Relay Therapeutics Announces Interim Clinical Data that Support RLY-4008 as a Highly Selective FGFR2 Inhibitor

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Interim data suggest that RLY-4008 is a highly selective FGFR2 inhibitor that has not shown to be limited by off-target toxicities of hyperphosphatemia (FGFR1) and diarrhea (FGFR4)

RLY-4008 demonstrated tumor shrinkage in all six pan-FGFR treatment-naïve FGFR2 fusion positive cholangiocarcinoma patients with three achieving confirmed partial responses

Interim data support potential clinical benefits of optimized inhibition of FGFR2 regardless of alteration (fusions, mutations, and amplifications), line of treatment or tumor type

Relay Therapeutics anticipates selecting a once daily recommended Phase 2 dose and initiating expansion cohorts prior to the end of 2021

Relay Therapeutics to host a conference call today at 12:30 pm E.T.

CAMBRIDGE, Mass., Oct. 08, 2021 (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 interim clinical data for RLY-4008, a highly selective irreversible and oral small molecule inhibitor of FGFR2, in a first-in-human trial in patients with FGFR2-altered cholangiocarcinoma and multiple other solid tumors. The data are being presented today at the virtual AACR-NCI-EORTC Molecular Targets Conference and suggest that RLY-4008 is the first investigational therapy designed to selectively bind to FGFR2 to avoid off-isoform toxicities for the treatment of patients with FGFR2-altered tumors.

As will be presented at the conference, study investigators reported robust inhibition of FGFR2 in the first 49 subjects that was not shown to be limited by off-target toxicities, including hyperphosphatemia and diarrhea, in the interim clinical data. The initial toxicity data suggest that certain dose levels administered can achieve >85% continuous inhibition of FGFR2. At those levels, acute toxicities that would limit dose intensity have generally not been observed to date. The interim clinical data included results from FGFR2-altered solid tumors, with approximately 80% of all patients treated achieving reductions in tumor size at the cut-off date of September 9, 2021. In pan-FGFRi treatment-naïve cholangiocarcinoma patients, RLY-4008 demonstrated tumor shrinkage in all six pan-FGFR treatment-naïve FGFR2 fusion positive cholangiocarcinoma patients, with three achieving confirmed partial responses. Three of these six patients remain on study and a fourth patient went on to surgery with curative intent. Relay Therapeutics anticipates selecting a once daily recommended Phase 2 dose and initiating expansion cohorts prior to the end of 2021.

“RLY-4008 clinical data exemplifies the power of the Relay Therapeutics Dynamo™ platform and approach to discovering innovative medicines,” said Don Bergstrom, M.D., Ph.D., executive vice president of R&D at Relay Therapeutics. “Not only has the platform succeeded in creating a selective and purpose-built investigational therapy, but the initial clinical evidence of RLY-4008 has also shown the potential to positively impact the course of disease for patients with FGFR2 altered cancers. We continue to evaluate the once daily dose schedule to determine which dose to take forward into expansion cohorts before year-end. Using the same approach, we are building a deep portfolio of precision medicine programs that have the potential to impact patients with the hard-to-treat diseases. Thank you to the patients, investigators and clinical trial teams who have put their faith in our investigational therapy.”

RLY-4008 First-in-Human Trial Interim Results

RLY-4008 is currently being evaluated in an ongoing dose-escalation first-in-human trial in patients with FGFR2 altered tumors regardless of prior FGFRi treatment. The study is designed to determine the maximum tolerated dose and recommended Phase 2 dosing as well as assess initial safety and tolerability. Approximately 125 patients are planned to enroll in the study, which is being conducted in two parts, a dose escalation (part 1) and a dose expansion (part 2). As of the cut-off date of September 9, 2021, 48 of the 49 patients enrolled had a primary FGFR2-alteration, of which a majority were FGFR2-fusion cholangiocarcinoma. Most patients had high disease burden with multiple prior treatments including pan-FGFR inhibitors, and several had FGFR2 resistance mutations detected by ctDNA at baseline. Patients were treated at nine different once daily (QD) or twice daily (BID) dose levels, ranging from 20 mg QD to 70 mg QD and 20 mg BID to 100 mg BID. As of the cut-off date, duration of treatment ranged from 4 to 45 weeks.

Initial Safety Analysis

RLY-4008 has generally been well tolerated in the 49 patients treated as of September 9, 2021. With regard to dosing, the QD schedule has been prioritized due to its preferable tolerability (only one dose limiting toxicity (DLT) observed across all dose levels) and high target coverage (lowest dose, 20 mg, exceeding 85% receptor occupancy). Within the BID dosing schedule there were five DLTs observed, and receptor occupancy ranged from 90% to 98% across the BID doses.

Across all QD doses only 16% of patients, all Grade 1 or 2, experienced hyperphosphatemia, a toxicity that has been shown to limit dose intensity for pan-FGFR inhibitors in other studies. These data indicate that RLY-4008 had little or no FGFR1 inhibition at the examined dose levels. Additionally, little or no diarrhea was observed with RLY-4008 treatment suggesting minimal or no FGFR4 inhibition in treated patients to date across dose levels. Together, the interim data suggest that RLY-4008 is a highly selective FGFR2 inhibitor in humans.

Most treatment emergent adverse events were low-grade adverse events and manageable. There have been no Grade 4 or 5 adverse events. Given that retinal toxicity has been observed with FGFRi treatment, the trial is designed to assess retinopathy and retinal pigment epithelial dystrophy (RPED) adverse events, which have been observed in seven patients (14%), three of which occurred in the QD regimen. All seven of these events were Grade 1-2, which were self-limiting or resolved upon treatment interruption.

To date, a maximum tolerated dose has not been reached and QD dose exploration is ongoing to determine the recommended Phase 2 dose (RP2D).

Initial Efficacy Analysis

The interim clinical data indicate that RLY-4008 has the potential to provide tumor reduction across a number of FGFR2 alterations and lines of treatment. Key interim data include:

- Promising early activity in FGFRi naïve cholangiocarcinoma FGFR2 fusion patients, with confirmed RECISTv1.1 partial responses observed in 3/6 patients with deep tumor regressions (-56% to -83%), and 3/6 patients continuing on treatment and a fourth who went on to surgery with curative intent.
- Radiographic tumor shrinkage and complete clearance of circulating tumor DNA (ctDNA) in 70% of patients with acquired resistance mutations (N=10), including molecular brake (N550) and gatekeeper (V565) mutations, suggesting the potential for RLY-4008 to treat or prevent on-target acquired resistance.
- Early signs of activity observed outside of FGFR2-fusion positive cholangiocarcinoma, including tumor reduction in 6 out of 8 evaluable patients with activating mutations (1 confirmed PR, 1 unconfirmed PR, and 4 SD (based on RECISTv1.1 criteria)) and 3 out of 3 patients with amplifications (all SD).
- Approximately 80% of all patients treated achieved radiographic tumor regressions; this was observed across all dose levels, tumor types and FGFR2 alterations, and in patients with prior FGFR inhibitor treatment.

Consistent with the preclinical profile, these early clinical data support Relay Therapeutics' belief that RLY-4008 has broad therapeutic potential across FGFR2 alterations and tumor types.

Relay Therapeutics anticipates selecting an RP2D and initiating expansion cohorts before the end of 2021. Relay Therapeutics also expects to give a data update from this ongoing first-in-human study in 2022.

Conference Call Information
Relay Therapeutics will host a live webcast and conference call today beginning at 12:30 pm E.T. to discuss the results. To access the live call, please dial (833) 540-1168 (domestic) or (929) 517-0359 (international) and refer to conference ID 4657916. A webcast of the conference call will be available under "News and Presentations" in the Media & Investors section of Relay Therapeutics' website at http://ir.relaytx.com. The archived webcast will be available on Relay Therapeutics' website approximately two hours after the conference call and will be available for 30 days following the call.

The data presentation from the AACR-NCI-EORTC Molecular Targets Conference is also available on the Relay Therapeutics website under "Publications/Presentations" near the bottom of https://relaytx.com/pipeline/.

About RLY-4008
RLY-4008 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, RLY-4008 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, RLY-4008 demonstrates strong activity against known clinical on-target resistance mutations in cellular and in vivo preclinical models. RLY-4008 is currently being evaluated in a first-in-human clinical trial designed to evaluate the safety and tolerability of RLY-4008 in patients with advanced or metastatic FGFR2-altered solid tumors. To learn more about the first-in-human clinical trial of RLY-4008, please visit here.

About Relay Therapeutics
Relay Therapeutics (Nasdaq: RLAY) is a clinical-stage precision medicines company transforming the drug discovery process by combining leading-edge computational and experimental technologies with the goal of bringing life-changing therapies to patients. Relay Therapeutics is the first of a new breed of biotech created at the intersection of disparate technologies. Relay Therapeutics' Dynamo™ platform integrates an array of leading-edge computational and experimental approaches designed to drug protein targets that have previously been intractable. Relay Therapeutics' initial focus is on enhancing small molecule therapeutic discovery in targeted oncology and genetic disease. 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 the timing of selecting a recommended Phase 2 dose, initiating expansion cohorts of its first-in-human clinical trial of RLY-4008 and a data update of RLY-4008; and potential therapeutic effects and clinical benefits of RLY-4008, including its potential efficacy and tolerability, and whether preliminary results from the first-in-human clinical trial of RLY-4008 will be predictive of the final results of the trial or any future clinical trials of RLY-4008. The words "may," "might," "will," "could," "would," "should," "expect," "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 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 and future operations; the delay of any current or planned clinical trials or the development of Relay Therapeutics' drug candidates; the risk that the results of its

clinical trials may not be predictive of future results in connection with future clinical trials; Relay Therapeutics' ability to successfully demonstrate the safety and efficacy of its drug candidates; the timing and outcome of Relay Therapeutics' 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' Quarterly Report on Form 10-Q for the quarter ended June 30, 2021, 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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