Cyclo Therapeutics Announces Publication of Phase 1 Data for Trappsol® Cyclo™ for the Treatment of Niemann-Pick Disease Type C1 (NPC1)

– Data published in official journal of the Society for Inherited Metabolic Disorders, Molecular Genetics and Metabolism

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

– Company advancing ongoing global pivotal Phase 3 study (TransportNPC™) evaluating Trappsol® Cyclo™ for NPC1

GAINESVILLE, FL – (Businesswire) – October 18, 2022 – 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 living with diseases, today announced the publication of positive data from its Phase 1 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. The manuscript titled, "Intravenous 2-hydroxypropyl-β-cyclodextrin (Trappsol® Cyclo™) demonstrates biological activity and impacts cholesterol metabolism in the central nervous system and peripheral tissues in adult subjects with Niemann-Pick Disease Type C1: Results of a phase 1 study" was published in the peer reviewed, official journal of the Society for Inherited Metabolic Disorders, *Molecular Genetics and Metabolism*.

Professor Caroline Hastings, MD, author of the published manuscript, Chair of the Company's Phase 3 Trappsol® Cyclo™ Program Steering Committee and Global Principal Investigator for the Company's ongoing TransportNPC™ study evaluating Trappsol® Cyclo™ for the treatment of NPC, added, "There remains a significant unmet need for a safe and effective therapy for NPC, a truly devastating neurodegenerative disease. The data seen to-date provide support for the capacity of Trappsol® Cyclo™ to stabilize disease progression with intravenous infusions in NPC. In these Phase 1 data, Trappsol® Cyclo™ cleared cholesterol from the liver and improved peripheral and central nervous system biomarkers of cholesterol homeostasis. I am pleased with the progress we've made and look forward to learning more about the full potential of Trappsol® Cyclo™ for the treatment of NPC."

About the Phase 1 Trial

The Phase 1 randomized, double-blind, parallel group study enrolled 13 subjects with NPC1 who received either 1500 mg/kg or 2500 mg/kg HPβCD intravenously every 2 weeks for a total of 7 doses (14 weeks). Subjects were 18 years or older, with a confirmed diagnosis of NPC1 and evidence of systemic involvement on clinical assessment. Pharmacokinetic evaluations in plasma and cerebrospinal fluid (CSF) were performed at the first and seventh infusions. Pharmacodynamic assessments included biomarkers of systemic cholesterol synthesis (serum lathosterol) and degradation (serum 4β-hydroxycholesterol), secondary sphingomyelin storage (plasma

lysosphingomyelin-509, now more accurately referred to as N-palmitoyl-Ophosphocholineserine [PPCS]), and CNS-specific biomarkers of neurodegeneration (CSF total Tau) and cholesterol metabolism (serum 24(S)-hydroxycholesterol [24(S)-HC]). Safety monitoring included assessments of liver and kidney function, infusion related adverse events, and hearing evaluations.

A total of ten subjects completed the study, with six (6) subjects at the 1500 mg/kg dose and four (4) subjects at the 2500 mg/kg dose. One subject withdrew following the first infusion after experiencing hypersensitivity pneumonitis, and 2 subjects withdrew after meeting a stopping rule related to hearing loss. Overall, Trappsol® Cyclo™ had an acceptable safety profile. The observed pharmacokinetic profile of Trappsol® Cyclo™ was similar following the first and seventh infusions, with a plasma half-life of 2 hours, a maximum concentration reached at 6 to 8 hours, and no evidence of accumulation. Serum biomarkers of cholesterol metabolism showed reduced synthesis and increased degradation. Compared to Baseline, filipin staining of liver tissue showed significant reductions of trapped unesterified cholesterol at both dose levels at Week 14. Plasma PPCS levels were also reduced. Trappsol® Cyclo™ was detected at low concentrations in the CSF (maximum, 33 μM) at both dose levels and persisted longer in CSF than in plasma. Total Tau levels in CSF decreased in most subjects. Serum levels of 24(S)-HC, a cholesterol metabolite from the CNS that is exported across the blood-brain barrier and into the circulation, decreased after both the first and seventh doses. Hence, pharmacodynamic assessments in both peripheral and CNS-related tissue show target engagement.

“These data reinforce our confidence in our Trappsol® Cyclo™ clinical program for the treatment of NPC. We believe that Trappsol® Cyclo™ has the ability to be a safe and effective treatment for both systemic and neurologic manifestations of NPC, an area of significant unmet need. We are pleased to publish these e data from our positive proof-of concept study in an important, scientific Journal such as *Molecular Genetics and Metabolism* and remain committed to exploring the potential of Trappsol® Cyclo™ as a potential life-changing medicine for the NPC community,” commented Lise Kjems, M.D. PhD. Chief Medical Officer of Cyclo Therapeutics.

Cyclo Therapeutics continues to advance enrollment in its ongoing pivotal Phase 3 study, TransportNPC™ evaluating Trappsol® Cyclo™ for the treatment of NPC1. The Phase 3 study intends to enroll at least 93 pediatric (age 3 years and older) and adult patients with NPC1 in at least 23 study centers in 9 countries. Eligible patients will be randomized 2:1 to receive either Trappsol® Cyclo™ or a placebo. Randomization will not be constrained based on patient age, nor will patient enrollment be gated by patient age. The study duration is 96 weeks and includes an interim analysis at 48 weeks. For more information about the Company’s Trappsol® Cyclo™ clinical program for the treatment of NPC1, visit www.ClinicalTrials.gov and reference identifiers NCT02939547, NCT02912793, NCT03893071 and NCT04860960.

Cyclo Therapeutics received Orphan Drug Designation for Trappsol® Cyclo™ to treat NPC1 in both the U.S. and EU and Fast Track and Rare Pediatric Disease Designations in the U.S. The Rare Pediatric Disease Designation is one of the chief requirements for sponsors to receive a Priority Review Voucher in the U.S. upon marketing authorization.

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 living with disease. The Company's Trappsol® Cyclo™, an orphan drug designated product in the United States and Europe, is the subject of four formal clinical trials for Niemann-Pick Disease Type C, a rare and fatal genetic disease, (www.ClinicalTrials.gov NCT02939547, NCT02912793, NCT03893071 and NCT04860960). The Company is conducting a Phase 2b clinical trial using Trappsol® Cyclo™ intravenously in early Alzheimer's disease based on encouraging data from an Expanded Access program for 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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