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): September 11, 2022

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.)**

399 Binney Street Cambridge, Massachusetts	**02139**
(Address of Principal Executive Offices)	**(Zip Code)**

Registrant's Telephone Number, Including Area Code: (617) 370-8837

(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, par value $0.001 per share	RLAY	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 September 11, 2022, Relay Therapeutics, Inc. (the "Company") issued a press release announcing late breaking interim clinical data from the Company's ReFocus trial for RLY-4008, an investigational, potent, selective and oral small molecule inhibitor of fibroblast growth factor receptor 2 ("FGFR2"), a copy of which is furnished herewith as Exhibit 99.1 to this Current Report on Form 8-K. The Company intends to host a conference call and live webcast to discuss the interim clinical data on September 12, 2022 at 8:00 a.m. E.T. The Company has made available a slide presentation to accompany the call, a copy of which is being furnished as Exhibit 99.2 to this Current Report on Form 8-K. The Company undertakes no obligation to update, supplement or amend the materials attached hereto as Exhibit 99.2.

The information in this Item 7.01, including Exhibit 99.1 and Exhibit 99.2 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.

On September 11, 2022, the Company announced interim clinical data for RLY-4008 that was presented at the European Society for Medical Oncology ("ESMO") Congress 2022.

The interim clinical data were based on an August 1, 2022 data cut-off date from both the dose escalation and dose expansion phases of the RLY-4008 clinical trial. The interim clinical data included a safety database of 195 patients, with 89 patients treated at the pivotal dose of 70 mg once daily ("QD") dose, of which 17 were pan-FGFR ("FGFRi") treatment-naïve FGFR2-fusion cholangiocarcinoma ("CCA") patients eligible for efficacy evaluation (patients with measurable disease who had opportunity for two or more tumor assessments to confirm response or discontinued treatment with less than two tumor assessments).

Key interim clinical data include:

- 15 out of 17 of the efficacy evaluable patients at the pivotal dose experienced a partial response resulting in an 88% interim overall response rate ("ORR"), with 14 confirmed partial responses and one unconfirmed partial response in an ongoing patient.
    - 13 out of 15 responders remain on treatment; one responder came off study to be resected with curative intent.
    - The two patients with the best response of stable disease remain on treatment.
- More broadly across all dose levels and schedules, 38 FGFRi-naïve FGFR2-fusion CCA patients were eligible for efficacy evaluation, of which 24 experienced a partial response resulting in a 63% interim ORR, with 22 confirmed partial responses and 2 unconfirmed partial responses.

The interim safety analysis as of the August 1, 2022 data cut-off date was generally consistent with the Company's analysis of the interim clinical data for RLY-4008 as of April 19, 2022 that was shared with the U.S. Food and Drug Administration ("FDA") as well as the Company's initial clinical data for RLY-4008 as of September 9, 2021 that was announced in October 2021. In particular:

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

Cautionary Note Regarding Forward Looking Statements

This Current Report on Form 8-K and certain 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 disclosures regarding additional clinical data updates and enrollment for RLY-4008 and initial clinical data for RLY-2608; the expected therapeutic benefits of its programs, including potential efficacy and tolerability; whether preliminary results from its preclinical or clinical trials will be predictive of the final results of the trials or any future clinical trials of its product candidates; the possibility that unconfirmed results from these trials will not be confirmed by additional data as the clinical trials progress; and the Company's expectations relating to its current and future interactions with the FDA, including its belief regarding a potential pivotal cohort. The words "may," "might," "will," "could," "would," "should," "plan," "anticipate," "intend," "believe," "expect," "estimate," "seek," "predict," "future," "project," "potential," "continue," "target" and similar words or expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

Any forward-looking statements 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 changing macroeconomic conditions or uncertain geopolitical factors where the Company 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 the Company's drug candidates; the risk that the results of its 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 its planned interactions with regulatory authorities; and obtaining, maintaining and protecting its intellectual property. These and other risks and uncertainties are described in greater detail in the section entitled "Risk Factors" in the Company's most recent Annual Report on Form 10-K and Quarterly Report on Form 10-Q, as well as any subsequent filings with the Securities and Exchange Commission. In addition, any forward-looking statements represent 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 Financial Statements and Exhibits.

99.1	Press release issued by Relay Therapeutics, Inc. on September 11, 2022, furnished herewith.
99.2	Corporate presentation, dated September 12, 2022, furnished herewith.
104	Cover Page Interactive Data File (embedded within Inline XBRL document)

SIGNATURES

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: September 12, 2022

By: /s/ Brian Adams
Brian Adams, J.D.
Chief Legal Officer

Late Breaking Data Presented at ESMO Congress 2022 Demonstrate Potential of RLY-4008 to Transform Treatment Options for Cholangiocarcinoma Patients with FGFR2-Driven Disease

88% overall response rate (15 out of 17) from interim data of pan-FGFR treatment (FGFRi)-naïve FGFR2-fusion cholangiocarcinoma (CCA) patients treated at the pivotal dose

Enrollment for the pivotal cohort anticipated to be completed in the second half of 2023

Relay Therapeutics to host a conference call on Monday, September 12, at 8:00 am E.T.

Cambridge, MA – September 11, 2022 – Relay Therapeutics, Inc. (Nasdaq: RLAY) today announced late breaking interim clinical data in an oral presentation for RLY-4008, an investigational, potent, selective and oral small molecule inhibitor of fibroblast growth factor receptor 2 (FGFR2), in a global phase 1/2 clinical trial in patients with FGFR2-altered CCA and multiple other solid tumors. The interim data presented today at the European Society for Medical Oncology (ESMO) Congress demonstrate an 88% overall response rate (ORR) at the pivotal dose of RLY-4008, 70 mg once daily (QD), as of August 1, 2022, and further support our hypothesis that selective inhibition of FGFR2 can improve the treatment for patients with FGFR2-driven tumors.

“We are thrilled to be sharing interim RLY-4008 data from patients treated at the pivotal dose with the ESMO community,” said Don Bergstrom, M.D., Ph.D., President of R&D at Relay Therapeutics. “We believe the interim ORR of 88% for these patients helps to demonstrate the potential power of our Dynamo platform to build transformative therapies for patients. Additionally, we continue to generate clinical data outside of CCA and anticipate sharing them in 2023. Beyond RLY-4008, we have a robust pipeline of precision medicine candidates, and we look forward to next presenting initial clinical data on our pan-mutant-selective PI3Kα inhibitor, RLY-2608, expected in the first half of 2023. Thank you to the patients, investigators and clinical trial teams who participate in clinical trials of our investigational therapies.”

Key Data Presented at ESMO Congress 2022

The data presented at the ESMO Congress were based on an August 1, 2022 data cut-off date from both the dose escalation and dose expansion phases of the trial. The interim data included a safety database of 195 patients, with 89 patients treated at the pivotal dose of 70 mg QD, of which 17 were FGFRi-naïve FGFR2-fusion CCA patients eligible for efficacy evaluation (patients with measurable disease who had opportunity for ≥2 tumor assessments to confirm response or discontinued treatment with <2 tumor assessments).

- 15 out of 17 of the efficacy evaluable patients at the pivotal dose experienced a partial response resulting in an 88% interim ORR (14 confirmed, 1 unconfirmed in an ongoing patient).
    - 13 out of 15 responders remain on treatment; 1 responder came off study to be resected with curative intent.
    - The two patients with best response of stable disease remain on treatment.

- More broadly across all dose levels and schedules, 38 FGFRi-naïve FGFR2-fusion CCA patients were eligible for efficacy evaluation, of which 24 experienced a partial response resulting in a 63% interim ORR (22 confirmed, 2 unconfirmed).

The interim safety analysis as of the August 1, 2022 cut-off date was generally consistent with the analysis from the June 2022 data disclosure:

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

The oral presentation from the ESMO Congress is available on the Relay Therapeutics website under Publications: https://relaytx.com/publications/.

Key Upcoming RLY-4008 Milestones

- The pivotal cohort of FGFRi-naïve FGFR2-fusion CCA patients is anticipated to be fully enrolled in the second half of 2023.
- Initial data from the non-CCA expansion cohorts are expected to be presented in 2023.
- The entirety of the dose escalation data is expected to be presented at a medical meeting or published by the end of the first half of 2023.

Conference Call Information

Relay Therapeutics will host a conference call and live webcast on September 12, 2022 at 8:00 am E.T. Registration and dial-in for the conference call may be accessed through Relay Therapeutics' website under Events in the News & Events section through the following link: https://ir.relaytx.com/news-events/events-presentations. An archived replay of the webcast will be available following the event.

About RLY-4008

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 demonstrated strong activity against known clinical on-target resistance mutations in cellular and *in vivo* preclinical models. RLY-4008 is currently being evaluated in a clinical trial in patients with advanced or metastatic FGFR2-altered solid tumors with a single arm, potentially registration-enabling cohort for FGFRi-naïve FGFR2-fusion CCA. To learn more about the clinical trial of RLY-4008, please visit here.

ReFocus Trial Background

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

About Relay Therapeutics

Relay Therapeutics (Nasdaq: RLAY) is a clinical-stage precision medicine company transforming the drug discovery process by combining leading-edge computational and experimental technologies with the goal of bringing life-changing therapies to patients. As the first of a new breed of biotech created at the intersection of disparate technologies, Relay Therapeutics aims to push the boundaries of what is possible in drug discovery. Its Dynamo™ platform integrates an array of leading-edge computational and experimental approaches designed to drug protein targets that have previously been intractable. Relay Therapeutics' initial focus is on enhancing small molecule therapeutic discovery in targeted oncology and genetic disease indications. For more information, please visit www.relaytx.com or follow us on Twitter.

Cautionary Note Regarding Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, implied and express statements regarding Relay Therapeutics' strategy, business plans and focus; the progress and timing of updates on the clinical development of the programs across Relay Therapeutics' portfolio, including the timing of disclosures regarding additional clinical data updates and enrollment for RLY-4008 and initial clinical data for RLY-2608; the expected therapeutic benefits of its programs, including potential efficacy and tolerability; 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; and Relay Therapeutics' expectations relating to its current and future interactions with the U.S. Food and Drug Administration, including its belief regarding a potential pivotal cohort. The words "may," "might," "will," "could," "would," "should," "plan," "anticipate," "intend," "believe," "expect," "estimate," "seek," "predict," "future," "project," "potential," "continue," "target" and similar words or expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

Any forward-looking statements in this press release are based on management's current expectations and beliefs, and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this press release, including, without limitation, risks associated with: the impact of changing macroeconomic conditions or uncertain geopolitical factors where 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 its planned interactions with regulatory authorities; and obtaining, maintaining and protecting its intellectual property. These and other risks and uncertainties are described in greater detail in the section entitled "Risk Factors" in Relay Therapeutics' most recent Annual Report on Form 10-K and Quarterly Report on Form 10-Q, as well as any subsequent filings with the Securities and Exchange Commission. In addition, any forward-looking statements represent Relay Therapeutics' views only as of today and should not be relied upon as representing its views as of any subsequent date. Relay Therapeutics explicitly disclaims any obligation to update any forward-looking statements. No representations or warranties (expressed or implied) are made about the accuracy of any such forward-looking statements.

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Exhibit 99.2

RELAY®
THERAPEUTICS

ESMO Disclosure Call Materials

September 2022

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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 and current and future preclinical studies of our product candidates; the timing of disclosures regarding our pipeline and additional clinical data for RLY-4008 and initial clinical data for RLY-2608; 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 competitive landscape and market opportunities for our product candidates; the potential strategic benefits 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; 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.

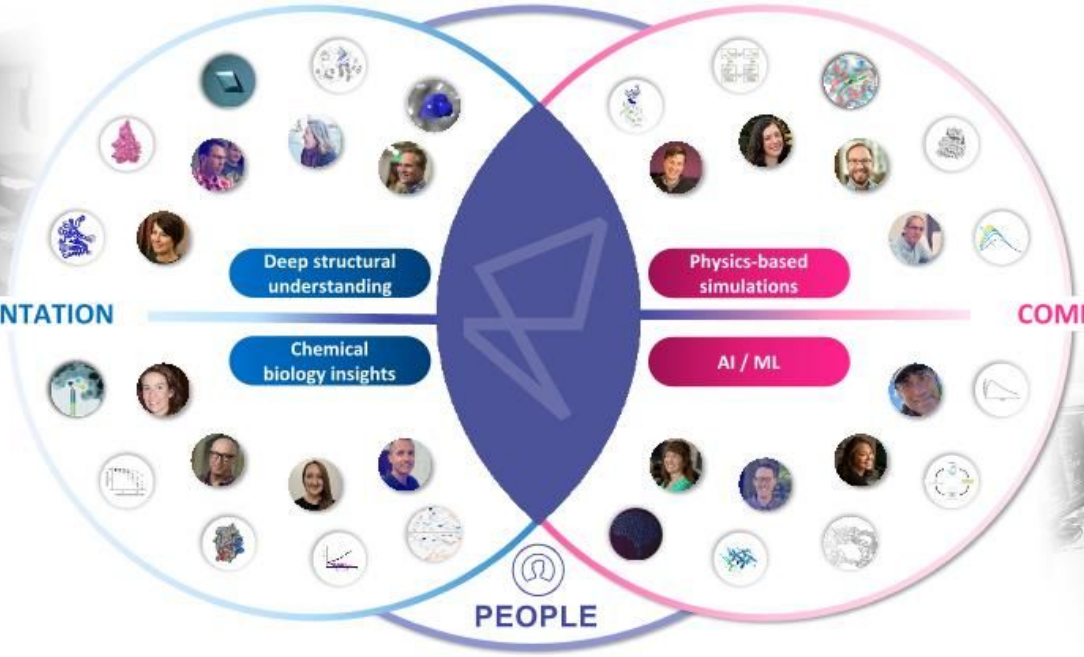
Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make due to a number of risks and uncertainties. These and other risks, uncertainties and important factors are described in the section entitled "Risk Factors" in our most recent Annual Report on Form 10-K and most recent Quarterly Report on Form 10-Q, 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.

This presentation contains trademarks, trade names and service marks of other companies, which are the property of their respective owners.

This presentation shall not constitute an offer to sell or the solicitation of an offer to buy securities of the Company.

Relay Tx – New Breed of Biotech



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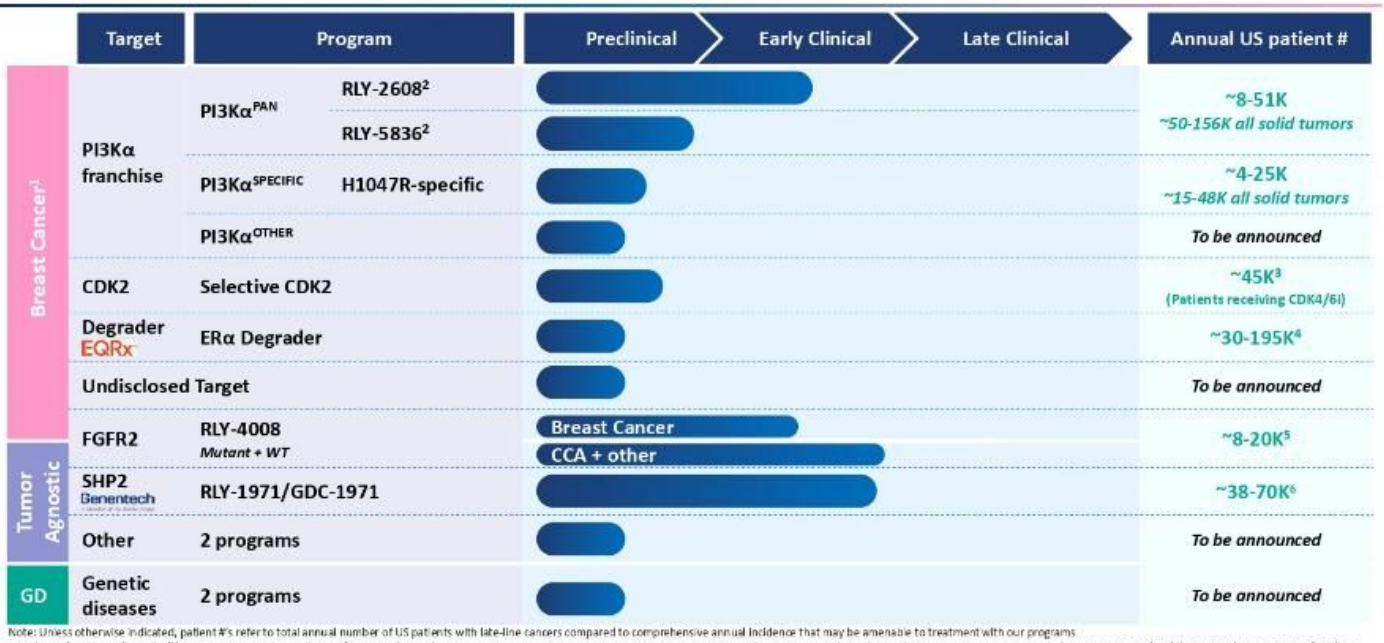
Relay Tx – Extensive Precision Medicine Focused Pipeline



Note: Unless otherwise indicated, 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

1. Unless otherwise indicated, all breast cancer patient numbers refer to HR+/HER2- breast cancer tumors 2. RLY-2608 covers H1047X, E542X, E545X hot spots 3. ~45k HR+/HER2- breast cancer patients expected to receive CDK 4/6 inhibitors in adjuvant setting, first-line setting, and second-line setting in 2023, per Decision Resources Breast Cancer Market Forecast, report dated February 2022 4. HR+/HER2- US late-line breast cancer patients compared to HR+/HER2- US incident breast cancer patients 5. FGFR2 altered late-line solid tumors compared to comprehensive annual FGFR2 altered incident solid tumors 6. SHP2 combo only includes KRAS G12C in lung and CRC, EGFR mutations in lung, and ALK fusions in lung

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Relay Tx – Anticipated Milestones

Breast Cancer Franchise

RLY-2608 (PI3Kα^{PAN})

Initial data in 1H 2023

Selective CDK2

Clinical start in 4Q 2023 or 1Q 2024

ERα Degrader

Development candidate nomination in 2023

Tumor Agnostic

RLY-4008 (Selective FGFR2)

✓ Additional data update in 2H 2022

Full dose escalation data in 1H 2023

Non-CCA expansion cohorts data in 2023

+ Pivotal cohort full enrollment in 2H 2023

GDC-1971 (RLY-1971, SHP2)

✓ Atezolizumab combo trial initiated

✓ Disclosed today

\+ New guidance issued today

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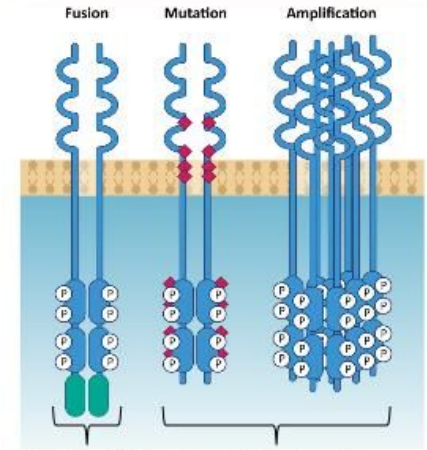
FGFR2 – Validated Target Present in Several Tumor Types

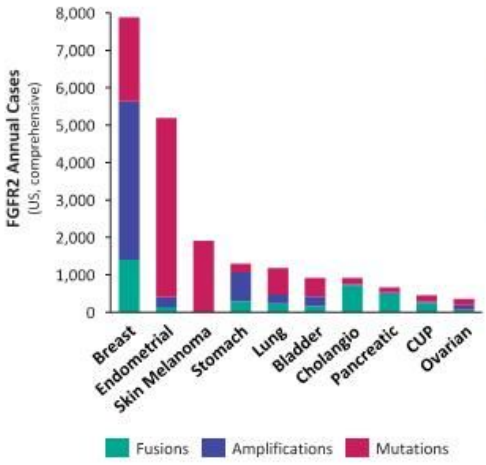
Three classes of driver alterations in FGFR2



~3K-5K patients in the US per year[1]

~5K-15K patients in the US per year[1]

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 targeted therapy	
FGFRi-resistant Cholangio-carcinoma			
Other FGFR2-altered solid tumors			

Sources: Image adapted from Babina IS, Turner NC. Nat Rev Cancer 2017;17: 318-332; 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

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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	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; FOLFOX – ABC-06 Publication in Lancet Oncology 2021

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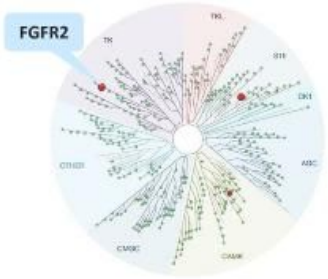
RLY-4008 – A Highly Selective and Irreversible FGFR2 Inhibitor

RLY-4008

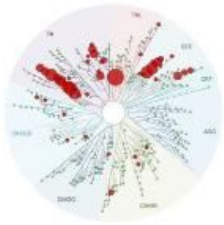


Percent Control

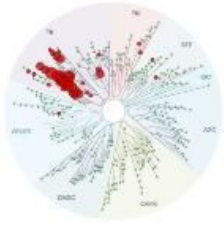
- 0%
- 0.1%
- 0.1-1%
- 1-5%
- 5-10%
- 10-35%
- > 35%

Pan-FGFR Inhibitors

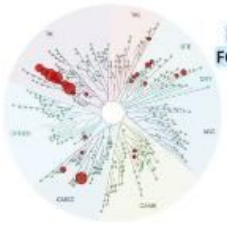
AZD4547



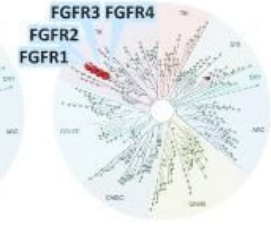
Erdafitinib



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

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RLY-4008 – Summary of Sept 2022 Interim Data Disclosure at ESMO

Favorable Interim Safety Profile

- Favorable Tolerability & Safety profile across 195 patients
- Highly Selective with no clinically significant off-target tox

Initial Efficacy Observed in Fusion+ CCA FGFRi-Naïve Patients

RLY-4008

88% ORR

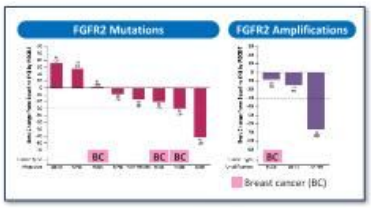
15 of 17 pt at pivotal dose (70 mg QD)[1]

63% ORR (24 of 38 pt)
fusion+ CCA FGFRi-naïve patients across all doses[2]

Approved pan-FGFRi

23-36% ORR[3]

Potential Outside of CCA



Early signs of activity in non-CCA patients, including breast cancer
(presented at Oct 2021 Triple Meeting)

CCA = Cholangiocarcinoma; ORR = Overall Response Rate; QD = once daily dosing; PR = partial response

1. ORR from interim data disclosure: 15 PRs at 70 mg QD: 14 confirmed PRs, 1 unconfirmed PR in an ongoing patient (confirmed ORR = 82%); 2. ORR from interim data disclosure: 24 PRs across all doses:22 confirmed PRs, 2 unconfirmed PR (confirmed ORR = 58%); 3. Referenced approved pan-FGFRi are Pemigatinib and Infigratinib; ORR based on prescribing information. These data are derived from different clinical trials at different points in time, with differences in trial design and patient populations. As a result, cross-trial comparisons cannot be made, and no head-to-head clinical trials have been conducted.

Data cut-off: August 01, 2022; efficacy analysis includes patients with measurable disease who had opportunity for ≥2 tumor assessments or discontinued treatment with <2 tumor assessments

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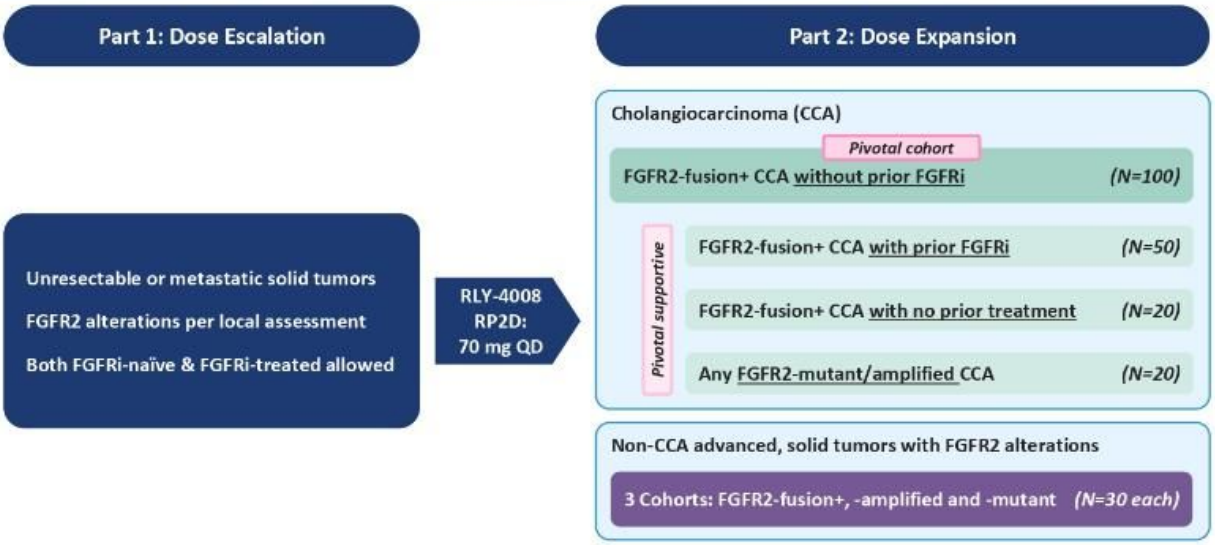
RLY-4008 – ReFocus Trial Design



Data cut-off: August 01, 2022; efficacy analysis includes patients with measurable disease who had opportunity for ≥2 tumor assessments or discontinued treatment with <2 tumor assessments

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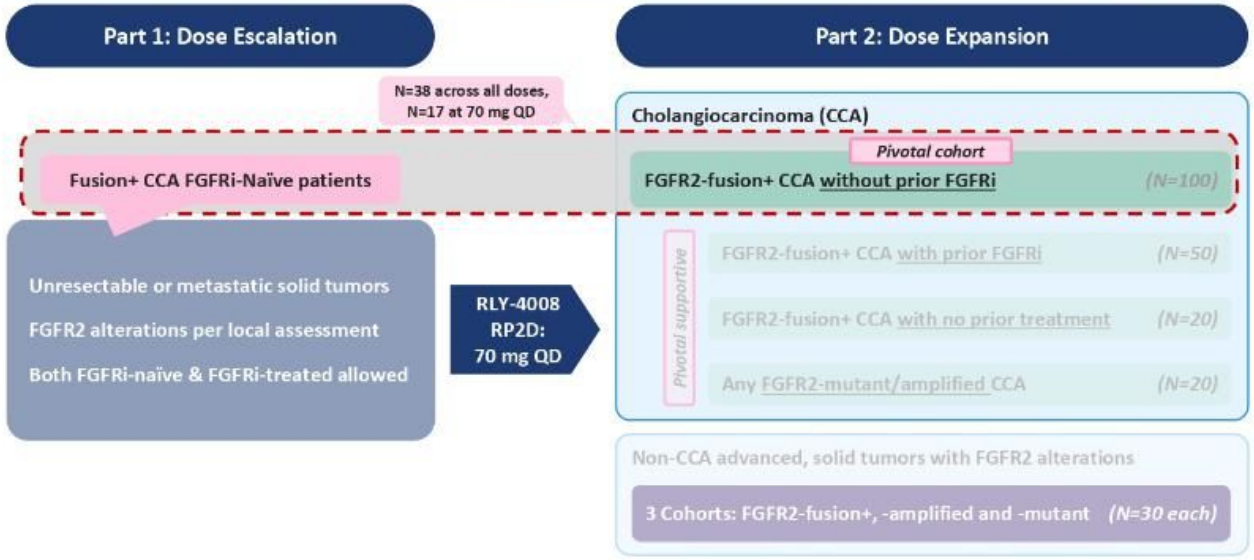
RLY-4008 –Continued Robust Activity Observed in FGFRi-Naïve CCA Patients



Interim Efficacy Data from Sept 2022 ESMO Disclosure Includes 38 Fusion+ CCA FGFRi-Naïve QD Patients (17 at 70 mg QD)

Data cut-off: August 01, 2022; efficacy analysis includes patients with measurable disease who had opportunity for ≥2 tumor assessments or discontinued treatment with <2 tumor assessments

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RLY-4008 – Patient Characteristics

Parameter	Fusion+ CCA FGFRi-Naïve[1]		Total (N=195)[2]
	70 mg QD (N=17)	All doses (N=38)	
Age (years), median (range)	57 (36-81)	58 (33-81)	59 (23-87)
Female, %	59%	58%	62%
Race, %			
White / Asian / Black / Unknown	41% / 24% / 0% / 35%	58% / 21% / 3% / 18%	63% / 15% / 4% / 18%
ECOG PS[3], %			
0	53%	50%	38%
1	47%	50%	58%
2	0%	0%	3%
Prior lines of systemic therapy, %			
0	0%	0%	2%
1	41%	47%	20%
2	47%	32%	29%
3+	12%	21%	49%
Baseline sum of target lesions (RECIST 1.1, mm), median (range)	57 (10-157)	63 (10-216)	79 (10-274)

1. Efficacy analysis includes patients with previously treated, FGFR2i-naïve CCA treated at the RP2D. Patients with measurable disease who had opportunity for ≥2 tumor assessments to confirm response or discontinued treatment with <2 tumor assessments
2. Patients in safety population who received ≥1 dose of RLY-4008 at any dose level
3. ECOG PS = Eastern Cooperative Oncology Group Performance Scale

Data cut-off: August 01, 2022; efficacy analysis includes patients with measurable disease who had opportunity for ≥2 tumor assessments or discontinued treatment with <2 tumor assessments

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RLY-4008 – Interim Response Data

FGFRi-Naïve Fusion+ CCA Patients at Pivotal Dose (70 mg QD)

Best RECIST Change (%) from Baseline Based on Investigator Evaluated Response for Fusion+ CCA FGFRi-Naïve Patients at 70 mg QD (N=17)

Approved Pan-FGFR Inhibitors Demonstrate 23-36% ORR in This Population[3]

1. Confirmed ORR = 82%: 14 confirmed PRs, 1 unconfirmed PR in an ongoing patient; 2. Complete tumor resection: R0 resection performed in curative intent, patient remains no evidence of disease as of 31 May 2022; 3. Referenced approved pan-FGFRi are Pemigatinib and Infigratinib; ORR based on prescribing information. These data are derived from different clinical trials at different points in time, with differences in trial design and patient populations. As a result, cross-trial comparisons cannot be made, and no head-to-head clinical trials have been conducted.

Data cut-off: August 01, 2022; efficacy analysis includes patients with measurable disease who had opportunity for ≥2 tumor assessments or discontinued treatment with <2 tumor assessments

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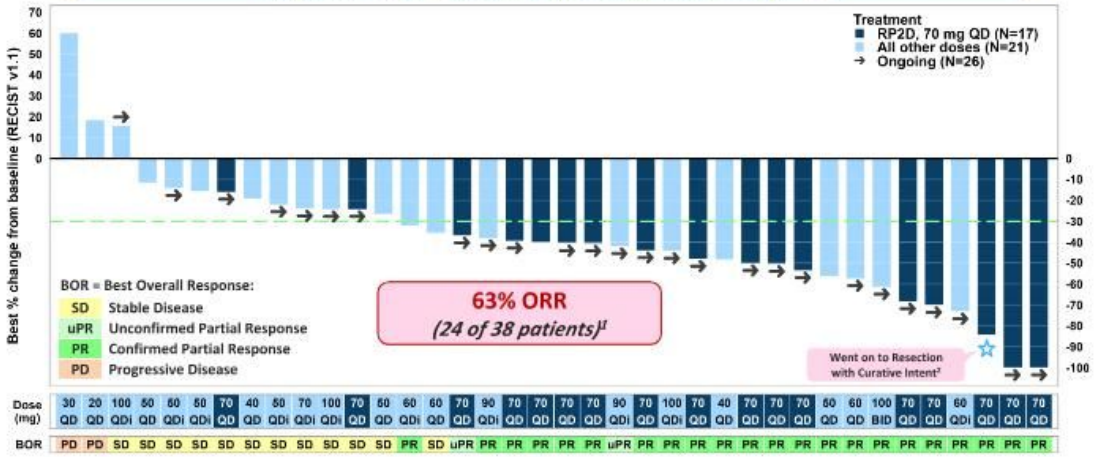
RLY-4008 – Interim Response Data

FGFRi-Naïve Fusion+ CCA Patients Across All Doses

Best RECIST Change (%) from Baseline Based on Investigator Evaluated Response for Fusion+ CCA FGFRi-Naïve Patients Across All Doses (N=38)



92% of Patients With Tumor Reduction Across All Dose Levels, Majority of Patients With Partial Response per RECIST 1.1

QDi = once daily dosing on an intermittent schedule (3 weeks on drug, 1 week off); BID = twice daily dosing

1. Confirmed ORR = 58%: 22 confirmed PRs, 2 unconfirmed PR
2. Complete tumor resection: R0 resection performed in curative intent, patient remains no evidence of disease as of 31 May 2022

Data cut-off: August 01, 2022; efficacy analysis includes patients with measurable disease who had opportunity for ≥2 tumor assessments or discontinued treatment with <2 tumor assessments

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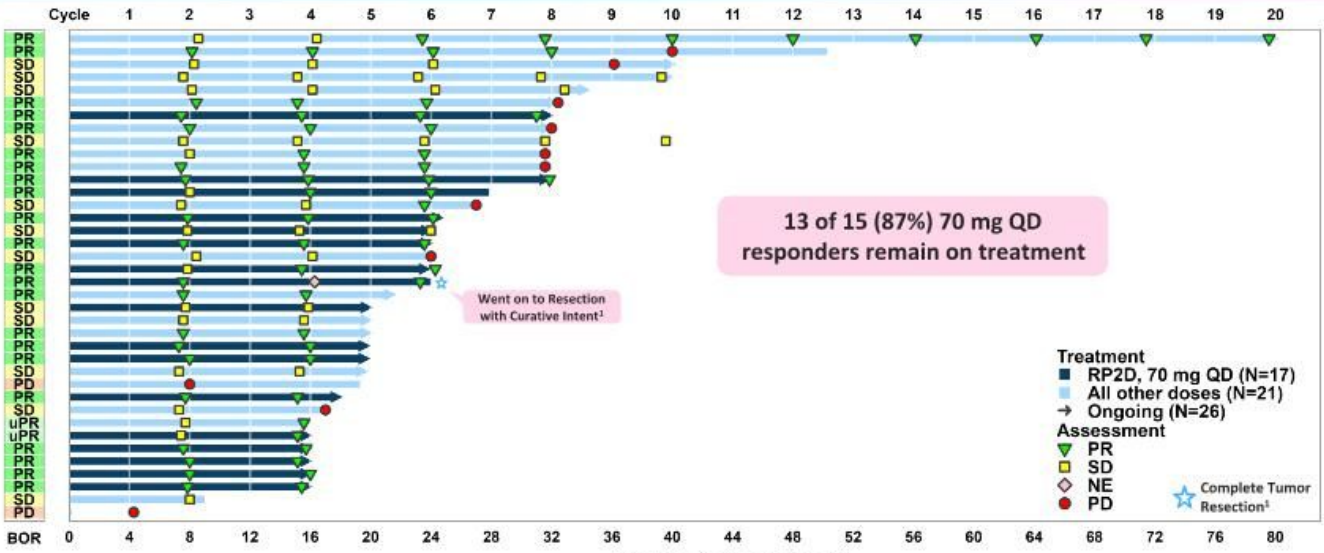
RLY-4008 – Time on Treatment for Fusion+ CCA FGFRi-Naïve Patients (All Doses)



BOR = Best Overall Response:
- SD Stable Disease
- uPR Unconfirmed Partial Response
- PR Confirmed Partial Response
- PD Progressive Disease

- Median duration of exposure: 5.5 months (range: <0.1 to 18.5 months)
- Median time to response: 1.8 months
- 12/38 (32%) Discontinued - 1 resection with curative intent, 8 PD, 1 AE, 2 withdrawal of consent

1. Complete tumor resection: R0 resection performed in curative intent, patient remains no evidence of disease as of 31 May 2022

Data cut-off: August 01, 2022; efficacy analysis includes patients with measurable disease who had opportunity for ≥2 tumor assessments or discontinued treatment with <2 tumor assessments

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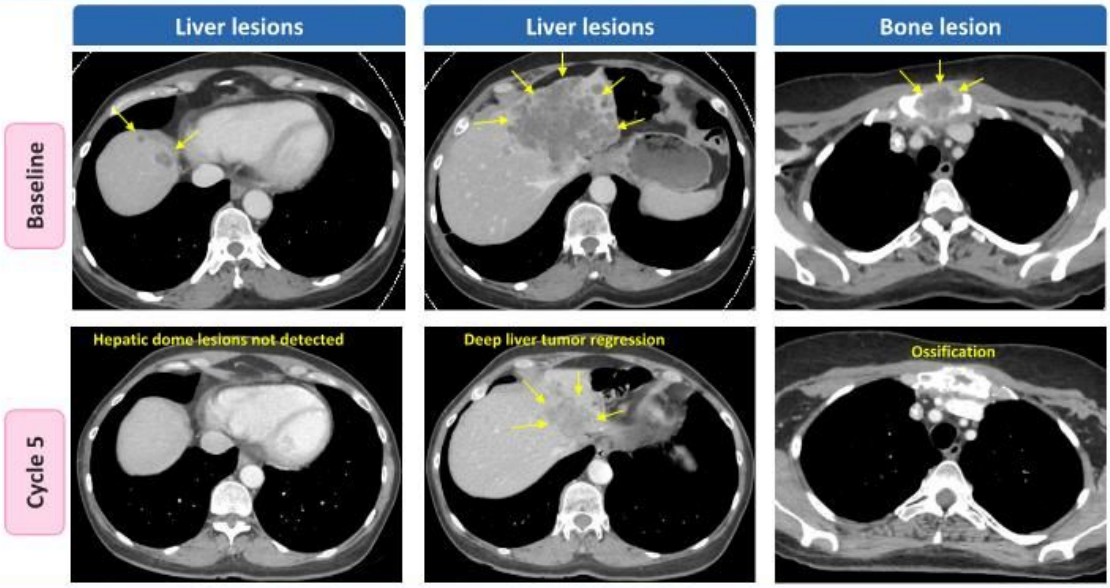
RLY-4008 – Patient Treated at 70 mg QD Resulted in 68% Tumor Regression



56-year-old Female With FGFR2-PLETHA4 Rearrangement ICC. Refractory to Gemcitabine/Cisplatin; Treated at 70 mg QD Dosing, Demonstrated Confirmed Partial Response per RECIST (-68%); Ongoing in Response

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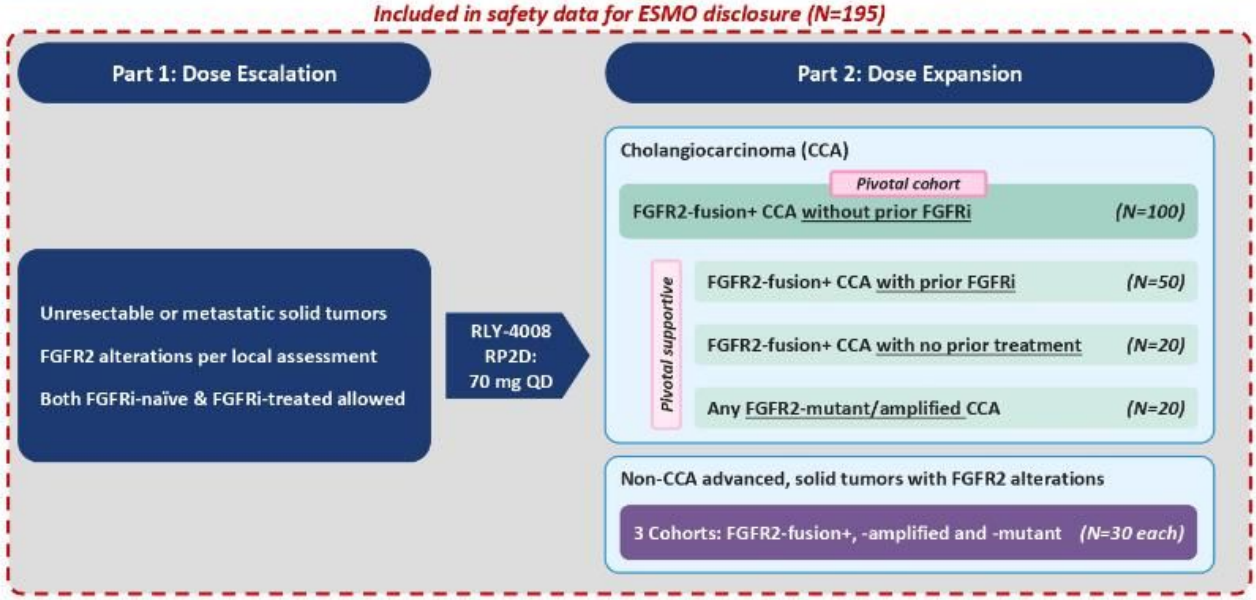
RLY-4008 – Interim Safety Data from ESMO Disclosure Includes 195 Patients



Data cut-off: August 01, 2022; efficacy analysis includes patients with measurable disease who had opportunity for ≥2 tumor assessments or discontinued treatment with <2 tumor assessments

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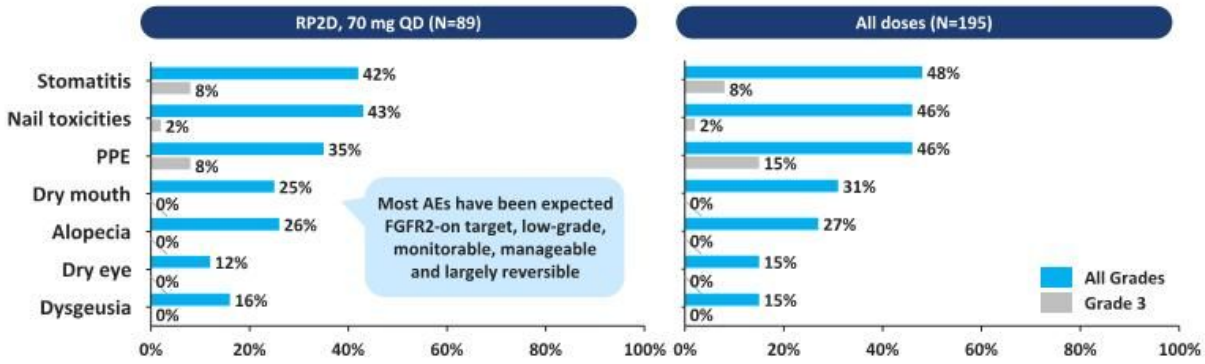
RLY-4008 – Treatment-Related Adverse Events (TRAEs) Interim Profile

TRAEs ≥ 15%



TRAE Dose Modification	RP2D, 70 mg QD (N=89)	All Doses (N=195)
Dose interruption (%)	42%	47%
Dose reduction (%)	27%	33%
Dose discontinuation (%)	1%	1%*

Doses at ≥40 mg QD result in 90%+ target inhibition

Clinically Insignificant Off-Target Hyperphosphatemia (12%, all Gr 1-2) and Diarrhea (4%, all Gr 1-2) Allow for Optimization of FGFR2 Inhibition

* 1 hypersensitivity, 1 retinal pigment epithelial detachment, both resolved

Data cut-off: August 01, 2022; efficacy analysis includes patients with measurable disease who had opportunity for ≥2 tumor assessments or discontinued treatment with <2 tumor assessments

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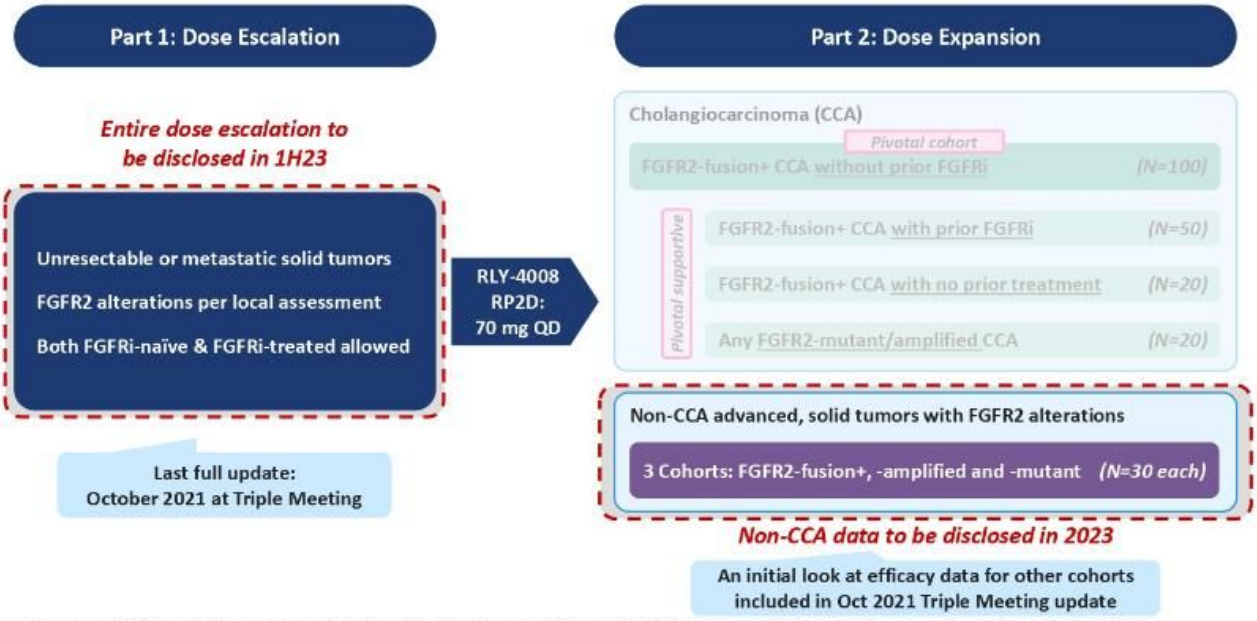
RLY-4008 – Additional Disclosures Expected in 2023



Data cut-off: August 01, 2022; efficacy analysis includes patients with measurable disease who had opportunity for ≥2 tumor assessments or discontinued treatment with <2 tumor assessments

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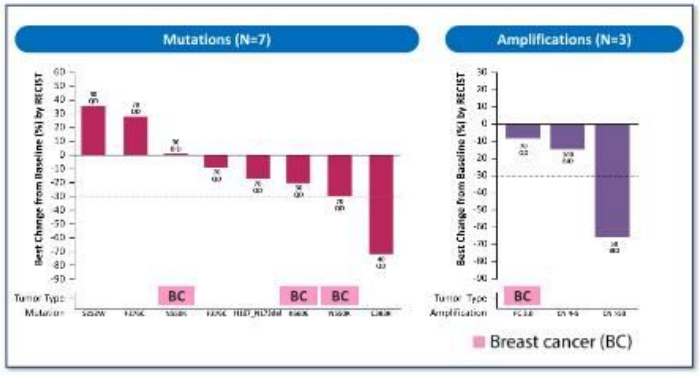
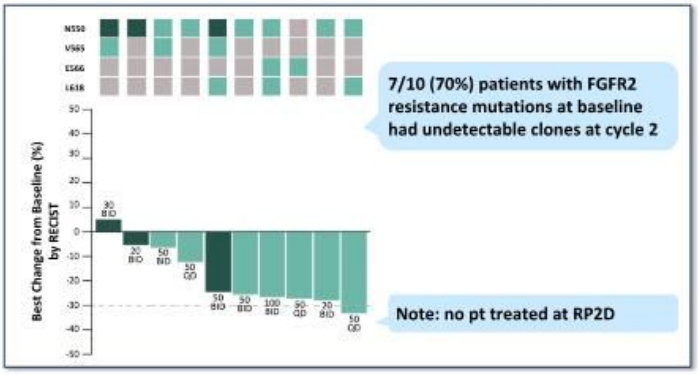
RLY-4008 – Observations from October 2021 Initial Clinical Data Disclosure

October 2021:
Presented at Triple Meeting *(data as of 09 September 2021)*

Tumor regression also observed across FGFR2 mutations (N=7) and amplifications (N=3)



Demonstrated activity against resistance mutations in pan-FGFRi-resistant cholangiocarcinoma (N=10)



Entire Dose Escalation Data Expected to be Disclosed in 1H 2023

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RLY-4008 – Summary of ESMO Disclosure and Anticipated Milestones

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RLY-4008 | Approved pan-FGFRi

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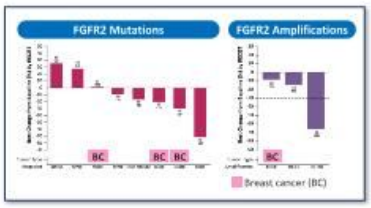

Early signs of activity in non-CCA patients, including breast cancer
(presented at Oct 2021 Triple Meeting)

1H 2023: Full dose escalation data

2H 2023: Pivotal cohort full enrollment

2023: Non-CCA expansion cohorts

CCA = Cholangiocarcinoma; ORR = Overall Response Rate; QD = once daily dosing; PR = partial response

1. ORR from interim data disclosure: 15 PRs at 70 mg QD: 14 confirmed PRs, 1 unconfirmed PR in an ongoing patient (confirmed ORR = 82%); 2. ORR from interim data disclosure: 24 PRs across all doses:22 confirmed PRs, 2 unconfirmed PR (confirmed ORR = 58%); 3. Referenced approved pan-FGFRi are Pemigatinib and Infigratinib; ORR based on prescribing information. These data are derived from different clinical trials at different points in time, with differences in trial design and patient populations. As a result, cross-trial comparisons cannot be made, and no head-to-head clinical trials have been conducted.

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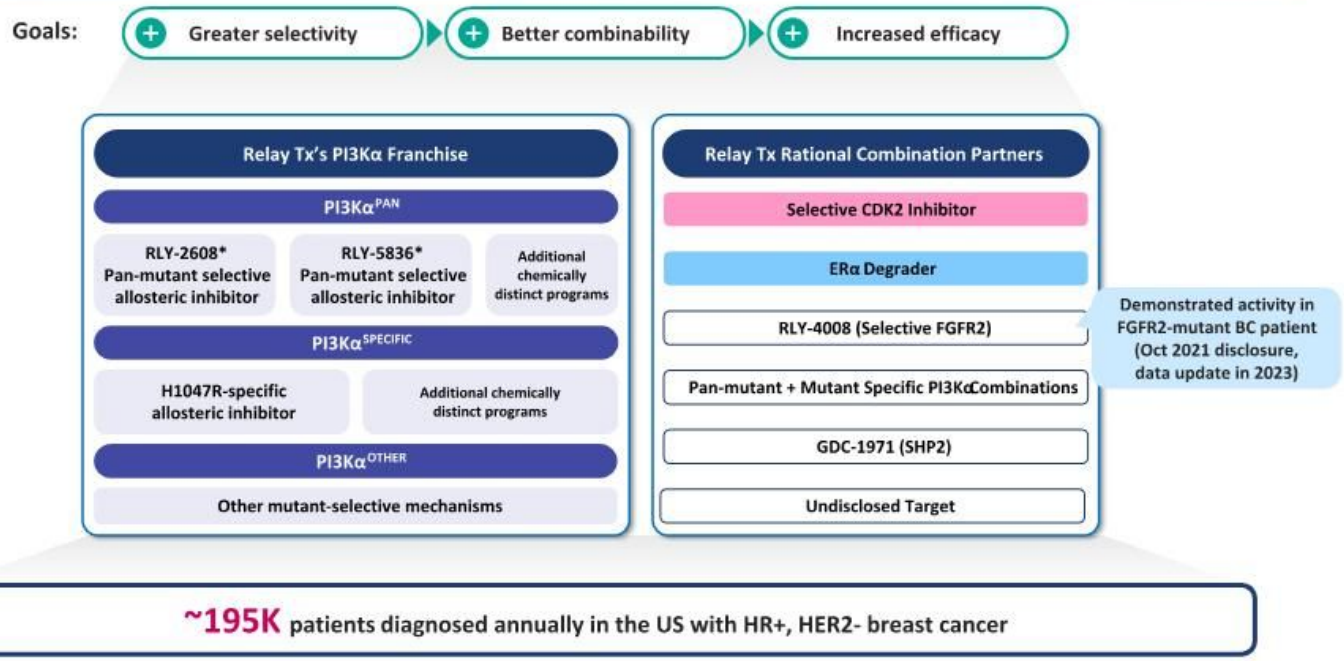
Relay Tx's Emerging Breast Cancer Franchise Addresses Large Opportunity



~195K patients diagnosed annually in the US with HR+, HER2- breast cancer

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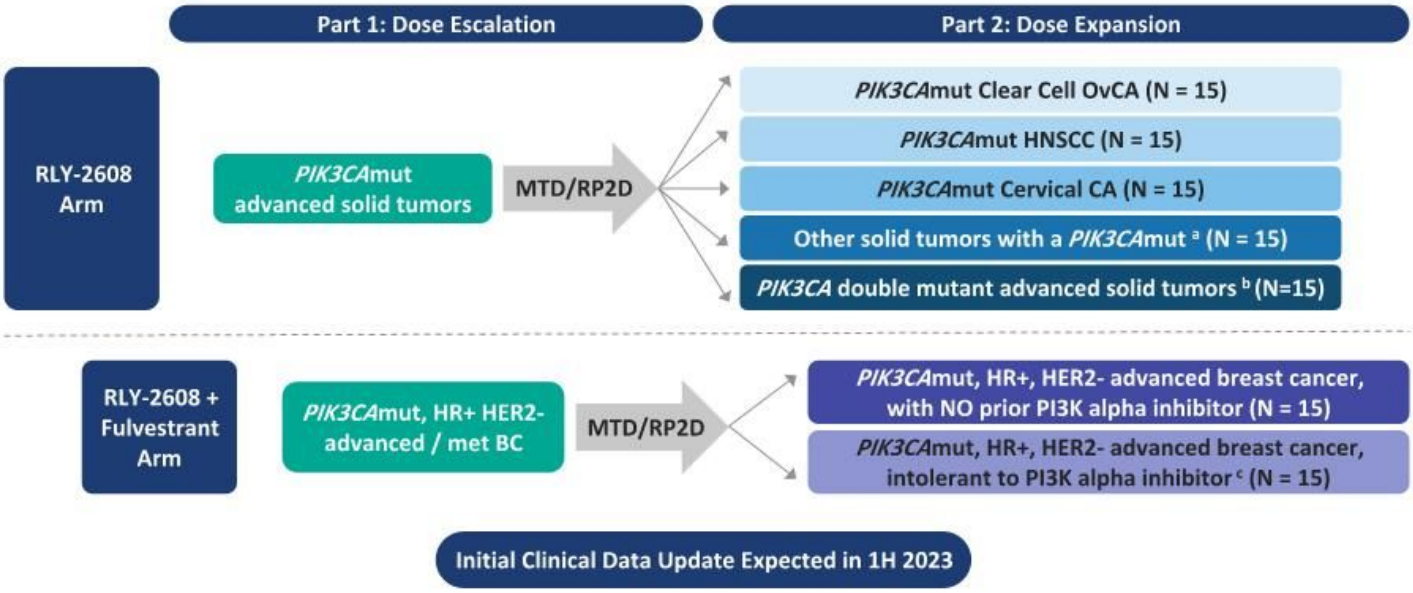
PI3Kα – RLY-2608 Trial Design



Initial Clinical Data Update Expected in 1H 2023

a. Excludes PIK3CAmut clear cell OvCA, HNSCC, and Cervical cancer patients; b. Double mutation defined as one major PIK3CA mutation (E542X, E545X, H1047X) + ≥1 additional PI3KCA mutation per local assessment; c. Intolerance to PI3K alpha inhibitors is defined as treatment discontinuation due to treatment-related AE (e.g., hyperglycemia, rash, diarrhea, stomatitis) other than severe hypersensitivity reaction and/or life-threatening reactions, such as anaphylaxis and Stevens-Johnson syndrome.

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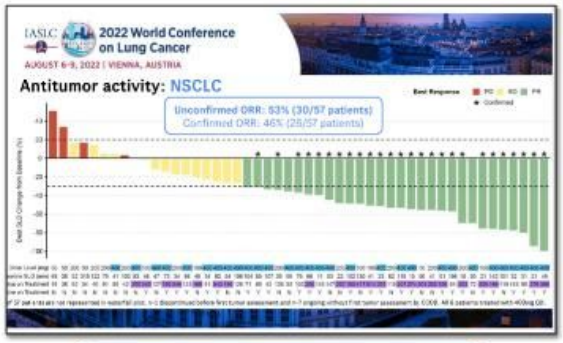
SHP2 – Genentech Global Collaboration for GDC-1971 (Formerly RLY-1971)

Two ongoing trials with GDC-1971:

GDC-1971
+
GDC-6036 (KRAS G12Ci)
initiated July 2021

GDC-1971
+
Atezolizumab (PD-L1 Ab)
initiated August 2022

Clinical Update for GDC-6036 Monotherapy at World Lung 2022 (Ph1)



Unconfirmed ORR: 53% (30/57 patients)
Confirmed ORR: 46% (26/57 patients)

Collaboration Provides Meaningful Economics to Relay Tx*

* As of June 30, 2022: $95 million in upfront & milestone payments received, plus an opt-in option for 50/50 profit share and up to $700M in potential additional total milestones, low-to-mid teen royalties on global net sales plus eligible to receive additional royalties upon approval of GDC-1971 and GDC-6036 in combination

Source: World Lung 2022 #OA03.04

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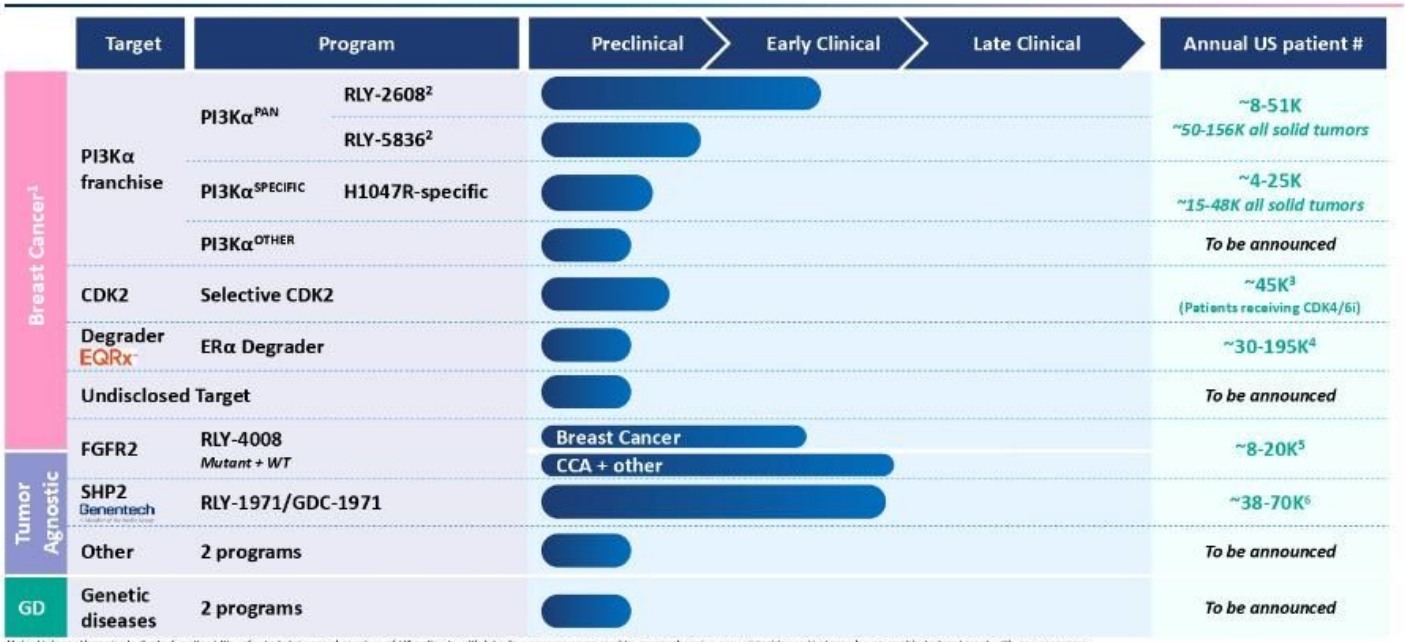
Relay Tx – Extensive Precision Medicine Focused Pipeline



Note: Unless otherwise indicated, 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

1. Unless otherwise indicated, all breast cancer patient numbers refer to HR+/HER2- breast cancer tumors 2. RLY-2608 covers H1047X, E542X, E545X hot spots 3. ~45k HR+/HER2- breast cancer patients expected to receive CDK 4/6 inhibitors in adjuvant setting, first-line setting, and second-line setting in 2023, per Decision Resources Breast Cancer Market Forecast, report dated February 2022 4. HR+/HER2- US late-line breast cancer patients compared to HR+/HER2- US incident breast cancer patients 5. FGFR2 altered late-line solid tumors compared to comprehensive annual FGFR2 altered incident solid tumors 6. SHP2 combo only includes KRAS G12C in lung and CRC, EGFR mutations in lung, and ALK fusions in lung

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Relay Tx – Capital, Team & Execution Focus to Deliver on Anticipated Milestones

RELAY THERAPEUTICS

Breast Cancer Franchise

RLY-2608 (PI3Kα^{PAN})

Initial data in 1H 2023

Selective CDK2

Clinical start in 4Q 2023 or 1Q 2024

ERα Degrader

Development candidate nomination in 2023

Tumor Agnostic

RLY-4008 (Selective FGFR2)

✓ Additional data update in 2H 2022

Full dose escalation data in 1H 2023

Non-CCA expansion cohorts data in 2023

+ Pivotal cohort full enrollment in 2H 2023

GDC-1971 (RLY-1971, SHP2)

✓ Atezolizumab combo trial initiated

$838M

Cash, cash equivalents and investments as of the end of 2Q 2022

Current cash, cash equivalents and investments are expected to be sufficient to fund current operating plan into 2025

✓ Disclosed today

\+ New guidance issued today

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