Rafael Holdings Announces Presentation of Preliminary Data from Ongoing Phase 3 TransportNPC™ Open-Label, Single-Arm Sub-Study in Patients Less Than 3 Years Old

First data on treatment of NPC1 with Trappsol® Cyclo™ (hydroxypropyl-beta-cyclodextrin) in this age group over a period of 48 weeks

At 48 weeks of the sub-study, 7 of 9 patients[1] showed stabilization or improvement in CGI-S score

Data presented at the15th International Congress of Inborn Errors of Metabolism (ICIEM)

NEWARK, N.J., Sept. 16, 2025 (GLOBE NEWSWIRE) -- Rafael Holdings, Inc. (NYSE: RFL; NYSE American: RFL-WT) announced today that data from Cyclo Therapeutics' Phase 3 TransportNPC™ open-label, single-arm sub-study evaluating Trappsol® Cyclo™ (hydroxypropyl-beta-cyclodextrin) for Niemann-Pick Disease Type C1 ("NPC1") were presented at the 15th International Congress of Inborn Errors of Metabolism (ICIEM).

The Company's ongoing TransportNPC™ study is a randomized, double-blind, placebo-controlled, parallel group, multicenter study designed to evaluate the safety, tolerability, and efficacy of 2,000 mg/kg doses of Trappsol® Cyclo™ administered intravenously and standard of care (SOC), compared to placebo administered intravenously and SOC alone, in patients with NPC1, a rare, genetic disease causing cholesterol accumulation in cells, leading to dysfunction primarily of the liver, lung, spleen and brain and premature death. The study duration is a 96-week study, with a 48-week comparative interim analysis. The TransportNPC™ study is the most comprehensive, controlled pivotal study with respect to patient size, global footprint, duration and clinical outcomes of an investigational therapy for NPC1. The study completed enrollment in May 2024. Additionally, the Company enrolled ten (10) patients in its single-arm sub-study per their adopted Pediatric Investigational Plan (PIP) treating newborns to 3 years of age. Two patients terminated participation in the sub-study after 48 weeks (caregiver decision). In accordance with the PIP, the sub-study will evaluate safety and tolerability, descriptive efficacy from both Investigator and patient perspectives via the Clinical Global Impression (CGI) scale and Pharmacokinetics. The sub-study is being conducted in countries outside of the United States per the Company's adopted PIP.

As part of the ICIEM Congress, Dr. Orna Staretz-Chacham, Senior neonatologist and metabolic specialist, Director of the Rare Disease Center at Soroka Medical Center, Israel and associate professor at the Faculty of Health Sciences, Ben-Gurion University of the Negev, Israel, and a Principal Investigator for the TransportNPC study presented a poster titled, "*Trappsol Cyclo Open Label Treatment in the TransportNPC Sub-Study in Patients Under the Age of 3 Diagnosed with Niemann Pick Disease Type C1."*

Summary Of Data Presented In Dr. Staretz-Chacham's Poster

- At baseline, sub-study patients had a mixture of very mild to severe disease based on the Clinical Global Impression - Severity (CGI-S) scale;
- Seven of nine patients who have reached 48 weeks participation in the study had an outcome of stabilization or improvement in CGI-S, with three patients showing improvement, and two patients showing deterioration of their CGI-S score;
- Adverse Event (AE) profile appears to be consistent with prior findings from earlier studies, and from the larger Phase 3 TransportNPC™ study that is irrespective of age and disease severity;
- As of May 14, 2025, there were 146 AEs, with the majority reported as mild (69%) or moderate (29%), 3 reported as severe and the remainder reported as Serious Adverse Events(SAEs) (14%); and
- No SAEs were considered by the principal investigators as related to or possibly related to study drug.

The potential clinical significance of these preliminary data, if any, will be evaluated based upon the full results of the sub-study.

Dr. Staretz-Chacham commented, "This growing body of promising preliminary findings from the TransportNPC™ sub-study continues to strengthen the potential of Trappsol® Cyclo™ to address the significant unmet medical need in the treatment of NPC1. Importantly, at 48 weeks, the clinical improvements seen in patients is encouraging, and we look forward to gathering additional data from this ongoing study and further evaluating the potential effect of Trappsol® Cyclo™ on progression of NPC1."

In addition to the poster presentation given by Dr. Staretz-Chacham, there was also an oral presentation given by Dr. Caroline Hastings, Pediatric hematologist oncologist, Director of Neuro-oncology, and Professor of Pediatrics at UCSF Benioff Children's Hospital Oakland, and a Principal Investigator for the TransportNPC titled, "*Hydroxypropyl-beta-cyclodextrin for the Long-Term Treatment of Niemann Pick Type C1: Efficacy and Safety Data from 4 Clinical Studies and the Ongoing Expanded Access Program."*

For more information about the Company's TransportNPC™ pivotal Phase 3 study, visit www.ClinicalTrials.gov and reference identifier 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 Trappsol® Cyclo™ (hydroxypropyl-beta-cyclodextrin)

Trappsol® Cyclo™ (hydroxypropyl-beta-cyclodextrin) is an investigational drug designed to deliver a first-in-class propriety cyclodextrin formulation that is administered intravenously (IV) in order to mobilize lysosomal cholesterol. Trappsol® Cyclo™ is designed to directly impact the root cause of Niemann-Pick Disease Type C1 (NPC1) by mobilizing cholesterol from late-stage endosomes and lysosomes. Trappsol® Cyclo™ has also been found in the completed Phase 1 study (CTD-TCNPC-101) and a Phase 2 study (CTD-TCNPC-201) to cross the blood-brain barrier after IV administration, suggesting that therapeutic concentrations have the potential to be reached in the central nervous system over the infusion time window. The potential clinical significance of those concentrations, if any, will be further evaluated based upon the results of the Phase 3 TransportNPC study.

About the Trappsol® Cyclo™ Study Program

The ongoing Phase 3 TransportNPC study is a prospective, randomized, double-blind, placebo-controlled study evaluating the safety and efficacy of Trappsol® Cyclo™ (hydroxypropyl-beta-cyclodextrin) administered intravenously (2000 mg/kg dose every 2 weeks) in patients aged 3 years and older with confirmed diagnosis of Niemann-Pick Disease Type C1 (NPC1) (CTD-TCNPC-301; NCT04860960). The TransportNPC study enrolled 94 patients in over 25 sites across 13 countries. The study duration is 96 weeks. An unblinded interim analysis was reviewed by an independent DMC when all patients reached 48 weeks. In June 2025, Cyclo Therapeutics announced the continuation of the study following the independent Data Monitoring Committee (DMC) review of safety and efficacy data at the prespecified 48-week interim analysis. As a result, the study is expected to continue for the full 96 weeks. A Phase 3 open-label extension study of up to 96 weeks follows the interventional study.

The primary endpoints of the Phase 3 TransportNPC study are the mean change in the 4-domain NPC Clinical Severity Scale (4D-NPC-CSS) score in the United States and the 5-domain NPC Clinical Severity Scale (5D-NPC-CSS) score in Europe. The 4D-NPC-CSS score (inclusive of ambulation, fine motor, speech, and swallow) and 5D-NPC-CSS score (inclusive of ambulation, fine motor, speech, swallow, and cognition) are measures of NPC disease progression that look at items that patients with NPC and their caregivers and physicians have identified as most relevant. Important secondary and exploratory endpoints will also be assessed across measures of disease activity.

As part of the Phase 3 study, a Phase 3 open-label sub-study is being conducted in NPC1 patients from birth to 3 years of age outside of the United States. Ten patients have been recruited and are continuing in the study. Outcomes for the sub-study include safety, clinical, and caregiver impression of the disease.

Cyclo Therapeutics has completed 2 studies, including a Phase 1 study (CTD-TCNPC-101; NCT02912793) and a Phase 2 study (CTD-TCNPC-201; NCT02912793). Patients who completed the Phase 1 study continue to receive Trappsol® Cyclo™ treatment in the ongoing Phase 1 open-label extension study (CTD-TCNPC-102; NCT03893071).

About Niemann-Pick Disease Type C1 (NPC1)

Niemann-Pick Disease Type C1 (NPC1) is a rare genetic disease that affects approximately 1 in 100,000 live births globally and often leads to premature death. NPC1 is characterized by an inability for cells to transport and process cholesterol, resulting in excessive amounts of cholesterol accumulating and damaging affected organs, including the liver, spleen, and brain. The disease can be life-limiting, with symptoms including progressive intellectual decline, loss of motor skills, seizures, and dementia. Approximately 95% of individuals with NPC have mutations in the NPC1 gene, and 5% have mutations in the NPC2 gene.

About Rafael Holdings, Inc.

Rafael Holdings, Inc. is a biotechnology company with interests in clinical and early-stage pharmaceutical companies including a 100% interest in Cyclo Therapeutics, LLC, a biotechnology company dedicated to developing Rafael's lead clinical candidate, Trappsol® Cyclo™ (hydroxypropyl-beta-cyclodextrin), which is being evaluated in clinical trials, including an ongoing phase 3 trial for the potential treatment of Niemann-Pick Disease Type C1 (NPC1), a rare, fatal, and progressive genetic disorder. Rafael also holds a majority interest in LipoMedix Pharmaceuticals Ltd., a clinical stage pharmaceutical company, Barer Institute Inc., a wholly owned preclinical cancer metabolism research operation, a majority interest in Cornerstone Pharmaceuticals, Inc., formerly known as Rafael Pharmaceuticals Inc., a cancer metabolism-based therapeutics company, a majority interest in Rafael Medical Devices, LLC, an orthopedic-focused medical device company developing instruments to advance minimally invasive surgeries, and a majority interest in Day Three Labs, Inc., a company which empowers third-party manufacturers to reimagine their existing cannabis offerings, enabling those third-party manufacturers to bring to market better, cleaner, more precise and predictable versions by utilizing Day Three's technology and innovation like Unlokt™.

About Cyclo Therapeutics, LLC

Cyclo Therapeutics, LLC ("Cyclo") is a wholly owned subsidiary of Rafael Holdings, Inc. (NYSE: RFL). Cyclo is a clinical-stage biotechnology company dedicated to developing life-changing medicines through science and innovation for patients and families living with rare and neurodegenerative diseases. The company's investigational drug Trappsol® Cyclo™ (hydroxypropyl-beta-cyclodextrin), which is orphan drug designated in the United States and Europe, is the subject of 4 formal clinical trials for Niemann-Pick Disease Type C1, a rare and fatal genetic disease, (www.ClinicalTrials.gov NCT02939547, NCT02912793, NCT03893071 and NCT04860960). Cyclo is also conducting a phase 2b clinical trial using Trappsol® Cyclo™ intravenously in early Alzheimer's disease (NCT05607615) based on encouraging data from an Expanded Access program for Alzheimer's disease (NCT03624842).

Forward Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this press release that do not relate to matters of historical fact should be considered forward-looking statements, including without limitation statements regarding our expectations surrounding the potential safety, efficacy, and regulatory and clinical progress of our product candidates; plans regarding the further evaluation of clinical data; and the potential of our pipeline, including our internal cancer metabolism research programs. These statements are neither promises nor guarantees, but involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements, including, but not limited to, those disclosed under the caption "Risk Factors" in our Annual Report on Form 10-K for the year ended July 31, 2024, and our other filings with the SEC. These factors could cause actual results to differ materially from those indicated by the forward-looking statements made in this press release. Any such forward-looking statements represent management's estimates as of the date of this press release. While we may elect to update such forward-looking statements at some point in the future, we disclaim any obligation to do so, even if subsequent events cause our views to change.

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[1] Patient 10 had not reached the 48 week treatment at the data cutoff used for this poster