Relay Therapeutics Announces Positive Interim Data for RLY-2608 Demonstrating Clinically Meaningful Progression Free Survival

Sep 09, 2024

9.2-month median PFS in heavily pre-treated patients with PI3Kα-mutated, HR+/HER2- metastatic breast cancer at RP2D

33% ORR across all patients & 53% ORR in patients with kinase mutations at RP2D

Favorable overall tolerability profile; at RP2D, only 2 patients discontinued treatment due to adverse events & only 1 patient experienced Grade 3 hyperglycemia

Data support planned initiation of 2L pivotal study in 2025

Triplet combination with ribociclib expected to move into dose expansion in 1H 2025 & triplet combination with atirmociclib (CDK4) remains on track to start before year-end

Relay Therapeutics to host a conference call today, September 9, at 8:00 a.m. ET

CAMBRIDGE, Mass., Sept. 09, 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 positive interim data for RLY-2608, the first known investigational allosteric, pan-mutant and isoform-selective inhibitor of PI3Kα. The data showed that despite heavy pre-treatment, patients with PI3Kα-mutated, HR+, HER2- locally advanced or metastatic breast cancer who received RLY-2608 600mg BID + fulvestrant demonstrated clinically meaningful progression free survival (PFS).

“These interim data suggest that by selectively targeting mutant PI3Kα, RLY-2608 has the potential to offer a level of benefit to patients that has not previously been possible with existing non-selective medicines, while also having significantly less toxicity,” said Don Bergstrom, M.D., Ph.D., President of R&D at Relay Therapeutics. “We are very encouraged to see that RLY-2608 + fulvestrant led to clinically meaningful progression free survival in heavily pre-treated patients with PI3Kα-mutated, HR+, HER2- metastatic breast cancer. We will move quickly to share these data with regulators and align on the design of a pivotal study, which we anticipate starting in 2025.”

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 alone, in combination with fulvestrant, and in combination with fulvestrant and ribociclib or atirmociclib (Pfizer’s selective CDK4 inhibitor). As of the August 12, 2024 interim data cut-off, the RLY-2608 + fulvestrant arm of the study 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 (17 in dose escalation and 47 in dose expansion). 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 currently proposed pivotal population. An abstract has been submitted for presentation at the San Antonio Breast Cancer Symposium, taking place December 10-13, 2024.

Patients were Heavily Pre-Treated

All 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:

- 45% of patients (n=29) 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% percent 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 patients who received the RP2D and did not have a PTEN or AKT co-mutation:

- Median PFS was 9.2 months across all mutations and 10.3 months among patients with kinase mutations
- Clinical benefit rate (CBR) was 57% across all patients (20 of 35 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 30 patients with measurable disease, one third achieved a partial response (PR) (33% objective response rate,

ORR; n=10; 8 confirmed, 1 confirmed post data cut-off date, 1 unconfirmed in an ongoing patient)
    - Nearly three quarters of patients experienced tumor reductions (73%; n=22)
- Among the 15 patients with measurable disease who had a kinase mutation, more than half achieved a PR (53% ORR; n=8; 7 confirmed, 1 confirmed post data cut-off date)
- Median follow-up was 7.5 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 95% 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 one patient experienced Grade 3 hyperglycemia; no Grade 4-5 hyperglycemia
- Only 25% 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 portion of the ReDiscover study is currently testing biologically active doses of RLY-2608
    - On track to identify a dose of RLY-2608 that is combinable with full-dose ribociclib
    - Initial safety data expected in the fourth quarter of 2024
    - Expect to initiate dose expansion cohort(s) in first half of 2025
- RLY-2608 + atirmociclib + fulvestrant triplet on track for initiation by the end of 2024

Anticipated RLY-2608 Next Steps

- Doublet – Breast Cancer:
    - Initiate 2L pivotal study of RLY-2608 + fulvestrant in 2025, pending regulatory discussions
- Triplets – Breast Cancer:
    - Report initial safety data for RLY-2608 + ribociclib + fulvestrant in the fourth quarter of 2024
    - Initiate RLY-2608 + ribociclib + fulvestrant triplet dose expansion cohort(s) in the first half of 2025
    - Initiate RLY-2608 + atirmociclib (CDK4) + fulvestrant triplet by the end of 2024
- Monotherapy – Solid Tumors:
    - Initiate RLY-2608 monotherapy solid tumor dose expansion cohort(s) by the end of 2024
- Monotherapy – Vascular Malformations:
    - Initiate vascular malformations study in the first quarter of 2025

Lirafugratinib Update

- Updated FGFR2 fusion tumor agnostic data, which have generally stayed consistent with the October 2023 disclosure, will be presented at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics, taking place October 23-25, 2024
- The company met with the FDA regarding the lirafugratinib regulatory path. The FDA suggested that the company first file a new drug application (NDA) in cholangiocarcinoma, followed by a tumor agnostic supplemental NDA for FGFR2 fusions with data from more patients and more follow up
- The company plans to seek a global commercialization partner for lirafugratinib in order to maintain focus on the remainder of the portfolio

Portfolio Prioritization is a Continued Focus

- The company continues to advance high-value next-generation programs:
    - Fabry disease: clinical start anticipated in the second half of 2025
    - NRAS: clinical start anticipated in the second half of 2025
- Ongoing streamlining of the research organization

Wholly-Owned Portfolio Provides Strategic Flexibility for Cash Runway

As of the end of the second quarter of 2024, cash, cash equivalents and investments were approximately $688 million, which the company expects to be sufficient to fund its current operating plan into the second half of 2026, assuming all current programs remain wholly owned and are fully

prosecuted.

Conference Call Information

Relay Therapeutics will host a conference call and live webcast today, Monday, September 9, 2024, at 8:00 a.m. ET. Registration and dial-in for the conference call may be accessed on 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 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 trial 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, including lirafugratinib 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 expected strategic benefits under Relay Therapeutics' clinical trial collaboration with Pfizer; 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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