Cyclo Therapeutics Meets Primary Efficacy Endpoint in Phase 1/2 Trial from Intravenous Trappsol® Cyclo™ in Rare Disease Niemann-Pick Type C1 (NPC1)

100% of patients who completed the trial improved or remained stable, and 89% met the efficacy outcome measure of improvement in at least 2 domains of the 17-domain NPC Severity Scale

Trial data suggest that Trappsol® Cyclo™ overcomes the NPC1 defect by removing trapped cholesterol from cells both systemically and in the central nervous system (CNS)

Pharmacokinetic analysis confirms that Trappsol® Cyclo™ crosses the blood-brain-barrier after intravenous infusion and further supports neurological benefit

GAINESVILLE, FL – (Businesswire) – March 25, 2021– Cyclo Therapeutics, Inc. (Nasdaq: CYTH) ("Cyclo Therapeutics" or the "Company"), a clinical stage biotechnology company dedicated to developing life-changing medicines through science and innovation for patients and families suffering from diseases, today announced topline data from its Phase 1/2 clinical trial, which demonstrated promising safety and efficacy results for Trappsol® Cyclo™ in the treatment of Niemann-Pick Disease type C1, a rare, genetic disease causing cholesterol accumulation in cells, leading to dysfunction of liver, lung, spleen and brain and premature death.

"These data continue to underpin our strong belief that Trappsol® Cyclo™ has the ability to be a safe and effective treatment for both systemic and neurologic manifestations of NPC. And, the data have informed our Phase 3 clinical trial design, allowing us to move forward with great confidence in the next crucial stage of drug development to meet the unmet need in the NPC community," said N. Scott Fine, Chief Executive Officer of Cyclo Therapeutics.

The multi-center, randomized, double-blind, parallel group trial without a placebo arm randomized 12 patients ranging in age from 2 to 39 years across clinical sites in the UK, Israel and Sweden. Patients were treated intravenously with Trappsol® Cyclo™, the Company's proprietary formulation of hydroxypropyl beta cyclodextrin, over 8-9 hours for a total of 24 doses in a 48-week treatment period. Three doses of Trappsol® Cyclo™ were evaluated: 1500 mg/kg, 2000 mg/kg, and 2500 mg/kg. All patients received study drug, and the top line data summarizes the results from all dose levels combined.

"These topline data represent a significant milestone for the Company, and even more importantly, for this patient population. We are incredibly pleased with the positive data demonstrated by Trappsol® Cyclo™ and are eager to advance our upcoming Phase 3

clinical trial in the coming quarter," commented Sharon Hrynkow, PhD the Company's Chief Scientific Officer and Senior VP for Medical Affairs. "We would like to extend our sincere gratitude to the patients, families and clinical teams that participated in the study. With the growing body of data in hand and our upcoming Phase 3 clinical trial, we are optimistic that Trappsol® Cyclo™ may provide a safe and efficacious treatment option for NPC where there remains significant unmet need."

Summary of Findings

Safety

- All dose groups showed a favorable safety profile, consistent with previously reported data from a companion Phase 1 clinical trial. 15 SAEs were reported in 5 patients. Of these, 3 were considered by the investigator to be at least possibly related to the study drug: one hearing related event resolved within a month (Grade 2); the 2 other events were in a pediatric patient related to infiltrated peripheral cannula which resolved quickly, and which did not interfere with study completion.

- Nine patients completed the trial and 3 were withdrawn by treating physicians. One patient was withdrawn at Week 24 due to intercurrent illness, another who had completed the 36 Week assessment was withdrawn due to COVID-19 travel restrictions which prohibited further participation. The third patient's parents refused to consent for efficacy assessments prior to Week 12, and the patient was withdrawn from the study and not replaced in keeping with the protocol. No patient was withdrawn due to concerns over safety of the drug.

First Efficacy Endpoint: *Improvement by at least one point in two domains of the 17-domain NPC Severity Scale (NPCSS) after 48 Weeks of treatment*

- Of the 9 patients who completed the study, 8 (89%) met the first efficacy endpoint. Patients improved in disease-related domains that included the ability to walk, speak, swallow, behavioral features, incontinence, fine motor skills, saccadic eye movements, and cognition.

- The 17-domain NPC Severity Scores for all patients between baseline and last available assessment showed overall improvement in 6 patients and worsening in 5. One patient had only baseline data and was excluded from the analysis. Based on natural history data with no intervention, patients would be expected to decline on average by 1.5 points over this time period. The 3 patients who were withdrawn from the study by treating physicians worsened by 6 and 8 points at their last assessment or had a single baseline score.

- NPC patients and caregivers report that improvement in any one of the following 5 domains would enhance their quality of life: ambulation, speech, swallow, fine motor skills and cognition. Of the 9 patients who completed the trial, 6 improved in at least one of these domains, and 2 improved in two of the domains. Further, 67%

percent showed improvement or stabilization in the total score of these 5 domains. This underpins selection of these domains to serve as a composite score for the Phase 3 clinical trial.

Second Efficacy Endpoint: Clinician Global Impression of Improvement at 48 Weeks

- Of the 9 patients who completed the study, all were rated as either improved or stable by clinicians at the end of the study. Clinicians rated 7 patients (78%) as improving to some degree at 48 weeks (Very Much Improvement to Minimal Improvement), with 2 patients as stable.

Additional Data Highlights

- Following single-dose kinetics at the three dose levels, 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 hours, and the median Tmax was 6 hours. Trappsol® Cyclo™ was measurable in cerebrospinal fluid (CSF) taken at intervals following the onset of intravenous infusion, indicating that it crossed the blood-brain-barrier. 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 the infusion.

- The pharmacodynamic endpoints measured in this study suggest that Trappsol® Cyclo™ clears cholesterol from cells and normalizes cholesterol metabolism. Serum lathosterol, an indicator of whole-body cholesterol synthesis, was reduced by 44% across all patients on average between baseline and 2 days after the first infusion, indicating that cholesterol synthesis was suppressed, most likely due to the release of trapped cholesterol. A concomitant rise in cholesterol metabolites, such as 4-beta-hydroxycholesterol, was observed peaking at day 5, further supporting the interpretation that Trappsol® Cyclo™ causes a bulk release of cholesterol from lysosomes and leads to subsequent processing of excess cholesterol for removal from the body. The levels of 4-beta-hydroxycholesterol diminished over the course of the 48 weeks, further suggesting that the pool of excess cholesterol found in NPC cells is reduced.

- Cholesterol metabolism in the CNS can be evaluated by the levels of serum 24S-hydroxycholesterol, a metabolite of CNS-derived cholesterol which is exported out of the brain and into the blood. Within 3 days of the first IV dose, serum 24S-hydroxycholesterol levels increased to 118% of baseline on average across all patients and then returned to baseline by day 8, suggesting that excess cholesterol in the CNS was metabolized following IV administration of Trappsol® Cyclo™, further supporting the neurologic efficacy outcomes observed in this trial.

- Tau is a biomarker found primarily in neurons within the CNS and present at elevated levels in the cerebrospinal fluid (CSF) of patients with neurodegenerative

disease. CSF tau levels were reduced by 31% in one patient and 72% in a second at 48 weeks. A third patient showed a 10% reduction at 24 weeks. Lumbar punctures for CSF assessments were optional in the study. These data suggest a neuroprotective effect, and they complement and extend data from the Phase 1 clinical trial showing a decrease in CSF tau after 14 weeks of treatment, which was the end of the Phase 1 clinical trial.

- Abdominal ultrasound data suggest that Trappsol® Cyclo™ reduces hepatosplenomegaly.

- Liver size was reduced on average by 16% in 3 patients and increased in 4 patients on average by 11% when comparing first and last available datapoint. Three patients showed no change, and data were not available for comparison for 2 patients.

- Spleen size was reduced by an average of 10% in 10 of 12 patients and was increased by 5% in one patient. One patient had a single data point and was not evaluable.

- Spinocerebellar ataxia was measured using the Scale for Assessment and Rating of Ataxia (SARA). An evaluation of all data averaged across patients showed overall improvement in all 8 domains of the tool. Fine motor skills were also assessed by a standardized bead-threading test, which showed improvement in 5 of the 6 patients able to perform this assessment.

For more information about the Phase 1/2 clinical trial, please visit clinicaltrials.gov and reference identifier NCT02912793.

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 dedicated to developing life-changing medicines through science and innovation for patients and families suffering from disease. The Company's Trappsol® Cyclo™, an orphan drug designated product in the United States and Europe, is the subject of three ongoing formal clinical trials for Niemann-Pick Disease Type C, a rare and 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, including, without limitation, statements regarding the satisfaction of closing conditions relating to the offering and the anticipated use of proceeds from the offering. 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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