Rapport Announces Positive Topline Results from Phase 2a Clinical Trial of RAP-219 in Patients with Focal Onset Seizures

September 8, 2025

- Trial met primary long episode endpoints with high statistical significance, and RAP-219 was generally well tolerated
- Patients achieved 77.8% reduction in clinical seizures (p=0.01), with 24% achieving seizure freedom for the 8-week treatment period (p<0.0001)
- Data support advancement of RAP-219 into Phase 3 registrational trials
- Company to host a conference call today at 8:00 a.m. ET

BOSTON and SAN DIEGO, Sept. 08, 2025 (GLOBE NEWSWIRE) -- Rapport Therapeutics, Inc. (Nasdaq: RAPP) (“Rapport” or the “Company”), a clinical-stage biotechnology company dedicated to the discovery and development of small molecule precision medicines for patients with neurological or psychiatric disorders, today announced that the Phase 2a clinical trial of RAP-219 (RAP-219-FOS-201) in patients with drug-resistant focal onset seizures met its primary endpoint, demonstrating a statistically significant reduction in long episodes (LEs) – an objective electrographic biomarker for clinical seizure reduction – compared with baseline over the 8-week treatment period. In the trial, RAP-219 also demonstrated a statistically significant and clinically meaningful reduction in clinical seizures compared with baseline. RAP-219 was generally well tolerated. The Company plans to advance RAP-219 into two Phase 3 pivotal trials in the third quarter of 2026. RAP-219 is a potential first-in-class, investigational TARPγ8-specific AMPAR negative allosteric modulator.

“Despite the available therapies, up to 40% of patients with focal epilepsy continue to experience seizures. There is still tremendous need for additional effective anti-seizure medications with novel mechanisms of action. Physicians and patients need new options that deliver meaningful benefits and the potential to offer the promise of seizure freedom,” said Jacqueline French, M.D., principal investigator of the study and professor in the Department of Neurology at NYU Langone Health's Comprehensive Epilepsy Center. “This trial represents the first time a novel antiseizure medication was evaluated in focal seizure patients using the RNS system with an objective biomarker of seizure activity. The magnitude of the reduction in clinical seizure frequency seen in this trial, and the corroboration of the clinical activity from the objective biomarker, give me confidence that a medication like RAP-219 has the potential to be a highly effective ASM for drug-resistant focal seizure patients."

RAP-219 Phase 2a Focal Onset Seizures Trial Design
The Phase 2a clinical trial of RAP-219 is a proof-of-concept, multi-center, open-label study designed to evaluate the efficacy, safety, and tolerability of RAP-219 in adult patients with drug-resistant focal onset seizures. The trial enrolled 30 patients with focal onset seizures who had an implanted RNS® System. Patients received 0.75 mg RAP-219 oral tablet daily for 5 days followed by 1.25 mg RAP-219 oral tablet daily for the remainder of the 8-week treatment period. The primary efficacy endpoint was the change in frequency of RNS-recorded long episodes (LEs) in patients with focal onset seizures evaluated both as the proportion of responders achieving ≥30% reduction in LEs from baseline, which has been demonstrated to be associated with ≥50% reduction in clinical seizures, and median percent change from baseline in LE frequency. Secondary endpoints include clinical seizure frequency reductions (assessed as median percent change from baseline, responder proportion who achieve a ≥50% reduction in seizure frequency, and seizure freedom), safety, and tolerability.

Topline Results
Topline efficacy and tolerability data shared today are for the treatment period (weeks 1-8). The Phase 2a trial 8-week follow-up period is currently ongoing.

Key Efficacy Results:

Efficacy findings from the Phase 2a trial achieved statistically significant results for primary LE endpoints and key secondary endpoints of clinical seizures. In the 8-week treatment period, 85.2% of patients achieved ≥30% reduction in LEs from baseline (p<0.0001), 72.0% achieved ≥50% reduction in clinical seizures from baseline (p<0.0001), and 24% of patients achieved seizure freedom (p<0.0001). Topline efficacy data are shown in the following table.

Outcome Measures for 8-Week Treatment Period		**RAP-219**
Long Episodes (LEs)— primary efficacy endpoint mITT: N=27	Patients with ≥30% reduction in LEs from baseline	85.2% (p<0.0001)
	Median reduction in LE frequency from baseline	71.0% (p=0.0001)

Clinical Seizures (CS)— key secondary endpoint mITT-CS: N=25	Patients with ≥50% reduction in clinical seizures from baseline	72.0% (p<0.0001)
	Patients who achieved seizure freedom	24.0% (p<0.0001)
	Median reduction in clinical seizure frequency from baseline	77.8% (p=0.01)
mITT: patients with ≥3 weeks of treatment, ≥70% adherence, and no RNS system detection or stimulation setting changes. mITT-CS: mITT with clinical seizures in prospective baseline. Statistical methods: For responder analysis for LEs, clinical seizure reduction ≥50%, and seizure freedom, two-tailed p-values were calculated using a one-sample exact binomial of proportions against a null hypothesis of 10%, 20%, and 1.5% respectively. For median reduction from baseline in LEs and clinical seizures, two-tailed p-values were calculated from the Wilcoxon signed rank test against a null hypothesis of 0% and 20%, respectively.		

Key Safety and Tolerability Results:

RAP-219 was generally well-tolerated in the trial, with the majority of treatment-emergent adverse events (TEAEs) being mild and a low discontinuation rate:

- No serious adverse events (SAEs) were reported during the treatment period
- All TEAEs reported were mild (78.5%) or moderate (21.5%) in severity (Grades 1 or 2)
- 3 (10%) patients discontinued treatment due to TEAEs
- The most common TEAEs reported (≥ 10% incidence) were dizziness (n= 8, 26.7%), headache (n = 5, 16.7%), fatigue (n = 4, 13.3%), fall (n = 3, 10.0%), nausea (n = 3, 10.0%), and somnolence (n = 3, 10.0%).

“The efficacy data and tolerability profile seen in the Phase 2a trial demonstrate RAP-219’s potential to be an important treatment for patients with drug-resistant focal onset seizures. What’s particularly encouraging is the consistency of the significant improvements seen in the long episode biomarker responses and the clinical seizure reductions,” said Abe Ceesay, chief executive officer of Rapport. “With these data and RAP-219’s emerging best-in-class profile, if approved, we believe RAP-219 could address a significant unmet need among patients, with the potential to support broad adoption among epileptologists and neurologists treating patients living with drug-resistant focal seizures.”

Trial Patient Demographics and Baseline Characteristics
The demographics and baseline characteristics of patients enrolled in the Phase 2a study are consistent with that of patients expected in future registrational trials. The trial enrolled 12 women and 18 men, and the mean age of patients enrolled was 40.1 years. The mean age of enrolled patients at the time of their first seizure was 16.6 years. Patients were taking a median of 3 concomitant antiseizure medications, with the highest proportion of patients taking lamotrigine (50%), levetiracetam (40%), and cenobamate (37%) medications.

“We are excited by the strength of these data in both the electrographic biomarker and clinical seizure reductions. These results give us the confidence to progress RAP-219 into its next stage of clinical development,” said Dr. Jeffrey Sevigny, M.D., chief medical officer of Rapport. “Importantly, the baseline characteristics of patients enrolled, together with the broad cortical expression of TARPγ8 and the robust results in the trial, give us confidence in the translatability of the data into the Phase 3 drug-resistant focal onset seizure patient population. Given the persistent unmet need in focal epilepsy, we plan to move into two Phase 3 trials using traditional clinical seizure endpoints, with initiation expected in the third quarter of 2026.”

Rapport plans to hold an end-of-Phase 2 meeting with the U.S. Food and Drug Administration (FDA) in the fourth quarter of 2025 and plans to initiate pivotal trials in the third quarter of 2026. The Company also expects to present additional efficacy analyses and 8-week follow-up results in 2026.

Additional RAP-219 Development Plans
By the end of 2025, Rapport plans to initiate an open-label long term safety trial to allow patients enrolled in the RAP-219-FOS-201 trial to continue on RAP-219. Preliminary results of the trial are expected in the second half of 2026.

Additionally, Rapport continues development of a long-acting injectable (LAI) formulation of RAP-219. Up to half of patients are nonadherent to prescribed ASMs, which can present a significant issue in optimizing treatment benefit and lead to potential breakthrough seizures. The Company believes a LAI formulation has the potential to improve patient adherence and expand the potential clinical utility across all of RAP-219’s indications.

Outside of epilepsy, Rapport is evaluating RAP-219 in a Phase 2 trial in bipolar mania. The trial is currently enrolling patients and is on track, with topline results expected in the first half of 2027. An update on the plan and timeline for initiation of a Phase 2 trial in diabetic peripheral neuropathic pain is expected later in 2025.

Conference Call Information

Rapport Therapeutics will host a conference call and live webcast at 8:00 a.m. ET / 5:00 a.m. PT on September 8, 2025, to discuss the data and provide a business update. Individuals interested in listening to the live conference call may do so by dialing (800) 715-9871 for U.S callers and (646) 307-1963 for other locations and reference conference ID 4762775, or from the webcast link in the “Investors” section of the Company's website at www.rapportrx.com. A webcast replay will be available in the investor relations section on the Company’s website for 90 days following the completion of the call.

About RAP-219
RAP-219 is a potential first-in-class, clinical-stage TARPγ8-specific AMPA receptor (AMPAR) negative allosteric modulator (NAM). Whereas AMPARs are distributed widely in the central nervous system, the receptor associated protein (RAP) TARPγ8 is expressed only in discrete brain regions, including the hippocampus and neocortex, where focal seizures often originate. By contrast, TARPγ8 has minimal expression in the hindbrain, where drug effects are often associated with intolerable adverse events. With this precision approach, the Company believes RAP-219 has the potential to provide a differentiated profile as compared to traditional neuroscience medications. Due to the role of AMPA biology in various neurological disorders and the selective targeting of TARPγ8, the Company believes RAP-219 has pipeline-in-a-product potential and is evaluating the compound as a transformational treatment for patients with focal onset seizures, bipolar disorder, and peripheral neuropathic pain.

About Rapport Therapeutics
Rapport Therapeutics is a clinical-stage biotechnology company dedicated to discovering and developing small molecule precision medicines for patients with neurological or psychiatric disorders. The Company’s founders have made pioneering discoveries related to the function of receptor associated proteins (RAPs) in the brain. Their findings form the basis of Rapport’s RAP technology platform, which enables a differentiated approach to generate precision small molecule product candidates with the potential to overcome many limitations of conventional neurology drug discovery. Rapport’s precision neuroscience pipeline includes the Company’s lead investigational drug, RAP-219, designed to achieve neuroanatomical specificity through its selective targeting of a RAP expressed in only discrete regions of the brain. The Company is currently pursuing RAP-219 as a potential treatment for drug-resistant focal onset seizures, bipolar mania and diabetic peripheral neuropathic pain. Additional preclinical and late-stage discovery stage programs are also underway, including targeting chronic pain and hearing disorders.

Availability of Other Information About Rapport Therapeutics
Rapport Therapeutics uses and intends to continue to use its Investor Relations website and LinkedIn (Rapport Therapeutics) as a means of disclosing material nonpublic information and for complying with its disclosure obligations under Regulation FD. Accordingly, investors should monitor the Company’s Investor Relations website and LinkedIn, in addition to following the Company’s press releases, SEC filings, public conference calls, presentations, and webcasts. The contents of the Company’s website or social media shall not be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended.

Forward-Looking Statements
Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934, each as amended. The words “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “plan,” “potential,” “predict,” “project,” “should,” “target,” “will,” “would” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. These forward-looking statements include, but are not limited to, express or implied statements regarding: the clinical development of RAP-219 for the treatment of focal onset seizures, bipolar mania, and diabetic peripheral neuropathic pain, including the initiation, timing, progress and results of the Company’s Phase 3 clinical trials in focal onset seizures, and a Phase 2 clinical trial of RAP-219 in bipolar mania, as well as other planned clinical trials; expectations for the activity, tolerability, and commercial potential of RAP-219; the future release of data from the ongoing 8-week follow-up period of the Phase 2a trial for RAP-219; expectations for a LAI formulation of RAP-219 and the potential of a LAI to improve patient adherence; the Company’s expectations for upcoming regulatory interactions; the potential of Rapport’s RAP technology platform; and expectations for Rapport’s uses of capital, expenses and financial results.

Forward looking statements are based on management’s current expectations and are subject to risks and uncertainties that could negatively affect Rapport’s business, operating results, financial condition and stock value. Factors that could cause actual results to differ materially from those currently anticipated include: risks relating to the Company’s research and development activities; Rapport’s ability to execute on its strategy including obtaining the requisite regulatory approvals on the expected timeline, if at all; uncertainties relating to preclinical and clinical development activities; the Company’s dependence on third parties to conduct clinical trials, manufacture its product candidates and develop and commercialize its product candidates, if approved; Rapport’s ability to attract, integrate and retain key personnel; risks related to the Company’s financial condition and need for substantial additional funds in order to complete development activities and commercialize a product candidate, if approved; risks related to regulatory developments and approval processes of the U.S. Food and Drug Administration and comparable foreign regulatory authorities; risks related to establishing and maintaining Rapport’s intellectual property protections; and risks related to the competitive landscape for Rapport’s product candidates; as well as other risks described in “Risk Factors,” in the Company’s Annual Report on Form 10-K and most recent Quarterly Report on Form 10-Q, as well as discussions of potential risks, uncertainties, and other important factors in Rapport’s subsequent filings with the Securities and Exchange Commission. Any forward-looking statements represent Rapport’s views only as of today and should not be relied upon as representing its views as of any subsequent date. Rapport expressly disclaims any obligation or undertaking to release publicly any updates or revisions to any forward-looking statements contained herein to reflect any change in its expectations or any changes in events, conditions or circumstances on which any such statement is based, except as required by law, and claims the protection of the safe harbor for forward-looking statements contained in the Private Securities Litigation Reform Act of 1995.

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