Rapport Therapeutics Presents RAP-219 Focal Onset Seizure Phase 2a Follow-up Period Results Demonstrating Sustained Seizure Reduction at the 2026 American Academy of Neurology Annual Meeting

April 21, 2026

Clinically meaningful efficacy demonstrated in the 8-week follow-up period (weeks 9-16), with a 90% median reduction in clinical seizures over baseline in weeks 9-12 and a 59% median reduction in clinical seizures over baseline in weeks 13-16

New data demonstrate that RAP-219 has a half-life of approximately 22 days

RAP-219 was generally well tolerated throughout treatment and follow-up periods

BOSTON and SAN DIEGO, April 21, 2026 (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 results from the follow-up period of its Phase 2a trial of RAP-219 in focal onset seizures (FOS) in a late-breaker podium presentation at the 2026 American Academy of Neurology (AAN) Annual Meeting, taking place April 18–22, 2026 in Chicago.

In the Phase 2a trial, patients received RAP-219 for 8 weeks and then entered an 8-week follow-up period after treatment ended to evaluate the effect of RAP-219 on long episodes (LEs) – an objective biomarker of epileptiform activity with >90% median concordance with electrographic seizures in this trial – and clinical seizures. Due to RAP-219's long half-life, therapeutic levels of RAP-219 were sustained, resulting in continued biomarker and clinical responses in the 8-week follow-up period. In the first four weeks of follow-up (weeks 9-12), RAP-219 showed even greater reductions in LEs and clinical seizures than were observed during the 8-week treatment period. Clinically meaningful improvements over baseline continued through the second four weeks of follow-up (weeks 13-16).

Consolidated Treatment Period and 8-Week Follow-up Period Results

Based on pharmacokinetic (PK) data collected across the Company's Phase 1 and Phase 2 trials and further supported by population PK modeling, RAP-219 is now estimated to have an approximately 22-day half-life, compared to the prior reported estimate of 14 days. RAP-219's plasma concentrations remained within the targeted therapeutic range over the 8-week follow-up period, with observed concentrations consistent with ≥75% receptor occupancy in weeks 9-12 and 60% to 75% receptor occupancy in weeks 13-16.

Patients experienced an 80% median reduction in LEs and 90% median reduction in clinical seizures compared to baseline in weeks 9-12 and a 68% median reduction in LEs and 59% median reduction in clinical seizures compared to baseline in weeks 13-16.

Median Percent Reduction	Treatment Period Weeks 1-4	Treatment Period Weeks 5-8	Follow-up Period Weeks 9-12	Follow-up Period Weeks 13-16
Long Episodes (LEs)	75% (n=27; p<0.0001)	75% (n=26; p=0.0029)	**80%** (n=27; p<0.0001)	**68%** (n=27; p=0.0317)
Clinical Seizures	85% (n=25; p=0.0007)	77% (n=24; p=0.0392)	**90%** (n=25; ns)	**59%** (n=25; p=0.0115)
Median percent change statistical comparisons used the Wilcoxon signed-rank test to determine if the median percentage change in LE from baseline was greater than 0% and if the median percent change in clinical seizures from baseline was greater than 20%. NS = not significant.				

Additionally, the Company evaluated LE and clinical seizure outcomes over weeks 1–12 and 1–16, which encompassed the 8-week treatment period and some or all of the subsequent follow-up. Patients experienced a 71% median reduction in LEs and 75% median reduction in clinical seizures compared to baseline in weeks 1-12 and a 69% median reduction in LEs and 68% median reduction in clinical seizures compared to baseline in weeks 1-16. Seizure freedom rates were 20% for weeks 1-12 and 12% for weeks 1-16, compared to 24% for the 8-week treatment period.

Outcome Measure	Treatment Period Weeks 1-8	Weeks 1-12 (Treatment Period Weeks 1-8 and Follow-up Period Weeks 9-12)	Weeks 1-16 (Treatment Period Weeks 1-8 and Follow-up Period Weeks 9-16)
Median Percent Reduction, Long Episodes (LEs)	71% (n=27, p=0.0001)	**71%** (n=27, p<0.0001)	**69%** (n=27, p=0.001)
Median Percent Reduction, Clinical Seizures	78% (n=25, p=0.01)	**75%** (n=25; p=0.0068)	**68%** (n=25, p=0.0072)
100% Responders (Clinical Seizure Freedom)	24% (n=25, p<0.0001)	**20%** (n=25, p<0.0001)	**12%** (n=25, p<0.0001)
Median percent reduction: Null hypothesis = 0.2 for CS, and 0 for LE, respectively. 100% responder (CS) null hypothesis = 0.015. Weeks 1–12 and 1–16 analyses were post-hoc exploratory. No multiplicity control was applied.			

RAP-219 was generally well tolerated during the follow-up period, with two patients experiencing mild (Grade 1) treatment-related adverse events. Three patients experienced a serious adverse event during the follow-up period; none were considered by the investigator to be related to RAP-219.

“Clinical outcomes improved further during the first four weeks after dosing ended, highlighted by a 90% reduction in clinical seizures, and consistent with the observed PK,” said William Motley, M.D., D. Phil., RAP-219 program leader. “These data demonstrate RAP-219’s treatment effect in focal onset seizures out to 16 weeks of therapeutic drug exposure and furthermore show a consistent dose-exposure-clinical outcome relationship that provides us confidence in the doses we’re advancing in Phase 3 trials.”

“We believe these follow-up period results underscore the sustained activity of RAP-219 beyond the 8-week treatment period,” said Jeffrey Sevigny, M.D., chief medical officer of Rapport. “Together with the treatment period data, these findings further support our view that RAP-219 has the potential to become a differentiated, best-in-class therapy and an important new treatment option for patients with focal onset seizures.”

Two pivotal Phase 3 trials of RAP-219 in FOS – *FOCUS 1* (RAP-219-FOS-301) and *FOCUS 2* (RAP-219-FOS-302) – are expected to be initiated in the second quarter of 2026. An open-label long-term safety trial (OLE) is currently underway to allow patients enrolled in the RAP-219 Phase 2a FOS trial to continue on RAP-219 treatment; initial data from the OLE are expected in the second half of 2026. Outside of FOS, Rapport is conducting a Phase 2 trial evaluating RAP-219 in bipolar mania, with topline results expected in the first half of 2027, and a Phase 3 trial in primary generalized tonic-clonic seizures is expected to begin in the first half of 2027. Additionally, Rapport continues development of a long-acting injectable (LAI) formulation of RAP-219, with Phase 1 initial PK results expected in 2027.

AAN Presentation Details

- **Title:** Efficacy and Tolerability of RAP-219, a Potential First-in-Class Negative Allosteric Modulator of γ8 Transmembrane AMPA Receptor Regulatory Protein: Impact on RNS Long Episodes and Clinical Seizures
- **Presenter:** William W. Motley, M.D., RAP-219 Program Leader at Rapport Therapeutics
- **Session Type:** Podium Presentation
- **Date & Time:** April 21, 2026; 3:54 PM CDT/4:54 PM ET

Additional information about the 2026 AAN Annual Meeting is available at www.aan.com.

About RAP-219 Phase 2a Trial in Focal Onset Seizures
The Phase 2a clinical trial of RAP-219 (NCT 06377930) was 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 adult 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. At the end of the treatment period, patients entered an 8-week follow-up period during which LEs, clinical seizures, safety and tolerability continued to be monitored.

About RAP-219
RAP-219 is an investigational and 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 potential treatment for patients with focal onset seizures, primary generalized tonic-clonic seizures, and bipolar mania. A long-acting injectable formulation of RAP-219 is also in development and could be the first of its kind in epilepsy.

About Rapport Therapeutics
Rapport Therapeutics is a clinical-stage biotechnology company dedicated to discovering and developing small molecule precision medicines for patients with neurological and psychiatric disorders. The Company's founders made pioneering discoveries related to the function of receptor associated proteins (RAPs) in the brain, which form the basis of Rapport's RAP technology platform. The platform 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, which is designed to achieve neuroanatomical specificity through selective targeting of a RAP expressed only in discrete regions of the brain. The pipeline is anchored by the Company's epilepsy portfolio, including FOS and primary generalized tonic-clonic seizures, as well as bipolar mania. The Company is also advancing additional discovery and preclinical programs leveraging its platform, including in chronic pain and migraine and in hearing and vestibular 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
This press release contains "forward-looking statements" within the meaning of Section 27A of the 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," "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 FOS, primary generalized tonic-clonic seizures, and bipolar mania, including the initiation, timing, progress, results and future data releases of our ongoing and planned clinical trials; the expected timing and initiation of the Company's *FOCUS 1 and FOCUS 2* Phase 3 trials; the expected timing and preliminary results of the OLE; the anticipated timing and topline results from the Company's Phase 2 trial evaluating RAP-219 in bipolar mania; the anticipated timing of the Phase 3 trial in primary generalized tonic-clonic seizures; the anticipated timing of a Phase 1 trial for the LAI formulation of RAP-219; the potential of Rapport's RAP technology platform; and expectations for the efficacy, tolerability, and commercial potential of RAP-219.

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, 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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