Cyclo Therapeutics Inc. Announces Positive Top Line Results from Phase I Trial and Interim Analysis of Phase I/II Trial using Trappsol® Cyclo™ Intravenously to Treat Patients with Niemann-Pick Disease Type C1 (NPC1)

Top line results of Phase I study confirm favorable safety and tolerability of Trappsol® Cyclo™ in patients with NPC1 and demonstrate biological responses for both dose groups.

An Unblinded Interim Analysis of Phase I/II study shows encouraging signals in efficacy for all dose groups as well as pharmacodynamic effects in cholesterol homeostasis across all dose groups.

Pharmacokinetic analysis confirms that Trappsol® Cyclo™ crosses the blood-brain-barrier after intravenous infusion for all dose groups in both trials.

Data from both studies are being used to inform dose selection for Cyclo Therapeutics' Phase III Pivotal Trial expected to recruit first patient in the second half of 2020.

Management to host webinar on May 20, 2020 to discuss data from the Phase I and Phase I/II trials, and plans for the global Phase III pivotal trial

GAINESVILLE, FL – (Businesswire) – May 20, 2020 – Cyclo Therapeutics, Inc. (OTCQB: CTDH), a clinical-stage biotechnology company that develops cyclodextrin-based products for the treatment of Niemann-Pick Disease Type C1 (NPC1) and Alzheimer's Disease, today announced Top Line data showing a favorable safety and tolerability profile for Trappsol® Cyclo™ as well as encouraging signals in efficacy for all dose groups (1500 mg/kg, 2000 mg/kg and 2500 mg/kg) evaluated in the treatment of NPC1. The data were derived from 25 patients participating in two clinical trials, a Phase I study that is now locked and a Phase I/II study for which the company conducted an unblinded interim analysis. Both trials used intravenous administration of Trappsol® Cyclo™ the company's proprietary formulation of hydroxypropyl beta cyclodextrin, given every two weeks.

"These results are exciting for the Company and for all of our stakeholders, especially the NPC patient community and the investors who have supported our clinical programs," said Company Chairman and CEO, N. Scott Fine. "With these data, we are

confident in our plans for our pivotal program, and we therefore expect to launch our global Phase III study using the intravenous route of administration of Trappsol® Cyclo™ for NPC1 by the end of 2020. We are deeply grateful to the physicians who lead our clinical sites and to the NPC patients, their families and caregivers for their unwavering commitment and support for our drug development program."

The Phase I study (NCT02939547) was designed to assess the safety, tolerability, pharmacokinetics (PK), and pharmacodynamics of Trappsol® Cyclo™ in NPC1 patients aged 18 years and older, administered by intravenous infusions over 8-9 hours. Following single- and multiple-dose kinetics at 1500mg/kg and 2500 mg/kg, the plasma profiles of Trappsol® Cyclo™ declined in a similar manner and there was no evidence of accumulation of the drug over time. The mean elimination half-life was approximately 2 hrs and median Tmax was between 6 and 8 hrs, irrespective of the dose. The PK profile in each patient is almost identical for each infusion.

Trappsol® Cyclo™ crossed the blood-brain-barrier as measured in cerebrospinal fluid (CSF) taken at intervals following the onset of intravenous infusion. The CSF:plasma ratio at 8 hrs was 2% increasing to 11-16% at 12 hrs, suggesting significant persistence of the drug in the CSF for several hours after the end of infusion.

The doses in both treatment groups affected cholesterol synthesis and metabolism as measured by cholesterol precursors, such as lathosterol, and cholesterol metabolites, such as 4-beta-hydroxysterol, in serum. Both dose groups showed a decrease in cholesterol precursors 2 – 3 days after infusion, and a concomitant increase in cholesterol metabolites until day 3 post-infusion. There was no difference in the level of the effect between dose groups. These data show that Trappsol® Cyclo™ at the low and the high dose group clears cholesterol from cells, along the lines that has been demonstrated previously in pre-clinical studies.

Tau, a neuron-specific biomarker of disease, decreased in cerebrospinal fluid as compared to baseline after 7 doses, suggesting its potential as a central nervous system (CNS) biomarker for neurodegeneration associated with NPC. Plasma levels of lysosphingomyelin-509, a biomarker for NPC disease, also showed a downward trend. Given the small number of patients in this study, it was not possible to differentiate the effects by dose.

Overall, both dose groups showed a highly favorable safety profile. The lower dose group (1500 mg/kg; 6 patients) had the least treatment-emergent adverse events (TEAE's) with 13 while the higher dose group (2500 mg/kg; 7 patients, 1 of whom was withdrawn and replaced) had 27 TEAEs. There were 3 Severe Adverse Events (SAEs) related to hearing in the study, all in the high dose group (2500 mg/kg) and all considered by the investigator to be related to the study treatment. On cessation of infusions, one patient recovered to baseline hearing levels; one improved but did not return to baseline; and one is awaiting further assessment. According to the investigator, none of the 3 patients nor their families perceived a change in hearing,

rather, the changes were detected by audiometry assessments as part of the study's normal screening protocol.

The Clinical Study Report for the Phase I trial is expected in August 2020.

All patients who completed the Phase I study opted to participate in the Extension Protocol (NCT03893071) (US-based patients) or to continue on the drug through Compassionate Use programs in their home countries (non-US patients). To date, the AE profile in the Extension Protocol is highly favorable. Patients in the Extension Protocol receive the drug every two weeks as in the Phase I study with home-based infusions under the care of qualified health professionals.

The Phase I/II study (NCT02912793) was designed to assess the safety, tolerability, pharmacokinetics (PK), pharmacodynamics and clinical outcomes of Trappsol® Cyclo™ in NPC1 patients aged 2 years and older. The study drug was administered by intravenous infusions over 8 – 9 hours as in the Phase I study. The unblinded interim analysis of the Phase I/II study was based on data from 12 patients: four patients had completed the trial by the cut-off date, two were withdrawn, and six are ongoing.

Following single-dose kinetics at 1500 mg/kg, 2000 mg/kg, and 2500 mg/kg, the plasma profiles of Trappsol® Cyclo™ declined in a similar manner and the increase in systemic exposure was approximately dose proportional. The elimination half-life was approximately 2 hrs and median Tmax was 6 hrs. Trappsol® Cyclo™ crossed the blood-brain-barrier as measured in cerebrospinal fluid (CSF) taken at intervals following the onset of intravenous infusion. The CSF:plasma ratio at 8 hrs was 2% increasing to 16% at 12 hrs, suggesting significant persistence of the drug in the CSF for several hours after the end of infusion.

All three dose groups have shown a favorable safety profile to date as exhibited by AE and SAE profiles.

Pharmacodynamic outcomes show that levels of cholesterol precursors decreased, and cholesterol metabolites increased, similar to findings in the Phase I study and showing an anticipated effect on cholesterol homeostasis. Also, as in the Phase I study, levels of tau decreased over time in CSF. The numbers of samples available at the time of evaluation precluded a determination of dose-dependency with respect to these biomarkers.

The major efficacy endpoint after 48 weeks of treatment (and as measured at 12-week increments for the interim analysis) is the 17-domain NPC Severity Score (NPCSS). It would be expected that after one year NPC patients with only standard of care and no interventional therapy would worsen their NPCSS by at least 1.5 points. Of the four patients who completed the study at the time of the data cut-off, 3 patients improved in their NPCSS by at least 3 points as compared to baseline while one patient worsened.

Spinocerebellar ataxia, a secondary outcome as measured by the Scale for Assessment and Rating of Ataxia, showed a clear improvement in some patients: the low patient number precluded establishing a dose dependent relationship.

Overall, while the limited sample size precluded definitive statements regarding efficacy and dose relationships, clinical observations within individual subjects provide a compelling justification to move forward with our global Phase III clinical program.

“With no approved therapy for NPC in the United States and only one approved therapy for NPC in Europe, there is a critical and urgent need for studies which show both safety and efficacy in treatment of NPC disease manifestations,” said Sharon Hrynkow, PhD, the Company’s Chief Scientific Officer and Senior Vice President for Medical Affairs. “We are pleased to share favorable safety findings and encouraging efficacy findings from our two early clinical trials, and we look forward to working with all of our partners and clinical sites globally to complete the Phase I/II study while simultaneously executing our plan for the global pivotal trial in the coming months.”

Cyclo Therapeutics Inc. will host a live webinar to discuss the data and to take questions on May 20, 2020 at 4:30 pm EDT. An opportunity to submit questions prior to the start of the webinar is available upon registration. To participate, please register at: Cyclo Therapeutics Clinical and Regulatory Update Call

About the Phase I Study Design:
“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, (NCT02939547). A single site, UCSF Benioff Children’s Hospital Oakland, with Co-Principal Investigators Caroline Hastings, MD and Benny Liu, MD, recruited all 12 patients for this study which was a double-blinded, randomized, parallel group trial with no placebo control. Patients received either 1500 mg/kg or 2500 mg/kg of Trappsol® Cyclo™ by slow intravenous infusion over 8-9 hours for a total of 7 doses in a 14 week treatment period. Patients were age 18 years and older.

Phase I/II Study Design:
“A Phase I/II Study to Evaluate the Safety and PK of IV Trappsol® Cyclo™ in Patients with Niemann-Pick Disease Type C (NPC1) and the Pharmacodynamic Effects of Treatment upon Markers of Cholesterol Metabolism and Clinical Outcomes,” (NCT02912793). A multi-center, double-blind, randomized, parallel group trial with no placebo involving clinical sites in UK, Israel and Sweden. EU Coordinating Investigator and site director Dr. Reena Sharma, Salford, UK. Additional sites at Birmingham Women and Children’s Hospital (Dr. Julian Raiman); HaEmek Medical Center, Afula, Israel (Dr. Ronen Spiegel); Soroka Medical Center, BeerSheva, Israel (Dr. Orna Chacham-Staretz); and Karolinska Institute, Stockholm, Sweden (Dr. Martin Paucar). Patients received either 1500 mg/kg, 2000 mg/kg or 2500 mg/kg of Trappsol® Cyclo™ by slow intravenous infusion over 8-9 hours for a total of 24 doses in a 48 week treatment period. Patients were age 2 years and older.

About Niemann-Pick Disease Type C:

Niemann-Pick Disease Type C1 is a rare genetic disease affecting 1 in 100,000 live births globally. NPC1 affects every cell in the body due to a defect in the NPC1 protein which is responsible for cholesterol processing in the cell. NPC causes symptoms in the brain, liver, spleen, lung and other organs and often leads to premature death. There are no approved drug therapies for NPC in the United States and only one approved therapy in Europe.

About Cyclo Therapeutics:

Cyclo Therapeutics, Inc. is a clinical-stage biotechnology company that develops cyclodextrin-based products for the treatment of Niemann-Pick Disease Type C and Alzheimer's Disease. The company's Trappsol® Cyclo™, an orphan drug designated product in the United States and Europe, is the subject of three formal clinical trials for Niemann-Pick Disease Type C, a rare and often fatal genetic disease, (ClinicalTrials.gov NCT02939547, NCT02912793 and NCT03893071). The company is planning an early phase clinical trial using Trappsol® Cyclo™ intravenously in Alzheimer's Disease based on encouraging data from an Expanded Access program for late-onset Alzheimer's Disease (NCT03624842). Additional indications for the active ingredient in Trappsol® Cyclo™ are in development. For additional information, visit the company's website: www.cyclotherapeutics.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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