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): January 09, 2023

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

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, 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.

Relay Therapeutics, Inc. (the "Company") will be conducting meetings with participants attending the 41st Annual J.P. Morgan Healthcare Conference (the "Conference") during the week of January 9, 2023. A copy of the slides to be presented by the Company at the Conference is furnished as Exhibit 99.1 to this Current Report on Form 8-K, which is incorporated herein by reference.

The information in this Item 7.01, including Exhibit 99.1 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 9.01 Exhibits.

99.1	41st Annual J.P. Morgan Healthcare Conference Company Presentation, dated January 2023, 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: January 9, 2023

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

RELAY®
THERAPEUTICS

JPM Presentation

January 2023

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 expected 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; 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.

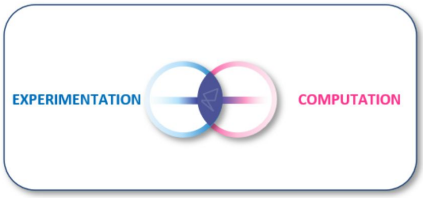
Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make due to a number of risks and uncertainties. These and other risks, uncertainties and important factors are described in the section entitled "Risk Factors"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

Relay Tx – Patient-Driven

New Breed of Biotech



Clear Focus

Targets & Therapeutic Areas	Validated Targets only	Oncology	Genetic diseases
Modalities	Small molecules	Degraders	Chaperones

$1.1B

Cash, cash equivalents and investments as of the end of 3Q 2022

Validated Approach

Clinical

- FGFR2 *RLY-4008*
- PI3Kα^{PAN} *RLY-2608*
- SHP2 *GDC-1971*

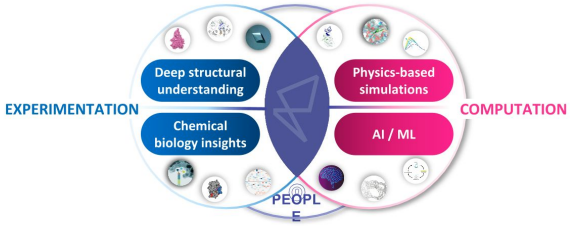
Pre-clinical

- PI3Kα^{PAN} *RLY-5836*
- Selective CDK2
- ERα Degrader

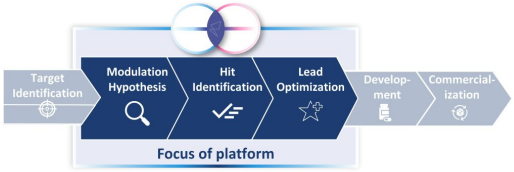
Execution-Focused

Relay Tx – Dynamo™ Platform

1 Dynamo™ Platform…



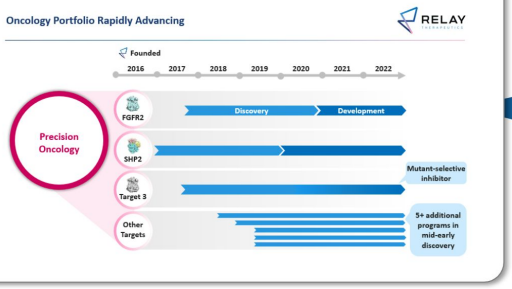
2 …is focused on making medicines



3 …aims to address selectivity on validated targets

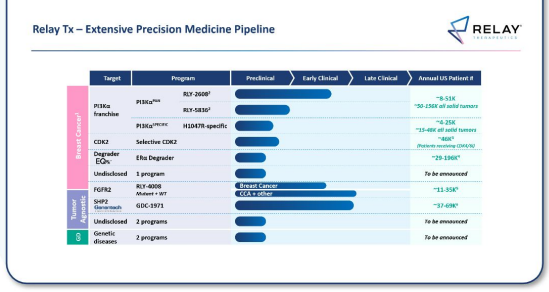
Relay Tx – Execution Focused

Jan 2020



Company	Programs
Private	2 disclosed targets
Preclinical	6+ unnamed programs
Purely research	

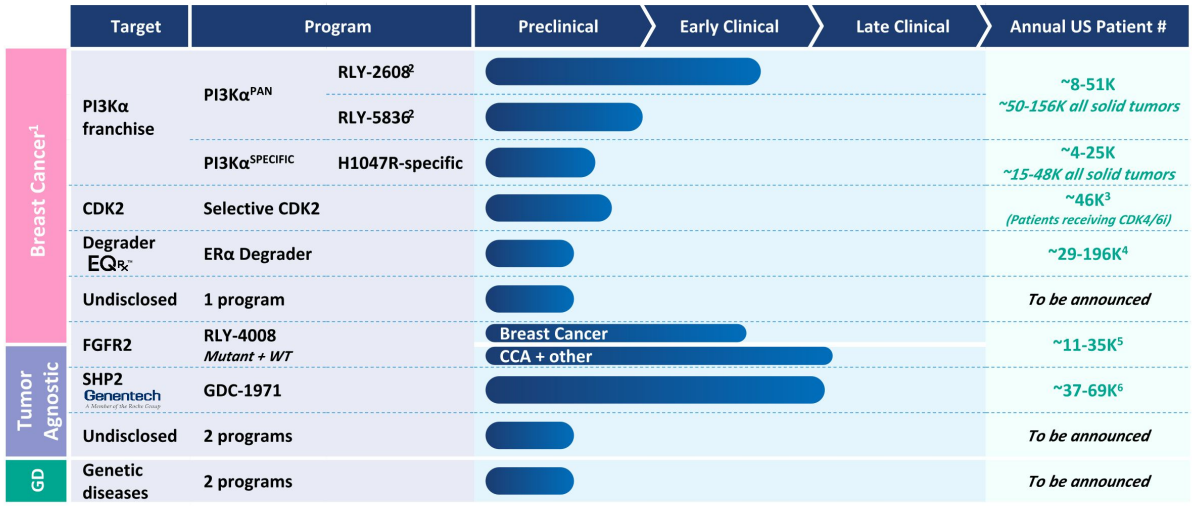
Jan 2023



Company	Programs
Public, clinical org	3 assets in clinic
Cash runway into 2025	5 disclosed programs
Presented clinical data at ESMO & Triple Meeting	5+ unnamed programs
	Platform: + ML-DEL and Automation

Source: Relay Tx presentation at JPM conference Jan 2020

Relay Tx – Extensive Precision Medicine 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, and breast cancer patient range assumes HR+/HER2- population 3. ~46k 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 June 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 including additional FGFR gene fusions and rearrangements resulting from truncation of the protein at exon 18 6. SHP2 combo only includes KRAS G12C in lung and CRC, EGFR mutations in lung, and ALK fusions in lung

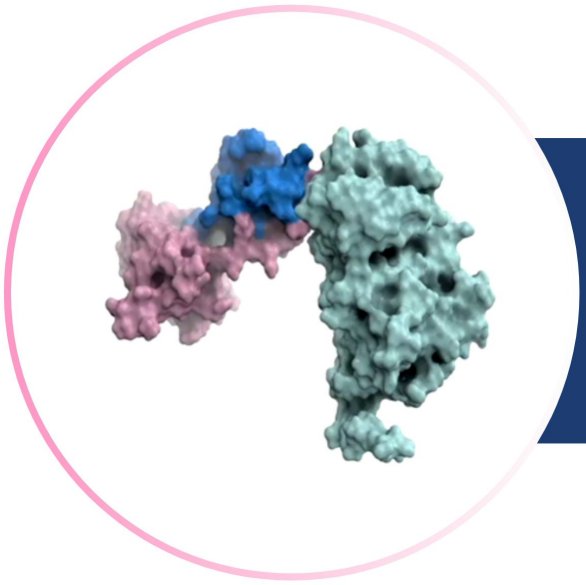
Relay Tx – Capital, Team & Execution Focus to Deliver

Breast Cancer Franchise			Tumor Agnostic		Undisclosed
 PI3Kα^{PAN}	 Selective CDK2	 ERα Degrader	 RLY-4008 (Selective FGFR2)	 GDC-1971 (SHP2)	 *To be announced*
RLY-2608 Initial data in 1H 2023 **RLY-5836** Clinical start in 2Q 2023	Clinical start in early 2024	Development candidate nomination in 2023	Full dose escalation data in 1H 2023 Non-CCA expansion cohorts data in 2H 2023 Pivotal cohort full enrollment in 2H 2023	Ongoing combo trials; Genentech controls data disclosures	*5+ undisclosed programs in preclinical development and additional early-stage efforts across platform*

$1.1B

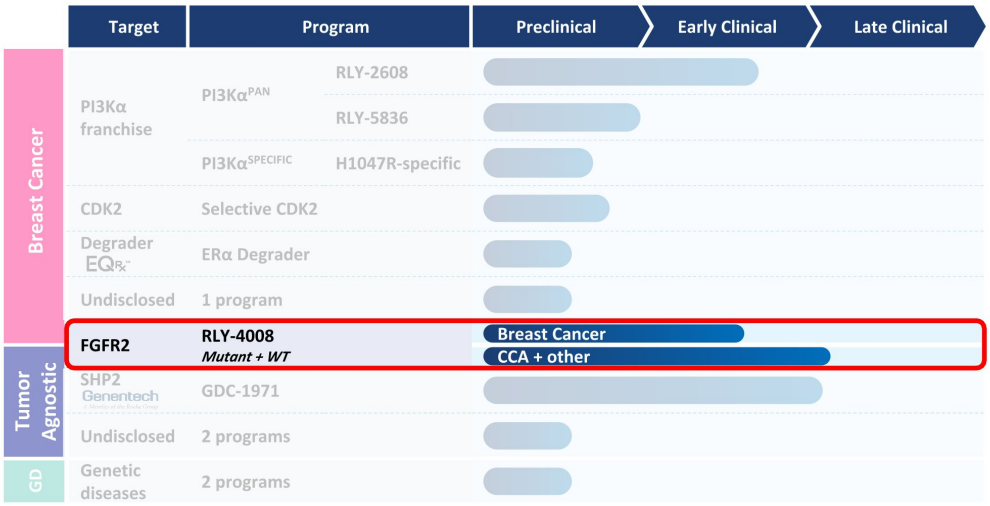
Cash, cash equivalents and investments as of the end of 3Q 2022

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



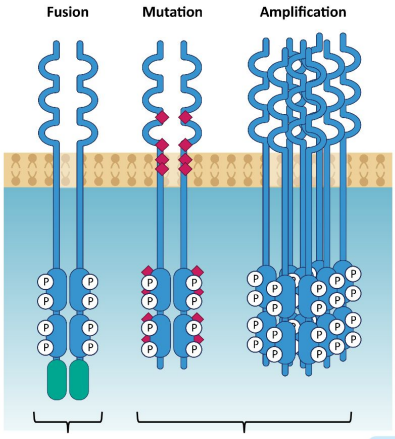
Relay Tx Programs

Relay Tx – Extensive Precision Medicine Pipeline



FGFR2 – Validated Target Present in Several Tumor Types

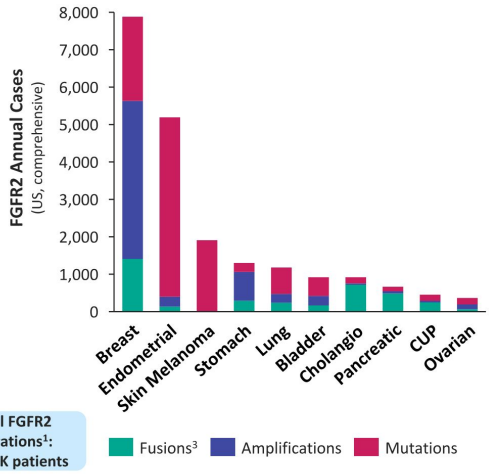
Three classes of driver alterations in FGFR2



Annual US Patient Count[1]

Total FGFR2 alterations[1]: ~10-23K patients

FGFR2 alterations are observed across multiple tumor types[2]



FGFR2-altered cancers remain a high unmet medical need

FDA approvals only in fusion+ CCA FGFRi-naïve patients

36-42% Objective Response Rate[4]

Limited treatment options for other FGFR2 driven cancers[5]

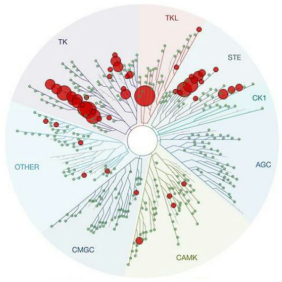
Sources: Image adapted from Babina IS, Turner NC. Nat Rev Cancer 2017;17: 318-332; Internal analysis based on third party industry data

1. All 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 including additional FGFR gene fusions and rearrangements resulting from truncation of the protein at exon 18; 2. Cholangio, cholangiocarcinoma (CCA); CUP, carcinoma unknown primary; 3. FGFR2 fusion estimates include del18 truncations; 4. Based on pemigatinib, erdafitinib, and futibatinib prescribing information; 5. Erdafitinib is approved for urothelial carcinoma with FGFR2/3 alterations

FGFR2 – Limitations of Current FGFR Inhibitor Landscape

Limited Selectivity

Approved Pan-FGFRis are non-specific across FGFR family



Limited Target Inhibition

Pemigatinib 13.5mg QD achieves 76% inhibition of FGFR2 at trough[1]

Limited Tolerability

High rates of off-target toxicity (esp. FGFR1,4)

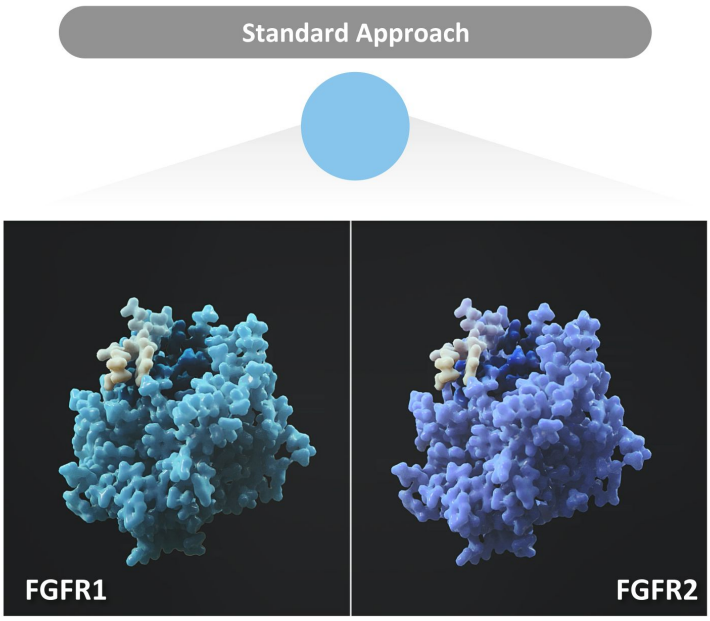
FDA Approved Compound	% of Patients with Hyperphosphatemia	% of Patients with Diarrhea
Pemigatinib	94%	47%
Futibatinib	88%	39%
Erdafitinib	76%	47%

Limited Efficacy

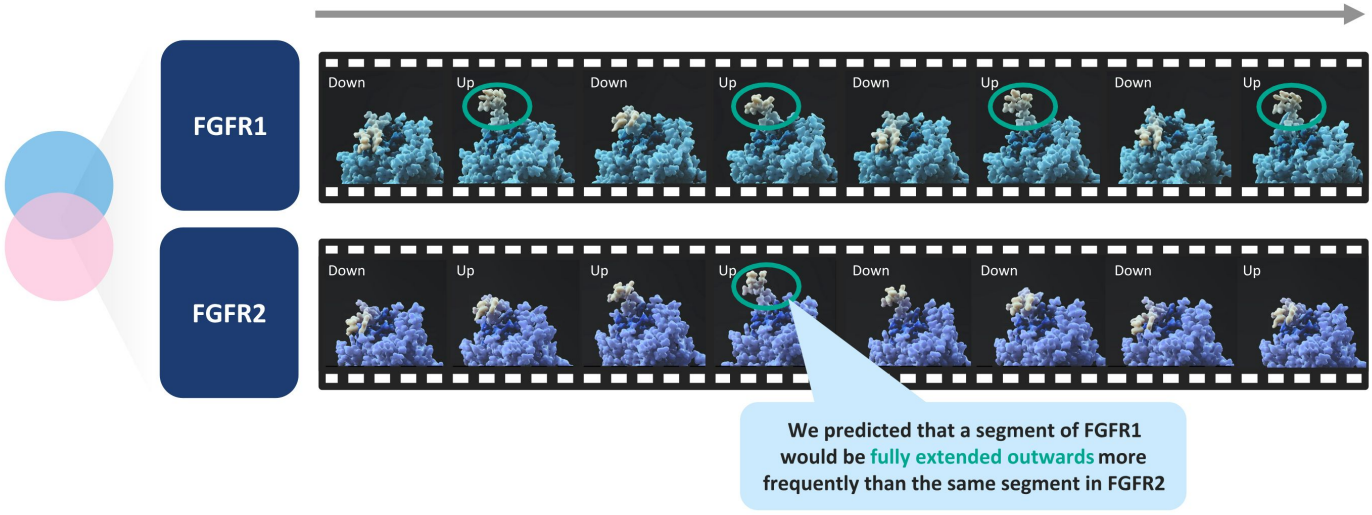
36-42% **Objective Response Rate** in Fusion+ CCA FGFRi-naïve pts

Sources: Pemigatinib – prescribing information; futibatinib – prescribing Information; erdafitinib – prescribing information
1. From pemigatinib NDA review documents: "Pemigatinib 13.5 mg daily provided 76% inhibition of ex vivo phosphorylated FGFR2α at trough"

FGFR2 – Standard Approach to Discovery Has Had Limited Success



FGFR2 – Increasing Resolution Reveals New Opportunities

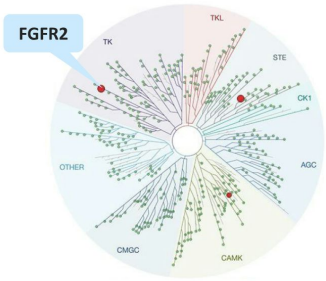


We predicted that a segment of FGFR1 would be fully extended outwards more frequently than the same segment in FGFR2

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

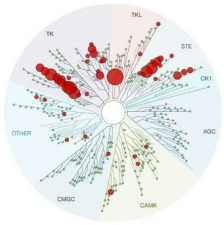
RLY-4008 – Is A Highly Selective and Irreversible Inhibitor

RLY-4008

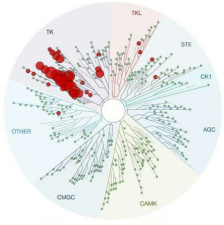


Pan-FGFR Inhibitors

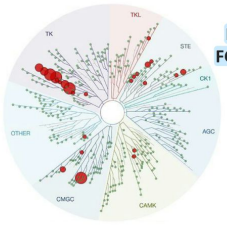
AZD4547



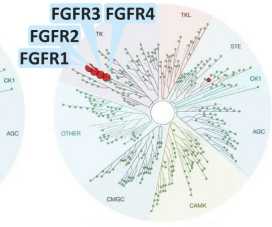
Erdafitinib



Pemigatinib



Futibatinib



Percent Control

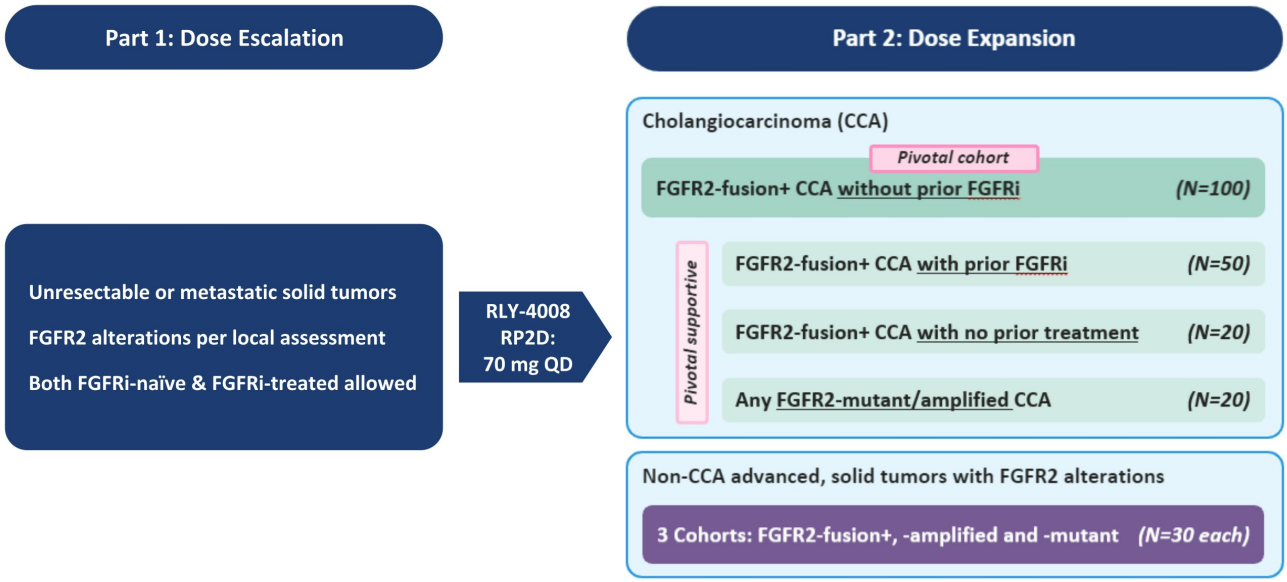
- 0%
- 0.1%
- 0.1-1%
- 1-5%
- 5-10%
- 10-35%
- > 35%

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

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

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)

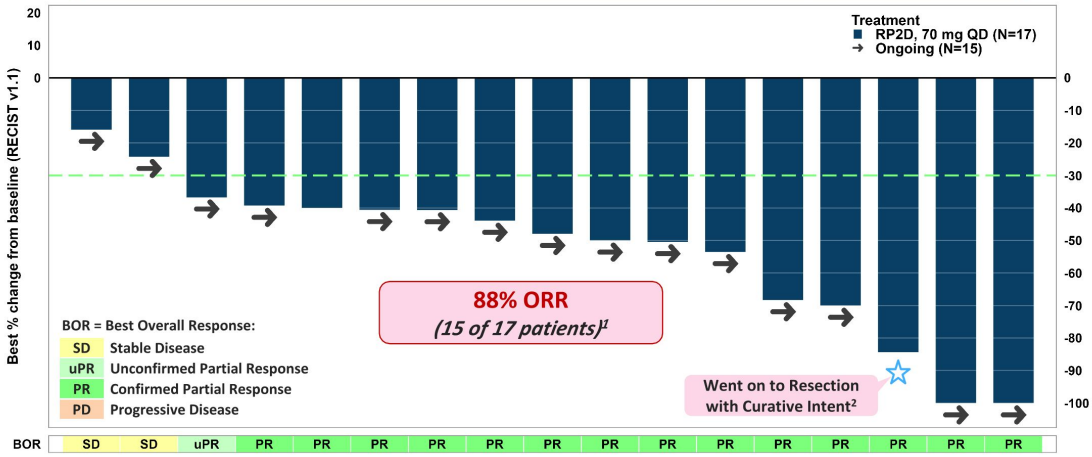
1. Efficacy analysis includes patients with previously treated, FGFR2i-naïve CCA treated at the RP2D. Patients with measurable disease who had opportunity for ≥2 tumor assessments to confirm response or discontinued treatment with <2 tumor assessments
2. Patients in safety population who received ≥1 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

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]

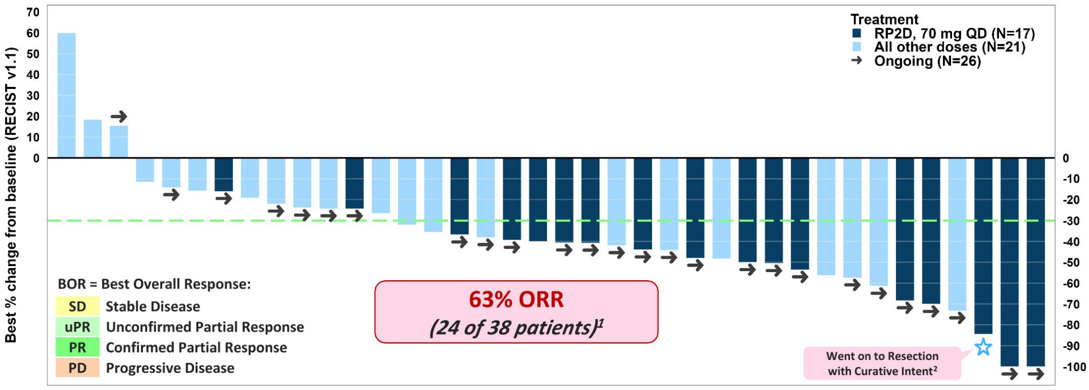
1. Confirmed ORR = 82%: 14 confirmed PRs, 1 unconfirmed PR in an ongoing patient; 2. Complete tumor resection: R0 resection performed in curative intent, patient remains no evidence of disease as of 31 May 2022; 3. Referenced approved pan-FGFRi are Pemigatinib and Infigratinib; ORR based on prescribing 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

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)



Dose (mg)	30 QD	20 QD	100 QDi	50 QD	50 QDi	50 QDi	70 QD	40 QD	50 QDi	70 QDi	100 QDi	70 QD	50 QD	60 QDi	60 QD	70 QD	90 QDi	70 QD	70 QD	70 QD	70 QD	90 QDi	70 QD	100 QDi	70 QD	40 QD	70 QD	70 QD	70 QD	50 QD	60 QD	100 BID	70 QD	70 QD	60 QDi	70 QD	70 QD	70 QD
BOR	PD	PD	SD	SD	SD	SD	SD	SD	SD	SD	SD	SD	SD	PR	SD	uPR	PR	PR	PR	PR	PR	uPR	PR	PR	PR	PR	PR	PR	PR	PR	PR	PR	PR	PR	PR	PR	PR	PR

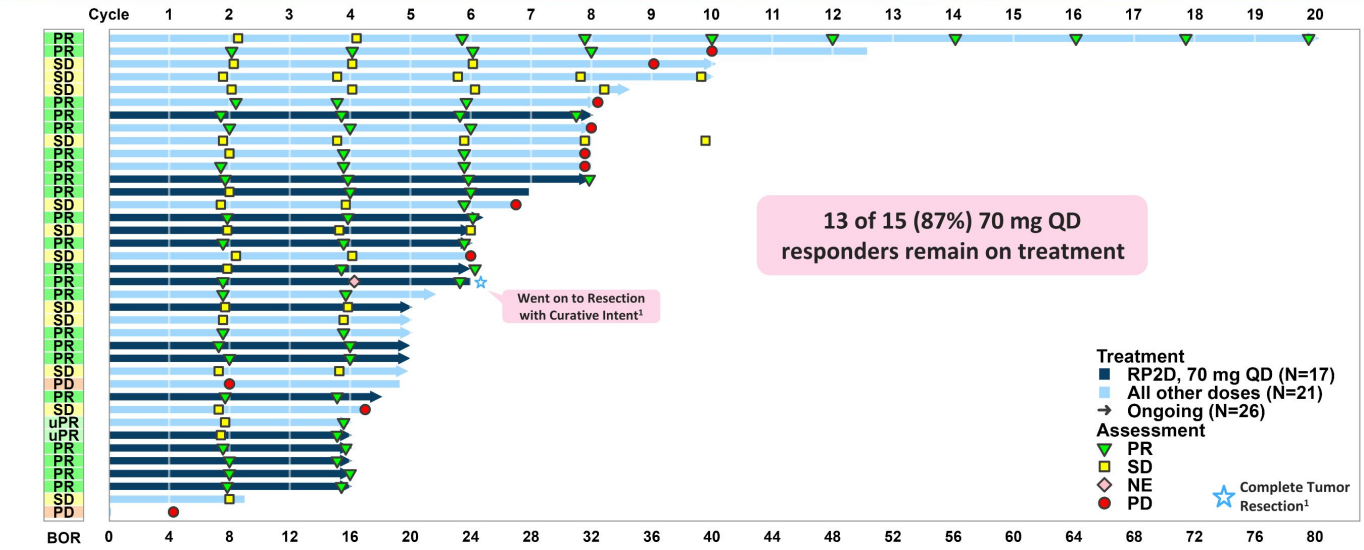
92% of Patients With Tumor Reduction Across All Dose Levels, Majority of Patients With Partial Response per RECIST 1.1

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

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

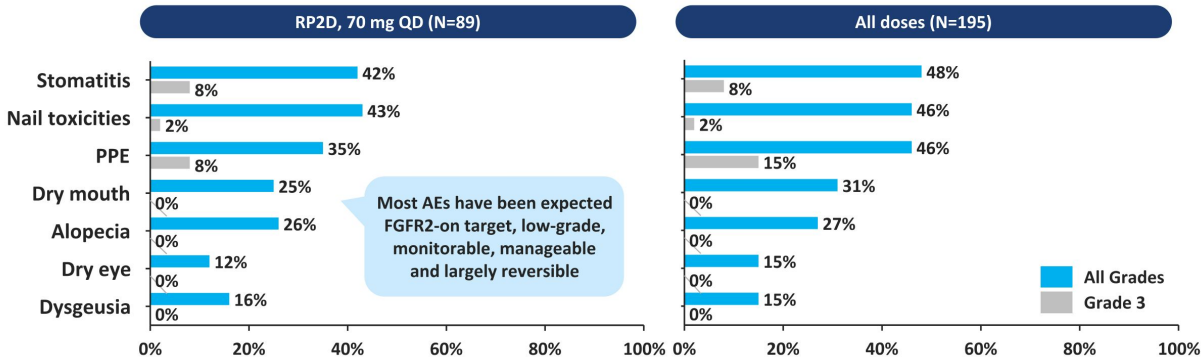
- Median duration of exposure: 5.5 months (range: <0.1 to 18.5 months)
- Median time to response: 1.8 months
- 12/38 (32%) Discontinued - 1 resection with curative intent, 8 PD, 1 AE, 2 withdrawal of consent

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

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

TRAEs ≥ 15%



Most AEs have been expected FGFR2-on target, low-grade, monitorable, manageable and largely reversible

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

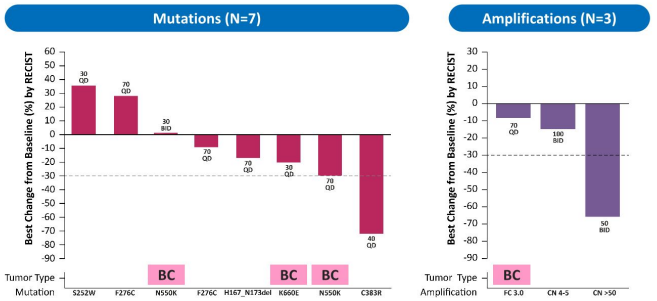
Clinically Insignificant Off-Target Hyperphosphatemia (12%, all Gr 1-2) and Diarrhea (4%, all Gr 1-2) Allow for Optimization of FGFR2 Inhibition

* 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

RLY-4008 Poised for Tumor Agnostic Validation Across FGFR2 Alterations

Tumor regression observed across FGFR2 mutations and amplifications in ReFocus Part 1 Dose Escalation Data



BC Breast Cancer

Continue to actively enroll tumor agnostic cohorts

Non-CCA advanced, solid tumors with FGFR2 alterations

- Non-CCA patients with FGFR2-fusion
- Non-CCA patients with FGFR2-amplification
- Non-CCA patients with FGFR2-mutation

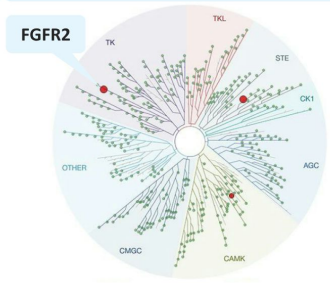
Data Disclosure From Tumor Agnostic Cohorts Anticipated in 2023

Data presented at 2021 ENA Meeting (data as of 09 September 2021)

Relay Tx Solution – Addressing Unmet Need Through Greater Selectivity

Favorable Selectivity[1]

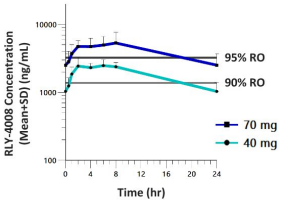
~200x selective for FGFR2 over FGFR1, ~5000x selective over FGFR4[2]



Most AEs have been expected FGFR2-on target, low-grade, monitorable, manageable and largely reversible

Favorable Target Inhibition[1]

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



Favorable Interim Tolerability[1]

Minimized key off-target toxicities[3]

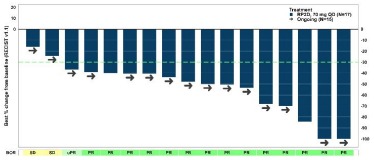
Hyper-phosphatemia[1]	Diarrhea	Discontinuation
12%	4%	1%

All Gr1-2

Favorable Interim Efficacy[1]

FGFR2 driven tumor shrinkage:

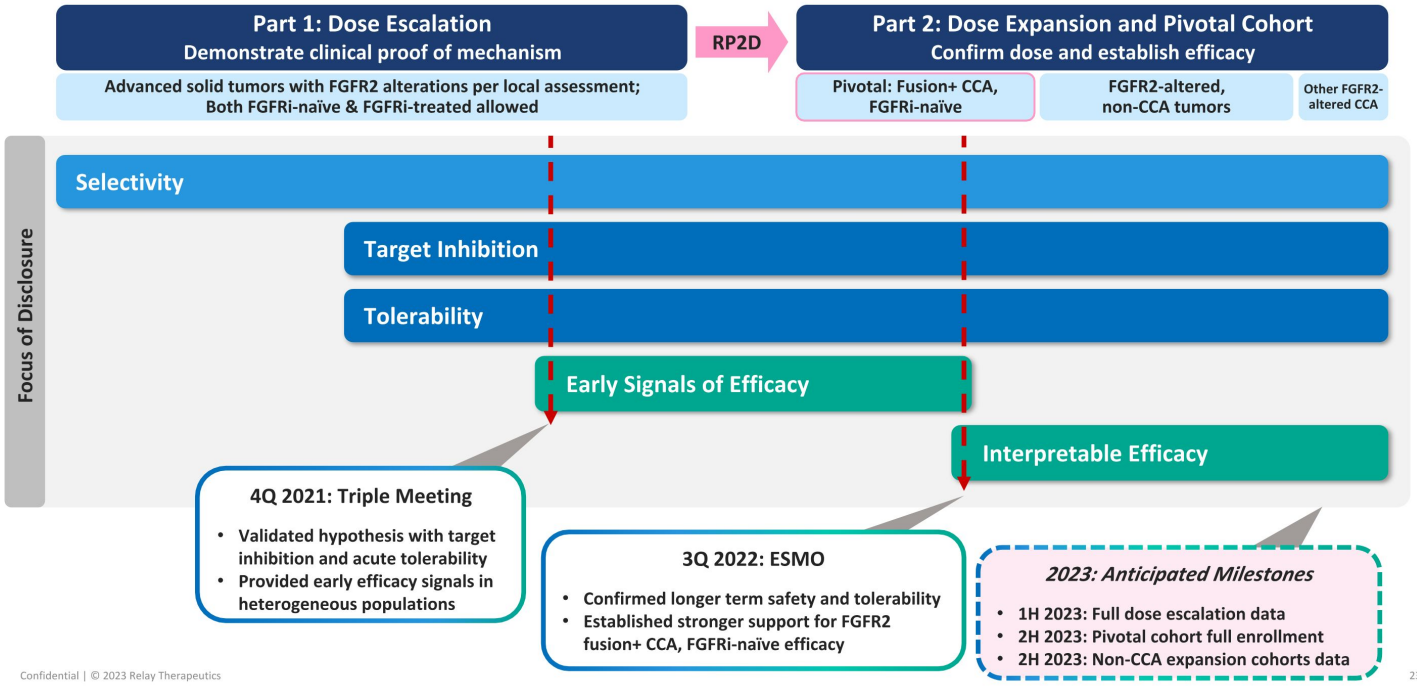
88% ORR in fusion+, FGFRi-naïve CCA
15 of 17 pts at 70mg QD pivotal dose
(based on interim data)



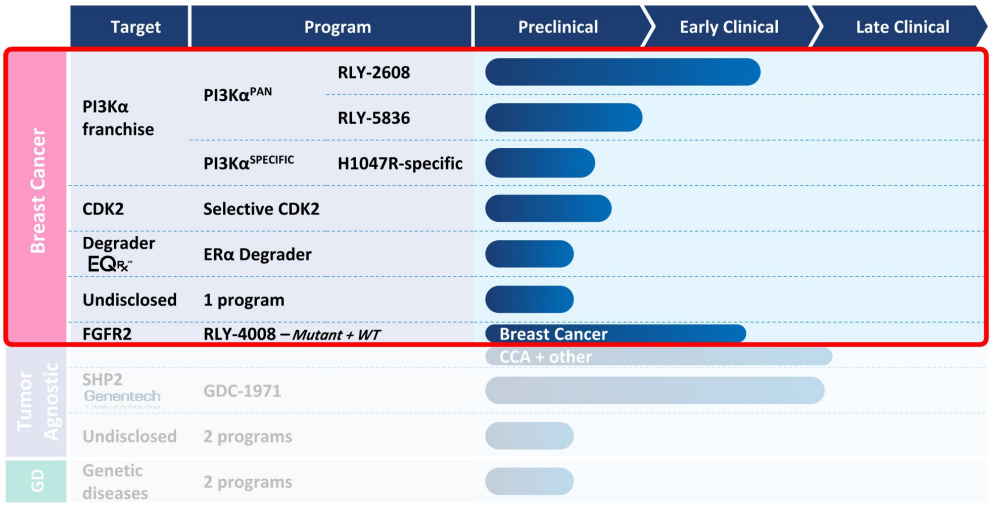
63% interim ORR for fusion+, FGFRi-naïve CCA across all doses

Sources: KINOMEscan™ by Eurofins DiscoverX; RLY-4008 data as presented at ESMO Congress 2022
1. Interim data as of 01 August 2022; 2. Single experiment that tested each compound run at 500nM against 468 targets in the absence of ATP and without preincubation; 3. Toxicity rates across all doses, n=195 patients

RLY-4008 – ReFocus Trial



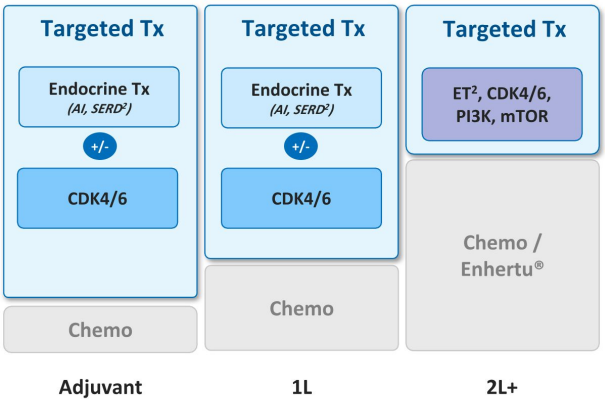
Relay Tx – Emerging Breast Cancer Franchise



Breast Cancer – Limitations of Current Standard of Care

~200k annual HR+/HER2- breast cancer patients in US, of whom ~60k advance to later lines of treatment

HR+/HER2- breast cancer standard of care[1]…



…is limited by efficacy of available treatments

Source: Internal analysis based on third party industry data
1. Standard of care for HR+/HER2- breast cancer is illustrative; 2. AI = Aromatase Inhibitor; SERD: Selective Estrogen Receptor Degrader; ET = Endocrine Therapy

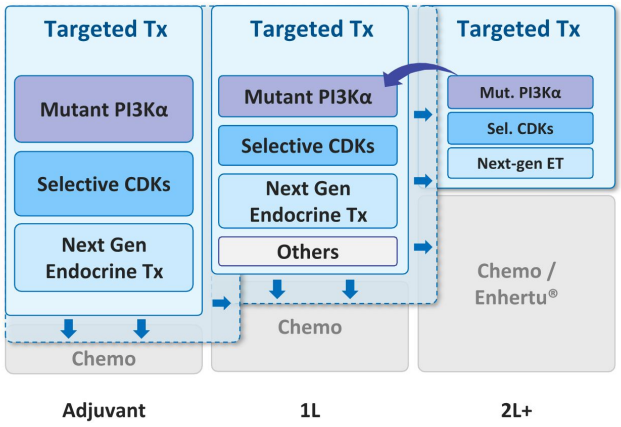
Relay Tx Solution – Highly Selective Breast Cancer Franchise

Relay Tx Solution

Relay Tx Breast Cancer Portfolio

- PI3Kα Franchise
  - RLY-2608 *(pan-mutant)*
  - RLY-5836 *(pan-mutant)*
  - H1047R *(mutant-specific)*
- Selective CDK2 Inhibitor
- ERα Degrader
- *Other Undisclosed Programs*

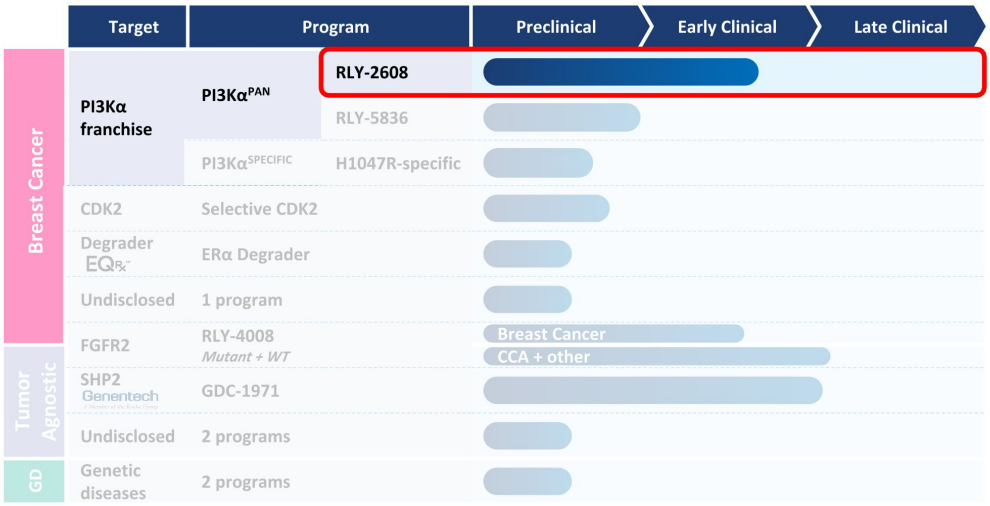
Aspirational future state standard of care (HR+/HER2- BC)[1]



Relay Tx aims to transform the standard of care for HR+/HER2- breast cancer

1. Aspirational future state standard of care for HR+/HER2- breast cancer is illustrative

Relay Tx – Extensive Precision Medicine Pipeline

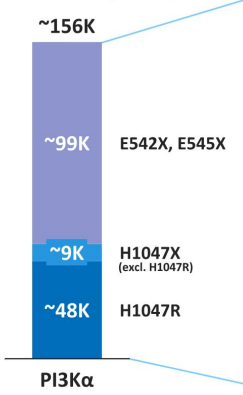


PI3Kα – Large Precision Oncology Opportunity

Pan-mutant selective drug is a significant clinical opportunity for solid tumors…

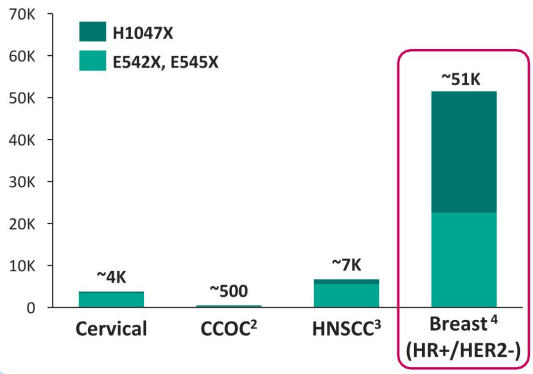
…with HR+/HER2- breast cancer as the single largest indication with PI3Kα mutations

US Patients – PI3Kα Solid Tumors Incidence (Annual)[1]



PI3Kα alterations observed across multiple tumor types – select indications

US Patients - Comprehensive Incidence (Annual)



HR+/HER2- breast cancer is the largest single indication with PI3Kα mutated patients

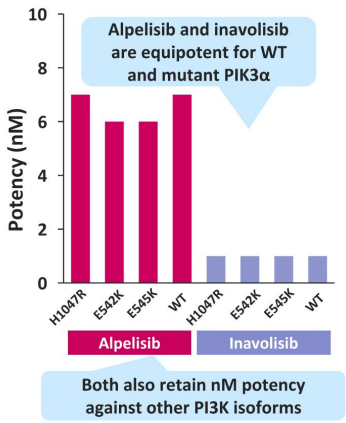
~30% Of HR+/HER2- breast cancer patients harbor a hotspot PI3Kα mutation[4]

Sources: Internal analysis based on third party industry data

1. Annual incidence of solid tumors with PI3Kα H1047R, PI3Kα H1047X, PI3Kα E542X + E545X alterations; 2. Clear Cell Ovarian Cancer; 3. Head & Neck Squamous Cell Carcinoma;
4. HR+/HER2- breast cancer patient population with a PI3Kα hotspot alteration; alterations include: H1047X, E542X, E545X

PI3Kα – Existing Inhibitors Have Limited Therapeutic Window

Limited Selectivity



Alpelisib and inavolisib are equipotent for WT and mutant PIK3α

Both also retain nM potency against other PI3K isoforms

Limited Target Inhibition

Regimen	Interruption	Reduction	Discont.
Alpelisib[6,7]	58%	38%	15%
Alpelisib + fulv[1]	74%	64%	25%
Inavolisib + fulv[8]	41%	18%	2%

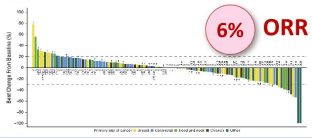
Alpelisib: Observed coverage (based on IC_{80}) at average clinical dose 9-13hr[7]

Limited Tolerability

Compound	All Gr3+ Tox	Hyperglycemia		GI Tox (all Gr)	Rash (all Gr)
		All Gr	Gr3+		
Alpelisib[1-7]	44-78%	33-65%	13-37%	33-60%	20-36%
Inavolisib[8-12]	33-54%	55-70%	5-22%	27-50%	7-27%

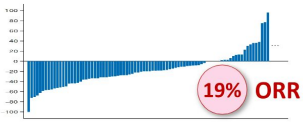
Limited Efficacy

Alpelisib Monotherapy Ph 1a[7]



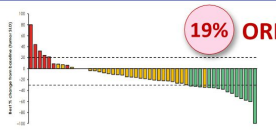
6% ORR

Alpelisib + fulvestrant Ph 2[4]



19% ORR

Inavolisib + fulvestrant Ph 1b[13]



19% ORR

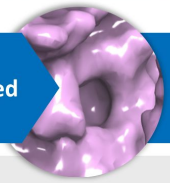
Note: fulv = fulvestrant; BC= breast cancer; all referenced studies are for their patient populations which are analogous to ongoing patient populations within RLY-2608 clinical trials; Alpelisib and fulvestrant are FDA approved, Inavolisib is in Phase 3 clinical trials

Sources: Alpelisib – 1. SOLAR-1: Andre 2019 N Engl J Med 380:1929, 2. Ph 1b: SABCS 2013 P2-16-14, 3. Ph 1b: SABCS 2014 PD5-5, 4. Ph 2 ByLIEVE: Rugo 2021 Lancet Oncol 22:489, SABCS 2021 #P1-18-03, 5. Ph 1b mono: Annals of Oncol 25 2014 (suppl 4), 6. Ph 2 mono: Savas Cancer Discov 2022 Sep 12:2058, 7. Ph 1a mono: Juric 2018 J Clin Oncol 36:1291; Inavolisib – 8. ASCO 2022 #1052, 9. SABCS 2020 #PS11-11, 10. AACR 2020 CT109, 11. SABCS 2019 OT1-08-04; 12. SABCS 2019 P1-19-46, 13. SABCS 2021 #P5-17-05;

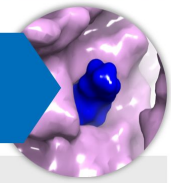
PI3Kα – Proprietary Insights Unlock Novel Approaches

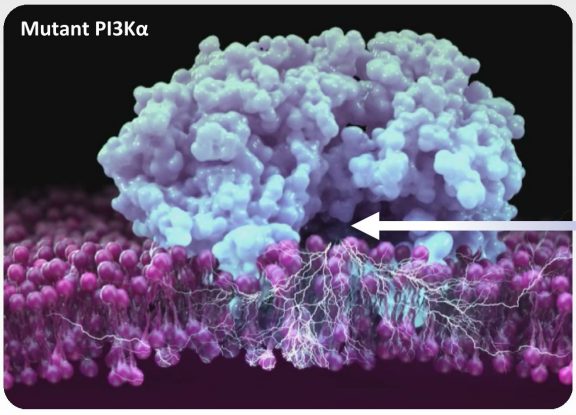
Solved first full-length structures of PI3Kα (mutant and wild-type)

Discovered novel allosteric pocket favored in mutant protein



Designed pan-mutant selective PI3Kα inhibitor ($PI3K\alpha^{PAN}$)

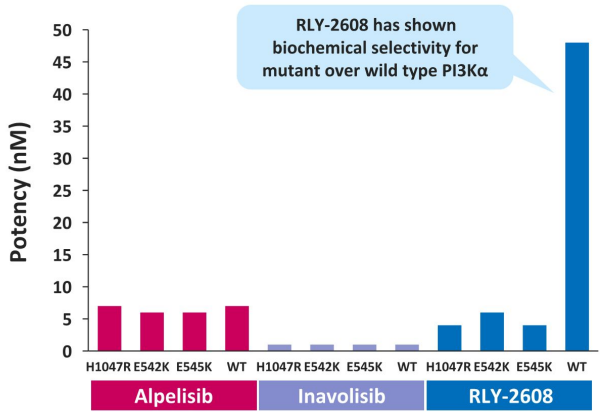




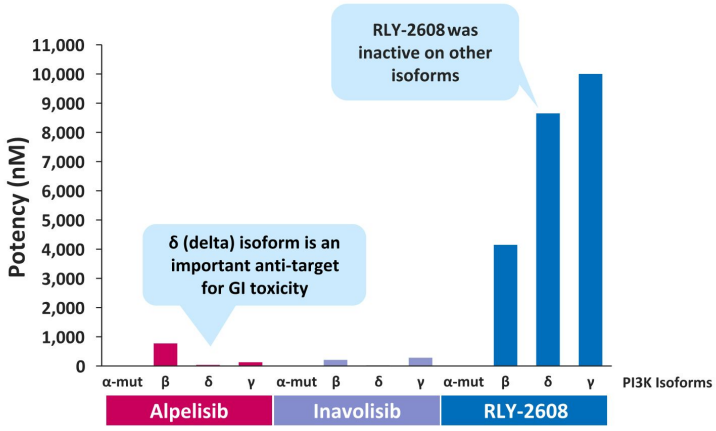
A differentiated understanding of the structure of PI3Kα and its relationship to function equips Relay Tx to design optimal mutant-selective inhibitors of PI3Kα

RLY-2608 – Mutant and Isoform Selectivity

Mutant vs. WT PI3Kα potency

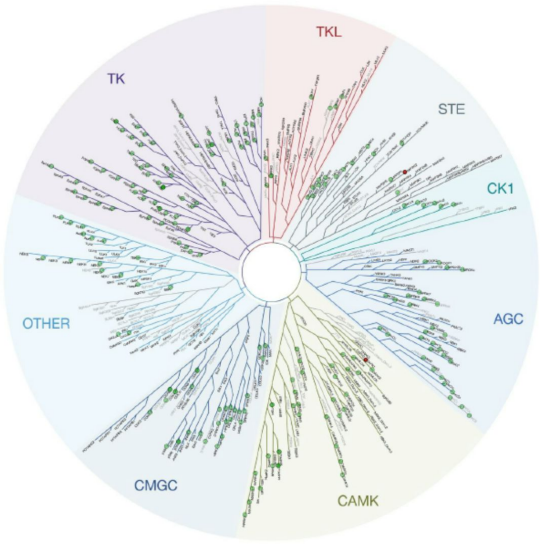


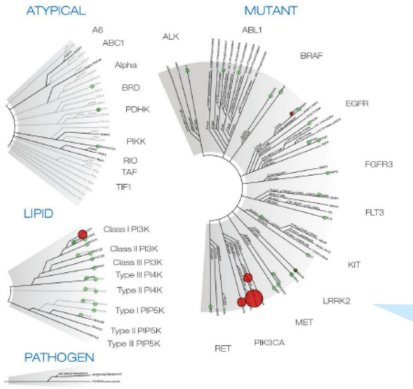
Mutant PI3Kα vs. other isoform potency



Source: RLY-2608 data as presented in 2021 AACR-NCI-EORTC Molecular Targets Conference poster presentation

RLY-2608 – Selective Across the Kinome





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

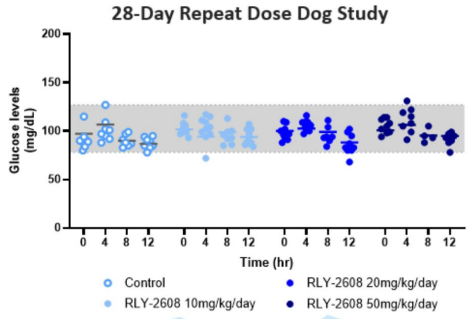
Kinase Inhibition @ 10 µM

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

Source: RLY-2608 data as presented in 2021 AACR-NCI-EORTC Molecular Targets Conference poster presentation

RLY-2608 – Reduced Impact on Glucose Homeostasis

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

Hyperglycemia Definitions (CTCAE v5.0)

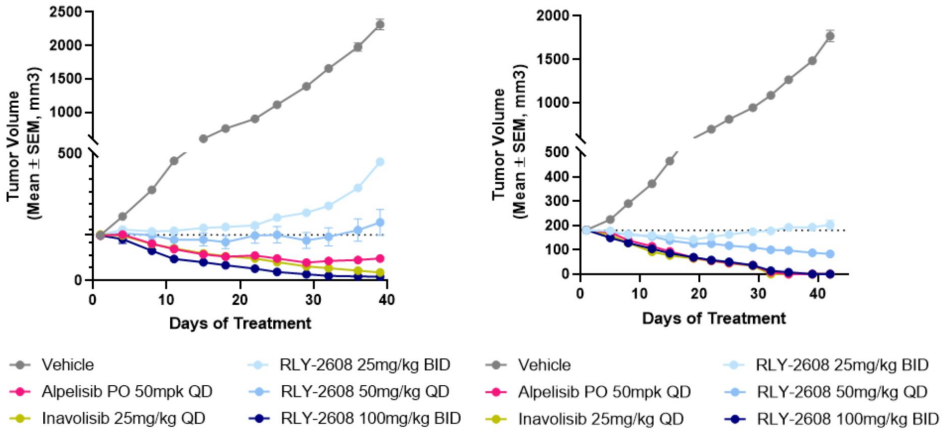
Grade	CTCAE Definition (v5.0)
Gr 1	Abnormal glucose above baseline, no medical intervention
Gr 2	Change in daily management from baseline for diabetic; oral antiglycemic agent initiated; workup for diabetes
Gr 3	Hospitilization indicated; insulin therapy initiated
Gr 4	Life-threatening consequences; urgent intervention indicated
Gr 5	Death

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

Source: NIH, Common Terminology Criteria for Adverse Events (CTCAE) version 5.0

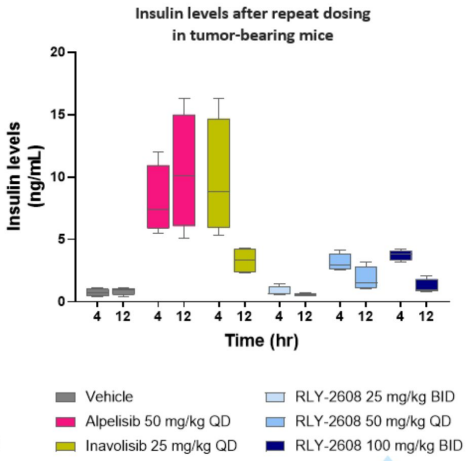
RLY-2608 – In Vivo Tumor Regressions

H1047R mutant (HCC1954) (mouse)



E545K mutant (MDAMB361) (mouse)[1]

RLY-2608 achieved active doses with less insulin than orthosteric inhibitors[2]



Consistent results for 1-hour time point[3]

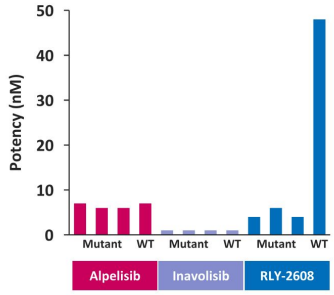
Source: RLY-2608 data as presented in 2021 AACR-NCI-EORTC Molecular Targets Conference poster presentation
1. This model also carries a second mutation at K567R; 2. HSC2 model; 3. Similar results observed in the same background strain at 1hr timepoint in the MCF7 (E545K) model

RLY-2608 – First Mutant Selective Inhibitor to Enter the Clinic

All Data Shown is Preclinical

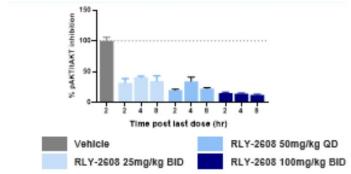
Favorable Selectivity

Limited potency against WT PI3Kα and other PI3K isoforms



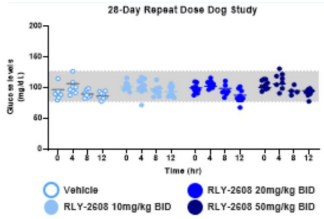
Favorable Target Inhibition

Maintains approx. 80% mutant PI3Kα inhibition in mouse model



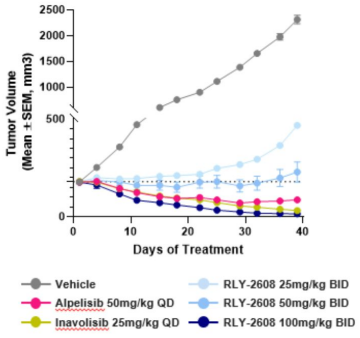
Favorable Tolerability

Manageable key toxicities, especially hyperglycemia shown in dog study

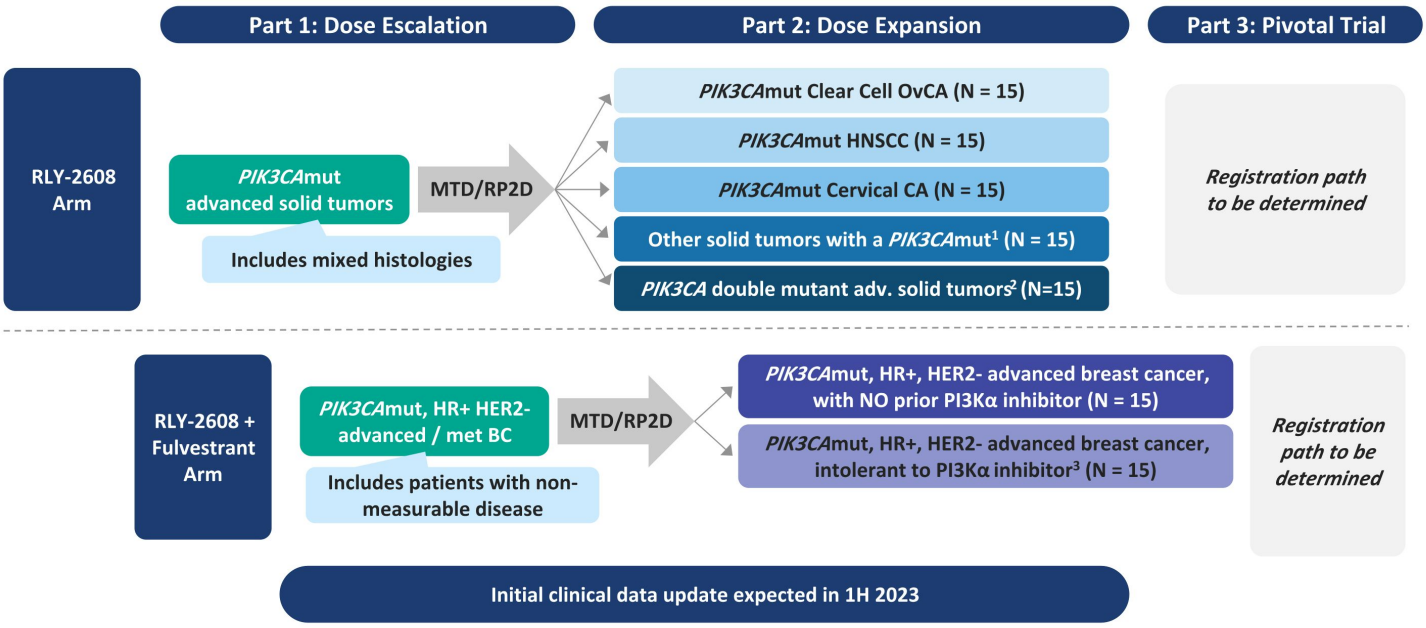


Favorable Efficacy

Robust tumor regression at tolerable doses in mouse model

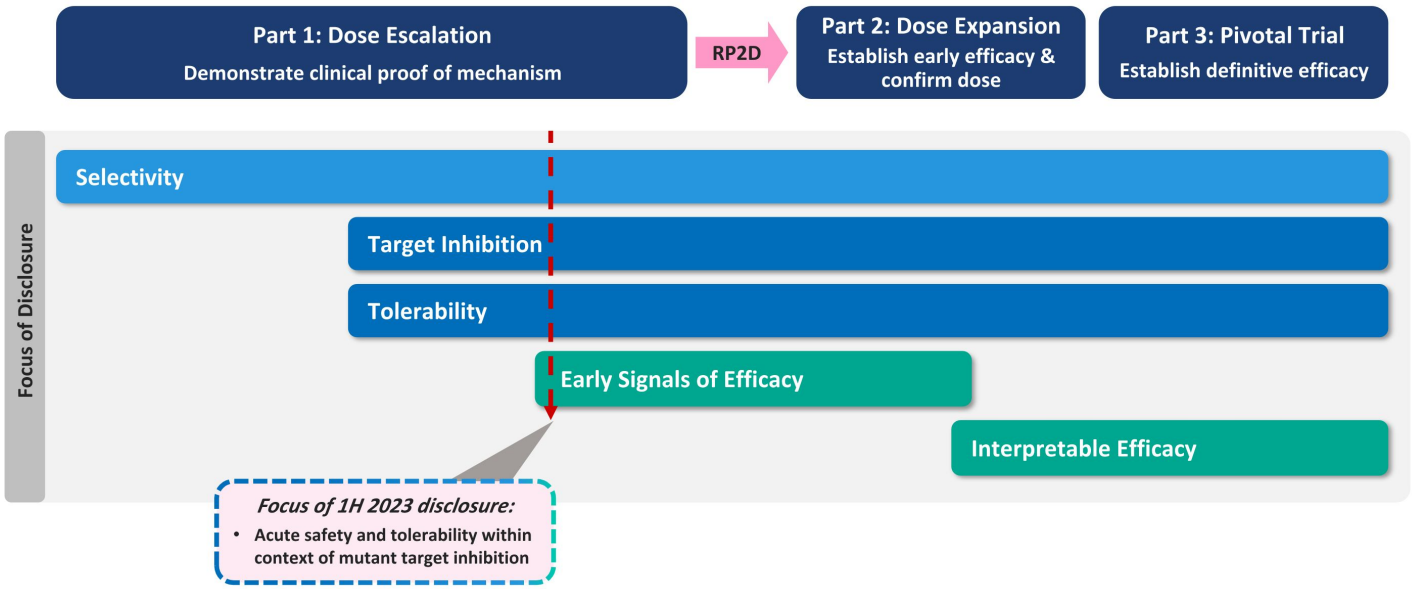


RLY-2608 –Trial Design

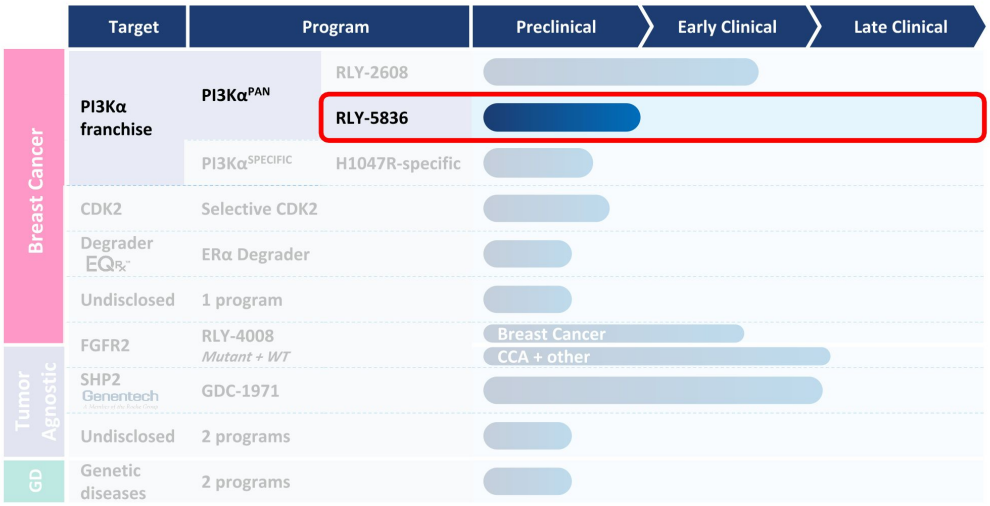


1. Excludes PIK3CAmut clear cell OvCA, HNSCC, and Cervical cancer patients; 2. Double mutation defined as one major PIK3CA mutation (E542X, E545X, H1047X) + ≥1 additional PI3KCA mutation per local assessment; 3. Intolerance to PI3Kα inhibitors is defined as treatment discontinuation due to treatment-related AE (e.g., hyperglycemia, rash, diarrhea, stomatitis) other than severe hypersensitivity reaction and/or life-threatening reactions, such as anaphylaxis and Stevens-Johnson syndrome.

RLY-2608 – Data Disclosure

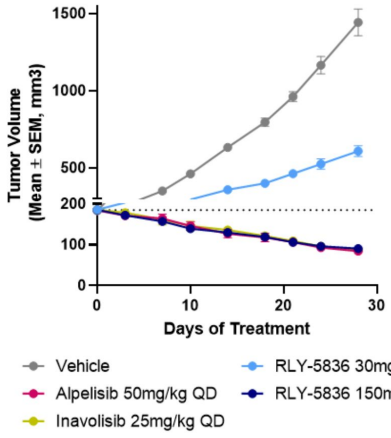


Relay Tx – Extensive Precision Medicine Pipeline

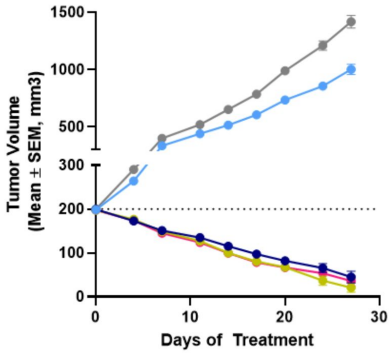


RLY-5836 – Similar Pre-clinical Profile, Different Chemical Properties from RLY-2608

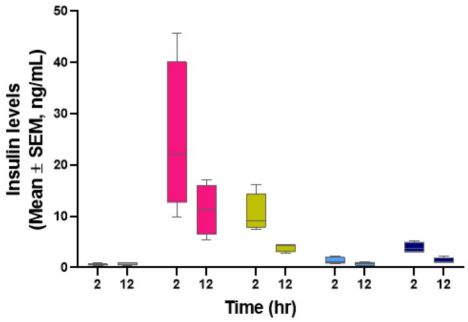
H1047R mutant (HCC1954) (mouse)



E545K mutant (MDAMB361) (mouse)[1]



RLY-5836 achieved active doses with less insulin than orthosteric inhibitors

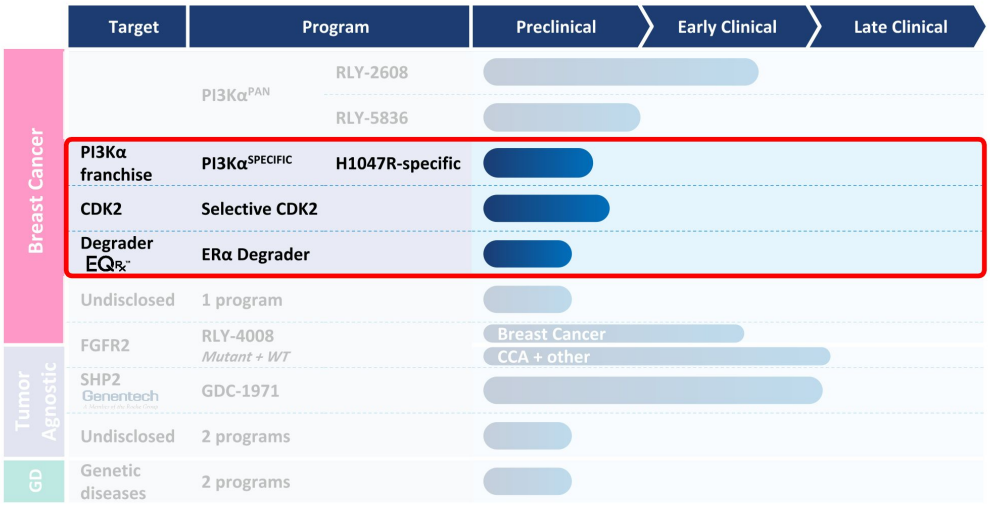


Clinical start anticipated in 2Q 2023

Source: Internal RLY-5836 data

1. This model also carries a second mutation at K567R

Relay Tx – Extensive Precision Medicine Pipeline



CDK2 – Highly Selective Inhibitors Identified

CDK2 is important in ER+ breast cancer

Patients receiving adjuvant CDK 4/6i ~23K

Patients receiving 1L CDK 4/6i ~18K

Patients receiving 2L CDK 4/6i ~5K

Higher CDK2 activity associated with worse response to CDK4/6 inhibition in ER+ breast cancer

Computational modeling enabled breakthrough speed

Collect MD frames

Extract features

Cluster frames & assign cluster populations

Novel workflow leverages MD and ML to predict selectivity without bias or intervention

Predict selectivity

First compound synthesized to identification of lead compounds in <1 year

Relay Tx's CDK2 inhibitors observed to be highly selective

		RTX-1	RTX-2
Biochemical Potency	CDK2/CycE IC_{50} (mM)	0.002	0.004
Biochemical Selectivity (fold over)	CDK1/CycB	260x	100x
	CDK4/CycD1	685x	273x
	CDK6/CycD3	630x	322x
	CDK9/CycT1	3990x	2380x
	GSK3b	70250x	68050x

Clinical start expected in early 2024

Source: Internal analysis based on third party industry data

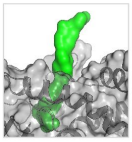
ERα Degrader – Rapidly Obtained Potent Compounds

Endocrine therapies are used in every line of therapy in HR+/HER2- Breast Cancer

Line of Therapy	Endocrine Tx
Adjuvant	Use of Endocrine Therapies
First Line	
Second Line +	

195k annual US patients with HR+/HER2- breast cancer

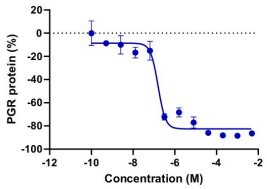
Relay Tx is leveraging rational design…

Traditional Approach	Relay Tx Approach
	

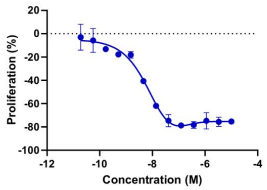
Multiple experimental tools deployed to develop conformational models that enable effective triage of degrader design ideas

…to obtain potent ERα degraders

Pathway suppression



Cellular proliferation

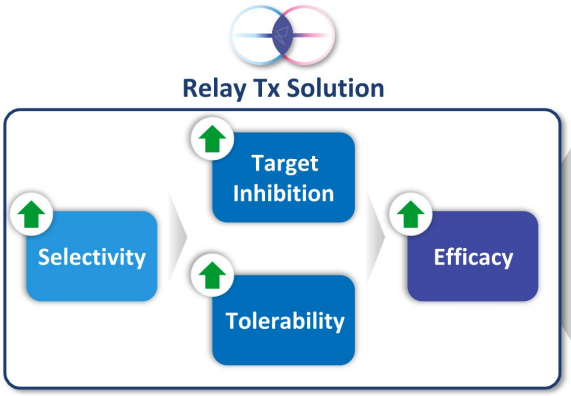


Development Candidate nomination expected in 2023

Source: Internal analysis based on third party industry data

Relay Tx Solution – Highly Selective Breast Cancer Franchise

The Relay Tx Solution…

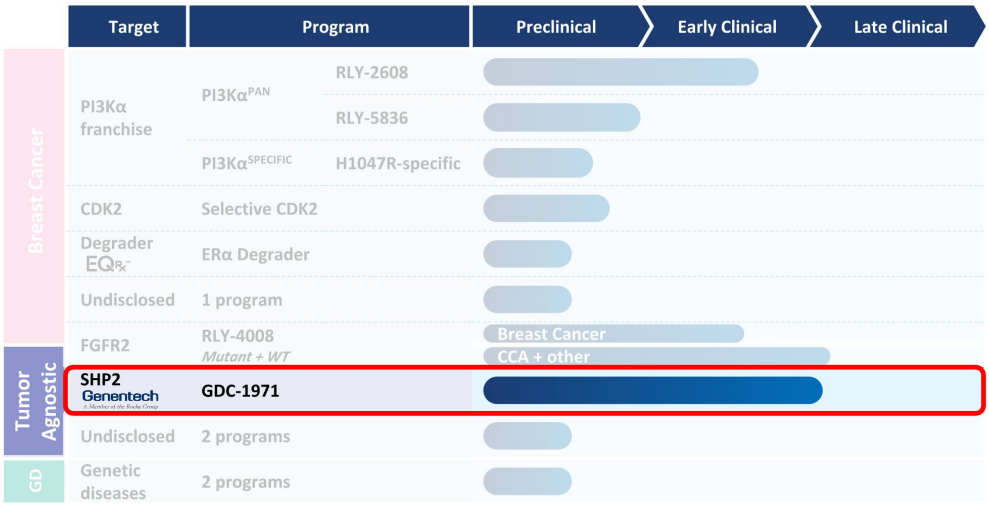


…aims to address selectivity on validated targets for breast cancer

Breast Cancer

Target	Program		Preclinical	Early Clin.	Late Clin.
PI3Kα franchise	PI3Kα^{PAN}	RLY-2608			
		RLY-5836			
	PI3Kα^{SPECIFIC}	H1047R-specific			
CDK2	Selective CDK2				
Degrader EQR$_x$™	ERα Degrader				
Undisclosed	1 program				
FGFR2	RLY-4008 *Mutant + WT*				

Relay Tx – Extensive Precision Medicine Pipeline



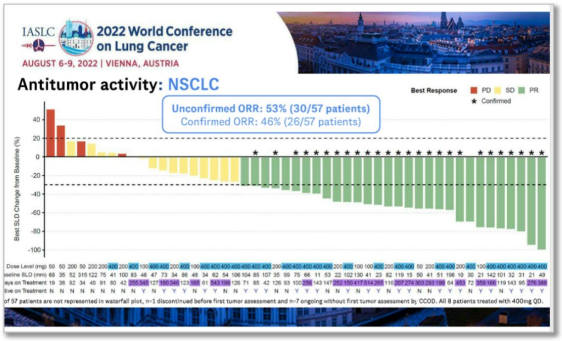
SHP2 – Genentech Global Collaboration for GDC-1971 (Formerly RLY-1971)

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



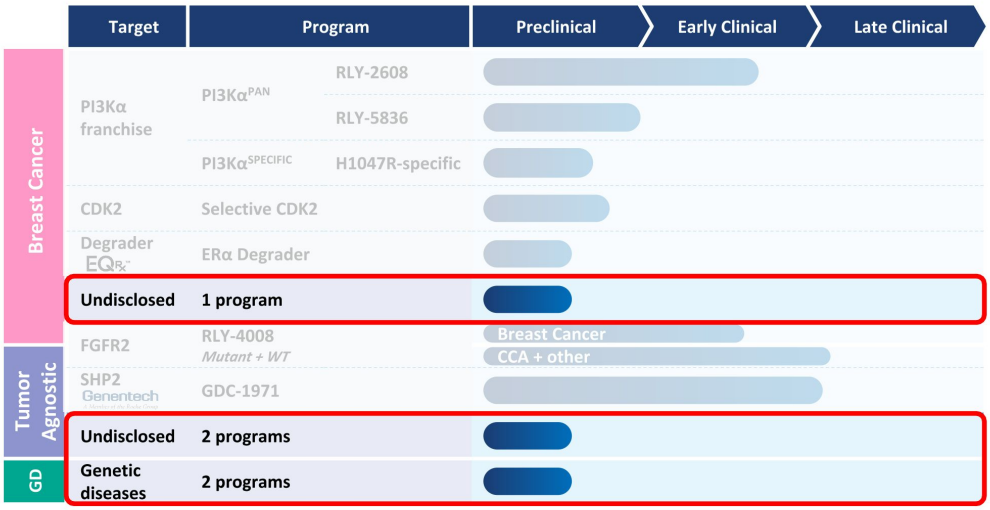
Unconfirmed ORR: 53% (30/57 patients)
Confirmed ORR: 46% (26/57 patients)

Collaboration provides meaningful economics to Relay Tx[1]

Source: World Lung 2022 #OA03.04

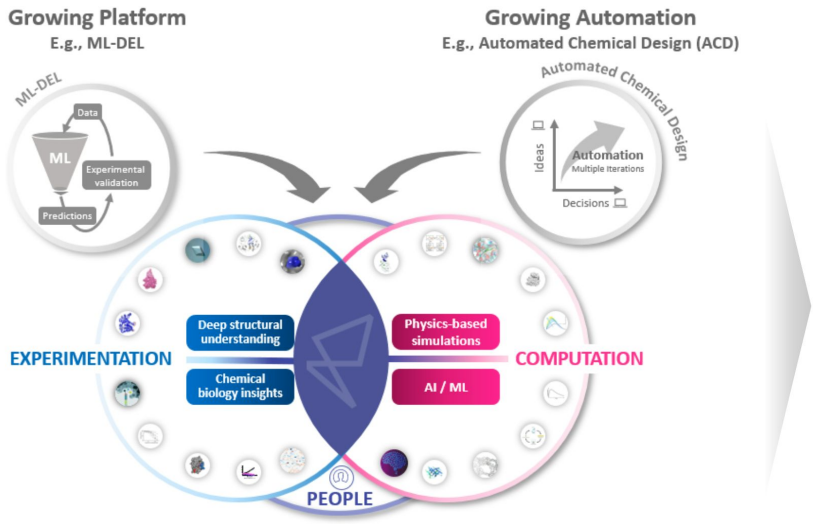
1. As of December 31, 2022: $105 million in upfront & milestone payments received, plus an opt-in option for 50/50 profit share and up to $690M in potential additional total milestones, low-to-mid teen royalties on global net sales plus eligible to receive additional royalties upon approval of GDC-1971 and GDC-6036 in combination

Relay Tx – Extensive Precision Medicine Pipeline



Relay Tx – The Dynamo™ Platform

Platform capabilities and expertise continue to expand

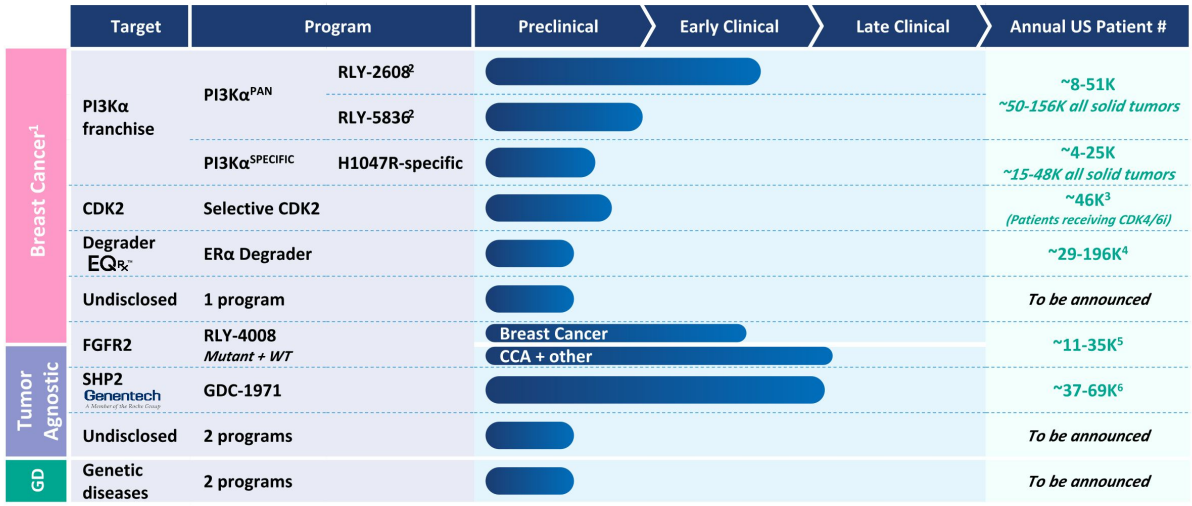


Enabling deep and diversified early pipeline

5+ Undisclosed Programs

- Inhibitors
- Degraders
- Chaperones
- New Modalities

Relay Tx – Extensive Precision Medicine 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, and breast cancer patient range assumes HR+/HER2- population 3. ~46k 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 June 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 including additional FGFR gene fusions and rearrangements resulting from truncation of the protein at exon 18 6. SHP2 combo only includes KRAS G12C in lung and CRC, EGFR mutations in lung, and ALK fusions in lung

Relay Tx – Capital, Team & Execution Focus to Deliver

Breast Cancer Franchise			Tumor Agnostic		Undisclosed
 PI3Kα^{PAN}	 Selective CDK2	 ERα Degrader	 RLY-4008 (Selective FGFR2)	 GDC-1971 (SHP2)	 *To be announced*
RLY-2608 Initial data in 1H 2023 **RLY-5836** Clinical start in 2Q 2023	Clinical start in early 2024	Development candidate nomination in 2023	Full dose escalation data in 1H 2023 Non-CCA expansion cohorts data in 2H 2023 Pivotal cohort full enrollment in 2H 2023	Ongoing combo trials; Genentech controls data disclosures	*5+ undisclosed programs in preclinical development and additional early-stage efforts across platform*

$1.1B

Cash, cash equivalents and investments as of the end of 3Q 2022

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

Relay Tx 2021 ESG Report – Continuing Our ESG Journey

Relay Tx's First Full ESG Annual Report

VALUE REPORTING FOUNDATION
SASB STANDARDS

SUSTAINABLE DEVELOPMENT GOALS

Patients

- 3 active clinical trials
- Committed to clinical trial patient safety
- Committed to product safety and quality

Note: Relay Tx is a development stage company

Community

- Our patients / future patients
- Our community in Cambridge and the broader Boston area
- The next generation of scientists

People

- 98% employee respondents agreed they "made the right decision to join Relay Tx"
- Turnover below industry average rates
- Diversity & inclusion advisory group
- Training and development opportunities
- Equitable compensation

Environment

- Responsible energy consumption
- Reducing water consumption
- Hazardous and lab waste management
- Non-hazardous waste management

Governance

- 7 Directors Total*
- The Nom/Gov and Audit Committees oversee ESG efforts, with the full BOD getting ~quarterly updates

29% Racial/Ethnic Diversity	43% Women
5yrs Average Tenure	71% Independence (Separate CEO and Chair Role)

*As of December 2021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THERAPEUTICS