

Rafael Holdings Announces Topline Results from the Pivotal Phase 3 TransportNPC™ Study of Trappsol® Cyclo™ in Niemann-Pick Disease Type C (NPC)

Trappsol® Cyclo™ did not achieve statistical significance but demonstrated a directionally favorable treatment effect versus placebo on the primary endpoint of change in the 4-domain NPC Clinical Severity Scale (4DNPCSS) at Week 96

A prespecified analysis in patients receiving background miglustat and/or leucine therapy, representing approximately 83% of the study population, showed a statistically significant effect on the 4DNPCSS

Trappsol® Cyclo™ demonstrated a well-tolerated safety and tolerability profile consistent with previous studies, with no new safety signals observed

Based upon its previously announced pre-NDA meeting, the Company remains on track to submit the NDA in the fourth quarter of 2026, consistent with prior guidance

Company to host investor conference call and webcast today, September 30, at 8:30 a.m. ET

NEWARK, N.J., Sept. 30, 2026 (GLOBE NEWSWIRE) -- Rafael Holdings, Inc. (NYSE: RFL) today announced topline efficacy and safety data from its Cyclo Therapeutics, LLC subsidiary's pivotal Phase 3 TransportNPC™ study (CTD-TCNPC-301) evaluating Trappsol® Cyclo™ (intravenous hydroxypropyl-β-cyclodextrin) in 94 patients diagnosed with Niemann-Pick Disease Type C (NPC). Trappsol® Cyclo™ was well tolerated and demonstrated a directionally favorable treatment effect on the primary endpoint, although the result did not achieve statistical significance. Notably, a prespecified analysis in patients receiving background miglustat and/or leucine therapy demonstrated a statistically significant and clinically meaningful treatment benefit. Based upon its previously announced pre-NDA meeting with the FDA, the Company remains on track to submit an NDA for Trappsol® Cyclo™ in the fourth quarter of 2026.

The Phase 3 TransportNPC™ Study

The global, double-blind, placebo-controlled Phase 3 TransportNPC™ study (CTD-TCNPC-301) enrolled 94 patients with NPC, ranging in age from 3 to 70 years. Patients were randomized to receive 2000 mg/kg of Trappsol® Cyclo™ administered intravenously every two weeks (n=63) or placebo (n=31) for a 96-week period to assess change in 4DNPCSS.

A prespecified analysis also evaluated change in 4DNPCSS among patients receiving background miglustat therapy and/or leucine (a food supplement available in some European countries), representing approximately 83% of the study population.

- **Primary endpoint:** Trappsol® Cyclo™ demonstrated a directionally favorable treatment effect compared with placebo, indicating slowing of disease progression by 64% on change in 4DNPCSS at Week 96 (LS mean change from baseline of 0.46 vs 1.28 points; difference 0.81 points [95% CI 2.04, 0.41]; p=0.19), the result did not achieve statistical significance.
- **Prespecified analysis:** Among patients receiving background miglustat and/or leucine therapy (n=78), Trappsol® Cyclo™ indicating slowing of disease progression by 71% compared with placebo at Week 96 (LS mean change from baseline of 0.46 vs 1.57 points; difference 1.11 points [95% CI 2.19, 0.02]; p=0.046).

Safety and Tolerability

Over the 96-week treatment period, the safety profile of Trappsol® Cyclo™ was well tolerated. Adverse events were largely consistent with the underlying disease. Treatment-emergent adverse events (TEAEs) were reported as follows: Trappsol® Cyclo™, 93.8%; placebo, 100.0%. Serious TEAEs occurred more frequently with Trappsol® Cyclo™, 35.9%, than with placebo 16.7%; however, serious TEAEs considered related to treatment were reported at similar rates 3.1% vs 3.3%. Hearing-related TEAEs were reported by 15.6% of participants receiving Trappsol® Cyclo™ and 13.3% receiving placebo, and most were mild or moderate in severity. One treatment-related event of bilateral deafness in the Trappsol® Cyclo™ group was severe. No TEAEs resulted in death, and one participant in the Trappsol® Cyclo™ group discontinued the study early because of a TEAE.

Separate Overall Survival Analysis

The Company also conducted a separate overall survival analysis comparing patients with infantile-onset NPC treated with Trappsol® Cyclo™ across its clinical development program with well-matched external controls from the International Niemann-Pick Disease Registry (INPDR). The external control cohort included patients with similar baseline characteristics and disease progression. Results from the analysis provide supportive evidence of a treatment-associated survival benefit with Trappsol® Cyclo™.

Specifically, these data indicated:

- **INPDR comparison:** Treatment with Trappsol® Cyclo™ (n=41) was associated with an 85% reduction in the risk of mortality compared with matched INPDR controls (n=93), HR=0.154; 95% CI: 0.025-0.950; p=0.044.
- **Expanded historical control analysis:** In a secondary analysis that expanded the control group to include additional matched historical cohorts from published natural history studies (n=133), treatment with Trappsol® Cyclo™ (n=41) was associated with a 94% reduction in the risk of mortality, HR=0.057; 95% CI: 0.011-0.306; p=0.0008.

The consistency and magnitude of the observed survival associations across both analyses provide additional supportive evidence for the potential clinical benefit of Trappsol[®] Cyclo[™] in patients with infantile-onset NPC.

"The Phase 3 TransportNPC study is the most comprehensive trial in NPC conducted to date," said Dr. Karen Mullen, Chief Medical Officer of Rafael Holdings. "We believe the totality of the data shared today provide a compelling rationale for the continued advancement of Trappsol Cyclo and its potential to offer clinically meaningful treatment benefit for those living with this devastating disease. We remain steadfast in our efforts to advance Trappsol Cyclo and are deeply grateful to the clinical investigators, patients, and caregivers whose courage and commitment were vital to completing this study."

"NPC is a devastating, heterogeneous disease, and preserving function and stabilizing symptoms are critical," said Dr. Caroline Hastings, Professor of Pediatric Hematology and Neurology at UCSF Benioff Children's Hospital Oakland. "As a clinician who has cared for these patients for many years, I am encouraged by the clinically meaningful TransportNPC results. The study was rigorously conducted, and its findings align with the two prior trials for Trappsol Cyclo across a decade of development. I am hopeful that these data can move us closer to delivering a much-needed therapeutic option for families facing profound unmet need."

NDA On Track for Fourth Quarter 2026

The Company remains on track to submit an NDA for Trappsol[®] Cyclo[™] to the U.S. Food and Drug Administration in the fourth quarter of 2026 based upon its previously announced pre-NDA meeting. The topline data, complete dataset and overall survival analysis remain subject to full analysis and FDA regulatory review. The Company also plans to present the full results at an upcoming medical meeting.

Conference Call Information:

Date: Wednesday, September 30, 2026

Time: 8:30 a.m. ET

Domestic Dial-in Number: 1-877-425-9470

International Dial-in Number: 1-201-389-0878

Conference ID:13763049

Webcast Participant Link: https://viaid.webcasts.com/starthere.jsp?ei=1777956&tp_key=73c1065384

About Rafael Holdings, Inc.

Rafael Holdings, Inc. is a biotechnology company that develops pharmaceuticals and holds interests in clinical and early-stage companies that develop pharmaceuticals and medical devices. Our lead candidate is Trappsol[®] Cyclo[™], and we have completed a pivotal Phase 3 study in NPC and are preparing for a planned NDA submission later this year. Niemann-Pick Disease Type C ("NPC") is a rare, fatal and progressive genetic disorder. We also hold interests in other clinical-stage and early-stage pharmaceutical development companies and an orthopedic-focused medical device company.

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. 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, the risk that the FDA may not accept for filing or approve an NDA for Trappsol[®] Cyclo[™] based on the available data, and those disclosed under the caption "Risk Factors" in our Annual Report on Form 10-K for the year ended July 31, 2025, our subsequent Quarterly Reports on Form 10-Q, 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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