Relay Therapeutics Announces Dosing of First Patient in First-in-Human Trial of RLY-2608 and Initiation of Expansion Cohorts for First-In-Human Trial of RLY-4008

Jan 04, 2022

Doses first patient in first-in-human trial of RLY-2608, a pan-mutant and isoform-selective PI3Kα inhibitor

Selects 70 mg once-daily dose for RLY-4008 and initiates expansion cohorts in patients with FGFR2-altered solid tumors, including cholangiocarcinoma and breast cancer

CAMBRIDGE, Mass., Jan. 04, 2022 (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 provided an update for two of its ongoing first-in-human trials, RLY-2608, the first known allosteric, pan-mutant and isoform-selective PI3Kα inhibitor in clinical development, and RLY-4008, a highly selective, irreversible and oral small molecule inhibitor of FGFR2.

"We now have three targeted therapeutics in clinical trials and a deep pipeline of preclinical precision medicine programs behind that, all with the potential to address major unmet medical needs for patients," said Sanjiv Patel, M.D., president and chief executive officer. "With our growing multi-disciplinary team, strong balance sheet and constant focus on execution, we believe we are well poised to accomplish our goal of delivering new medicines to patients. 2021 was a pivotal year for Relay Therapeutics, having disclosed promising clinical data for RLY-4008, and we are confident this is only the beginning of what this platform and team can do."

RLY-2608 First-in-Human Trial

For RLY-2608, Relay Therapeutics dosed the first patient in a first-in-human trial for patients with advanced solid tumors with a PIK3CA (PI3Kα) mutation.

The first-in-human trial for RLY-2608 is designed to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics and preliminary antitumor activity, and will consist of two separate arms. The first arm will assess RLY-2608 as a single agent for patients with unresectable or metastatic solid tumors with PI3Kα mutation, while the second arm will evaluate RLY-2608 in combination with fulvestrant for patients with PI3Kα-mutant, HR+, HER2– locally advanced or metastatic breast cancer. Each arm will have two parts, first a dose escalation part to determine the maximum tolerated dose and/or recommended phase 2 dose, followed by a dose expansion part to evaluate RLY-2608 in genomically defined populations.

In the dose expansion part of the trial for RLY-2608 as a single agent, patients with the following unresectable or metastatic solid tumors with a PI3Kα mutation per local assessment will be enrolled in the following groups: 1) clear cell ovarian cancer; 2) head and neck squamous cell carcinoma; 3) cervical cancer; 4) other solid tumors; and 5) unresectable or metastatic solid tumors with PIK3CA double mutations defined as major (E542X, E545X, or H1047X), plus ≥1 additional PI3Kα mutations. For RLY-2608 in combination with fulvestrant, men or postmenopausal women with HR+, HER2– advanced or metastatic breast cancer patients with PI3Kα mutations will be enrolled in the following groups: 1) patients who have not received prior treatment with a PI3Kα inhibitor; and 2) patients who are intolerant to PI3Kα inhibitors. The trial is designed to enroll approximately 190 patients between both arms.

RLY-4008 Expansion Cohorts

Relay Therapeutics initiated expansion cohorts last month for the first-in-human trial for RLY-4008 in patients with FGFR2-altered cholangiocarcinoma, breast cancer and other solid tumors.

The ongoing first-in-human trial for RLY-4008 is designed to evaluate the safety, tolerability, pharmacokinetics and anti-tumor efficacy. Following a thorough assessment of the dose escalation data, the expansion portion of the trial has been initiated at a dose of 70 mg once daily.

The expansion part of the trial has five cohorts planned to evaluate genetically defined populations: 1) intrahepatic cholangiocarcinoma (ICC) patients with an FGFR2 fusion previously treated with a pan-FGFR inhibitor; 2) ICC patients with an FGFR2 fusion not previously treated with a pan-FGFR inhibitor; 3) patients with an FGFR2 fusion and solid tumor other than ICC; 4) advanced, unresectable solid tumor patients with focal FGFR2 amplification; 5) advanced, unresectable solid tumor patients with an oncogenic FGFR2 mutation.

Relay Therapeutics will continue to monitor the dose escalation data and expansion cohorts to determine if other doses or schedules should be evaluated.

About RLY-2608

RLY-2608 is the lead program of multiple preclinical efforts to discover and develop mutant selective inhibitors of PI3Kα. PI3Kα is the most frequently mutated kinase in all cancers, with oncogenic mutations detected in about 13% of patients with solid tumors. 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 (H1047X, E542X and E545X), 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.

About RLY-4008

RLY-4008 is a potent and selective oral small molecule inhibitor of FGFR2, a receptor tyrosine kinase that is frequently altered in many cancers, including cholangiocarcinoma, breast cancer, gastric cancer and endometrial cancer. FGFR2 is one of four members of the FGFR family, a set of closely related proteins with highly similar protein sequences and properties. Interim clinical data support RLY-4008 as the first highly selective FGFR2 inhibitor that has not shown to be limited by off-target toxicities of hyperphosphatemia (FGFR1) and diarrhea (FGFR4). These initial data suggest RLY-4008 has a manageable safety profile and drives tumor regression across multiple FGFR2 alterations and tumor types. RLY-4008 is currently being evaluated in a first-in-human trial designed to evaluate the safety, tolerability, pharmacokinetics and anti-tumor efficacy of RLY-4008 in patients with advanced or metastatic FGFR2-altered solid tumors. To learn more about the first-in-human 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 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 plans and timelines for the clinical development of RLY-2608 and RLY-4008, including plans and timelines for pursuing development in the dose expansion part of the trial; potential therapeutic effects and anticipated clinical benefits of RLY-4008 and RLY-2608, as a monotherapy and in combination; the potential of RLY-2608 to be among the largest precision oncology medicine opportunities ever; the potential of RLY-2608 to be more tolerable and effective than existing therapies; whether preclinical or early clinical results of RLY-2608 and RLY-4008 will be predictive of future clinical trials; and Relay Therapeutics' strategy, business plans and focus. 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 we have operations or do business, as well as on the timing and anticipated results of our 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 our 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' most recent Annual Report on Form 10-K or 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.

Contact:
Pete Rahmer
Chief Corporate Development Officer
617-322-0715
prahmer@relaytx.com

Media:
Dan Budwick
1AB
973-271-6085
dan@1abmedia.com