Relay Therapeutics Announces Efficacy Subset Analysis of Zovegalisib (RLY-2608) + Fulvestrant in Breast Cancer Patients Pre-Treated with SERD or with ESR1 Mutations at SABCS 2025

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Efficacy data remain consistent with previous disclosures, showing 10.3-month median PFS in all patients and 11.4-month median PFS in 2L patients

Subset analyses show broad activity in patients with PI3Kα-mutated, HR+/HER2- metastatic breast cancer, regardless of prior fulvestrant or other SERD exposure, or ESR1 *mutation status*

Phase 3 ReDiscover-2 trial in CDK4/6-experienced breast cancer ongoing

CAMBRIDGE, Mass., Dec. 12, 2025 (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 a subset analysis of interim clinical data for zovegalisib (RLY-2608), the first known investigational allosteric, pan-mutant and isoform-selective inhibitor of PI3Kα. These data are being presented today at the 2025 San Antonio Breast Cancer Symposium (SABCS).

“Data presented today demonstrate the robust activity of zovegalisib + fulvestrant across subgroups of patients whose baseline characteristics are known to affect outcomes, such as prior fulvestrant or SERD and *ESR1* mutation status,” said Don Bergstrom, M.D., Ph.D., President of R&D at Relay Therapeutics. “The broad range of activity highlights the importance of selectively targeting the driver of disease, mutant PI3Kα, and gives us confidence that the data observed to date should translate to our ongoing Phase 3 trial, ReDiscover-2.”

ReDiscover – Zovegalisib First-in-Human Study

Zovegalisib is currently being evaluated in ReDiscover, an ongoing first-in-human study, which was designed to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics and preliminary antitumor activity of zovegalisib in combination with fulvestrant, and in combination with fulvestrant and CDK inhibitors.

As of the data cut-off date of October 15, 2025, 118 patients had enrolled into the zovegalisib + fulvestrant arm of the ReDiscover study. Across all doses, all patients had received a significant level of prior therapy in the advanced setting, including at least one prior endocrine therapy and at least one prior CDK4/6 inhibitor. Among the 64 patients who received 600mg twice daily (BID) fasted, 44% of patients (n=28) had received two or more prior lines of therapy, 52% of patients (n=33) had received prior SERD (includes fulvestrant or oral SERD), and 29% of patients (n=18) had detectable *ESR1* mutations at baseline.

Efficacy Consistent Across Subset Populations

The data cut-off date was October 15, 2025 for this analysis. The total efficacy population consisted of 52 zovegalisib + fulvestrant patients who received 600mg BID fasted and did not have a PTEN or AKT co-mutation. Median follow-up was 20.2 months.

The median progression free survival (PFS) was 10.3 months for all patients. Among the total of 31 patients with measurable disease, objective response rate (ORR) was 39%. For second line (2L) patients, median PFS was 11.4 months and ORR was 47%.

Efficacy was generally consistent across other subsets of patients. For patients who received prior SERD, median PFS was 11.4 months and ORR was 44% (7/16), and for patients who had a detectable *ESR1* mutation at baseline, median PFS was 8.8 months and ORR was 60% (6/10).

The overall tolerability profile remained consistent with mutant-selective PI3Kα inhibition, with treatment-related adverse events that were mostly low-grade, manageable and reversible.

Anticipated Zovegalisib Next Steps

- Breast Cancer
  - Continued enrollment of Phase 3 ReDiscover-2 trial of zovegalisib + fulvestrant in PI3Kα-mutated, CDK4/6 pre-treated, HR+/HER2- advanced breast cancer
  - Continued dose escalation in Phase 1/2 ReDiscover trial, advancing triplet cohorts that will inform which regimen could be used in a future frontline metastatic trial
- Vascular Malformations
  - Continued enrollment of ongoing Phase 1/2 ReInspire clinical trial in vascular malformations

The data presentation from SABCS is available on the Relay Therapeutics website in the “Publications/Presentations” section through the following link: https://relaytx.com/publications/.

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 malformations. Zovegalisib has the potential, if approved, to address nearly 500,000 patients 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 malformations. 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's 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 malformations. Relay's pipeline also includes late-stage research 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; the expected therapeutic benefits and potential efficacy and tolerability of zovegalisib , both as a monotherapy and in combination with other agents, and its other programs; the clinical data for zovegalisib; the interactions with regulatory authorities and any related approvals; and the potential 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; 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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