Holdings may not receive FDA approval for its drug candidate despite significant time and financial investments. Regulatory approval to market and sell a drug does not guarantee that the drug will penetrate the market, and sales may not meet expectations.

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