UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): October 7, 2021

RELAY THERAPEUTICS, INC.
(Exact name of Registrant as Specified in Its Charter)

Delaware	**001-39385**	**47-3923475**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

Relay Therapeutics, Inc.
399 Binney Street, 2nd Floor
Cambridge, Massachusetts 02139
(Address of principal executive offices, including zip code)

(617) 370-8837
(Registrant's telephone number, including area code)

Not Applicable
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.001 par value per share	**RLAY**	**The Nasdaq Global Market**

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

On October 7, 2021, Relay Therapeutics, Inc. (the "Company") issued a press release announcing preclinical data for RLY-2608, a copy of which is furnished herewith as Exhibit 99.1. In addition, on October 8, 2021, the Company issued a press release announcing interim clinical data from its ongoing dose-escalation first-in-human clinical trial of RLY-4008 (the "RLY-4008-101 Trial"), a copy of which is furnished herewith as Exhibit 99.2. The Company intends to host a conference call to discuss the interim clinical data from its RLY-4008-101 Trial and preclinical data for RLY-2608 on October 8, 2021 at 12:30 p.m. E.T. The Company has made available a slide presentation to accompany the call, a copy of which is being furnished as Exhibit 99.3 to this Current Report on Form 8-K. The Company undertakes no obligation to update, supplement or amend the materials attached hereto as Exhibit 99.3.

The information in this Item 7.01, including Exhibit 99.1, Exhibit 99.2 and Exhibit 99.3 attached hereto, is intended to be furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such filing.

Item 8.01 Other Events.

RLY-2608

On October 7, 2021, at the AACR-NCI-EORTC Molecular Targets Conference, the Company announced preclinical data for RLY-2608, its inhibitor of cancer-associated mutant variants H1047X, E542X, and E545X of phosphoinostide 3-kinase alpha ("PI3Kα"). RLY-2608 is the lead program of the Company's multiple preclinical efforts to discover and develop mutant selective inhibitors of PI3Kα.

The data show that in preclinical models, RLY-2608 preferentially binds mutant PI3Kα at a novel allosteric site discovered by the Company's Dynamo™ platform. In biochemical and cellular assays, RLY-2608 inhibited the three major classes of PI3Kα oncogenic mutations (H1047X, E542X and E545X) while sparing wild-type PI3Kα. The data further suggest that RLY-2608 is also highly selective against other PI3K family members and exquisitely selective across the kinome. The data suggest that projected clinically relevant doses of RLY-2608 achieved tumor regression in PIK3CA mutant in vivo xenograft models representing H1047R and E545K mutations with significantly reduced impact on glucose metabolism compared to non-mutant selective active site inhibitors. In higher species, dosing of RLY-2608 resulted in exposures exceeding 90% inhibition of mutant PI3Kα in cells without resulting in elevated glucose levels or histopathological changes associated with dysregulation of glucose metabolism that are seen with non-mutant selective inhibitors.

The Company believes these results support advancement of RLY-2608 into clinical development as a differentiated mechanism of mutant PI3Kα inhibition. In addition, the Company believes that due to the preclinical selectivity that RLY-2608 has shown against the PI3Kα mutant variants H1047X, E542X, and E545X, RLY-2608 could potentially address over 100,000 patients per year in the United States. The Company expects to initiate a first-in-human clinical trial of RLY-2608 in the first half of 2022, subject to submission of an investigational new drug application and acceptance by the FDA.

RLY-4008

On October 8, 2021, at the AACR-NCI-EORTC Molecular Targets Conference, the Company will also announce interim clinical data from the RLY-4008-101 Trial of its investigational fibroblast growth factor receptor 2 ("FGFR2") inhibitor, RLY-4008, in patients with FGFR2 altered tumors regardless of prior FGFR inhibitor treatment. The clinical trial 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 trial, which is being conducted in two parts, a dose escalation (part 1) and a dose expansion (part 2).

The Company believes the interim clinical data suggest robust inhibition of FGFR2 in the first 49 subjects that was not shown to be limited by off-target toxicities, including hyperphosphatemia and diarrhea. 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 having achieved reductions in tumor size as of September 9, 2021 (the "Data Cut-off Date"). In pan-FGFR inhibitor 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. The Company plans to select a once daily recommended Phase 2 dose and initiate expansion cohorts of the RLY-4008-101 Trial prior to the end of 2021.

As of the Data Cut-off Date, 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 circulating tumor DNA ("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 Data Cut-off Date, duration of treatment ranged from 4 to 45 weeks.

Initial Safety Analysis

The interim clinical data of the RLY-4008-101 Trial indicate that RLY-4008 has generally been well tolerated in the 49 patients treated as of the Data Cut-Off Date. With regard to dosing, the QD dosing schedule has been prioritized due to its preferable tolerability (as only one dose limiting toxicity ("DLT") was observed across all dose levels) and high target coverage (lowest dose of 20 mg exceeded 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 FGFR inhibitor treatment, the trial is designed to assess retinopathy and retinal pigment epithelial dystrophy adverse events, which have been observed in seven patients (14%), three of which occurred in the QD dosing regimen. All seven of these events were Grade 1-2, which were self-limiting or resolved upon treatment interruption.

Initial Efficacy Analysis

The interim clinical data of the RLY-4008-101 Trial 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 FGFR inhibitor naïve cholangiocarcinoma FGFR2 fusion patients, with confirmed RECISTv1.1 partial responses observed in 3 out of 6 patients with deep tumor regressions (-56% to -83%) and 3 out of 6 patients continuing on treatment and a fourth who went on to surgery with curative intent.
- Radiographic tumor shrinkage and complete clearance of 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 partial response, ("PR"), 1 unconfirmed PR, and 4 stable disease ("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 of RLY-4008, these early clinical data support the Company's belief that RLY-4008 has broad therapeutic potential across FGFR2 alterations and tumor types.

Cautionary Note Regarding Forward Looking Statements

This Current Report on Form 8-K and certain of the materials furnished or filed herewith contain 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: the Company's strategy, business plans and focus; the progress and timing of updates on the clinical development of the programs across the Company's 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 the timing of initiation of a first-in-human clinical trial of RLY-2608; potential therapeutic effects and clinical benefits of RLY-2608 and RLY-4008, and whether preclinical or preliminary results from the Company's ongoing trials of its product candidates will be predictive of the final results of the trial or any future clinical trials; and the potential target patient population of RLY-2608. 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 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 Current Report on Form 8-K or the materials furnished or filed herewith, including, without limitation, risks associated with: the impact of COVID-19 on countries or regions in which the Company has operations or does business, as well as on the timing and anticipated results of the Company's clinical trials, strategy and future operations; the delay of any current or planned clinical trials or the development of the Company's drug candidates; the risk that the results of the Company's clinical trials may not be predictive of future results in connection with future clinical trials; the Company's ability to successfully demonstrate the safety and efficacy of its drug candidates; the timing and outcome of the Company's 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 the Company's 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 the Company's views only as of today and should not be relied upon as representing its views as of any subsequent date. The Company 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.

Item 9.01. Exhibits

(d) Exhibits

99.1	Press release for RLY-2608 issued by Relay Therapeutics, Inc. on October 7, 2021, furnished herewith.
99.2	Press release for RLY-4008 issued by Relay Therapeutics, Inc. on October 8, 2021, furnished herewith.
99.3	Corporate presentation, dated October 2021, furnished herewith.
104	Cover Page Interactive Data File (embedded within Inline XBRL document).

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

RELAY THERAPEUTICS, INC.

Date: October 8, 2021

By: /s/ Brian Adams
Brian Adams, J.D.
General Counsel

Relay Therapeutics Announces Preclinical Data that Support RLY-2608 as the First Known Allosteric Pan-Mutant Selective Inhibitor of PI3Kα

RLY-2608 preferentially binds mutant PI3Kα at a novel allosteric site discovered by the Dynamo™ platform

Preclinically, achieved tumor regressions in vivo with significantly reduced impact on glucose metabolism compared to active site inhibitors

RLY-2608's pan-mutant inhibition has the potential to address over 100,000 patients per year in the U.S.

Cambridge, MA – October 07, 2021 – 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 shared preclinical data at the virtual AACR-NCI-EORTC Molecular Targets Conference for RLY-2608, the first allosteric, pan-mutant (H1047X, E542X and E545X) and isoform-selective PI3Kα inhibitor.

The data presented at the conference show that in preclinical models, RLY-2608 preferentially binds mutant PI3Kα at a novel allosteric site discovered by the Dynamo™ platform. Scientists at Relay Therapeutics solved the full-length structure of PI3Kα, performed long time-scale molecular dynamic simulations to elucidate differences in motion between wild-type (WT) and mutant PI3Kα, and leveraged these insights to enable the design of RLY-2608. In biochemical and cellular assays, RLY-2608 inhibited the three major classes of PI3Kα oncogenic mutations (H1047X, E542X and E545X) while sparing WT PI3Kα. The data further suggest that RLY-2608 is also highly selective against other PI3K family members and exquisitely selective across the kinome. The data suggest that projected clinically relevant doses of RLY-2608 achieved tumor regression in *PIK3CA* mutant in vivo xenograft models representing H1047R and E545K mutations with significantly reduced impact on glucose metabolism compared to non-mutant selective active site inhibitors. In higher species, dosing of RLY-2608 resulted in exposures exceeding 90% inhibition of mutant PI3Kα in cells without resulting in elevated glucose levels or histopathological changes associated with dysregulation of glucose metabolism that are seen with non-mutant selective inhibitors.

These results support advancement of RLY-2608 into clinical development as a differentiated mechanism of mutant PI3Kα inhibition with the first-in-human study anticipated to start in the first half of 2022. RLY-2608 is the lead program of multiple preclinical efforts at Relay Therapeutics to discover and develop mutant selective inhibitors of PI3Kα.

RLY-2608 has the potential to address over 100,000 patients per year in the United States, one of the largest patient populations for a precision oncology medicine. Selectivity for all three mutation hot spots (H1047X, E542X and E545X) has the potential to effectively double the addressable patient population compared to selectivity for only H1047X.

“The data shared today provide another proof point that we’re developing what we believe to be the first known pan-mutant selective allosteric inhibitor of PI3Kα,” said Don Bergstrom, M.D., Ph.D., executive vice president of R&D at Relay Therapeutics. “We believe RLY-2608 has the potential to address a significant unmet medical need in a large population and have validated our approach for developing mutant selective inhibitors of PI3Kα. RLY-2608 is only the start of our PI3Kα efforts, and by leveraging our Dynamo™ platform, we plan to build a franchise around this target for the long-term.”

Conference Call Information

Relay Therapeutics will host a live webcast and conference call tomorrow, October 8, beginning at 12:30 pm E.T. to discuss the results of this presentation and the RLY-4008 presentation tomorrow. 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” at https://relaytx.com/pipeline/.

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 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 on path to initiate a first-in-human clinical trial in the first half of 2022, subject to submission of an investigational new drug application and acceptance by the FDA.

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 initiation of a first-in-human clinical trial of RLY-2608; potential therapeutic effects and anticipated clinical benefits of RLY-2608; Relay Therapeutics’ plans to build a franchise around PI3Kα; the potential target patient population of RLY-2608; and whether preclinical results of RLY-2608 will be predictive of future clinical trials of RLY-2608. 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.

Contact:

Pete Rahmer
Senior Vice President, Corporate Affairs and Investor Relations
617-322-0715
prahmer@relaytx.com

Media:

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

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

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, MA – October 08, 2021 – 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.

Contact:
Pete Rahmer
Senior Vice President, Corporate Affairs and Investor Relations
617-322-0715
prahmer@relaytx.com

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

RELAY®
THERAPEUTICS

Corporate Update Call: Data Presentations at AACR-NCI-EORTC Molecular Targets Conference

October 2021

Disclaimer

This presentation contains forward-looking statements and information about our current and future prospects and our operations and financial results, which are based on currently available information. All statements other than statements of historical facts contained in this presentation, including statements regarding our strategy, future financial condition, future operations, projected costs, prospects, plans, objectives of management and expected market growth, are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as ''aim,'' ''anticipate,'' ''assume,'' ''believe,'' ''contemplate,'' ''continue,'' ''could,'' ''design,'' ''due,'' ''estimate,'' ''expect,'' ''goal,'' ''intend,'' ''may,'' ''objective,'' ''opportunity,'' ''plan,'' ''predict,'' ''positioned,'' ''potential,'' ''seek,'' ''should,'' ''target,'' ''will,'' ''would'' and other similar expressions that are predictions of or indicate future events and future trends, or the negative of these terms or other comparable terminology. These forward-looking statements include express or implied statements about the initiation, timing, progress and results of our current and future clinical trials, including the cohort expansion of our ongoing clinical trial for RLY-4008, the initiation of a clinical trial for RLY-2608 and additional data disclosures for RLY-4008 and RLY-2608, and current and future preclinical studies of our product candidates; the potential therapeutic benefits of our product candidates, including potential efficacy and tolerability, and combination potential of our product candidates; whether preliminary results from our preclinical or clinical trials will be predictive of the final results of the trials or any future clinical trials of our product candidates; the possibility that unconfirmed results from these trials will not be confirmed by additional data as the clinical trials progress; the market opportunities for our product candidates; the expected strategic benefits and potential receipt of payments under our collaborations; our ability to successfully establish or maintain collaborations or strategic relationships for our product candidates; expectations regarding current and future interactions with the U.S. Food and Drug Administration (FDA); our ability to manufacture our product candidates in conformity with the FDA's requirements; the capabilities and development of our Dynamo™ platform; our financial performance; the effect of the COVID-19 pandemic, including mitigation efforts and economic effects, on any of the foregoing or other aspects of our business operations, including but not limited to our preclinical studies and future clinical trials; our plans to develop, manufacture and commercialize our current product candidates and any future product candidates; and the implementation of our business model and strategic plans for our business, current product candidates and any future product candidates.

Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make due to a number of risks and uncertainties. These and other risks, uncertainties and important factors are described in the section entitled "Risk Factors" in our 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. Any forward-looking statements represent our views only as of the date of this presentation and we undertake no obligation to update or revise any forward-looking statements, whether as a result of new information, the occurrence of certain events or otherwise. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. No representations or warranties (expressed or implied) are made about the accuracy of any such forward-looking statements.

Certain information contained in this presentation relates to or is based on studies, publications, surveys and other data obtained from third-party sources and our own internal estimates and research. While we believe these third-party studies, publications, surveys and other data to be reliable as of the date of this presentation, we have not independently verified, and make no representation as to the adequacy, fairness, accuracy or completeness of, any information obtained from third-party sources. In addition, no independent source has evaluated the reasonableness or accuracy of our internal estimates or research and no reliance should be made on any information or statements made in this presentation relating to or based on such internal estimates and research.

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Relay Tx Has Delivered Against All Key Objectives

Programs

	Goal Set at Time of July 2020 IPO	Status
RLY-4008 *(FGFR2)* 	Initiate Phase 1 clinical trial in 2H 2020	✓
	Limit off-target toxicities / be highly selective for FGFR2	✓
	Show initial data to support promising tolerability	✓
	Show initial data demonstrating potential for tumor reduction across a number of FGFR2 alterations and lines of treatment	✓
	Potentially increase addressable population	✓
RLY-2608 *(PI3Kα)* 	Design molecule with PI3Kα isoform selectivity	✓
	Design molecule with H1047X mutant selectivity • *Additional mutant selectivity demonstrated in E545X and E542X, potentially increasing addressable patient population to ~100K*	✓
	Begin IND-enabling studies in 2021	✓
RLY-1971 *(SHP2)*	Identify strategic development path • *Genentech partnership*	✓

Dynamo™ Platform and Capabilities

Goal Set at Time of July 2020 IPO	Status
Continue platform evolution • *ZebiAI acquisition*	✓
Build team out across all key functions	✓
Prove clinical development execution • *Excellent enrollment of 2 Phase 1 studies during a global pandemic*	✓
Expand scope of research (genetic diseases)	✓
Create scale in research	✓

Clear focus on execution

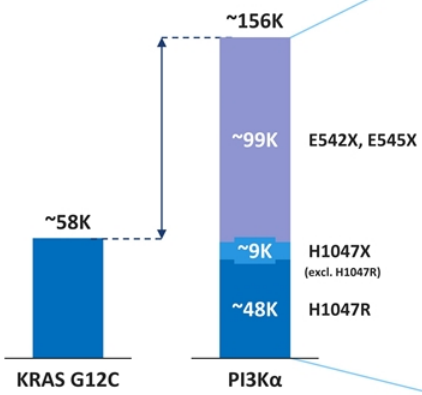
FGFR2 – Highlights from Recent RLY-4008 Interim Clinical Data Disclosure

Source: RLY-4008 data as presented at 2021 AACR-NCI-EORTC Molecular Targets Conference

PI3Kα Opportunity Is Among the Largest Ever for Precision Oncology

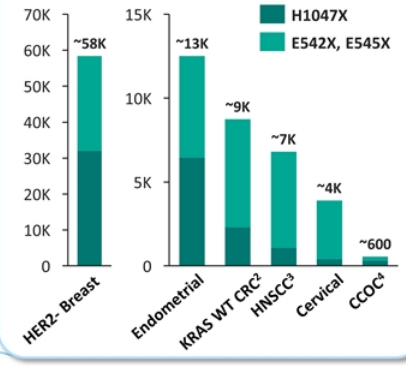
Pan-mutant selective drug represents significant clinical opportunity

US Patients – Solid Tumors Incidence (Annual)[1]

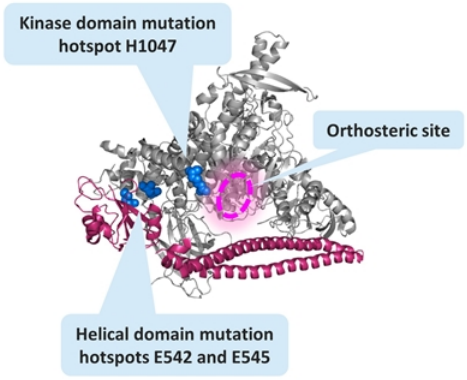


PI3Kα alterations observed across multiple tumor types – select indications

US Patients - Comprehensive Incidence (Annual)



Relay Tx has a unique understanding of PI3Kα



First gen — Pan-PI3K/mTOR inhibitors: Significant toxicity

2010s — Pan-PI3K inhibitors: Significant toxicity

2019 — PI3Kα-predominant inhibitor (alpelisib): PFS benefit with limited TI

Today — **Pan-mutant selective inhibitor needed**

Sources: FoundationInsights® database; SEER

1. Annual incidence of solid tumors with KRAS G12C, PI3K H1047R, PI3K H1047X, PI3K E542X + E545X alterations; 2. KRAS wild-type colorectal cancer; 3. Head & Neck Squamous Cell Carcinoma; 4. Clear Cell Ovarian Cancer

PI3Kα – Highlights from Recent RLY-2608 Preclinical Data Disclosure

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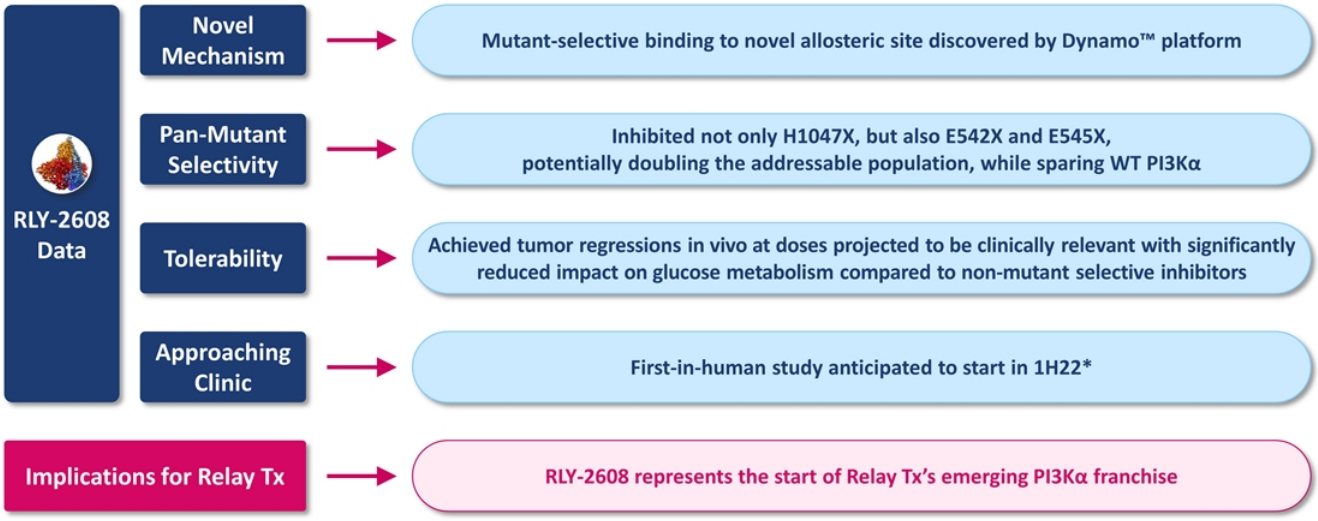


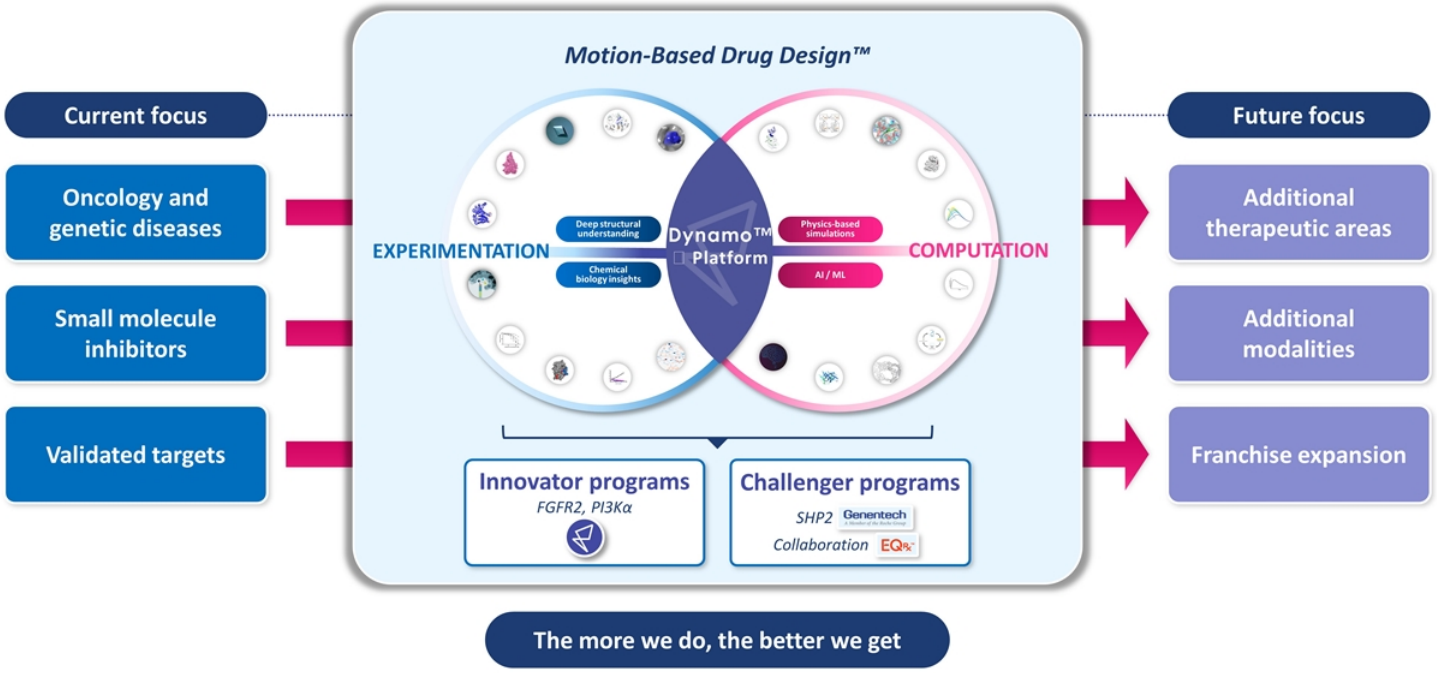
*Subject to submission and acceptance of IND by the FDA

Relay Tx – We Have Validated Our Approach

Elucidation of novel disease biology → **Selection of validated targets** → **Creation of new medicines** → **Execution of precision medicines clinical trials** → Commercialization and generation of real world data

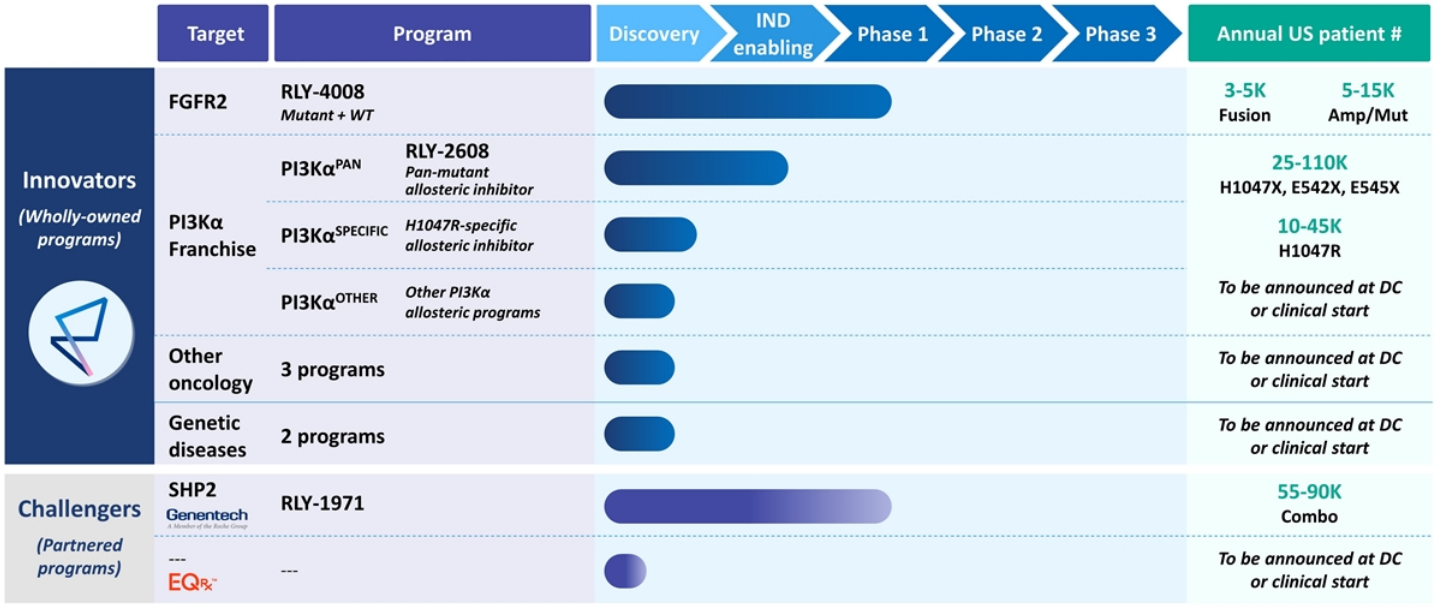
				DISCOVERY				IND ENABLING	CLINICAL
				Selection of Validated Target	Motion-Based Hypothesis	Supporting Preclinical Data	Selection of DC	Clinical Execution	Supporting Early Clinical Data
Innovators *(Wholly owned programs)*	**FGFR2**		**RLY-4008**	✓	✓	✓	✓	✓	✓
	PI3Kα Franchise	**PI3Kα^{PAN}**	**RLY-2608** *Pan-mutant allosteric inhibitor*	✓	✓	✓	✓	○	○
		PI3Kα^{SPECIFIC}	*H1047R-specific allosteric inhibitor*	✓	✓	✓	○	○	○
	Additional Oncology Programs *(3)*			✓	✓	✓	○	○	○
	Genetic Disease Programs *(2)*			✓	✓	✓	○	○	○
Challengers *(Partnered programs)*	**SHP2** Genentech *A Member of the Roche Group*		**RLY-1971**	✓	✓	✓	✓	✓	✓

Relay Tx – Our Vision

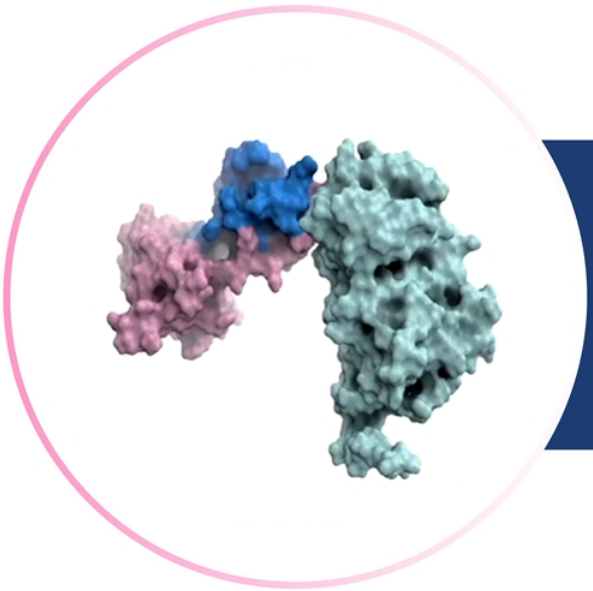


The more we do, the better we get

Extensive Precision Medicines Pipeline

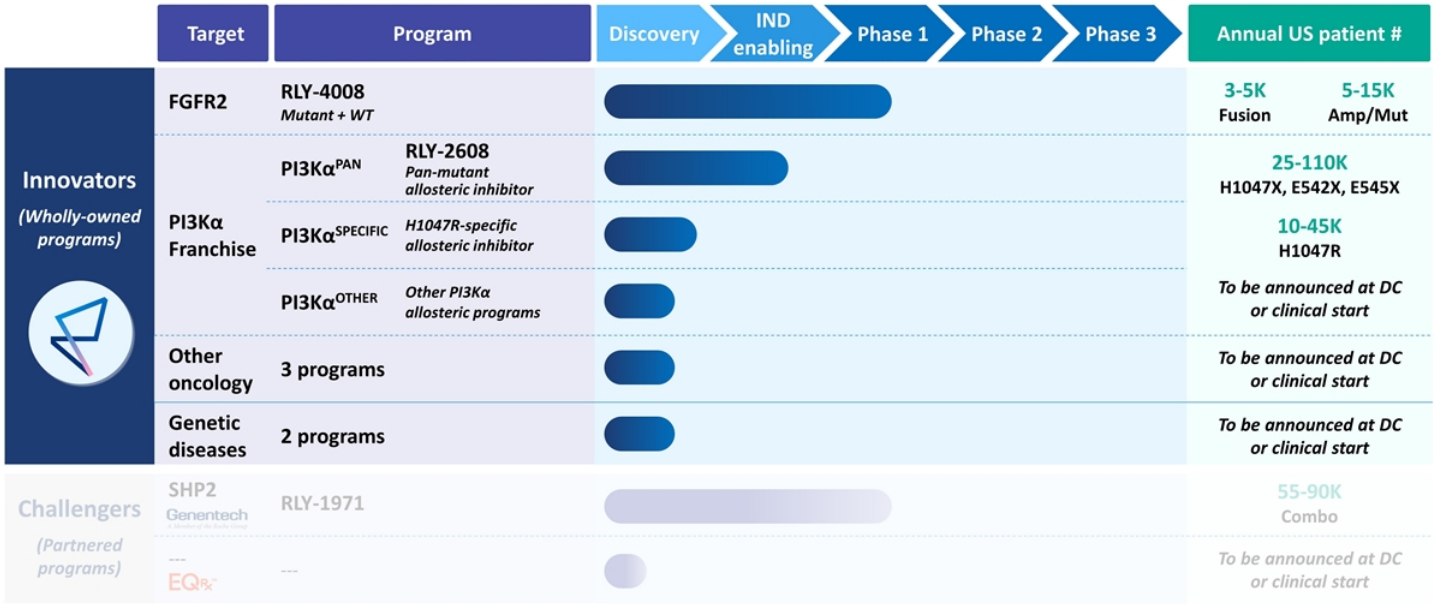


Note: Patient #'s refer to total annual number of US patients with late-line cancers compared to comprehensive annual incidence that may be amenable to treatment with our programs



Relay Tx Programs

Extensive Precision Medicines Pipeline – Innovators



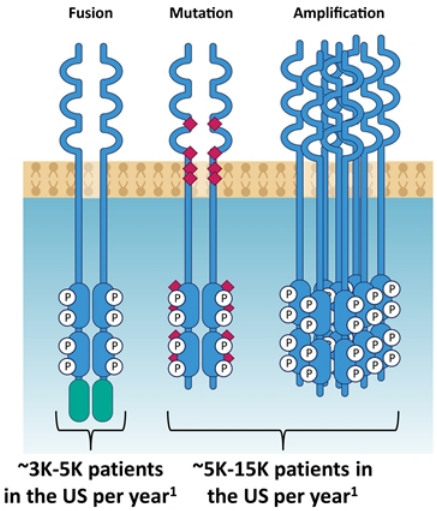
Note: Patient #'s refer to total annual number of US patients with late-line cancers compared to comprehensive annual incidence that may be amenable to treatment with our programs

FGFR2 – Highlights from Recent RLY-4008 Interim Clinical Data Disclosure

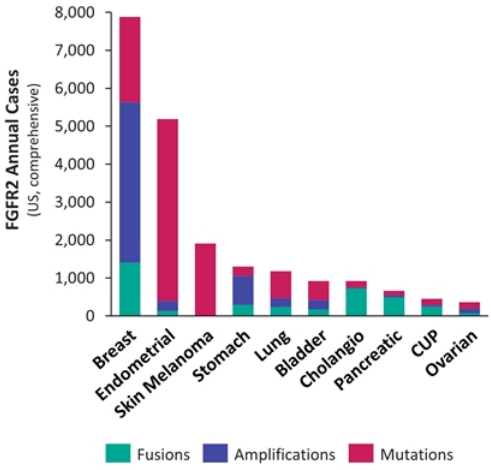
Source: RLY-4008 data as presented at 2021 AACR-NCI-EORTC Molecular Targets Conference

FGFR2 – Validated Target Present in Several Tumor Types

Three classes of driver alterations in FGFR2



FGFR2 alterations are observed across multiple tumor types[2]



FGFR2-altered cancers remain a high unmet medical need

Current FDA Accelerated Approvals for FGFR2-Altered Cancers

Tumor Type	FGFR2 Fusion & Rearrangement	FGFR2 Oncogenic Mutation	FGFR2 Amplification
FGFRi-naïve Cholangio-carcinoma	23-36% ORR Pemigatinib Infigratinib	No FDA-approved therapy	
FGFRi-resistant Cholangio-carcinoma			
Other FGFR2-altered solid tumors			

Sources: FoundationInsights® database, using 8 copies as the threshold for amplification, and including only mutations with known or likely functional significance; SEER and ACS databases
1. Patient #'s refer to total annual number of US patients with late-line cancers vs. comprehensive annual incidence that may be amenable to treatment with our programs; 2. Cholangio, cholangiocarcinoma; CUP, carcinoma unknown primary

FGFR2 – Selective Inhibitor Required to Address Large Unmet Medical Need

Second Line:
FGFRi Treatment Naïve Precedent

FGFRi treatment naïve patient population

Compound	Company	Stage	FGFR2 Selective	Response Rate	Dosing Schedule	% of Patients with Hyperphosphatemia[1]	% of Patients with Diarrhea	% of Patients Discontinued or Dose Reduced
Pemigatinib	Incyte	Approved[3]	No	36% (ICC)	2 weeks on, 1 week off	94%	47%	23%
Infigratinib	QED therapeutics	Approved[3]	No	23% (ICC)	3 weeks on, 1 week off	90%	24%	75%
Futibatinib	TAIHO ONCOLOGY, INC.	Phase 2/3	No	42% (ICC)	Once daily dosing	91%	~28%	56%
Erdafitinib	janssen	Approved[3]	No	32% (Urothelial Carcinoma)	Personalized dosing based on phosphate levels[2]	76%	47%	66%

[1] As defined by increased serum phosphate; except for infigratinib which is not specified
[2] Initial dose (8 mg QD) adjusted to 9 mg QD only in absence of hyperphosphatemia
[3] Currently have accelerated approval

High toxicity limits efficacy of non-selective FGFR inhibitors

Late-Line:
Retreating with Chemo Precedent

Regimen	Trial	Stage	Population	Response Rate	Progression-Free Survival *(median)*	Overall Survival *(median)*	% Deaths Due to Chemo	% of Patients Discontinued or Dose Reduced
FOLFOX Chemotherapy	ABC-06	Phase 3	All Comers, 2L	3% (ICC)	3.3 months (ICC)	5.7 months (ICC)	4%	74%

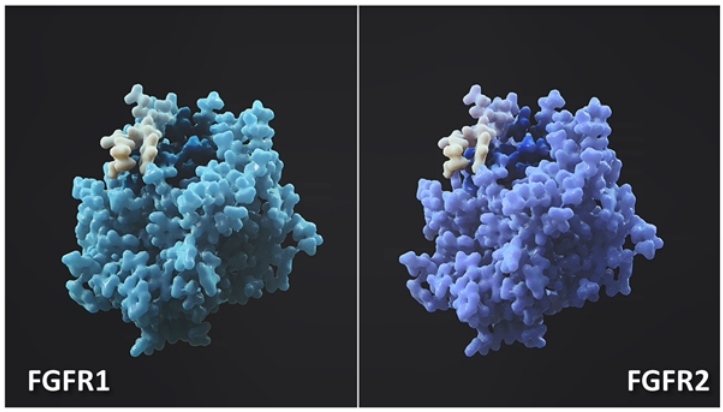
Late-line treatment with chemotherapy can be highly toxic and only results in incremental efficacy

A selective inhibitor of FGFR2 with broad activity against acquired resistance mutations is necessary to address significant unmet need in patients with FGFR2-altered tumors

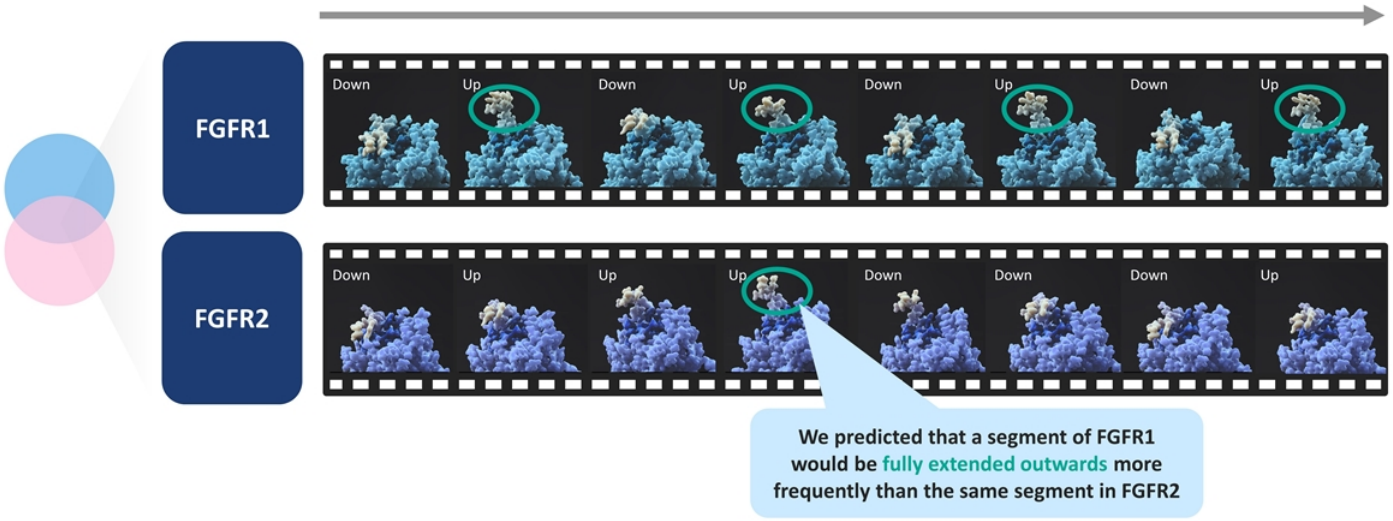
Sources: Pemigatinib – Prescribing information; Infigratinib – Prescribing information; Futibatinib/TAS-120 – AACR 2021 (diarrhea %s approximated from presentation); Erdafitinib – Prescribing information; N.R. = not reported; FOLFOX – ABC-06 Publication in Lancet Oncology 2021

FGFR2 – Standard Approach to Discovery Has Had Limited Success

Standard Approach



FGFR2 – Increasing Experimental Resolution Reveals New Opportunities



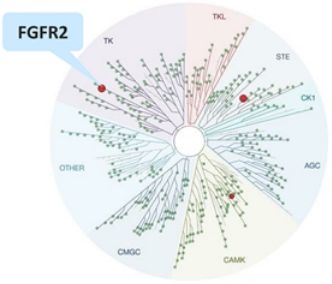
We predicted that a segment of FGFR1 would be fully extended outwards more frequently than the same segment in FGFR2

Exploiting the dynamic difference between FGFR1 and FGFR2 enabled Relay Tx to design a selective FGFR2 inhibitor

FGFR2 – RLY-4008 Is Potentially the First Highly Selective Irreversible FGFR2 Inhibitor

RELAY THERAPEUTICS

RLY-4008

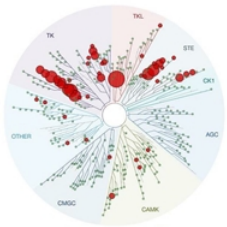


Percent Control

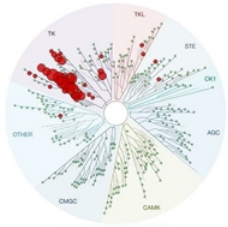
- 0%
- 0.1%
- 0.1-1%
- 1-5%
- 5-10%
- 10-35%
- > 35%

Pan-FGFR Inhibitors

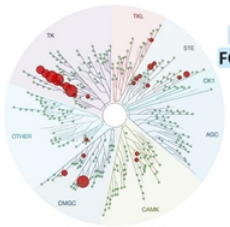
AZD4547



Erdafitinib



Pemigatinib



Futibatinib

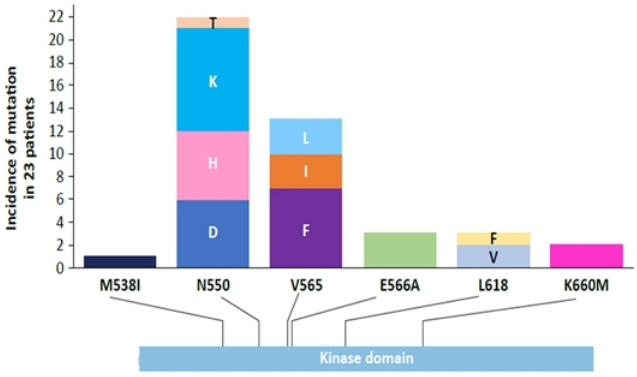
Percent Control

- 0%
- 0.1%
- 0.1-1%
- 1-5%
- 5-10%
- 10-35%
- > 35%

Note: Single experiment that tested each compound run at 500nM against 468 targets in the absence of ATP and without preincubation
Source: KINOMEscan™ by Eurofins DiscoverX

FGFR2 – RLY-4008 Designed to be Active Against Resistance Mechanisms

Reported on target resistance mutations for pan-FGFR inhibitors



Activity against acquired resistance mutations

	Gatekeeper			Molecular Brake			Other		
	V565F	V565L	V565I	N550K	E566A	K642N	L618V	K660M	M538I
RLY-4008									
Pemigatinib									
Infigratinib									
Futibatinib									
Erdafitinib									
Debio-1347									

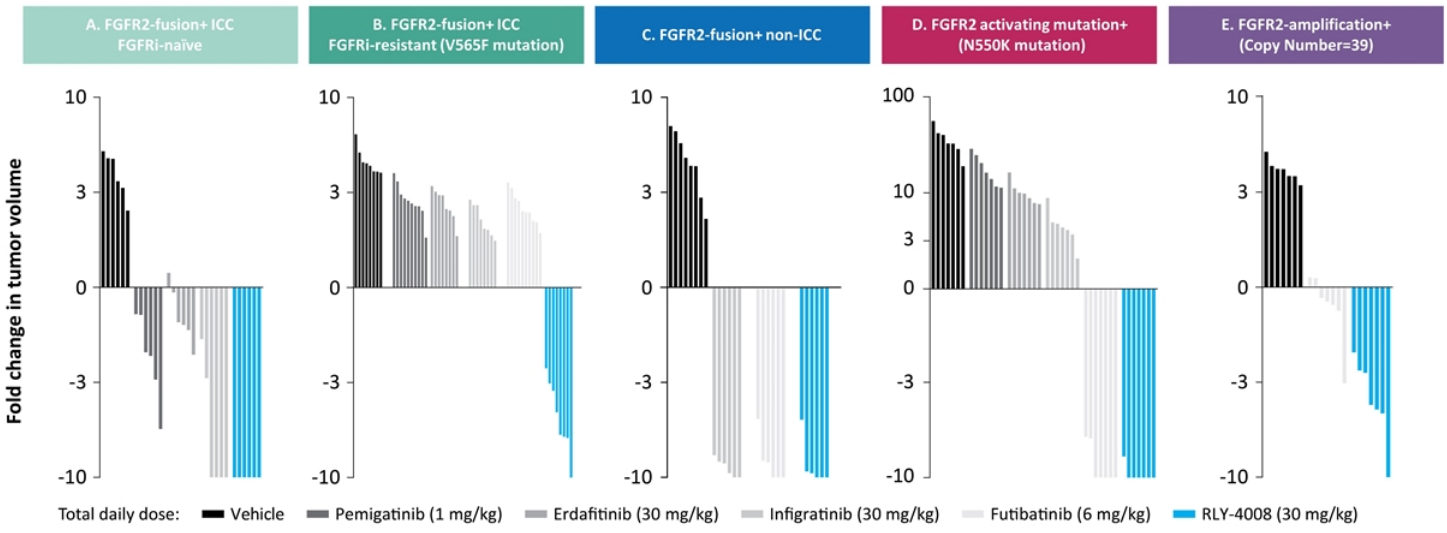
KEY: Potency Fold Change

1 25 >50

Decreasing potency on resistance mutation

Note: Left figure adapted from: Goyal L et al. 32nd EORTC/AACR/NCI Virtual Symposium. Abstract 49 and Varghese AM et al. JCO Precision Oncology. 2021;5: 44-50. Heat map displaying fold-change in potency (IC_{50}) for the indicated inhibitors against FGFR2 WT and the indicated FGFR2 mutant. Numbering of mutant residues refers to the FGFR2 IIIb isoform. Fold-change of 1 indicates equivalent potency on FGFR2 WT and the indicated FGFR2 mutant.

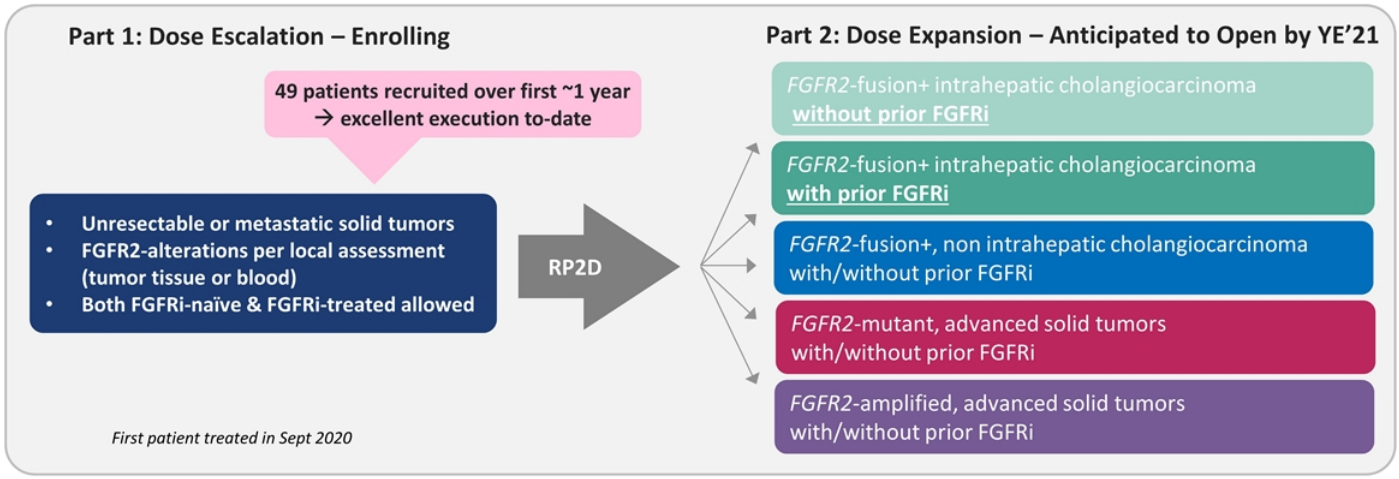
FGFR2 – RLY-4008 Has Potent *In Vivo* Antitumor Activity Against Primary FGFR2 Alterations and Common Resistance Mutations



Note: End-of-treatment waterfall plots (change in tumor volume) for tumor models treated with 30 mg/kg RLY-4008 or the indicated pan-FGFRi used at doses equivalent to their recommended human doses.
CC6702 cholangiocarcinoma xenograft with FGFR2-TTC28 fusion **(Figure A)**; ICC13-7 cholangiocarcinoma xenograft harboring FGFR2-OPTN fusion with an V565F gatekeeper resistance mutation introduced by CRISPR **(Figure B)**; Gastric adenocarcinoma PDX, FGFR2-WDR11 fusion **(Figure C)**; AN3 CA endometrial adenocarcinoma xenograft, with FGFR2 N550K activating mutation **(Figure D)**; and SNU-16 gastric carcinoma xenograft with FGFR2 amplification (FGFR2 copy number=39) **(Figure E)**.
ICC: Intrahepatic cholangiocarcinoma.

FGFR2 – RLY-4008 First-in-Human (FIH) Study Design

Key Objectives:
MTD/RP2D, safety, pharmacokinetics, biomarkers (ctDNA, tumor markers), preliminary anti-tumor activity



Orally dosed; BID and QD schedules explored using the Bayesian Optimal Interval Escalation (BOIN) design; Starting dose was 50 mg BID

MTD, maximum tolerated dose; RP2D: recommended phase 2 dose.

FGFR2 – RLY-4008 FIH Study: Baseline Characteristics

Parameter	Total (N=49)
Sex, n (%)	
Female	29 (59%)
Male	20 (41%)
Age (years), median (range)	**60 (23-87)**
Race, n (%)	
White	38 (78%)
Asian	6 (12%)
Black/African American	4 (8%)
Unknown	1 (2%)
ECOG PS, n (%)	
0-1	46 (94%)
2	3 (6%)
Prior lines of systemic therapy, n (%)	
1	9 (18%)
2	11 (23%)
3+	29 (59%)

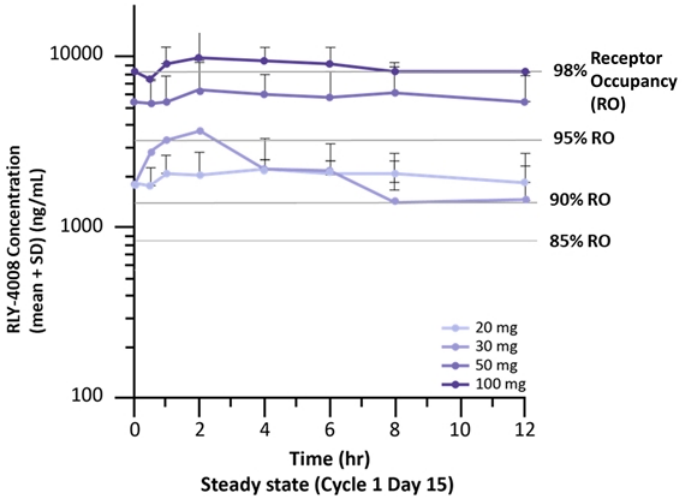
Parameter	Total (N=49)
Tumor types, n (%)	
Cholangiocarcinoma (CCA)	40 (82%)
Breast cancer	4 (8%)
Endometrial cancer	1 (2%)
Prostate adenocarcinoma	1 (2%)
Soft-tissue sarcoma*	1 (2%)
Uterus	1 (2%)
Melanoma (rectum)	1 (2%)
Baseline sum of target lesions (RECIST v1.1, cm), median (range)	**9.3 cm (1.4-22.0)**
FGFR2 oncogenic alteration, n (%)	**48/49 (98%)**
FGFR2 fusion	32 (67%)
FGFR2 mutation	12 (25%)
FGFR2 amplification	4 (8%)

Source: RLY-4008 data as presented at 2021 AACR-NCI-EORTC Molecular Targets Conference
ECOG, Eastern Cooperative Oncology Group; PS, performance status; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1.
*Soft tissue sarcoma patient enrolled in dose escalation without a documented oncogenic FGFR2 genomic alteration.

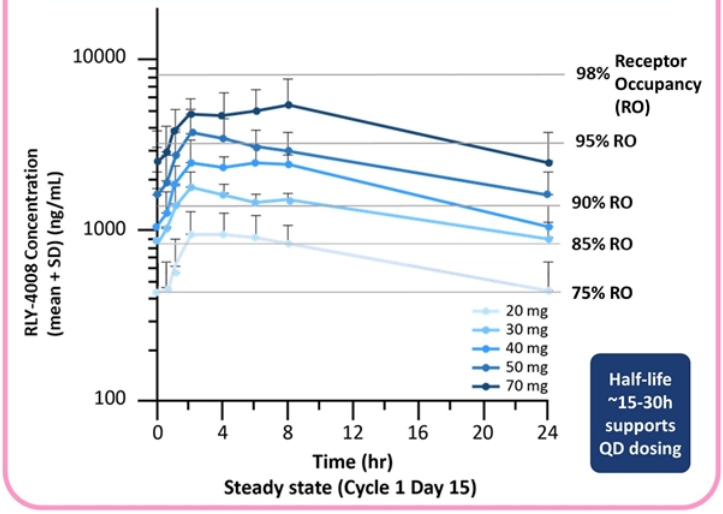
Preliminary data as of 09-Sept-2021

FGFR2 – RLY-4008 FIH Study: Pharmacokinetics and Predicted Receptor Occupancy Support QD Dosing

RLY-4008 BID Schedule



RLY-4008 QD Schedule



Half-life ~15-30h supports QD dosing

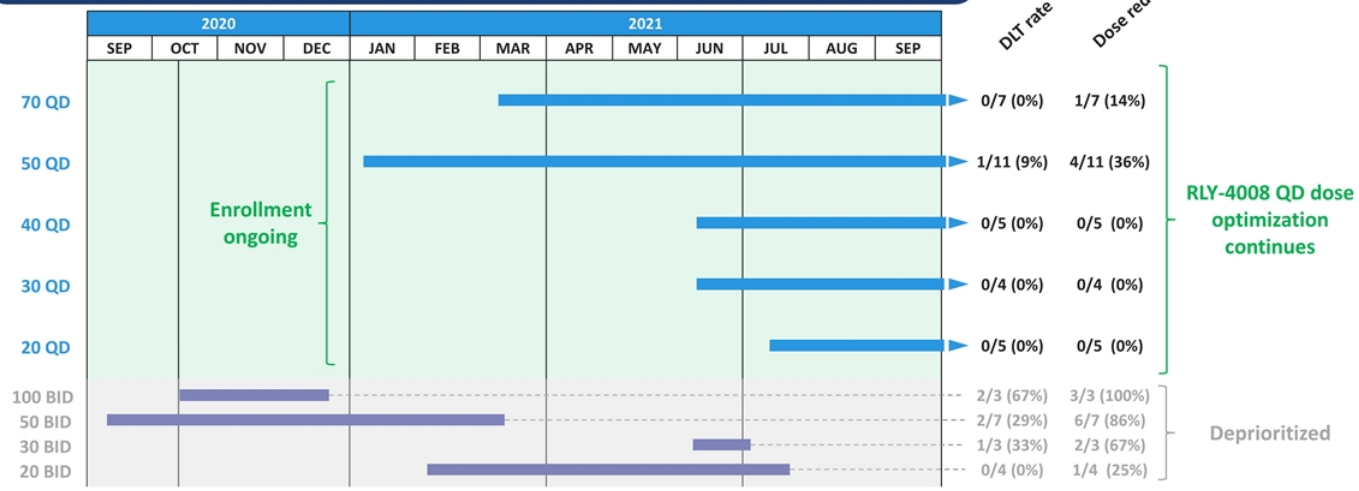
RLY-4008 showed ≥85 % predicted median receptor occupancy (based on modeling) across all dose levels
Pemigatinib 13.5mg QD achieves 76% inhibition of FGFR2 at trough*

Source: RLY-4008 data as presented at 2021 AACR-NCI-EORTC Molecular Targets Conference; Pemigatinib – NDA Multi-Disciplinary Review Document, pg 70
BID, twice a day; QD, once a day; RO, receptor occupancy. Predicted receptor occupancy: projected level of engagement of oncogenic FGFR2 at given plasma concentration. Error bars correspond to the standard deviation measures.
*Pemigatinib label: 13.5 mg orally once daily for 14 days followed by 7 days off therapy treatment regimen

Preliminary data as of 09-Sept-2021

FGFR2 – RLY-4008 FIH Study: Parallel Bayesian Dose Optimization Ongoing

Dose cohort enrollment periods – Bayesian dose optimization with enrichment (ongoing)

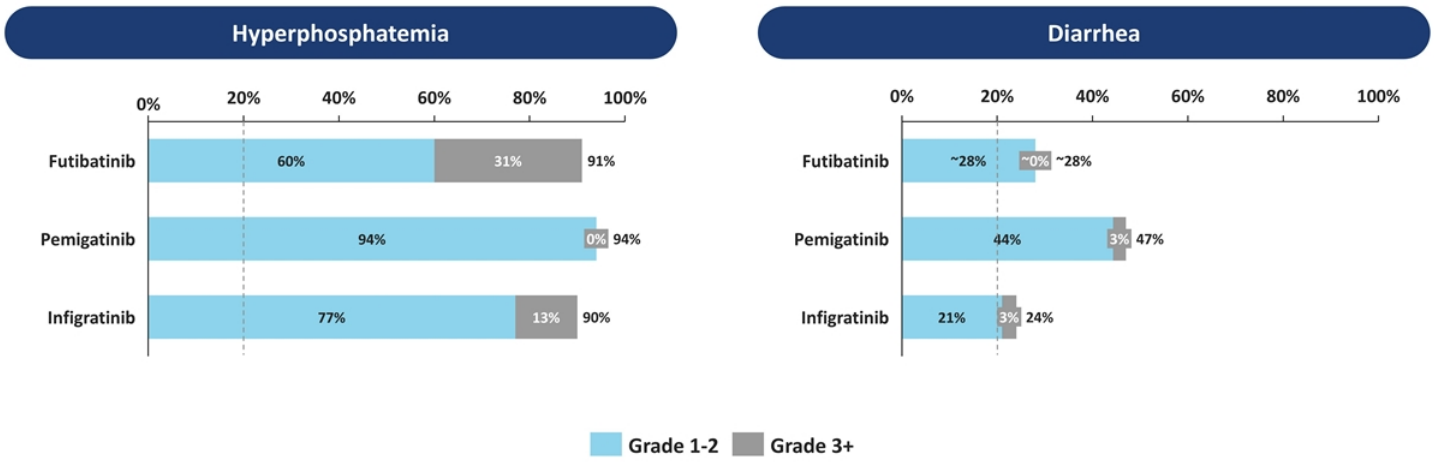


MTD not defined per protocol, RP2D selection is ongoing with the QD dosing schedule

Source: RLY-4008 data as presented at 2021 AACR-NCI-EORTC Molecular Targets Conference

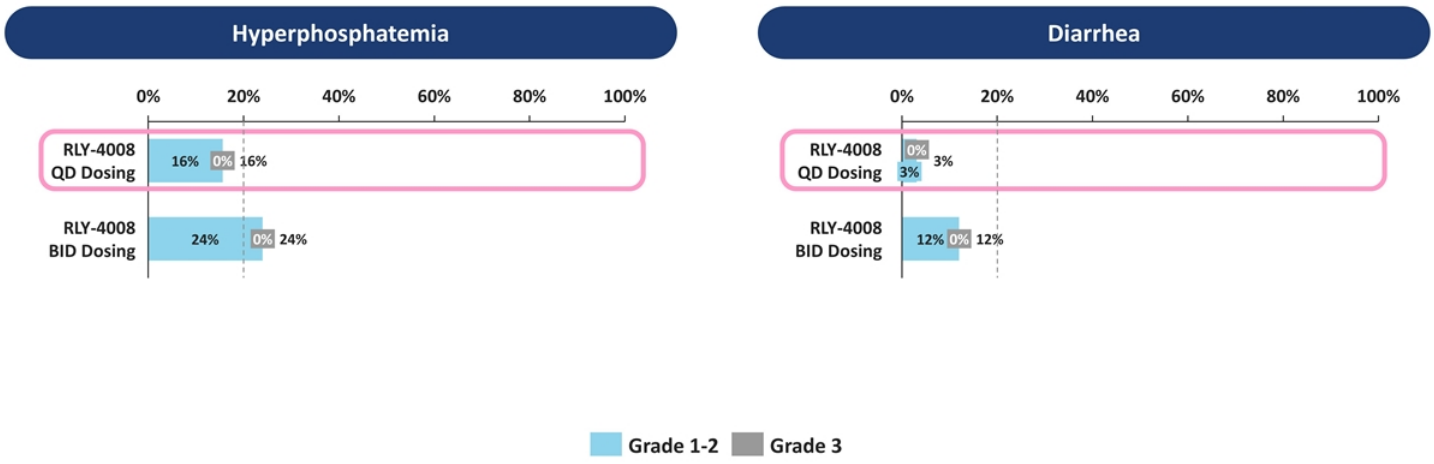
Preliminary data as of 09-Sept-2021

Tolerability Profile of Pan-FGFR Inhibitors for Relevant FGFR1 and FGFR4 AEs



Sources: Infigratinib (Truseltiq) Prescribing Information; Pemigatinib (Pemazyre) Prescribing Information; Futibatinib – AACR 2021 Presentation (Goyal et al) (diarrhea %s approximated from presentation)

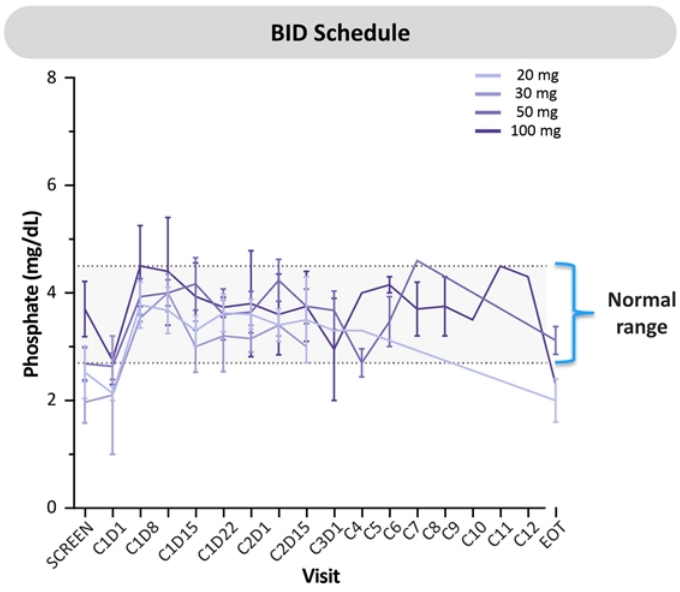
FGFR2 – RLY-4008 FIH Study: Initial Evidence of RLY-4008's FGFR2 Selectivity

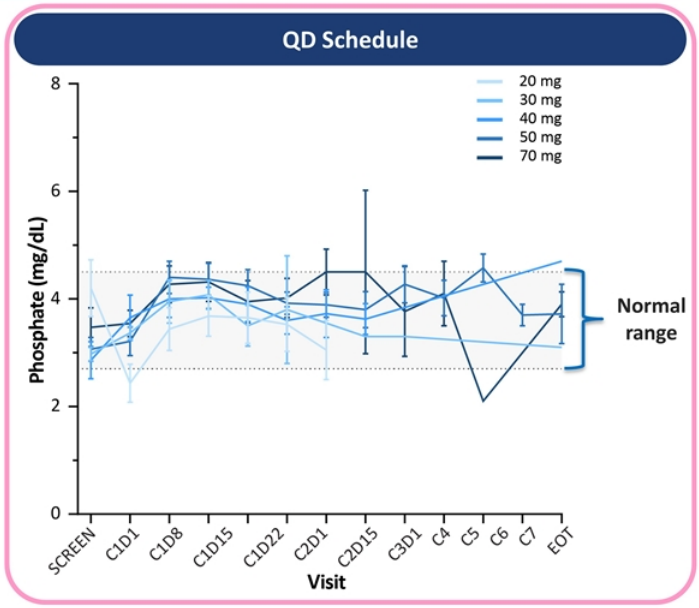


Source: RLY-4008 data as presented at 2021 AACR-NCI-EORTC Molecular Targets Conference

Preliminary data as of 09-Sept-2021

FGFR2 – RLY-4008 FIH Study: Initial Support for FGFR1- and FGFR4-Inhibition Sparing in the Clinic



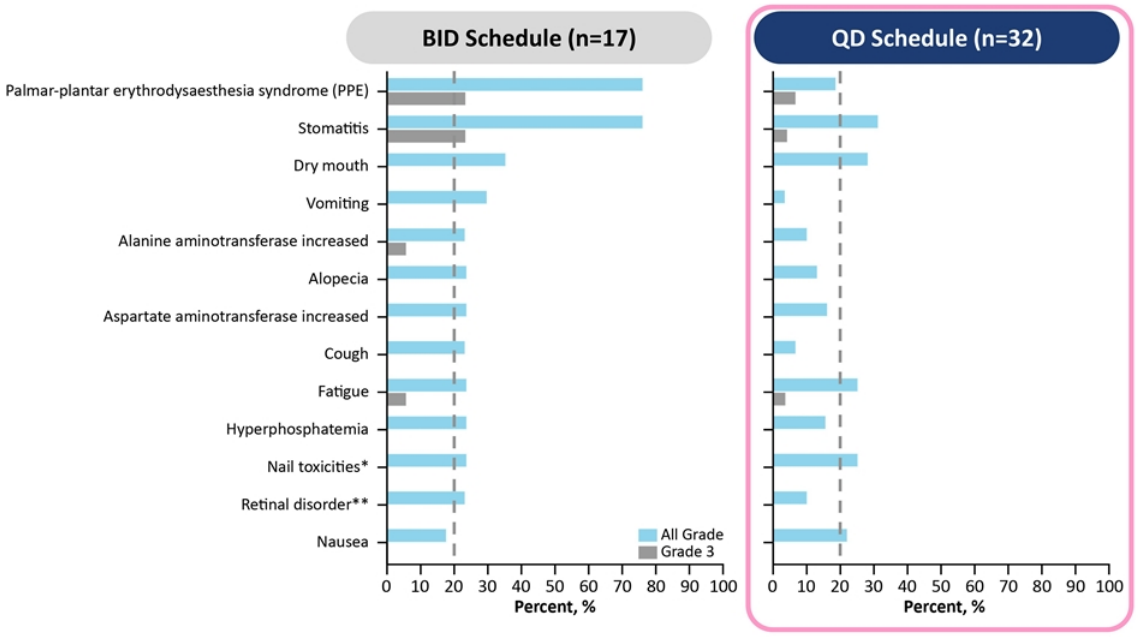


FGFR1 sparing: Hyperphosphatemia: n=9/49 (18%) patients, all low grade (Grade 1-2). Only 1/49 (2%) patients was prescribed phosphate binders.
FGFR4 sparing: Diarrhea: n=3/49 (6%) patients, all low grade (Grade 1-2) and unrelated.

Source: RLY-4008 data as presented at 2021 AACR-NCI-EORTC Molecular Targets Conference
EOT, End of Treatment

Preliminary data as of 09-Sept-2021

FGFR2 – RLY-4008 FIH Study: Treatment-Emergent Adverse Events (TEAEs) ≥ 20%



No Grade 4-5 AE

Most AEs are low-grade, including hyperphosphatemia and diarrhea
- TEAEs profile consistent with FGFR1- and FGFR4-sparing

Retinopathy/Retinal Pigment Epithelial Detachment (RPED):
- 7 cases
- BID n=4/17 (24%)
- QD n=3/32 (9%)
- All events were Gr 1-2, self-limiting or resolved upon treatment interruption

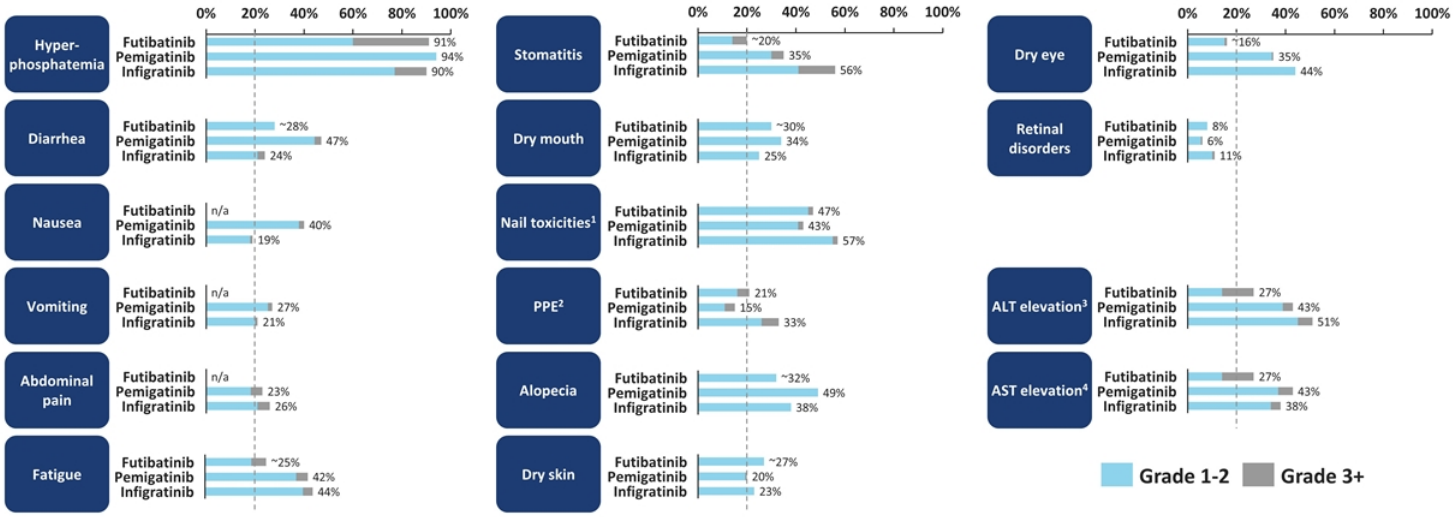
RLY-4008 QD dosing
Dry eye: 9% all grades, 0% grade 3+
Corneal AEs: 13% all grades, 0% grade 3+

Bemarituzumab (Phase 2)
Dry eye: 26% all grades, 3% grade 3+
Corneal AEs: 67% all grades, 24% grade 3+

Source: RLY-4008 data as presented at 2021 AACR-NCI-EORTC Molecular Targets Conference; Bemarituzumab ASCO 2021 Presentation. This presentation notes corneal AEs are defined by Standardised MedDRA Queries (SMQ) of corneal disorders, which includes dry eye.
*Included preferred terms of nail disorder, nail discoloration, nail ridging, onychalgia, onychoclasis, onycholysis, onychomadesis, paronychia.
**Included preferred terms of retinal pigment epithelium detachment, retinopathy, blurred vision, subretinal fluid.

Preliminary data as of 09-Sept-2021

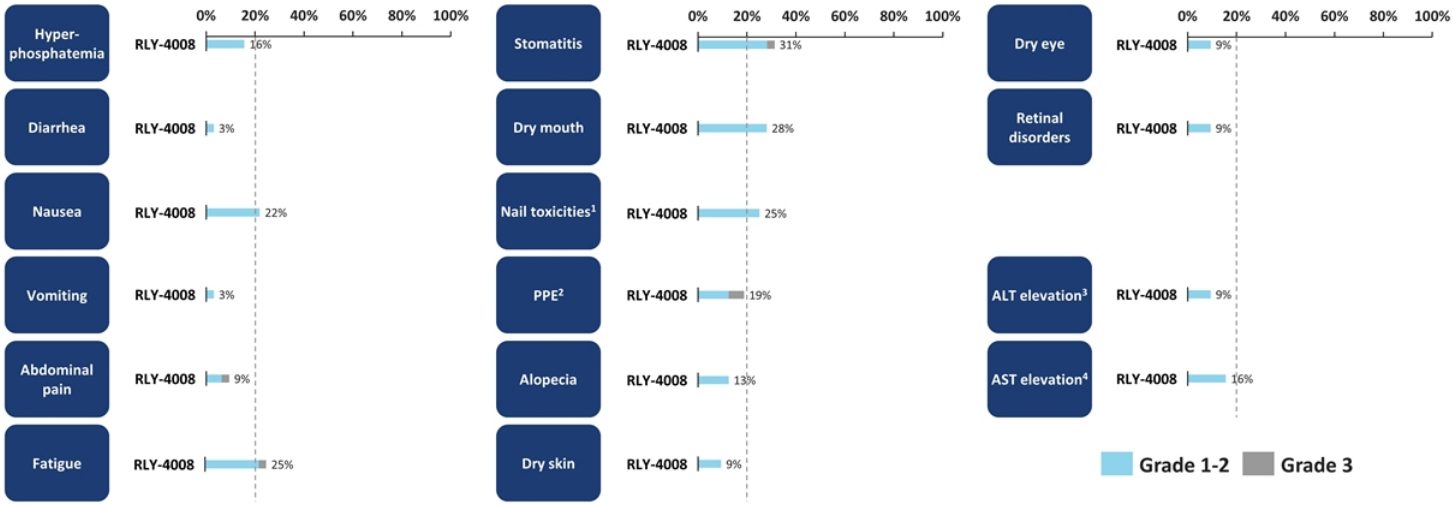
Tolerability Profile of Pan-FGFR Inhibitors



Sources: Infigratinib (Truseltiq) Prescribing Information; Pemigatinib (Pemazyre) Prescribing Information; Futibatinib – AACR 2021 Presentation (Goyal et al) (%s approximated from presentation for dry eye, alopecia, dry skin, diarrhea, fatigue, dry mouth, stomatitis)
1. Nail toxicities Includes onycholysis, nail disorder, nail discoloration, onychomadesis, paronychia; 2. PPE stands for Palmar plantar erythrodysesthesia syndrome (hand foot syndrome); 3. alanine transaminase;
4. aspartate aminotransferase

FGFR2 – RLY-4008 FIH Study:
Promising Emerging Tolerability Profile of FGFR2 Selective Targeting

RLY-4008 data reflect QD population only, with QD dose optimization ongoing



On-target AEs have been mostly low grade (no Gr 4/5, < 10% in the QD dosing regimen), and all of them have been reversible, manageable with dose modification or no intervention and monitorable

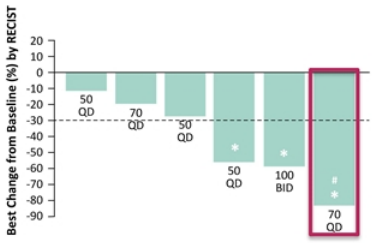
Source: RLY-4008 data as presented at 2021 AACR-NCI-EORTC Molecular Targets Conference

1. Nail toxicities Includes onycholysis, nail disorder, nail discoloration, onychomadesis, paronychia; 2. PPE stands for Palmar plantar erythrodysesthesia syndrome (hand foot syndrome); 3. alanine transaminase; 4. aspartate aminotransferase

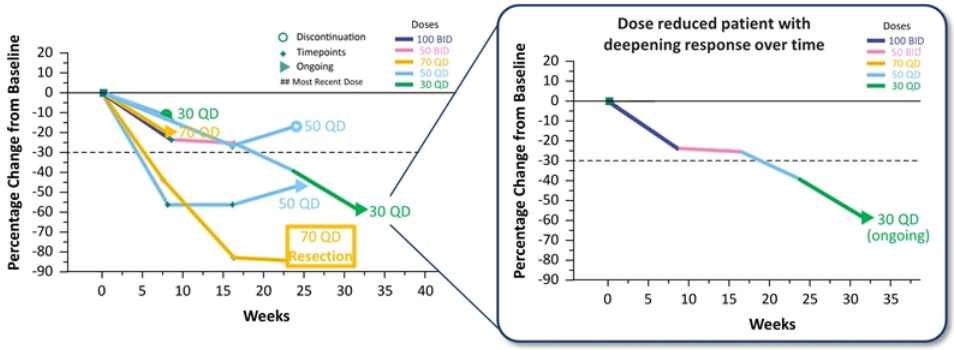
Preliminary data as of 09-Sept-2021

FGFR2 – RLY-4008 FIH Study: RLY-4008 Induced Radiographic Tumor Regression in FGFR Inhibitor-Naïve FGFR2-Fusion+ Cholangiocarcinoma

Best RECIST change from baseline



Relative change from baseline in tumor size



3/6 patients exhibit a confirmed PR

3/6 patients ongoing on treatment, and 1 patient had resection with curative intent

Pan-FGFR benchmark in this population is 23-36% ORR

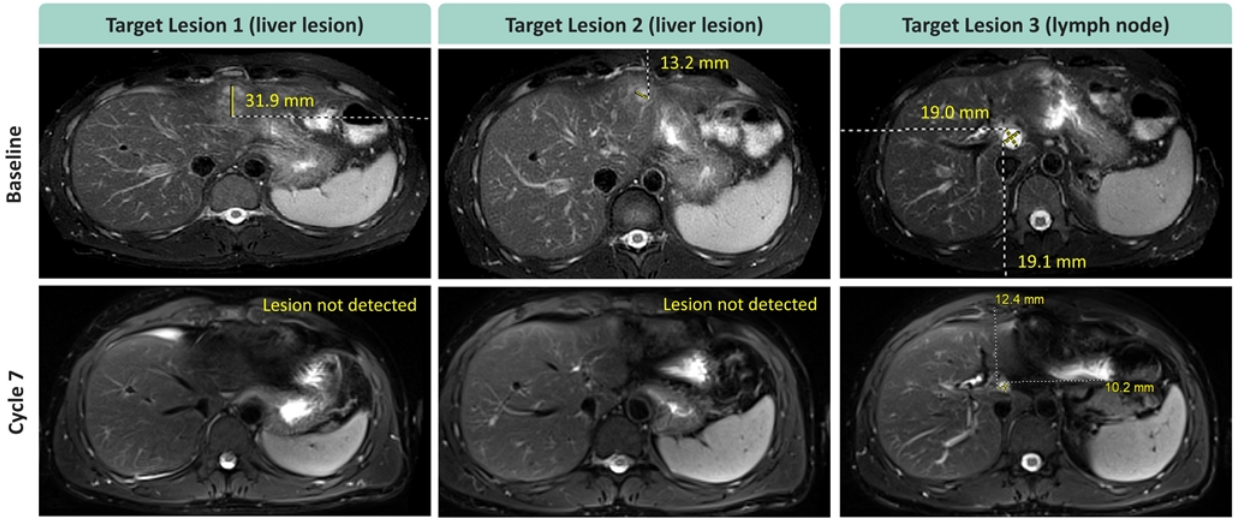
Source: RLY-4008 data as presented at 2021 AACR-NCI-EORTC Molecular Targets Conference
*Confirmed PR; #Tumor resection after data cut off.
FGFRi, fibroblast growth factor receptor inhibitor PR, partial response.

Preliminary data as of 09-Sept-2021

FGFR2 – RLY-4008 FIH Study: RLY-4008 Resulted in Near Complete Regression in a Patient with FGFR2-Fusion, FGFRi-Naïve Cholangiocarcinoma, Leading to Surgical Resection

35-year-old male with FGFR2-FLIP1 fusion ICC. Prior treatment: Gemcitabine/Cisplatin

70 mg QD dosing (no dose modification). Relevant AEs: Gr 1 dry eye, Gr 1 onycholysis, Gr 2 stomatitis



31.9 mm → Not detected

13.2 mm → Not detected

19.0 mm → 10.2 mm

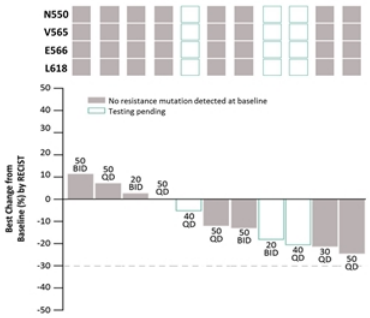
Confirmed PR (near CR) -83% by RECIST v1.1

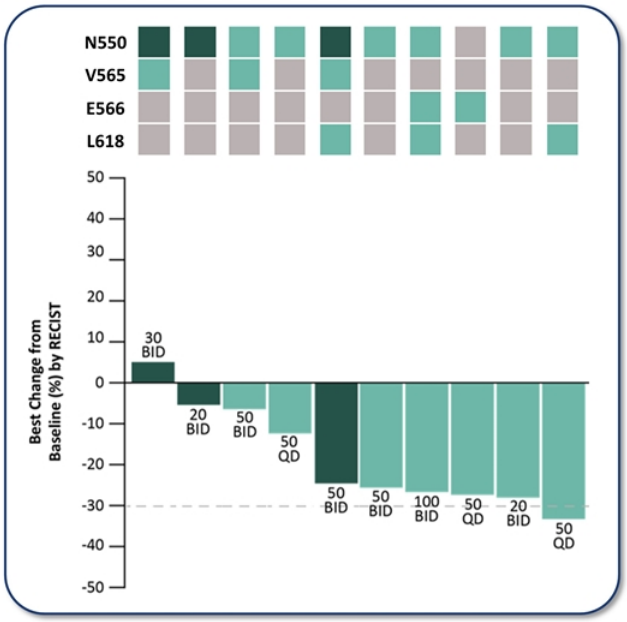
Patient underwent resection with curative intent

Source: RLY-4008 data as presented at 2021 AACR-NCI-EORTC Molecular Targets Conference

Courtesy: Dr. V. Sahai (U Michigan)

FGFR2 – RLY-4008 FIH Study: RLY-4008 Exhibited Activity in Pan-FGFR Inhibitor Resistant FGFR2-Fusion Cholangiocarcinoma Regardless of FGFR2 Resistance Mutations





Resistance mutation cleared at C2D1

Resistance mutation not cleared at C2D1

No resistance mutation at baseline

Testing pending

13/21 (62%) patients with tumor reduction > 10%

7/10 (70%) patients with FGFR2 resistance mutations at baseline had all identified resistance mutations rendered undetectable at C2D1

Clearance of resistance clones implies greater duration in earlier line patients

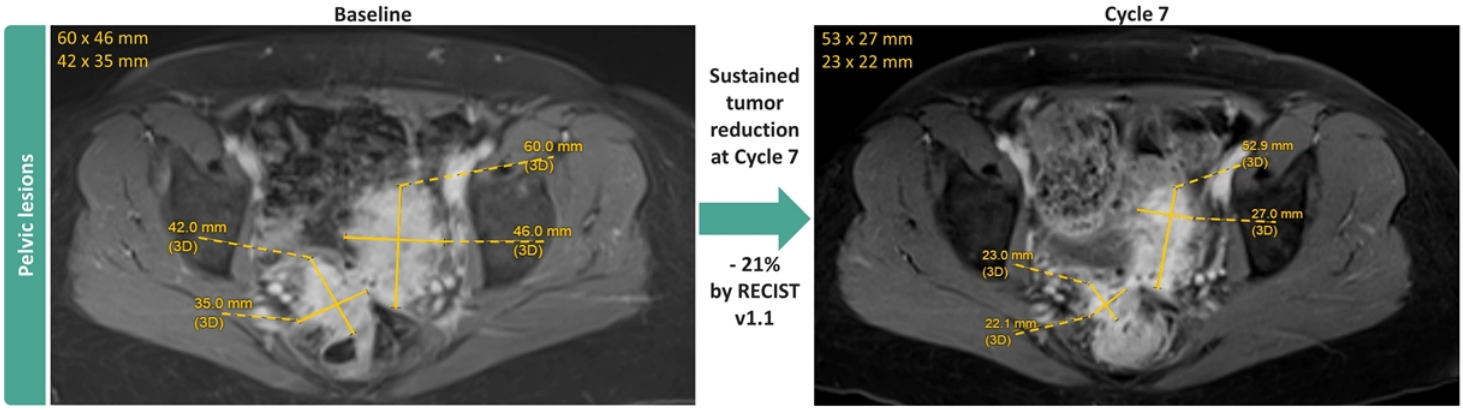
Source: RLY-4008 data as presented at 2021 AACR-NCI-EORTC Molecular Targets Conference

Note: (N550, N549), (V565, V564), (E566, E565), (L618, L617) are different terminology for the same mutated site; ctDNA, circulating DNA; FGFRi, fibroblast growth factor receptor inhibitor

Preliminary data as of 09-Sept-2021

FGFR2 – RLY-4008 FIH Study: RLY-4008 Produced Tumor Regression in a Patient with FGFR2-Fusion+ Cholangiocarcinoma Pretreated with Futibatinib

51-year-old female with FGFR2-CIT fusion ICC. Prior treatments: Gemcitabine/Cisplatin, Futibatinib



Antitumor activity:

Sustained tumor reduction at C7 (-21% per RECIST v1.1)

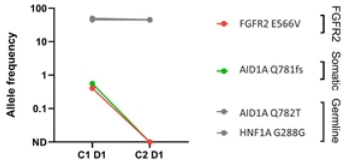
Safety and tolerability:

No dose interruption or modification

RLY-4008 treatment is ongoing (50 mg QD)

ctDNA:

Baseline FGFR2-E566V mutation is undetectable at C2D1



Source: RLY-4008 data as presented at 2021 AACR-NCI-EORTC Molecular Targets Conference
Note: E566 and E565 are different terminology for the same mutated site
Courtesy: Dr. L. Goyal (Mass. General Hospital)

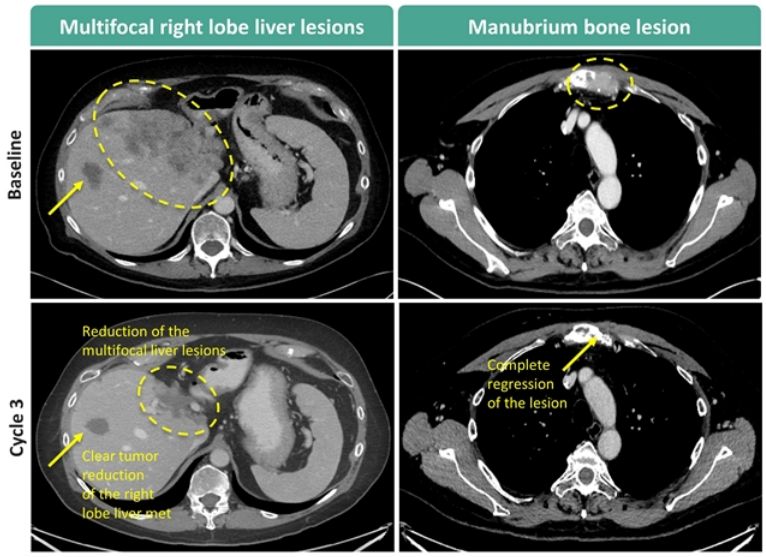
Preliminary data as of 09-Sept-2021

FGFR2 – RLY-4008 FIH Study: Yet to Be Confirmed Partial Response with 30mg QD in FGFR2 Fusion+ CCA Pretreated with Infigratinib

Unconfirmed PR

RELAY THERAPEUTICS

65-year-old male with FGFR2-WAC fusion CCA and 3 FGFR2 resistance mutations: N550K, N550D, V565I. Prior FGFR treatment: Infigratinib. RLY-4008 treatment is ongoing at C3 (30 mg QD).



PR (cycle 3)
-72% by RECIST v1.1
(pending confirmation)

Chest pain resolution within 2 weeks of initiating RLY-4008 dosing

No dose interruption
No dose reduction

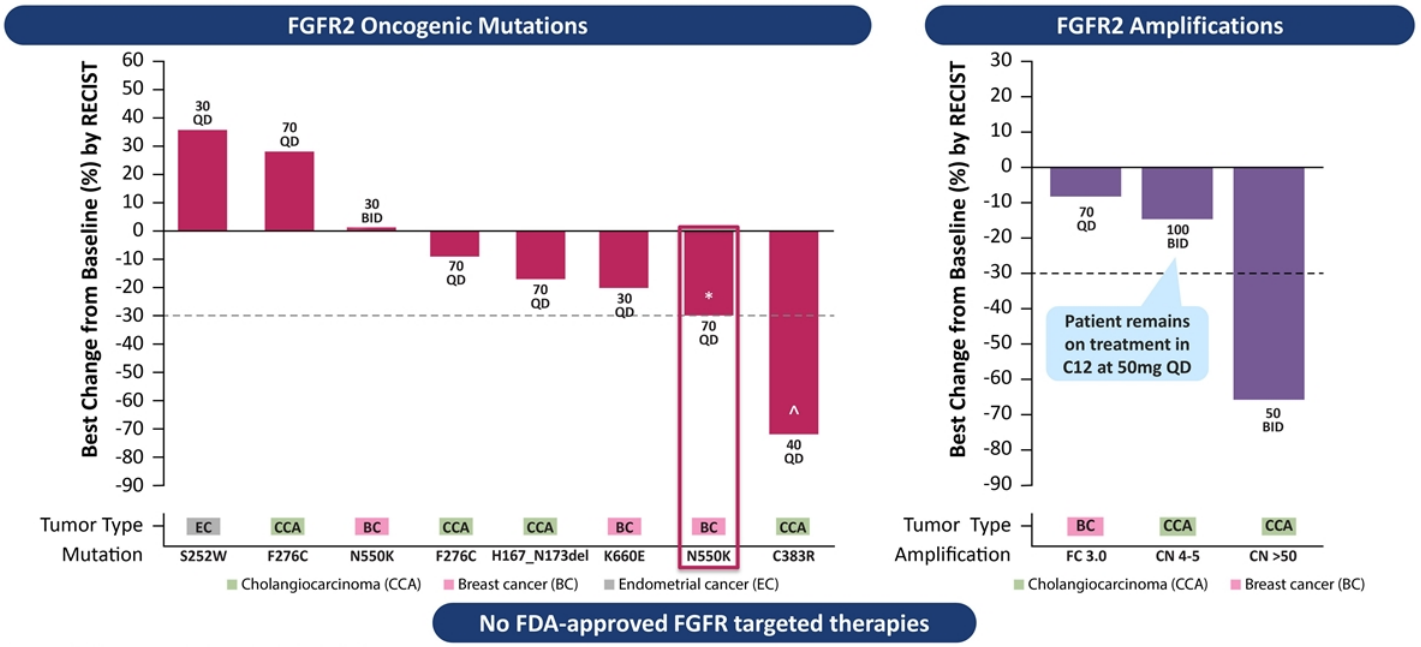
Efficacy data received after data lock and not included in the October 8 AACR-NCI-EORTC Molecular Targets Conference presentation data

Note: (N550, N549), (V565, V564) are different terminology for the same mutated site

Courtesy: Dr. V. Subbiah (MD Anderson)

Data as of 01OCT21- post data lock

FGFR2 – RLY-4008 FIH Study: RLY-4008 Showed Radiographic Tumor Regression in FGFR2 Oncogenic Mutations and in FGFR2 Amplifications



No FDA-approved FGFR targeted therapies

Source: RLY-4008 data as presented at 2021 AACR-NCI-EORTC Molecular Targets Conference
*Confirmed PR with increased tumor reduction after data cut; ^PR pending confirmation.
FC, fold change; CN, copy number.

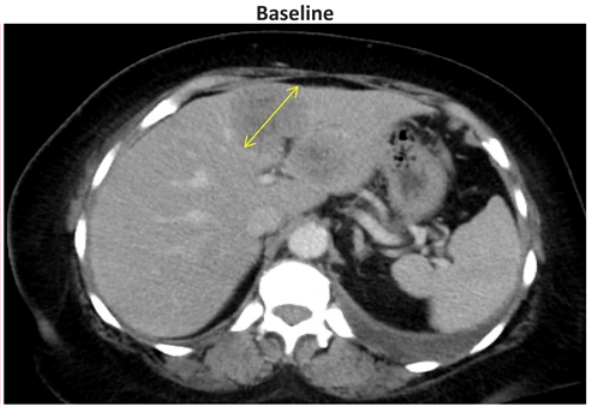
Preliminary data as of 09-Sept-2021

FGFR2 – RLY-4008 FIH Study: RLY-4008 Resulted in Confirmed PR in a Patient with Heavily Pretreated FGFR2 N550K Mutant Breast Cancer

60-year-old female with breast cancer ER+ HER2- ESR1 mut PIK3CA mut FGFR2 N550K-mut, 12 prior lines of therapy including Alpelisib (PI3Ki) + Palbociclib (CDKi)

Liver lesion

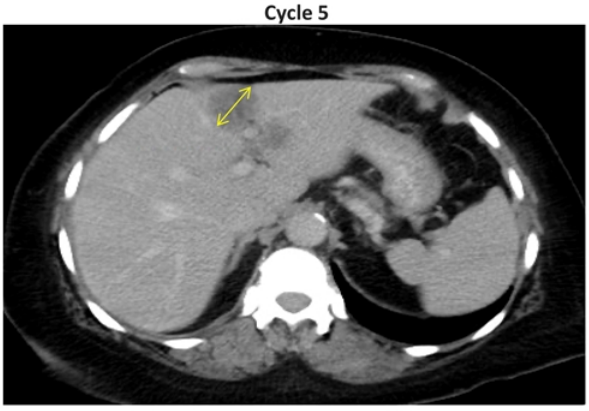
Baseline



Confirmed PR at Cycle 5

- 41% by RECIST v1.1

Cycle 5



Antitumor activity:

Confirmed PR at Cycle 5: -41% (after data cut off), initial PR at Cycle 3 : -30%

Significant reduction in CA 15-3 by Cycle 2: –62%

Safety and tolerability

Relevant AEs: G2 PPE, G1 stomatitis, G1 nail changes

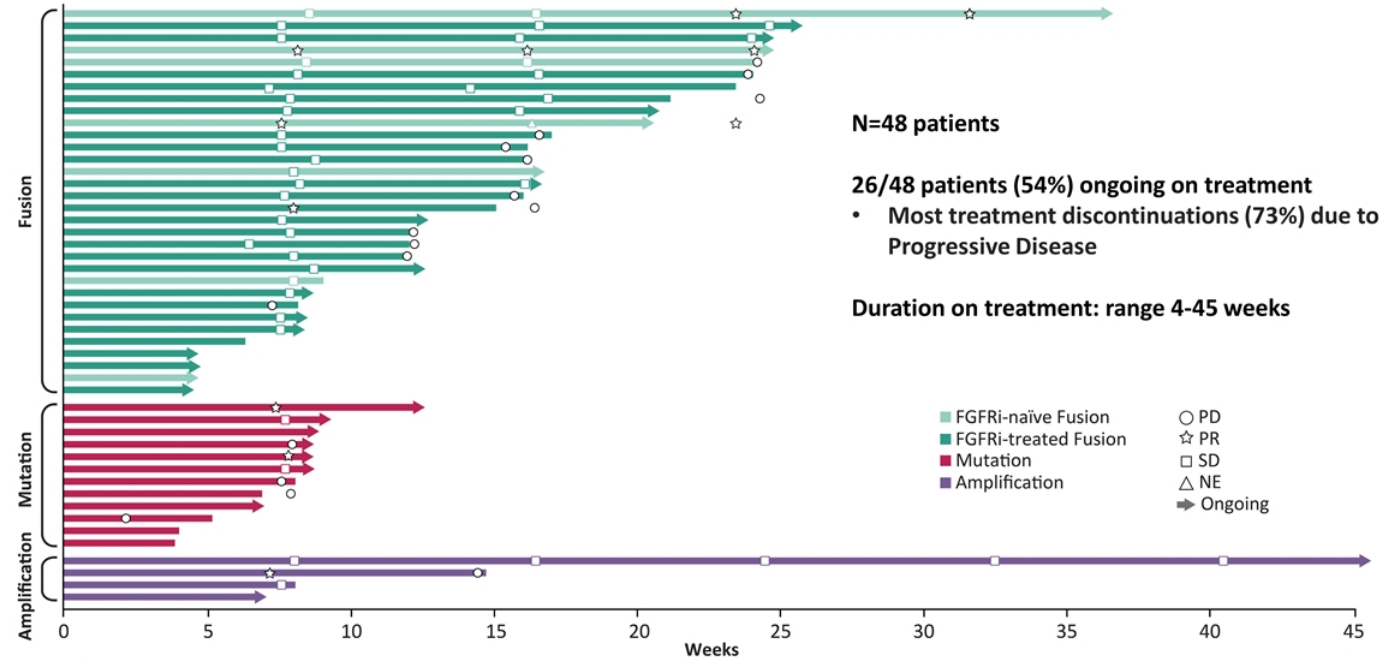
No dose reduction; RLY-4008 treatment is ongoing (70 mg QD)

First ever known reported response in FGFR2 mutated breast cancer for an FGFR inhibitor

Source: RLY-4008 data as presented at 2021 AACR-NCI-EORTC Molecular Targets Conference
Note: N550 and N549 are different terminology for the same mutated site
Courtesy: Dr. A. Schram (MSKCC)

Preliminary data as of 09-Sept-2021

FGFR2 – RLY-4008 FIH Study:
Time on Treatment and Response by FGFR2-Alteration



N=48 patients

26/48 patients (54%) ongoing on treatment

- **Most treatment discontinuations (73%) due to Progressive Disease**

Duration on treatment: range 4-45 weeks

Source: RLY-4008 data as presented at 2021 AACR-NCI-EORTC Molecular Targets Conference
FGFRi, fibroblast growth factor receptor inhibitor; NE, not evaluable; PR, partial response; PD, progressive disease; SD, stable disease.

Preliminary data as of 09-Sept-2021

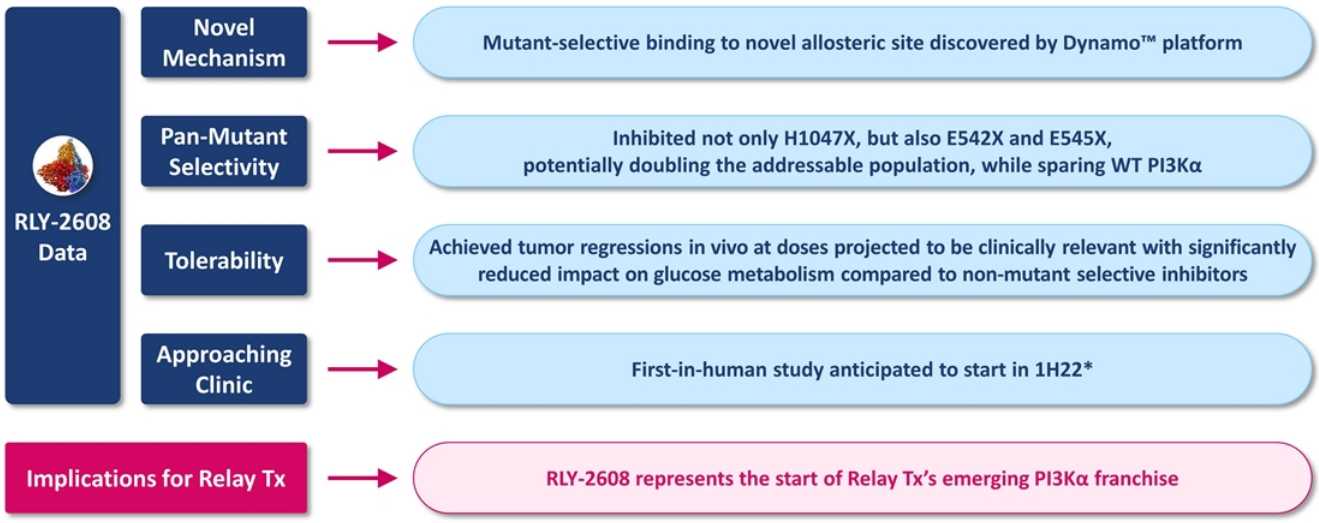
FGFR2 – RLY-4008 FIH Study: RLY-4008 Initial Observations

Selectivity Data	**RLY-4008 is potentially the first highly selective FGFR2 inhibitor in the clinic that targets driver alterations and FGFR inhibitor resistance mutations**
Safety and Tolerability Data	**Robust FGFR2 inhibition observed with ≥ 85% receptor occupancy and minimal off-isoform toxicity to-date across a wide dose range** **Promising QD PK and generally well-tolerated profile**
Early Efficacy Data	**Encouraging anti-tumor activity** • **FGFRi-naïve, FGFR2-fusion+ cholangiocarcinoma: 3/6 patients with confirmed partial responses** • **FGFRi-resistant, FGFR2-fusion+ cholangiocarcinoma: 62% patients showed tumor shrinkage ≥10%** • **Early signs of activity also observed in FGFR2-mutant and -amplified tumors, beyond cholangiocarcinoma** **Interim results support selective targeting of FGFR2 and suggest RLY-4008 has potential to overcome FGFRi resistance**

Source: RLY-4008 data as presented at 2021 AACR-NCI-EORTC Molecular Targets Conference

Preliminary data as of 09-Sept-2021

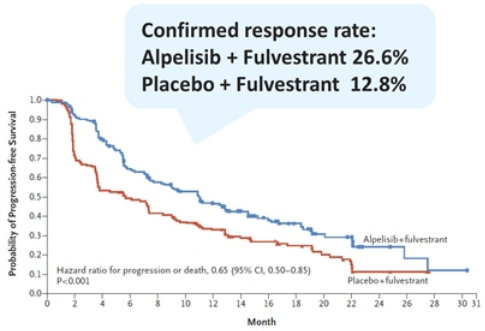
PI3Kα – Highlights from Recent RLY-2608 Preclinical Data Disclosure



*Subject to submission and acceptance of IND by the FDA

PI3Kα – Existing Inhibitors Establish POC but Have Limited Therapeutic Window

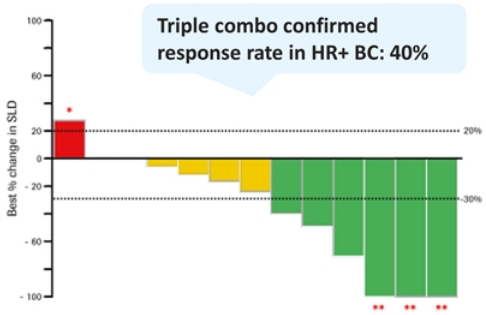
Alpelisib + fulvestrant vs. placebo + fulvestrant



- Dose modifications: 64%
- Hyperglycemia: 64% (36% Grade 3/4)
- GI toxicity: 58%
- Rash: 36%

André F et.al., N Engl J Med. 2019 May 16;380(20):1929-1940

GDC-0077 + fulvestrant + palbociclib



- Dose modifications: 36%
- Hyperglycemia: 61% (23% Grade 3/4)
- GI toxicity: 48%
- Rash: 19%

Data from Phl/Ib Inavolisib Combination Trial in HR+, HER2-, *PIK3CA*mut mBC presented at SABC 2020

PI3Kα – Relay Tx Has a Unique Understanding of PI3Kα

KRAS experience teaches us pan-mutant coverage is required

Similarities between PI3K and KRAS:

- ✓ Clear oncogenic driver
- ✓ Mutations cluster at a few key hotspots
- ✓ Hotspot mutations can occur with multiple different alleles

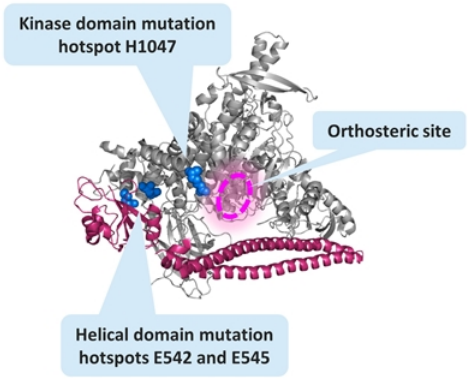
KRAS G12C

Examples of on-target resistance mechanisms

- KRAS G13D
- KRAS G12V
- KRAS Y96D

On-target resistance to mutation-specific inhibitors can result in escape via different allele at same site or mutation at another hotspot

Relay Tx has a unique understanding of PI3Kα



RLY-2608 (pan-mutant selective) is the foundation of our franchise

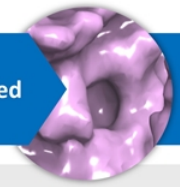
PI3Kα Franchise		
	PI3Kα^{PAN}	**RLY-2608** *Pan-mutant allosteric inhibitor*
	PI3Kα^{SPECIFIC}	*H1047R-specific allosteric inhibitor*
	PI3Kα^{OTHER}	*Other PI3Kα allosteric programs*

Source: Hata, Helst, & Corcoran et al, *Cancer Discovery* 2021

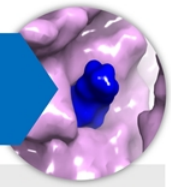
PI3Kα – Proprietary Insights Unlock Additional Approaches

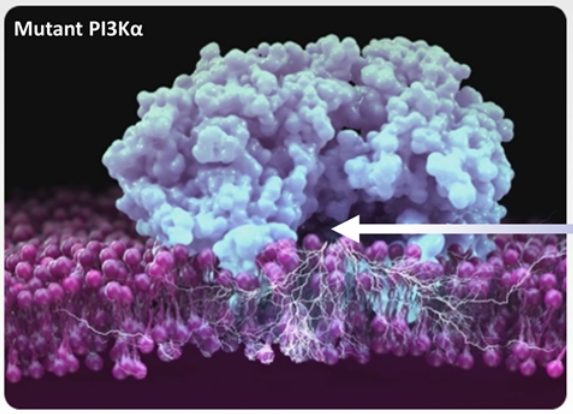
Solved first full-length structures of PI3Kα (mutant and wild-type)

Discovered novel allosteric pocket favored in mutant protein



Designed mutant selective PI3Kα inhibitor

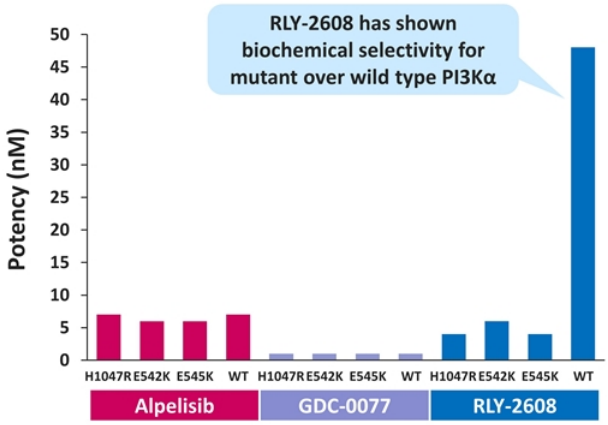




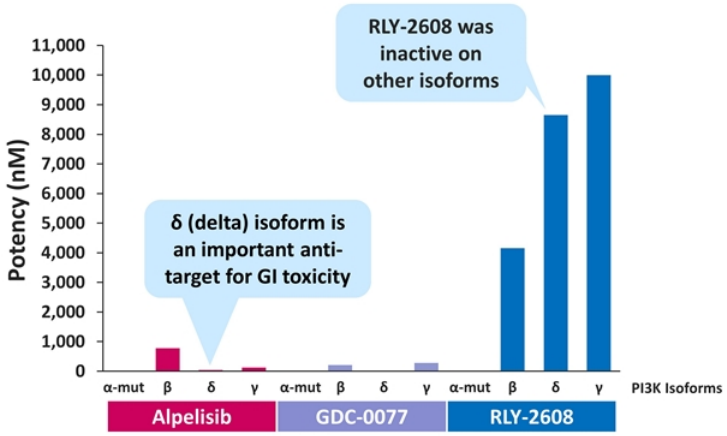
A differentiated understanding of the structure of PI3Kα and its relationship to function equips Relay Tx to design optimal mutant-selective inhibitors of PI3Kα

PI3Kα – RLY-2608 Has Shown Mutant and Isoform Biochemical Selectivity

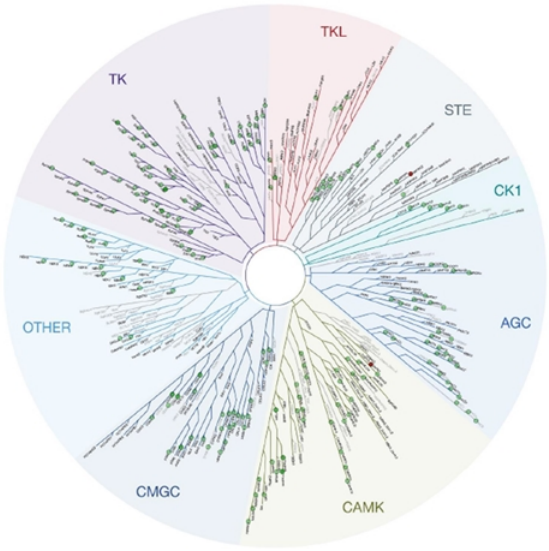
Mutant vs. WT PI3Kα potency

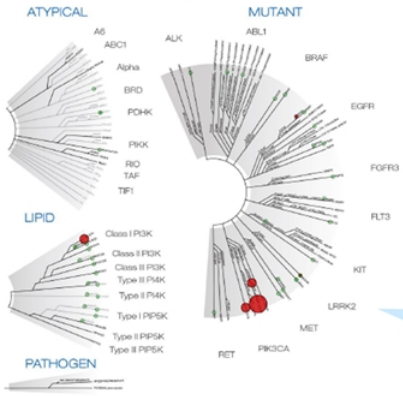


Mutant PI3Kα vs. other isoform potency



PI3Kα – RLY-2608 Is Selective Across the Kinome





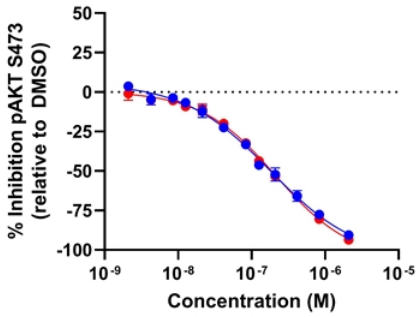
RLY-2608 inhibited only PI3Kα, with preferential inhibition of mutant

Kinase Inhibition @ 10 µM R

- >80% inhibition
- 20-80% inhibition
- < 20 % inhibition

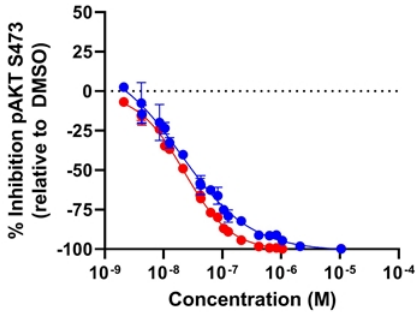
PI3Kα – RLY-2608 Inhibited Mutant PI3Kα More Potently in Cells

Alpelisib



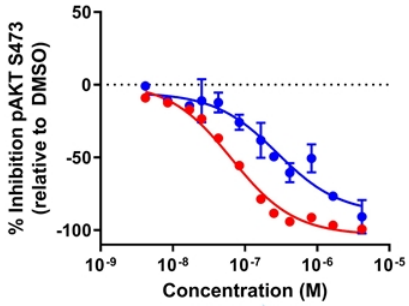
Orthosteric binders were equipotent between WT and mutant

GDC-0077



MCF10A Parental
MCF10A *PIK3CA* mutant

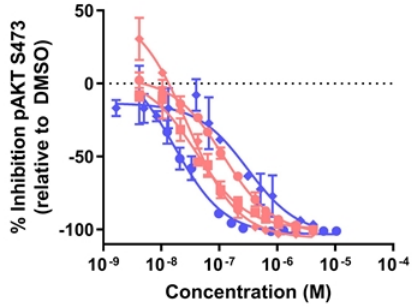
RLY-2608



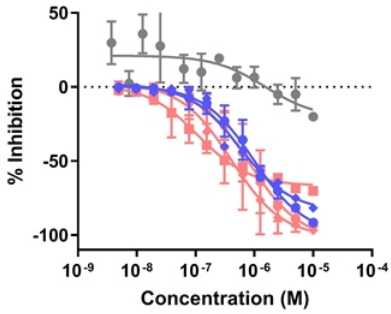
RLY-2608 was more potent against mutant cells

PI3Kα – RLY-2608 Potently Inhibited Signaling and Viability in *PIK3CA* Mutant Cancer Cell Lines

pAKT



Viability

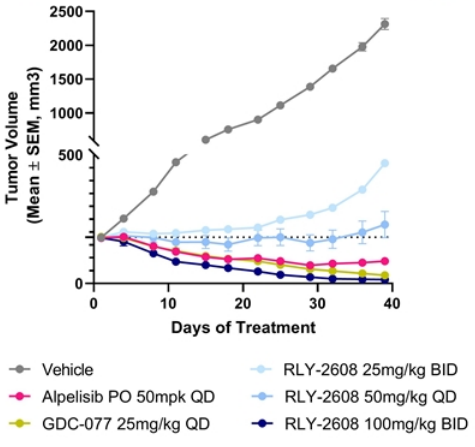


Activity observed in both kinase and helical domain mutant cell lines

- HCC1954 (H1047R)
- T47D (H1047R)
- CAL33 (H1047R)
- MDAMB361 (E545K;K567R)
- MCF7 (E545K)
- HCC1428 (WT)

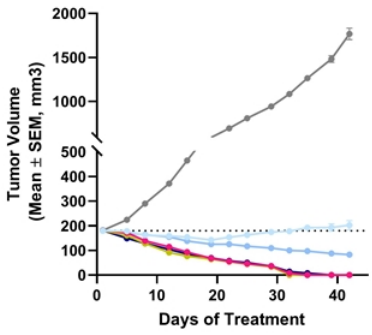
PI3Kα – In Vivo Tumor Regressions Across Both Mutation Hotspots (Mouse Study)

H1047R mutant (HCC1954) (mouse)



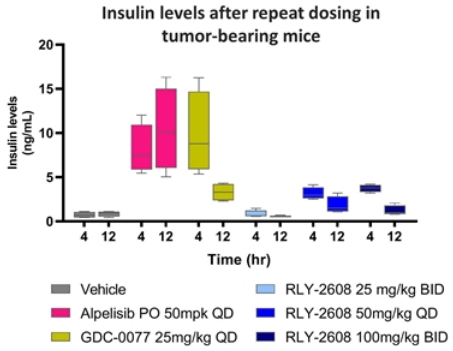
Vehicle
Alpelisib PO 50mpk QD
GDC-077 25mg/kg QD
RLY-2608 25mg/kg BID
RLY-2608 50mg/kg QD
RLY-2608 100mg/kg BID

E545K mutant (MDAMB361) (mouse)[1]



Vehicle
Alpelisib PO 50mpk QD
GDC-077 25mg/kg QD
RLY-2608 25mg/kg BID
RLY-2608 50mg/kg QD
RLY-2608 100mg/kg BID

RLY-2608 achieved max efficacy with less insulin than orthosteric inhibitors[2]



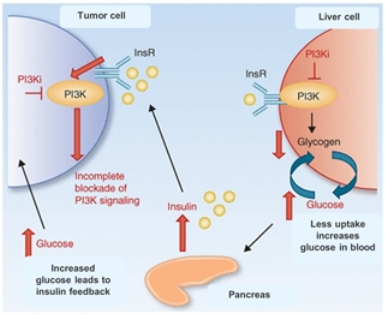
Consistent results for 1-hour time point[3]

IND enabling studies initiated, with clinical start expected in 1H 2022[4]

1. This model also carries a second mutation at K567R; 2. HSC2 model; 3. Consistent results observed at 1hr timepoint in MCF7 (E545K) model; 4. Subject to submission and acceptance of IND by the FDA

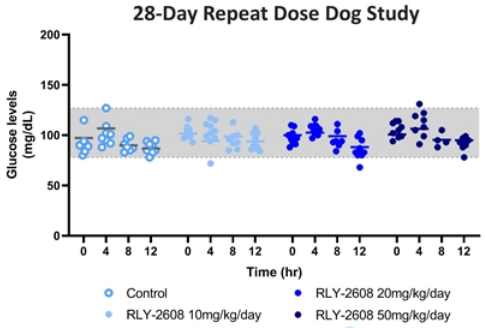
PI3Kα – RLY-2608 Had Reduced Impact on Glucose Homeostasis (28-Day Dog Study)

Inhibition of WT PI3Kα leads to hyperglycemia



Adapted from Hanker Cancer Disc 2019

Repeat dosing of RLY-2608 did not cause hyperglycemia in tox species (dog)

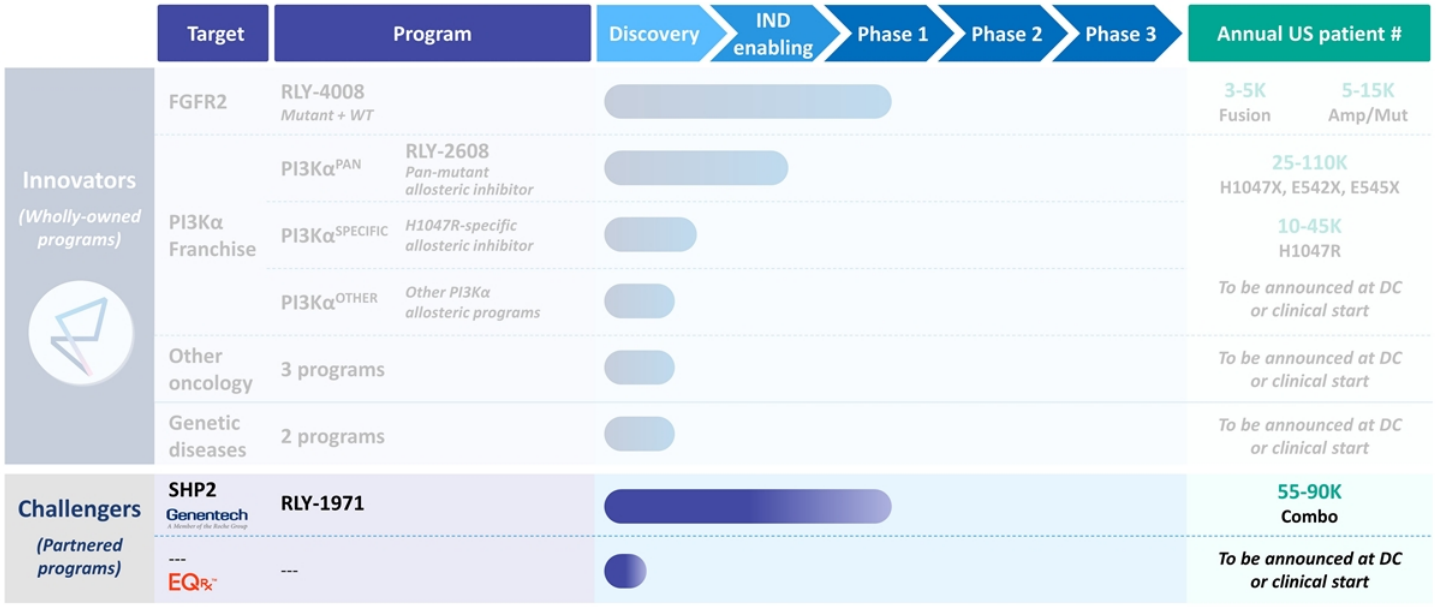


Equivalent exposures to efficacious mouse doses

Projected human oral bioavailability ~60% and half-life ~16h

In higher species, dosing of RLY-2608 for 28 days showed no histopathological or ophthalmic findings associated with hyperglycemia

Extensive Precision Medicines Pipeline – Challengers



Note: Patient #'s refer to total annual number of US patients with late-line cancers compared to comprehensive annual incidence that may be amenable to treatment with our programs

What To Expect From Relay Tx

Nearer-term milestones

Innovators

- **RLY-4008 (FGFR2)** — Expansion cohorts open by 2021 year end; Additional data update expected in 2022
- **RLY-2608 (PI3Kα^{PAN})** — Clinical start expected in 1H 2022*; Add'l preclinical data at SABCS (Dec 2021)
- **Next target in pipeline** — Next target to be disclosed in 1H 2022

Challengers

- **RLY-1971 (SHP2)** — GDC-6036 (KRAS G12C) combo trial initiated in July 2021

Medium-term drivers

- 5 additional innovator programs
- Pursuit of challenger targets through partnerships
- Continued evolution of our Dynamo™ platform
- Continued expansion of pipeline scope and scale

$671M

Cash, cash equivalents and investments as of the end of Q2 2021

Execution focus underpins value creation

*Subject to submission and acceptance of IND by the FDA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THERAPEUTICS