

CTD announces encouraging top-line data from two ongoing clinical trials of Trappsol® Cyclo™ administered intravenously in Niemann Pick Disease Type C (NPC)

ALACHUA, FL – (Marketwired) – October 3, 2018 – CTD Holdings, Inc. (OTCQB: CTDH), a clinical stage biotechnology company that develops cyclodextrin-based products for the treatment of disease, today announced initial findings from two clinical trials utilizing its proprietary formulation of hydroxypropyl beta cyclodextrin (HPBCD), Trappsol(R) Cyclo(TM), administered intravenously (IV) in NPC patients. Both studies began dosing in subjects in the third quarter of 2017.

“We are pleased to be able to share our initial findings from both of our clinical trials using Trappsol(R) Cyclo(TM) for NPC disease.” said N. Scott Fine, CTD Chairman and CEO. “This announcement comes after many consultations with NPC families and patients, who helped us design our trials and who support us at every step, and after much work with our partners and investor base. It is gratifying and hopeful for all of us to be able to give this progress report.”

CTD reports on the first four patients in each of the studies. The Phase I trial in the United States is a 14-week treatment study with IV dosing every two weeks (see ClinicalTrials.gov [NCT02939547](https://clinicaltrials.gov/ct2/show/study/NCT02939547).) The Phase I/II trial in the EU and Israel is a 48-week treatment study also with IV dosing every two weeks (see ClinicalTrials.gov [NCT02912793](https://clinicaltrials.gov/ct2/show/study/NCT02912793)). Both trials are double-blinded and randomized with no control groups. Patients averaged in age of 28.1 years old; 5 are female, 3 are male. All received drug at either 1500 mg/kg, 2000mg/kg or 2500 mg/kg and the results as presented remained blinded in relation to the actual doses administered. Because the studies remain blinded, CTD is not able to provide a full analysis of the data. Definitive conclusions are therefore not possible. The report here focuses on major findings as exhibited in clear data trends.

Safety of the study drug was assessed in March 2018 for both studies. At the time, the drug was well tolerated with no serious safety signals observed. A full Safety Review Committee (SRC) will be conducted for each trial in the near future as specified in the SRC charter. We comment here on one of the most important safety questions posed by NPC patients and their families, namely, the potential for a drug-related effect on hearing or ototoxicity. At the time of this review, no clinically significant or permanent hearing problems were observed from IV dosing of Trappsol(R) Cyclo(TM) as measured by standard audiometric testing. Two subjects did experience mild hearing events, one a transient high-frequency loss which resolved within weeks after initial detection and another tinnitus of mild severity which resolved within 48 hrs. A third, more severe loss was measured by audiometry in the high frequency range, but this loss was not perceptible to the subject and it resolved by the time of the next regularly scheduled visit. The audiologist attributed this event to a conductive rather than sensorineural loss.

Study investigators consider these hearing events unrelated to the study drug, relating them instead to air travel or concurrent symptoms of an upper respiratory tract illness.

Both trials examine markers of cholesterol metabolism as important pharmacodynamic measurements. Following IV administration of Trappsol(R) Cyclo(TM), individual measurements from the patients of lathosterol, a validated serum marker of whole-body cholesterol synthesis, decreased along with two other cholesterol precursors, lanosterol and desmosterol. In addition to the suppression of whole-body cholesterol synthesis, there was a concomitant rise in cholesterol metabolites as measured by oxysterols.

Dr. Benny Liu, whose groundbreaking work paved the way for use of cyclodextrins in NPC, and who is Co-Investigator for one of the CTD clinical trials and a practicing gastroenterologist at Highland Hospital, Alameda Health System, Oakland, CA, said, "The fact that IV Trappsol(R) Cyclo(TM) administration is correlated with a decrease in whole-body cholesterol synthesis along with increases in cholesterol clearance metabolites is consistent with what we saw in the NPC mouse model after systemic treatment with cyclodextrin. Trapped cholesterol is being released and cleared from cells, and cells are responding by suppressing cholesterol synthesis, since the released cholesterol can now be 'sensed' by appropriate cellular mechanisms, and excess cholesterol is being excreted and removed."

Another biomarker analyzed in all patients was lysosphingomyelin-509, a validated diagnostic tool for NPC and a marker for severity of NPC disease (Giese et al. Orphanet Journal of Rare Diseases (2015) 10:78). Lysosphingomyelin-509 shows a clear downward trend in 7 of 8 subjects who received multiple doses. In one subject there was an initial decrease in lysosphingomyelin-509, consistent with findings for other subjects, followed by an increase after 6 weeks of treatment. While preliminary, the overall trend suggests that repeated dosing intravenously with Trappsol(R) Cyclo(TM) correlates with a decrease in this marker for severity of NPC disease.

The company asked treating physicians for subjective views on the patients' and caregivers' experiences in the study, while full evaluation of standardized scores, including the NPC Severity Scores, proceeds. Comments received focused on the spectrum of possible outcomes, from one subject who showed some progression of disease, to two subjects who showed stabilization overall but with aspects of improvement (tandem gait, motor ability), to several subjects with improvements in engagement and awareness and improvements in gait and dystonia, and one subject who had not spoken for two years who began to speak following the first infusion. While the benefit subsided for this last subject, it was seen again following the next infusion, and with each administration dystonic movements improved significantly, along with improvements in continence.

"We look forward to presenting the full set of data at an upcoming scientific conference as well as presenting the data to regulators in the EU and US. Our expectation is that we will complete enrollment for both studies by the end of 2018 and begin to work with

regulators on our next steps toward market approval,” said Dr. Sharon Hrynkow, CTD’s Senior VP for Medical Affairs.

About CTD Holdings:

CTD Holdings, Inc. is a clinical-stage biotechnology company that develops cyclodextrin-based products for the treatment of disease with unmet medical need. The company’s Trappsol(R) Cyclo(TM), an orphan drug designated product in the United States and Europe, is used to treat Niemann-Pick Disease Type C, a rare and fatal genetic disease, on a compassionate use basis as well as in two ongoing formal clinical trials (ClinicalTrials.gov [NCT02939547](#) and [NCT02912793](#)). Additional indications for the active ingredient in Trappsol(R) Cyclo(TM) are in development. For additional information, visit the company’s website: www.ctd-holdings.com

Safe Harbor Statement:

This press release contains “forward-looking statements” about the company’s current expectations about future results, performance, prospects and opportunities. Statements that are not historical facts, such as “anticipates,” “believes” and “expects” or similar expressions, are forward-looking statements. These statements are subject to a number of risks, uncertainties and other factors that could cause actual results in future periods to differ materially from what is expressed in, or implied by, these statements. The factors which may influence the company’s future performance include the company’s ability to obtain additional capital to expand operations as planned, success in achieving regulatory approval for clinical protocols, enrollment of adequate numbers of patients in clinical trials, unforeseen difficulties in showing efficacy of the company’s biopharmaceutical products, success in attracting additional customers and profitable contracts, and regulatory risks associated with producing pharmaceutical grade and food products. These and other risk factors are described from time to time in the company’s filings with the Securities and Exchange Commission, including, but not limited to, the company’s reports on Forms 10-K and 10-Q. Unless required by law, the company assumes no obligation to update or revise any forward-looking statements as a result of new information or future events.

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