Relay Therapeutics Announces Updated Interim Data for RLY-2608 + Fulvestrant Demonstrating Continued Maturation of Clinically Meaningful Progression Free Survival

December 11, 2024

New interim data show 11.4-month median PFS in 2L patients with PI3Kα-mutated, HR+/HER2- metastatic breast cancer at RP2D

39% confirmed ORR across all patients & 67% in patients with kinase mutations at RP2D

Data support planned initiation of 2L pivotal study in 2025

Next-generation triplet combination with atirmociclib (CDK4-selective) initiated & ribociclib triplet combination ongoing

Relay Therapeutics to host a conference call today, December 11, at 7am ET (6am CT)

SAN ANTONIO, Dec. 11, 2024 (GLOBE NEWSWIRE) -- Relay Therapeutics, Inc. (Nasdaq: RLAY), a clinical-stage precision medicine company transforming the drug discovery process by combining leading-edge computational and experimental technologies, today announced updated interim clinical data for RLY-2608, the first known investigational allosteric, pan-mutant and isoform-selective inhibitor of PI3Kα. The updated data show a median progression free survival (PFS) of 11.4 months in second line (2L) patients with PI3Kα-mutated, HR+, HER2- locally advanced or metastatic breast cancer who received RLY-2608 600mg twice daily (BID) + fulvestrant. These data are being presented today at the San Antonio Breast Cancer Symposium (SABCS) 2024.

“These updated data help build on previously reported results that show a level of benefit that had not previously been seen with non-selective PI3Kα inhibitors,” said Don Bergstrom, M.D., Ph.D., President of R&D at Relay Therapeutics. “We are particularly encouraged to see even greater benefit observed in the patients in which we are working to start a pivotal study next year; in these 2L patients, RLY-2608 + fulvestrant demonstrated a median progression free survival that is more than twice that of the existing standards-of-care.”

ReDiscover – RLY-2608 First-in-Human Study

RLY-2608 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 RLY-2608 in combination with fulvestrant, and in combination with fulvestrant and ribociclib or atirmociclib (Pfizer’s selective CDK4 inhibitor).

The RLY-2608 + fulvestrant arm of the study, as of the November 4, 2024 interim data cut-off for this arm, had enrolled 118 patients with PI3Kα-mutated, HR+, HER2- locally advanced or metastatic breast cancer across all doses in both the dose escalation and dose expansion portions of the study, including 64 patients at the company’s recommended Phase 2 dose (RP2D) of 600mg BID. Among these 64 patients, 31 had a kinase mutation and 33 had a non-kinase mutation. Twelve patients also had a PTEN or AKT co-mutation and were therefore excluded from the efficacy analysis, consistent with the planned pivotal population.

The RLY-2608 + ribociclib + fulvestrant arm of the study continues to enroll patients with PI3Kα-mutated, HR+, HER2- locally advanced or metastatic breast cancer in dose escalation. The RLY-2608 + atirmociclib + fulvestrant arm of the study has recently been initiated.

Patients were Heavily Pre-Treated

All RLY-2608 + fulvestrant patients across doses 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 the RP2D:

- 41% of patients (n=26) had received two or more prior lines of therapy
- 52% of patients (n=33) had received a prior selective estrogen-receptor degrader (SERD), such as fulvestrant or a novel SERD
- 25% of patients (n=16) had received chemotherapy or an ADC
- 59% of patients (n=38) had visceral metastases
- 34% of patients (n=22) had a BMI of at least 30 and/or HbA1c of at least 5.7%

Promising Efficacy Data in Proposed Pivotal Population

Among the 52 RLY-2608 + fulvestrant patients who received the RP2D and did not have a PTEN or AKT co-mutation:

- The median PFS was 9.2 months for all patients and 11.4 months for 2L patients
    - Median PFS was 11.4 months for patients with kinase mutations
- Clinical benefit rate (CBR) was 67% across all patients (32 of 48 CBR-evaluable patients; CBR defined as the proportion of patients with complete response, partial response or stable disease for at least 24 weeks)
- Among the 31 patients with measurable disease, 12 achieved a partial response (PR) (39% confirmed objective response

rate, ORR)
    - Nearly three quarters of patients experienced tumor reductions (74%; n=23)
- Among the 15 patients with measurable disease who had a kinase mutation, two thirds achieved a PR (67% confirmed ORR; n=10)
- Median follow-up was 9.5 months

Maintained Meaningfully Differentiated Tolerability Profile

RLY-2608 + fulvestrant was generally well tolerated in the 118 patients treated across all doses as of the data cut-off date. The overall tolerability profile consisted of mostly low-grade treatment-related adverse events (TRAEs) that were manageable and reversible. Safety outcomes were generally as expected across dose levels based on exposure and consistent with mutant-selective PI3Kα inhibition. Among the 64 patients who received the RP2D:

- The low rate of TRAE-related dose modifications allowed for 94% median dose intensity
- Only two patients discontinued treatment due to TRAEs (Grade 1 pruritis; Grade 1 nausea, loss of appetite)
- The majority of hyperglycemia was Grade 1; only two patients (3%) experienced Grade 3 hyperglycemia; no Grade 4-5 hyperglycemia
- Only 31% of patients experienced a Grade 3 TRAE; no Grade 4-5 TRAEs

Continued Progression of Front-Line Breast Cancer Regimens

Two front-line triplet regimens are being progressed – one with the existing CDK4/6 standard-of-care ribociclib and one with Pfizer's investigative selective-CDK4 inhibitor atirmociclib. RLY-2608 + ribociclib + fulvestrant dose escalation is ongoing with biologically active doses of RLY-2608. The RLY-2608 + atirmociclib + fulvestrant arm of the ReDiscover study has been initiated.

Anticipated RLY-2608 Next Steps

- Breast Cancer:
    - Initiate 2L pivotal study of RLY-2608 + fulvestrant in 2025
    - Disclose complete Phase 1/2 data in 2025
- Vascular Malformations:
    - Initiate vascular malformations study in the first quarter of 2025

Cash balance will be operationalized to preserve ability to complete 2L pivotal study

As of the end of the third quarter of 2024, cash, cash equivalents and investments were approximately $840 million.

Conference Call Information

Relay Therapeutics will host a conference call and live webcast today, December 11, 2024, at 7:00 a.m. ET (6:00 a.m. CT). 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.

The data presentation from the San Antonio Breast Cancer Symposium is also available on the Relay Therapeutics website in the "Publications/Presentations" section through the following link: https://relaytx.com/pipeline/.

About RLY-2608

RLY-2608 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, with oncogenic mutations detected in about 14% of patients with solid tumors. RLY-2608 has the potential, if approved, to address more than 300,000 patients per year in the United States, one of the largest patient populations for a precision oncology 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 RLY-2608, 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 RLY-2608. RLY-2608 is currently being evaluated in a first-in-human study designed to treat patients with advanced solid tumors with a PIK3CA (PI3Kα) mutation. For more information on RLY-2608, please visit here.

About Relay Therapeutics

Relay Therapeutics is a clinical-stage precision medicine company transforming the drug discovery process by combining leading-edge computational and experimental technologies with the goal of bringing life-changing therapies to patients. As the first of a new breed of biotech created at the intersection of complementary techniques and technologies, Relay Therapeutics aims to push the boundaries of what's possible in drug discovery. Its 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. Relay Therapeutics' initial focus is on enhancing small molecule therapeutic discovery in targeted oncology and genetic disease indications. For more information, please visit www.relaytx.com or follow us on Twitter.

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 RLY-2608, both as a monotherapy and in combination with other agents, and its other programs, as well as the clinical data for RLY-2608; the interactions with regulatory authorities and any related approvals; the potential market opportunity for RLY-2608; the cash runway projection and the expectations regarding Relay Therapeutics' use of capital and expenses. 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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