



Rapport Therapeutics Announces Positive Topline Results from its Phase 2 Trial of RAP-219 for the Treatment of Bipolar Mania

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The trial met the primary and secondary endpoints with statistically significant placebo-adjusted improvements at Week 3 in the YMRS total score (3.1 points; $p=0.045$) and CGI-BP Severity of Mania score (0.4 points; $p=0.024$)

RAP-219-treated patients had a 15.4-point mean reduction in YMRS total score from baseline at Week 3

All 11 items measured by the YMRS improved numerically compared to placebo at Week 3, with improvements in irritability, thought content, disruptive-aggressive behavior, and sexual interest reaching nominal significance

RAP-219 was well tolerated; all treatment-emergent adverse events during the treatment period were mild or moderate

Company to host a conference call today at 8:00 a.m. ET

BOSTON and SAN DIEGO, Oct. 20, 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 and psychiatric disorders, today announced positive topline results from its Phase 2 trial of RAP-219 in adults with acute bipolar mania. The trial met its primary endpoint, with RAP-219 achieving a 3.1-point placebo-adjusted improvement in the Young Mania Rating Scale (YMRS) total score at Week 3 (mean reduction from baseline of 15.4 points with RAP-219 versus 12.3 points with placebo ($p=0.045$)). RAP-219 was well-tolerated, with no severe treatment emergent adverse events (TEAEs) or serious adverse events (SAEs) observed over the treatment period. These results establish clinical proof-of-concept for RAP-219 and its novel TARPγ8-selective mechanism in bipolar mania, supporting progression to Phase 3 trials which are expected to begin in the second half of 2027.

"For people with bipolar disorder, the challenge isn't just finding a treatment that's efficacious. It's finding one they can tolerate and stay on," said Abraham N. Ceesay, chief executive officer of Rapport. "Side effects drive discontinuation, and discontinuation drives relapse. RAP-219 has the potential to break that cycle with the first new mechanism of action for bipolar mania in decades. Together with our positive Phase 2 focal epilepsy data, these results strengthen RAP-219's profile across each indication we are pursuing and show it delivering on its potential as a pipeline-in-a-product with two indications that both represent multibillion dollar market opportunities. We look forward to engaging with the FDA on Phase 3 in bipolar mania, alongside our ongoing Phase 3 epilepsy programs."

This randomized, double-blind, placebo-controlled Phase 2 trial, conducted in the United States, enrolled 253 adults with bipolar I disorder (BD) experiencing an acute manic episode (YMRS $\geq$ 25 at baseline). During the screening period, all treatments indicated for BD and all anxiolytics and hypnotics were discontinued. Lorazepam was allowed as a rescue medication at protocol-defined doses, and its use required an AE to be recorded, regardless of whether the symptom(s) were judged to be due to a pre-existing condition.

Eligible patients received 0.75 mg of RAP-219 once daily (following a two- or four- day titration) or placebo for three weeks in an inpatient setting. Mean baseline YMRS total score was 36.9 in the RAP-219 arm and 35.8 in the placebo arm. Topline efficacy and safety data reported are from the three-week treatment period. Safety data from the eight-week post-treatment period will be presented at a future medical conference.

RAP-219 Demonstrated Statistically Significant Improvement in Manic Symptoms

- The trial met its primary endpoint, with RAP-219 achieving a statistically significant 3.1-point least squares (LS) mean improvement over placebo in YMRS total score at Week 3 ($p=0.045$).
- RAP-219-treated patients had an LS mean decrease of 15.4 points in YMRS total score at Week 3 from a baseline of 36.9.
- All 11 YMRS items improved on RAP-219 compared to placebo at Week 3, with improvements in irritability, thought content, disruptive-aggressive behavior, and sexual interest reaching nominal significance ($p<0.05$).
- RAP-219 showed progressive improvement in the placebo-adjusted YMRS scores over the 3-week treatment period (0.9 at Week 1, 2.2 at Week 2, and 3.1 at Week 3).
- RAP-219 also demonstrated a statistically significant improvement in mania severity score versus placebo at Week 3 as measured by the Clinical Global Impression—Bipolar Version (CGI-BP) mania severity scale, the pre-specified secondary endpoint (0.4; $p=0.024$).

RAP-219 Was Well-Tolerated

During the three-week treatment period, based on safety and tolerability data^{*}:

- The incidence of treatment-emergent adverse events (TEAEs) was similar between RAP-219 and placebo (51.6% vs 52.8%), as was the incidence of psychiatric TEAEs (34.9% vs 33.1%).
- All TEAEs were mild or moderate in severity, and there were no serious adverse events (SAEs); 3.2% of patients on RAP-219 discontinued due to a TEAE compared with 0.8% placebo.
- TEAEs occurring in ≥5% of participants in either group (RAP-219 vs placebo) were agitation (16.7% vs 9.4%), insomnia (14.3% vs 15.0%), restlessness (8.7% vs 7.9%), anxiety (7.1% vs 5.5%), headache (5.6% vs 10.2%), and nausea (5.6% vs 1.6%). Those considered treatment related by the investigator were agitation (3.2% vs 1.6%), insomnia (3.2% vs 0.8%), restlessness (1.6% vs 0%), anxiety (0.8% vs 0.8%), headache (0.8% vs 4.7%), and nausea (3.2% vs 0.8%).
 - The most common TEAE on RAP-219 was agitation, generally occurring in the first week and lasting a median duration of two days in both the RAP-219 and placebo groups. In both groups, this was considered unrelated in >80% of patients.
- Adverse effects commonly associated with current bipolar mania medications, including orthostatic hypotension, akathisia, and extrapyramidal symptoms were not reported. Somnolence was reported less often with RAP-219 (0.8%) than placebo (3.1%).

“In this proof-of-concept study, RAP-219 demonstrated statistically significant improvement across measures of mania symptoms as well as a favorable tolerability profile,” said Jeffrey Sevigny, M.D., chief medical officer of Rapport. “This is important because tolerability issues lead many patients to discontinue their therapies. These results continue to build our confidence in the safety profile of RAP-219, and the insights learned from this study will guide us in optimizing the Phase 3 design in bipolar mania. Finally, we are deeply grateful to everyone who made this study possible, including participating patients and their families, the investigators and site staff, and our dedicated employees.”

“There hasn’t been a new mechanism to treat bipolar mania in decades. In this study, RAP-219 achieved statistically significant improvement in manic symptoms with an encouraging tolerability profile, underscoring the promise of this novel mechanism,” said Gary Sachs, M.D., founding director of the Bipolar Clinic and Research Program at Massachusetts General Hospital and associate clinical professor of psychiatry at Harvard Medical School. “Importantly, clinical benefit was seen consistently across all measures, with the greatest improvements in symptoms that tend to drive hospitalization for acute mania patients. What is encouraging about the tolerability profile is what was not seen on RAP-219--the somnolence, akathisia, and extrapyramidal symptoms that often cause patients to discontinue treatment. Based on these results, RAP-219 has the potential to become a mainstay of treatment for acute mania.”

Next Steps and Upcoming Milestones

Rapport plans to meet with the U.S. Food and Drug Administration (FDA) in the first quarter of 2027 to discuss the Phase 2 data and registrational trial design for RAP-219 in bipolar mania. Initiation of two Phase 3 trials of RAP-219 in acute bipolar mania is expected in the second half of 2027. Additional data from the Phase 2 trial will be presented at a future medical meeting.

Upcoming milestones include:

- Focal onset seizures (FOS): FOCUS 1 and FOCUS 2 pivotal Phase 3 trials are enrolling.
- FOS open-label long-term safety trial: Initial data from the long-term open-label extension of the Phase 2a trial are expected in the fourth quarter of 2026.
- Bipolar mania: End-of-Phase 2 meeting with the FDA expected in the first quarter of 2027; initiation of two Phase 3 pivotal trials expected in the second half of 2027.
- Long-acting injectable (LAI): Phase 1 pharmacokinetic (PK) data for an LAI formulation of RAP-219 are expected in the third quarter of 2027.
- Primary generalized tonic-clonic seizures (PGTCS): Phase 3 trial is expected to begin in the first half of 2027.
- RAP-641: Phase 1 preliminary results are expected in the second half of 2027.
- Financial position: As of June 30, 2026, Rapport had \$436.1 million in cash, cash equivalents and short-term investments, excluding restricted cash, expected to fund operations into the second half of 2029, beyond expected topline data from the Company’s Phase 3 program in focal onset seizures.

^{*} Safety and tolerability data as of interim database lock, September 16, 2026.

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 October 20, 2026, 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. and Canadian callers and (646) 307-1963 for other locations and reference conference ID 3120573, 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 “Investors” section of the Company’s website for 90 days following the completion of the call.

About the Young Mania Rating Scale (YMRS)

The Young Mania Rating Scale (YMRS) is a clinician-administered tool used to measure the severity of manic symptoms in people with bipolar disorder. It is the most widely used rating scale in mania research. The YMRS assesses 11 core symptoms of mania: elevated mood, increased activity and energy, sexual interest, sleep, irritability, speech, thought disorder, thought content, disruptive or aggressive behavior, appearance, and insight. Four of these symptoms (irritability, speech, thought content, and disruptive or aggressive behavior) are weighted more heavily to reflect their clinical significance. Clinicians rate each symptom from a clinical interview and the patient’s reported symptoms over the preceding 48 hours. Total scores range from 0 to 60, with higher scores indicating more severe mania.

About the Clinical Global Impression–Bipolar Version (CGI-BP)

The Clinical Global Impression–Bipolar Version (CGI-BP) is a clinician-rated scale adapted from the widely used Clinical Global Impression scale to assess illness severity and change in people with bipolar disorder. Clinicians rate mania, depression, and overall bipolar illness separately. The CGI-BP mania severity score reflects the clinician’s overall judgment of how severe a patient’s manic symptoms are, based on clinical experience with patients with bipolar disorder. Scores range from 1 (normal, not ill) to 7 (among the most extremely ill patients), with higher scores indicating more severe mania. CGI-BP mania severity is commonly used as a complement to symptom-based scales such as the YMRS by capturing the clinician’s overall view of illness severity.

About RAP-219

RAP-219 is an investigational and potential first-in-class, clinical-stage TARPγ8-specific AMPA receptor (AMPA) 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, PGTCs and bipolar mania, including the initiation, timing, progress, results and future data releases of our ongoing and planned clinical trials, including the long-term open-label extension of the Phase 2a trial in FOS, the FOCUS 1 and FOCUS 2 pivotal Phase 3 trials, the Phase 1 trial for a long-acting injectable formulation of RAP-219, the Phase 1 trial for RAP-641 and the Phase 3 trial of RAP-219 in PGTCs; expectations and timing of upcoming regulatory interactions, including an End-of-Phase 2 Meeting with the FDA for RAP-219 the anticipated planning activities for a potential Phase 3 trial in

bipolar mania; expectations for a LAI formulation of RAP-219; the potential of the Company's RAP technology platform; expectations for the efficacy, tolerability, and commercial potential of RAP-219; and expectations for the Company's uses of capital, expenses and financial results, including its expectations regarding cash runway into the second half of 2029.

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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