Rafael Holdings Announces Continuation of its Phase 3 Study for the Treatment of Niemann-Pick Disease Type C1 (NPC1) Following Independent Data Monitoring Committee (DMC) Review of Prespecified 48-Week Interim Data

Phase 3 TransportNPC study to continue based on the independent DMC review of safety and efficacy data at prespecified 48-week interim analysis

Data on the investigational candidate Trappsol® Cyclo™ (hydroxypropyl-beta-cyclodextrin), indicates that it is well-tolerated and has a safety profile consistent with the previously completed phase 1 and 2 studies and ongoing phase 1 open-label extension study

NEWARK, N.J., June 18, 2025 (GLOBE NEWSWIRE) -- Rafael Holdings, Inc. (NYSE: RFL; NYSE American: RFL-WT) announced today that its subsidiary Cyclo Therapeutics' 96-week pivotal phase 3 TransportNPC study evaluating intravenous (IV) Trappsol® Cyclo™ for the potential treatment of Niemann-Pick Disease Type C1 (NPC1) will continue based on the independent Data Monitoring Committee (DMC) review of safety and efficacy data at the prespecified 48-week interim analysis. Additionally, the Food and Drug Administration (FDA) has accepted the statistical analysis plan for the TransportNPC study. These developments underscore the company's continuing commitment to advancing its lead investigational candidate through late-stage clinical development to support global regulatory and commercial readiness.

"NPC is a rare, fatal, and progressive genetic disease, and there is a need for safe and effective treatment that addresses its root cause," said Howard S. Jonas, CEO of Rafael Holdings. "The recommendation made by the independent DMC to continue the study to 96 weeks, boosts our determination to the continued clinical evaluation of the potential of TrappsolCyclo as a systemic and neurological treatment option for people living with NPC1. We recently enhanced our financial position with the closing of a $25 million rights offering earlier this month which will support our strategic objectives."

"It is a privilege to lead and continue the TransportNPC study, the most comprehensive, controlled pivotal study of an investigational therapy for NPC ever conducted in terms of patient size, global footprint, duration, and clinical outcomes," commented N. Scott Fine, Chief Executive Officer of Cyclo Therapeutics. "We are grateful to the study participants, their families, investigators, and clinical trial sites who are dedicated to this important research."

About Trappsol® Cyclo™ (hydroxypropyl-beta-cyclodextrin)

Trappsol® Cyclo™ (hydroxypropyl-beta-cyclodextrin) is a first-in-class propriety cyclodextrin formulation administered intravenously (IV) that mobilizes lysosomal cholesterol. TrappsolCyclo is designed to directly impact the root cause of Niemann-Pick Disease Type C1 (NPC1) by mobilizing cholesterol from late-stage endosomes and lysosomes. TrappsolCyclo has also been shown to cross the blood-brain barrier after IV administration, suggesting that therapeutic concentrations are reached in the central nervous system over the infusion time window. The potential clinical significance of those concentrations will be evaluated based upon the results of the phase 3 TransportNPC study.

About the TrappsolCylco Study Program

The phase 3 TransportNPC study is a prospective, randomized, double-blind, placebo-controlled study evaluating the safety and efficacy of TrappsolCyclo (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 and recommended to continue the study 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 TrappsolCyclo 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 them 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), an orphan drug designated product 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 TrappsolCyclo 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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