# Relay Therapeutics Announces Initial RLY-4008 (lirafugratinib) Data Demonstrating Durable Responses Across Multiple FGFR2-Altered Solid Tumors

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*35% ORR in patients with FGFR2 fusions (excluding CCA) & 40% ORR in patients with FGFR2-altered HR+/HER2- breast cancer*

*RLY-4008 commercialization plans to focus on broader tumor agnostic opportunities*

*Clinical focus on PI3Kα mutant selective programs, with plans to initiate RLY-2608 triplet combinations in HR+/HER2- breast cancer by YE 2023*

*Pipeline updates extend cash runway by 1 year into 2H2026*

*Relay Therapeutics to host a conference call today, October 12, at 5:30 p.m. ET*

BOSTON, Oct. 12, 2023 (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 initial clinical data for RLY-4008 (lirafugratinib) in patients with FGFR2-altered solid tumors. The data demonstrate activity across several sub-groups, including patients with FGFR2-fusion tumors and patients with FGFR2-altered HR+/HER2- breast cancer. These data are being presented today at the 2023 AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics.

“These data provide important early evidence that RLY-4008, or lirafugratinib, has the potential to help both patients with FGFR2-fusion cholangiocarcinoma as previously reported, as well as those with multiple other types of FGFR2-altered tumors,” said Don Bergstrom, M.D., Ph.D., President of R&D at Relay Therapeutics. “We are excited by the potential for lirafugratinib to help many more patients and are focused on advancing this opportunity as well as our PI3Kα programs, with the initiation of a RLY-2608 triplet combination trial this year.”

**ReFocus Trial**

Lirafugratinib is currently being evaluated in the two-part global Phase 1/2 ReFocus trial in patients with FGFR2-altered tumors. The first part of the study (dose escalation) is complete, and the second part of the study (dose expansion) is ongoing at the 70mg QD recommended Phase 2 dose. The dose expansion portion of the study includes four cholangiocarcinoma (CCA) arms and three (non-CCA) tumor agnostic arms (1: FGFR2 fusions, 2: FGFR2 amplifications and 3: FGFR2 mutations).

As of the August 23, 2023 cut-off date, the three tumor agnostic arms of the study had enrolled 84 FGFR inhibitor-naïve patients who were efficacy evaluable across 18 tumor types, including 26 patients with FGFR2 fusions, 34 patients with FGFR2 amplifications and 24 patients with FGFR2 mutations. Across these arms of the study, enrolled patients had received a median of approximately three prior lines of therapy, with the vast majority (94%) having received prior chemotherapy/ADC and nearly half (45%) having received prior targeted therapies.

**Encouraging Initial FGFR2-Fusion Tumor-Agnostic Signal with Promising Durability**

In patients with FGFR2 fusions, there was consistent activity across a range of tumor types.

- Nine of 26 patients experienced a partial response (PR) (35% overall response rate (ORR))
- Sixty-three percent of confirmed responders experienced a duration of response of at least 6 months as of the data cut-off date
- There were 11 tumor types represented amongst enrolled patients with FGFR2 fusions, including pancreatic (n=6), ovarian (n=3), gastric (n=3), non-small-cell lung (NSCLC, n=2), and breast (n=2)

**Compelling Response Rate with Multiple Long-Term Responses in Heavily Pre-Treated Patients with HR+/HER2- Breast Cancer**

The study enrolled 14 patients with breast cancer across all FGFR2 alterations, 10 of whom had HR+/HER2- breast cancer.

- Four of the 10 HR+/HER2- patients achieved PRs (40% ORR)
  - Three of the four responders remain on treatment, with the longest duration of response 72 weeks and ongoing as of the data cut-off date
  - All responders had a duration of response of at least 6 months
- All 14 patients were very heavily pre-treated, with a median of six prior lines of therapy
  - All patients had received prior targeted therapies

- Nearly all patients had received prior chemotherapy/ADC (93%)
- The vast majority of patients had received prior endocrine therapy (79%) and prior CDK4/6 (71%)

**Early Tumor-Agnostic Signal in FGFR2-Amplifications**

There were signals of activity in patients with a range of FGFR2-amplified tumor types.

- Eight of 34 patients experienced a PR (24% ORR)
  - PRs seen across tumor types, including gastric, breast, colorectal, and esophageal
- Six patients remain on treatment as of data cut-off, including four responders, one patient with stable disease and one patient who continued treatment beyond disease progression
- Forty-three percent of confirmed responders experienced a duration of response of at least 6 months

**Additional Signals**

Early, promising efficacy signals were seen in patients with FGFR2-fusions and amplifications across eight tumor types, including gastric, breast, pancreatic, NSCLC, ovarian, colorectal, esophageal, and carcinoma of unknown primary origin. In addition, three of the 24 patients with FGFR2 mutations achieved a PR (breast, gastric and ameloblastic tumors).

**Safety Data Remain Generally Consistent with Previously Reported Profile**

The safety analysis from the tumor agnostic cohorts, as of the data cut-off date, was generally consistent with the analysis from the 2022 ESMO data disclosure.

- Most treatment-related adverse events were expected FGFR2 on-target, low-grade, monitorable, generally manageable and largely reversible
- There were no observed Grade 4 or 5 adverse events
- Off-target toxicities of hyperphosphatemia and diarrhea continued to be clinically insignificant

**Lirafugratinib Next Steps**

- Continue enrollment in the three tumor agnostic cohorts
  - The company expects to report additional clinical data and a regulatory update in 2024
- Enrollment is complete in the pivotal expansion cohort in patients with FGFR2-fusion CCA who have not previously received an FGFR inhibitor
- Near-term commercial readiness activities for CCA will be paused and aligned with the broader tumor agnostic opportunity

The AACR-NCI-EORTC presentation and poster are available on the Relay Therapeutics website under Publications: https://relaytx.com/publications/.

**Pipeline Updates**

The company will continue to prioritize and expand further PI3Kα mutant selective development, including:

- RLY-2608: continue ongoing ReDiscover trial with focus on RLY-2608 + fulvestrant cohorts
  - Initiate triplet combination with RLY-2608 + fulvestrant + CDK4/6 by the end of 2023
- Next PI3Kα clinical data update expected in 2024
- Additionally, Relay Therapeutics has decided to pause further development efforts on RLY-2139 (CDK2 inhibitor)

**Cash Runway Extended**

With the decision to pause CCA commercial readiness and RLY-2139 development, Relay Therapeutics expects its cash, cash equivalents and investments will be sufficient to fund its current operating plan into the second half of 2026.

**Conference Call Information**

Relay Therapeutics will host a conference call and live webcast today, Thursday, October 12, 2023, at 5:30 p.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-4008 (lirafugratinib)**

RLY-4008 (lirafugratinib) is a potent, selective and oral small molecule inhibitor of FGFR2, a receptor tyrosine kinase that is frequently altered in certain cancers. FGFR2 is one of four members of the FGFR family, a set of closely related proteins with highly similar protein sequences and properties. Preclinically, lirafugratinib demonstrated FGFR2-dependent killing in cancer cell lines and induced regression in in vivo models, while minimal inhibition of other targets was observed, including other members of the FGFR family. In addition, lirafugratinib demonstrated strong activity against known clinical on-target resistance mutations in cellular and in vivo preclinical models. Lirafugratinib is currently being evaluated in a clinical trial in patients with advanced or metastatic FGFR2-altered solid tumors with a single arm, potentially registration-enabling cohort for FGFRi-naïve FGFR2-

fusion CCA. To learn more about the clinical trial of lirafugratinib, please visit here.

**ReFocus Trial Background**

RLY-4008 (lirafugratinib) is currently being evaluated in a global Phase 1/2 clinical trial (ReFocus) in patients with FGFR2-altered CCA and multiple other solid tumors including a single-arm, potentially registration-enabling cohort for FGFRi-naïve FGFR2-fusion CCA. The Phase 1 dose escalation has been completed, and 70 mg QD has been selected as the registrational dose. The expansion cohorts were initiated in December 2021 and now consist of seven different cohorts based on FGFR2 alteration and tumor type. Of the seven cohorts, the potential pivotal cohort consists of approximately 100 previously treated, FGFRi-naïve FGFR2-fusion CCA patients.

**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 updates on the clinical development of the programs across Relay Therapeutics' portfolio, including RLY-4008; the expected therapeutic benefits of its programs; and the expected cash runway. 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 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, or public health epidemics or outbreaks of an infectious disease, such as COVID-19, 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 of any current or planned clinical trials or the development of Relay Therapeutics' drug candidates; the risk that the preliminary 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; 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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