Relay Therapeutics Announces Clinical Data for Zovegalisib plus Atirmociclib Triplet Combination Supportive of Further Development in Frontline Metastatic Breast Cancer

Apr 27, 2026

Zovegalisib + atirmociclib + AI selected as triplet regimen for frontline development

Compelling efficacy and tolerability data for zovegalisib triplet in median 3L patients

44% ORR in heavily pre-treated, CDK4/6-experienced patients (median third-line); ORR is similar across kinase and non-kinase PIK3CA mutations

Phase 3 frontline trial in endocrine sensitive patients expected to initiate in early 2027, subject to regulatory feedback

Supply agreement in place with Pfizer to supply atirmociclib for the Phase 3 frontline trial

Relay Therapeutics to host a conference call today, April 27, at 8:30am ET

CAMBRIDGE, Mass., April 27, 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 plans to move zovegalisib + atirmociclib, Pfizer's investigational, potential first-in-class CDK4 inhibitor, into Phase 3 development for frontline patients with PI3Kα-mutated, HR+/HER2- metastatic breast cancer.

"While PI3Kα inhibition has demonstrated meaningful benefit in breast cancer, its use in the frontline setting has been limited by tolerability challenges with earlier agents," said Don Bergstrom, M.D., Ph.D., President of R&D at Relay Therapeutics. "We believe that combining the selective profiles of zovegalisib and atirmociclib with endocrine therapy has the potential to enable a well-tolerated, all-oral triplet regimen, and these initial data support advancing this combination into Phase 3 development for patients with frontline metastatic breast cancer."

Zovegalisib + Atirmociclib Data Demonstrate Potential Best-in-Class Triplet Profile

Zovegalisib is currently being evaluated in ReDiscover, an ongoing first-in-human study designed to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics and preliminary antitumor activity of zovegalisib in combination with fulvestrant and CDK inhibitors in patients with PI3Kα-mutated, HR+/HER2- metastatic breast cancer. These data are from the zovegalisib + atirmociclib + fulvestrant dose finding portion of the study.

As of the April 13, 2026 data cut-off date, 69 total patients were enrolled, with 62 patients at or below the potential Phase 3 dose and 34 patients with measurable disease evaluable for response. All patients had previously received a CDK4/6 inhibitor and at least one prior endocrine therapy in the advanced setting and could have received a PI3K pathway inhibitor. These heavily pre-treated patients had received a median of 2 prior therapies (21% received 3+ prior therapies) in the metastatic setting with 63% having visceral disease, 29% having received chemotherapy, and 47% being pre-diabetic. The median follow-up was 7.4 months.

Expansion cohorts of zovegalisib + atirmociclib + fulvestrant and zovegalisib + atirmociclib + aromatase inhibitor (AI) in the ReDiscover study are ongoing.

Safety and Tolerability of Triplet is Critical for Potential Long-Term Treatment in Frontline Endocrine Sensitive Breast Cancer

Early safety and tolerability data for zovegalisib in combination with atirmociclib and fulvestrant (N=62) reinforce the potential of this regimen moving forward in frontline endocrine sensitive patients. As of the April 13, 2026 data cut-off date:

- Only two patients (3%) discontinued zovegalisib and six patients (10%) dose reduced zovegalisib due to treatment-related adverse events (TRAEs)
- Adverse events were consistent with those previously reported by each molecule
  - Grade 3 hyperglycemia was 0% despite 47% of patients being pre-diabetic
- Overall grade 3+ TRAE rate in these median third-line patients is 40%
  - Neutropenia accounts for the majority of the grade 3+ events
  - No instance of febrile neutropenia was observed

Overall Response Rate in Median Third Line Patients is Approaching ORR Seen in Frontline Breast Cancer with Standard of Care

As of the April 13, 2026 data cut-off date, 34 patients had measurable disease to be evaluated for response:

- Objective response rate (ORR) was 44% (15/34) and was also 44% in both kinase and non-kinase patients
  - ORR in these heavily pre-treated patients has approached that of current standard of care doublets in 1L patients, ranging from 53% to 55% ORR

    - Nearly all patients experienced tumor reduction (85%, 29/34)
- 48 of 62 patients (77%) remain on study as of the data cut-off date, with a median follow-up of 7.4 months
    - The data are not yet mature enough to estimate median progression-free survival

Pharmacokinetics

Pharmacokinetic analyses demonstrated that atirmociclib increased the exposure of zovegalisib by about two and half-fold (regardless of atirmociclib dose), while zovegalisib had no impact on atirmociclib exposure. Subject to regulatory feedback, the potential Phase 3 dose of zovegalisib will be 150mg twice daily (BID), which maintains average concentration of zovegalisib just below IC90 throughout the dosing interval.

Preliminary Phase 3 Trial Design in Frontline Endocrine Sensitive Patients

The planned study, subject to regulatory feedback, is a randomized Phase 3 trial evaluating zovegalisib in combination with atirmociclib and aromatase inhibitor (AI) in frontline endocrine sensitive patients with PIK3CA-mutated, HR+/HER2- advanced or metastatic breast cancer.

- **Population:** Frontline endocrine sensitive patients with HR-positive, HER2-negative advanced or metastatic breast cancer harboring a PIK3CA mutation
- **Experimental arm:** Zovegalisib + atirmociclib + AI
- **Control arm:** CDK4/6 inhibitor (investigator's choice) + AI
- **Key endpoints:** Median progression-free survival (primary) and overall survival (secondary)

Pfizer to Supply Atirmociclib and Palbociclib Through Supply Agreement

Pfizer has agreed to supply atirmociclib for the experimental arm in combination with zovegalisib and the palbociclib portion of the control arm for use in the planned study. Relay Tx will sponsor, fully operationalize and fund the planned Phase 3 trial. Relay Tx retains full global rights for zovegalisib.

Next Steps

- Conduct regulatory interactions to finalize Phase 3 design and dose with the goal of initiating the study in early 2027
- Continued execution of Phase 1/2 dose finding and expansion as part of the ReDiscover study, allowing for larger sample size and longer follow up at potential Phase 3 dose for future disclosures
- Continued execution of ongoing ReDiscover-2 Phase 3 trial in second line breast cancer
- Present initial data for zovegalisib in vascular anomalies at ISSVA 2026 (May 20, 2026 in Philadelphia)

Conference Call Information

Relay Therapeutics will host a conference call and live webcast today, April 27, at 8:30 a.m. ET. Registration and dial-in for the conference call 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.

About Zovegalisib

Zovegalisib is the lead 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 (PI3Kα) 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 PI3Kα-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 and timing of the clinical development of the programs across Relay Therapeutics' portfolio, including the timing of initiation of a frontline Phase 3 clinical trial for zovegalisib in combination with atirmociclib and AI; the timing of clinical data readouts for zovegalisib; the expected therapeutic benefits and potential efficacy and tolerability of zovegalisib, both as a monotherapy and in combination with other agents, including the combination of zovegalisib and atirmociclib, and its other programs; the clinical data for zovegalisib; the interactions with regulatory authorities and any related approvals; the potential commercialization and market opportunity for zovegalisib; and the expected strategic benefits under Relay Therapeutics' clinical trial supply agreement with Pfizer. 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 today 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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