Relay Therapeutics Announces Initial Clinical Data Demonstrating That Zovegalisib Has Potential for Differentiated Safety and Efficacy in Patients with PIK3CA-Driven Vascular Anomalies

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Promising initial efficacy data with 60% volumetric response rate across doses and 29% at the lowest tested dose of 100mg twice daily (BID) with all patients ongoing*

Interim investigator- and patient-reported outcomes show 89% and 79% of patients achieved clinical improvement at week 12, respectively, and support the potential of zovegalisib to drive clinically meaningful benefit for patients

Evaluation across a wide dose range confirms potential therapeutic window, with interim safety profile supportive of chronic dosing and no patients discontinuing treatment due to adverse events

Expansion cohorts for adults and adolescents opened at 400mg once daily (QD) and 300mg BID; pediatric dose-finding is ongoing

Company to host conference call today, Tuesday, May 19, 2026 at 8:00 am ET

CAMBRIDGE, Mass., May 19, 2026 (GLOBE NEWSWIRE) -- Relay Therapeutics, Inc. (Nasdaq: RLAY), a clinical-stage, small molecule precision medicine company developing potentially life-changing therapies for patients living with cancer and genetic disease, today announced initial clinical data from the Phase 2 RelnspIre trial of zovegalisib in vascular anomalies signaling the advantage of PI3Kα mutant-selective inhibition. Vascular anomalies are a group of rare disorders characterized by abnormal development of blood vessels, lymphatic vessels and surrounding tissues. As of the April 15, 2026 data cut-off date, in the Part 1 dose randomization portion of the study for adults and adolescents ages 12 and up, 60% of patients achieved a volumetric response at the earliest time point (12 weeks) and nearly all patients experienced symptomatic improvement at 12 weeks while maintaining a safety and tolerability profile showing the potential for chronic use. The data are being presented at the International Society for the Study of Vascular Anomalies (ISSVA) World Congress 2026, taking place in Philadelphia.

“These data demonstrate, for the first time, the promise of PI3Kα mutant-selective inhibition for patients with vascular anomalies,” said Don Bergstrom, M.D., Ph.D., President of R&D at Relay Therapeutics. “The combination of robust volumetric responses, symptomatic improvement, and a safety profile that supports chronic dosing underscores the potential of zovegalisib to meaningfully change the treatment paradigm for this underserved population. These early results strengthen our conviction in zovegalisib’s differentiated profile and its potential ability to deliver lasting benefit for patients and families affected by vascular anomalies.”

RelnspIre – Zovegalisib Study in PIK3CA-Driven Vascular Anomalies

Zovegalisib is currently being evaluated in an ongoing Phase 2 study designed to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics, and efficacy of zovegalisib in adults and children with vascular anomalies driven by PIK3CA mutations.

The study consists of three age groups: Group 1 is adults and adolescents 12 years or older, Group 2 is pediatrics 6-11 years old, and Group 3 is pediatrics 2-5 years old. For each age group, there is a 3-part design: Part 1 is dose selection, Part 2 is dose expansion featuring open-label basket design with exploratory single-arm dose cohorts across various patient subpopulations, and Part 3 is potentially a randomized study.

The data reported today are from Part 1 of the study in the adults and adolescents cohort (patients 12 years or older), which featured randomized dose selection across three doses. As of the April 15, 2026 data cut-off date, 32 total patients were enrolled and randomized to the following dose cohorts: N=11 at 100mg BID, N=11 at 300mg BID, and N=10 at 400mg BID. Of the patients enrolled, 22 had PIK3CA-related overgrowth spectrum (PROS), 8 had a lymphatic malformation (LM), and 2 had a venous malformation (VeM). 23 patients (72%) had prior treatment with sirolimus and/or alpelisib, which was allowed in the study.

Expansion cohorts (Part 2) for 12 and older patients have been opened at 400mg once daily (QD) and 300mg BID and are enrolling.

Unless indicated otherwise, all data reported are as of the April 15, 2026 data cut-off date.

Initial Efficacy Data Demonstrated Meaningful Volumetric Lesion Regression

Of the 32 patients enrolled, 20 have been evaluated for efficacy per volumetric response assessment by blinded independent central review (BICR), which is assessed by MRI every 12 weeks. The remaining 12 patients had not reached the 12-week timepoint. A response is defined by a 20% or greater reduction in target lesion(s) volume from baseline.

Of the 20 response-evaluable patients, 15 had PROS, 4 had a LM, and 1 had a VeM. Of patients with a confirmed PIK3CA mutation, 25% of patients had a kinase mutation and 55% had a non-kinase mutation, while 20% had no PIK3CA mutation documented at the time of data cut-off. 65% had been previously treated with alpelisib or sirolimus (35% had been treated by both). All 32 patients remained on treatment as of the data cut-off date.

For the 20 response-evaluable patients:

- 60% of patients had a volumetric response with all responses coming at the first MRI
    - Of the 13 patients treated at 300mg BID or 100mg BID, 8 (62%) had a volumetric response
    - Of the 13 patients previously treated with alpelisib and/or sirolimus, 8 (62%) had a volumetric response
    - Responses were observed in patients with PROS and LM
    - Responses were observed across a spectrum of PIK3CA mutations
- Four responding patients had a 24-week scan, and all showed confirmation of response with deepening of reduction of lesion volume
- 95% of patients experienced lesion reduction
- After the data cut-off date, one 100mg BID patient that did not have a volumetric response as of the data cut-off date has converted to an unconfirmed response, resulting in a 100mg BID volumetric response rate of 43% (3/7), a volumetric response rate of 69% (9/13) for patients treated at 300mg BID or 100mg BID, and a volumetric response rate of 65% (13/20) across doses
    - None of the other response-evaluable patients' response statuses have changed since the data cut-off date

Initial Patient and Clinician Reported Outcomes Showed Meaningful Clinical Improvement at 12 Weeks

Clinical outcome assessments of symptoms, including investigator- and patient-global impression of change (IGIC and PGIC) and pain measured by investigator assessment of disease-related signs and symptoms (IADRSS), are being measured as secondary endpoints in the study. IGIC, PGIC, and IADRSS measures are each a seven point, single-item scale asking patients and clinicians to rate how their condition has improved or worsened since the start of treatment.

At week 12, IGIC and PGIC scores demonstrated clinical improvement in 89% and 79% of patients, respectively, and IADRSS Pain scores demonstrated clinical improvement for 71% of pain symptoms. Clinical outcome scores across all three measures trended towards further improvement for later timepoints.

Relay Therapeutics has developed a fit-for-purpose patient-reported outcome (PRO) tool specifically for use within the trial patient population, which is in the process of being incorporated into the ReInspire trial.

Initial Safety and Tolerability Data Demonstrated a Clear Path to Identifying a Chronic Dose of Zovegalisib

The safety profile of zovegalisib was assessed across a wide dose range, spanning from 100mg BID to 400mg BID (the dose being evaluated in the ongoing Phase 3 trial in metastatic breast cancer). The overall tolerability profile was generally as expected and consistent with mutant-selective PI3Kα inhibition. Rates of treatment-related adverse events (TRAEs) and dose modifications were proportional to dose level, allowing for further dose optimization intended to identify go-forward doses suitable for chronic treatment.

Among the 22 patients treated at 100mg and 300mg BID:

- Dose reductions were seen in 23% of patients, with no dose discontinuations
    - Median dose intensity was >99%
- Only 2 patients (9%) experienced a Grade 3+ TRAE
- Common adverse events associated with wild-type PI3Kα inhibition were low-grade, manageable, and reversible
    - No rash or stomatitis of any grade was observed, and no grade 3 hyperglycemia or diarrhea was observed
- No prophylactic treatment was administered for management of any adverse event

The 400mg BID dose, while not a formal maximum tolerated dose, showed a safety profile that was not optimal for this patient population and is deprioritized for further development.

Anticipated Next Steps

- Vascular Anomalies
    - 400mg QD and 300mg BID have been selected as expansion doses, with enrollment ongoing
    - Continued execution of the ReInspire trial of zovegalisib in vascular anomalies:
        - Enrollment of expansion cohorts for adults and adolescents (ages 12 and up)
        - Enrollment of Part 1 dose escalation cohort for pediatrics(ages 6-11)
        - Implementation of the fit-for-purpose PRO tool
- Breast Cancer
    - Continued execution of the Phase 3 ReDiscover-2 trial of zovegalisib + fulvestrant in PI3Kα-mutated, CDK4/6 pre-treated, HR+/HER2- advanced breast cancer
    - Continued frontline Phase 3 readiness activities for zovegalisib + atirmociclib + aromatase inhibitor, intended to initiate in early 2027, subject to regulatory feedback

Data Presentation and Conference Call Information

Relay Therapeutics will host a conference call and live webcast today, May 19, at 8:00 a.m. ET. Registration and dial-in for the conference call, as well

as the data presentation, may be accessed through Relay Therapeutics' website under Events in the News & Events section through the following link: https://ir.relaytx.com/news-events/events-presentations. An archived replay of the webcast will be available following the event. An abstract for these data will be presented tomorrow, May 20 from 4:45pm-4:49pm ET. No additional or new data will be in the presentation.

About Vascular Anomalies

Vascular anomalies (VAs) are a group of rare disorders characterized by abnormal development of blood vessels, lymphatic vessels and surrounding tissues. These conditions can vary widely in presentation and severity and may cause chronic pain, swelling, disfigurement, impaired mobility, bleeding and other serious complications that can significantly impact quality of life. PIK3CA-driven vascular anomalies are a subset of these disorders caused by mutations in the PIK3CA gene, including conditions such as PIK3CA-related overgrowth spectrum, lymphatic malformations and venous malformations. Approximately 170,000 patients in the U.S. are estimated to be living with PIK3CA-driven vascular anomalies. Current systemic treatment options are limited and may be associated with tolerability challenges that can restrict long-term use.

About Zovegalisib

Zovegalisib is the lead investigational program in Relay Therapeutics' efforts to discover and develop mutant-selective inhibitors of PI3Kα, the most frequently mutated kinase in all cancers and all vascular anomalies. Zovegalisib has the potential, if approved, to address a significant portion of the approximately 140,000 patients with HR+/HER2- breast cancer with a PI3Kα mutation and the estimated 170,000 patients with vascular anomalies driven by a PI3Kα mutation per year in the United States, one of the largest patient populations for a precision medicine.

Traditionally, the development of PI3Kα inhibitors has focused on the active, or orthosteric, site. The therapeutic index of orthosteric inhibitors is limited by the lack of clinically meaningful selectivity for mutant versus wild-type (WT) PI3Kα and off-isoform activity. Toxicity related to inhibition of WT PI3Kα and other PI3K isoforms results in sub-optimal inhibition of mutant PI3Kα with reductions in dose intensity and frequent discontinuation. The Dynamo® platform enabled the discovery of zovegalisib, the first known allosteric, pan-mutant, and isoform-selective PI3Kα inhibitor, designed to overcome these limitations. Relay Therapeutics solved the full-length cryo-EM structure of PI3Kα, performed computational long time-scale molecular dynamic simulations to elucidate conformational differences between WT and mutant PI3Kα, and leveraged these insights to support the design of zovegalisib. Zovegalisib is currently being evaluated in multiple metastatic breast cancer studies and a first-in-human study designed to treat patients with PIK3CA mutation driven vascular anomalies. For more information on zovegalisib, please visit here.

About Relay Therapeutics

Relay Therapeutics (Nasdaq: RLAY) is a clinical-stage, small molecule precision medicine company developing potentially life-changing therapies for patients living with cancer and genetic disease. Relay Therapeutics' Dynamo® platform integrates an array of leading-edge computational and experimental approaches designed to drug protein targets that have previously been intractable or inadequately addressed. The company's lead clinical asset, zovegalisib, is the first pan-mutant selective PI3Kα inhibitor to enter clinical development and is currently in a Phase 3 clinical trial (ReDiscover-2) in HR+/HER2- metastatic breast cancer. Zovegalisib is also being investigated in a group of genetic disease indications called PIK3CA-driven vascular anomalies. Relay Therapeutics' pipeline also includes programs for NRAS-driven solid tumors and Fabry disease. For more information, please visit www.relaytx.com or follow us on LinkedIn.

Cautionary Note Regarding Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, implied and express statements regarding Relay Therapeutics' strategy, business plans and focus; the progress, timing and results of the clinical development of the programs across Relay Therapeutics' portfolio; the progress of enrollment and timing of clinical data readouts for zovegalisib; the expected therapeutic benefits and potential, efficacy, safety and tolerability of zovegalisib, both as a monotherapy and in combination with other agents, and its other programs; the therapeutic potential of the clinical data for zovegalisib; the potential uses, implementation and development of Relay Therapeutics' patient-reported outcome tool; the execution of the Phase 3 ReDiscover-2 trial of zovegalisib + fulvestrant; the execution of the frontline Phase 3 readiness activities for zovegalisib + atirmociclib + aromatase inhibitor as well as the timing of any such trial; the interactions with regulatory authorities and the timing of any regulatory updates or approvals, and any related actions or decisions; and the potential commercialization and market opportunity for zovegalisib. The words "may," "might," "will," "could," "would," "should," "plan," "anticipate," "intend," "believe," "expect," "estimate," "seek," "predict," "future," "project," "potential," "continue," "target" and similar words or expressions, or the negative thereof, are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

Any forward-looking statements in this press release are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this press release, including, without limitation, risks associated with: the impact of global economic uncertainty, geopolitical instability and conflicts, or public health epidemics or outbreaks of an infectious disease on countries or regions in which Relay Therapeutics has operations or does business, as well as on the timing and anticipated results of its clinical trials, strategy, future operations and profitability; significant political, trade or regulatory developments, such as tariffs, beyond Relay Therapeutics' control; the delay or pause of any current or planned clinical trials or the development of Relay Therapeutics' drug candidates; the risk that the preliminary or interim results of its preclinical or clinical trials may not be predictive of future or final results in connection with future clinical trials of its product candidates and that interim and early clinical data may change as more patient data become available and are subject to audit and verification procedures; Relay Therapeutics' ability to successfully demonstrate the safety and efficacy of its drug candidates; the timing and outcome of its planned interactions with regulatory authorities; and obtaining, maintaining and protecting its intellectual property. These and other risks and uncertainties are described in greater detail in the section entitled "Risk Factors" in Relay Therapeutics' most recent Annual Report on Form 10-K and Quarterly Report on Form 10-Q, as well as any subsequent filings with the Securities and Exchange Commission. In addition, any forward-looking statements represent Relay Therapeutics' views only as of the date of this press release and should not be relied upon as representing its views as of any subsequent date. Relay Therapeutics explicitly disclaims any obligation to update any forward-looking statements. No representations or warranties (expressed or implied) are made about the accuracy of any such forward-looking statements.

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**After the data cut-off date, one 100mg BID patient that did not have a volumetric response as of the data cut-off date has converted to an unconfirmed response. Taking this additional response into account, the volumetric response rate across doses would be 65% and the volumetric response rate at the 100mg BID dose would be 43%.*