

CTD Reports Initial Data for Two Clinical Trials of Trappsol® Cyclo™ Provided Intravenously for Patients with Niemann-Pick Disease Type C

ALACHUA, Fla., Feb. 07, 2019 (GLOBE NEWSWIRE) -- CTD Holdings, Inc. (OTCQB: CTDH), a clinical stage biotechnology company that develops cyclodextrin-based products for the treatment of disease with unmet medical need, reports initial results from its two clinical trials using the company's proprietary formulation of hydroxypropyl beta cyclodextrins (HPBCDs), Trappsol® Cyclo™, intravenously in patients with Niemann-Pick disease type C. Results were presented at two scientific conferences, WORLDSymposium (We're Organizing Research on Lysosomal Diseases), held Feb. 4 – 8, 2019, Orlando, Florida and the 13th Annual Brains for Brain (B4B) symposium organized under the auspices of the European Task Force on Brain and Neurodegenerative Lysosomal Storage Diseases, January 24-26, 2019. CTD's presentations were on February 6 and January 26, respectively. (Here are links to: [WORLDSymposium Poster 1](#), [WORLDSymposium Poster 2](#), and to the [B4B presentation](#)).

Niemann-Pick disease type C is a rare and fatal genetic disorder characterized by cholesterol accumulation in every cell of the body. There are no approved treatments in the United States, and only one in the EU. NPC patients may have a range of symptoms, including enlarged liver or spleen, respiratory challenges, and neurologic deficits, including cognitive decline. Hydroxypropyl beta cyclodextrins (HPBCDs) have been found in animal studies to release cholesterol from cells, normalize cholesterol homeostasis, delay symptom onset, and increase lifespan. CTD's compassionate use program with Trappsol® HPBCD began in 2009, providing significant data which supported the launch of its formal trials.

At both conferences, data were presented on the first four patients in the Phase I trial, "A Phase I Study to Evaluate the Single and Multiple-dose Pharmacokinetics of Intravenous Trappsol® Cyclo™ (HP-β-CD) in Patients With Niemann-Pick Disease Type C (NPC-1) and the Effects of Dosing Upon Biomarkers of NPC Disease," (ClinicalTrials.gov [NCT02939547](#)) and the first four patients in the Phase I/II trial, "A Phase I/II Study to Evaluate the Safety and PK of IV Trappsol® Cyclo™ (HP-β-CD) in Patients With Niemann-Pick Disease Type C (NPC-1) and the Pharmacodynamic Effects of Treatment Upon Markers of Cholesterol Metabolism and Clinical Outcomes," (ClinicalTrials.gov [NCT02912793](#)).

"We are delighted to share initial data from our two clinical trials," said N. Scott Fine, Chairman and CEO of CTD Holdings. "For our company, it is exciting to reach milestones with interim data for both trials and to share them with peers in the scientific and medical communities. For the NPC patient community and all of CTD's stakeholders, this is an important and positive moment."

Both of CTD's trials are completing enrollment in the US, Europe and Israel.

Investigators who treated the first patients are Caroline Hastings, MD, UCSF Benioff Children's Hospital Oakland, CA, and Benny Liu, MD, Alameda Health System, Oakland and UCSF Benioff Children's Hospital Oakland, CA (for the Phase I trial); and Reena Sharma, MD, Salford Royal NHS Foundation Trust, Salford, UK (also Coordinating PI for the EU/Israel trial); Martin Paucar-Arce, MD, Karolinska Institute, Stockholm, Sweden; and Orna Staretz-Chacham MD, Soroka Medical Center, BeerSheva, Israel (for the Phase I/II trial). Dr. Hastings is also Senior Clinical Advisor to the Phase I/II trial.

Patients in the Phase I trial were randomized to receive one of two doses (1500 mg/kg or 2500 mg/kg) administered intravenously over 8 to 9 hours twice monthly for a period of 14 weeks (7 doses). Patients in the Phase I/II trial were randomized to receive one of three doses (1500 mg/kg, 2000mg/kg or 2500 mg/kg) administered intravenously over 8 to 9 hours twice monthly for a period of 48 weeks (24 doses). Both trials are randomized, double-blinded, and with no control group. Results presented at both conferences were blinded with respect to dose.

The following are highlights of CTD's initial data:

Safety:

The review of individual and cumulative safety data to date has shown the study drug to be well tolerated with no

serious safety signals observed. In particular, no clinically significant or permanent hearing problems were observed from dosing of Trappsol® Cyclo™ given intravenously as measured by standard audiometric testing.

Pharmacokinetics:

This is a measure of how the drug is metabolized by the body. CTD measured the amount of drug in the blood plasma to determine how quickly the body processed the drug. Trappsol® Cyclo™ as measured in plasma peaks at 6 to 8 hours following the start of intravenous drug infusion, and it rapidly cleared from the body, with a half-life of 1-2 hours. This means that the drug is available to body tissues for a limited period of time, after which it is cleared (through the kidneys).

Trappsol® Cyclo™ is found in the cerebrospinal fluid (CSF), the liquid which surrounds the brain and spinal cord, starting at 4 hours after the start of intravenous infusion and continues to enter the CSF even after the end of infusion. Levels of drug are 30 ug/ml to 450 ug/ml. This means that the drug crosses the blood-brain-barrier. It may explain why Trappsol® Cyclo™ in compassionate use programs has been linked to neurologic benefits. Additional analysis is underway to further understand these findings. The full interpretation will not be available until trials are unblinded.

Impact on cholesterol metabolism:

Since the drug has an affinity for cholesterol, it is important to understand if Trappsol® Cyclo™ releases cholesterol from cells, as has been seen in animal models of the disease. Measurements of cholesterol precursors and metabolites from serum of NPC patients taken following intravenous infusion of the drug show that the drug causes cells to reduce cholesterol synthesis and to increase cholesterol degradation, in keeping with the understanding that Trappsol® Cyclo™ clears cholesterol from cells.

Impact on biomarkers for NPC disease:

Two biomarkers for NPC disease are reduced with successive administration of Trappsol® Cyclo™ provided intravenously in both clinical trials. Lysosphingomyelin-509, measured in plasma, is a validated biomarker for NPC disease severity. Levels show a clear downward trend with successive dosing: in 3 of 4 patients in the Phase I/II study, there was a 30% to 50% reduction of this biomarker by Week 10. The second biomarker is tau, a neuron-specific protein that increases in the CSF in conjunction with neuronal degradation and disease. After intravenous administration of the drug, tau is reduced between 10% and 50% in 5 of the initial patients in both trials for which significant data are available. Additional data points on biomarkers will assist interpretation.

Clinical efficacy:

Blinded results from standardized tests for ataxia, cognitive capacity, and NPC Severity Scores and Global Impression of Disease in the Phase I/II trial show variation among patients in terms of outcome measures. However, three of four patients showed improvement in one or more outcome measures, including ataxia, speech and overall well-being.

“The initial data from both studies are encouraging overall,” said Dr. Hastings. “The positive safety profile, coupled with data showing for the first time that Trappsol® Cyclo™ crosses the blood-brain-barrier, are important findings. Furthermore, these data are contributing to important insights on understanding mechanism of action of the drug on cholesterol homeostasis. Disease stabilization as well as improvements in disease specific features are observed, suggesting a positive correlation with the biochemical findings.”

Once the trials are unblinded, the company will report additional outcomes.

“We look forward to sharing these data with FDA, EMA and other regulatory authorities as we work toward approval of the drug and as we design and launch our global pivotal trial,” said Sharon Hrynkow, PhD, CTD’s Senior Vice President for Medical Affairs.

CTD Holdings gratefully acknowledges the many patients and families who are participating in the current trials and all those who contributed compassionate use data to support CTD’s trial applications with regulatory authorities. CTD also gratefully acknowledges its partners at Alan Boyd Consultants (UK), Aptus Clinical, Emmes, Synteract, Medpace Bioanalytical Labs, Centogene, Oxford University, Accenture, and ProductLife. We thank Professor David Begley, Kings College London, for critical review of pK data.

About CTD Holdings:

CTD Holdings, Inc. is a clinical-stage biotechnology company that develops cyclodextrin-based products for the treatment of disease. The company’s Trappsol® Cyclo™, 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 (Clinical Trials.gov [NCT02939547](#) and [NCT02912793](#)). Additional indications for the active ingredient in Trappsol[®] Cyclo[™] 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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