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 10, 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

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 40th Annual J.P. Morgan Healthcare Conference (the "Conference") during the week of January 10, 2022. 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	40th Annual J.P. Morgan Healthcare Conference Company Presentation, dated January 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: January 10, 2022

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

Exhibit 99.1

RELAY®
THERAPEUTICS

40th Annual J.P. Morgan Healthcare Conference Company Presentation

January 2022

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; 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, Growth-Oriented

New Breed of Biotech

Validated Approach

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

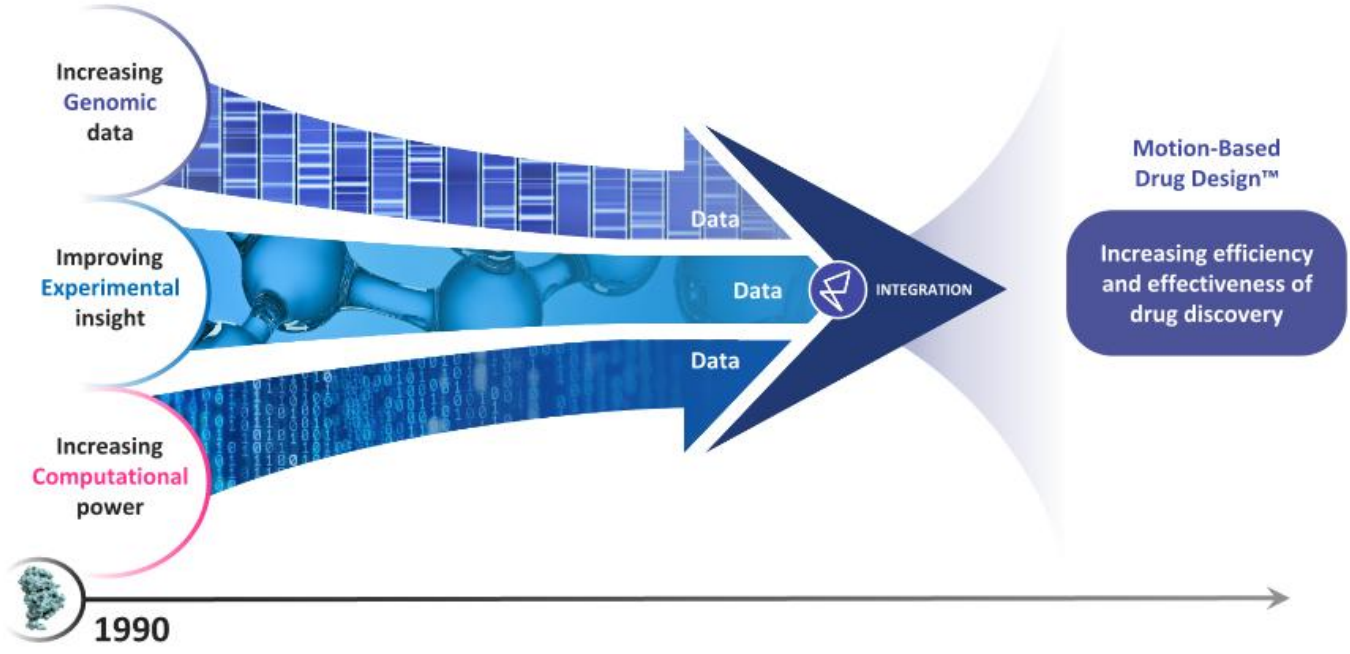
Clear Focus

Validated Targets	Therapeutic Areas	Modalities
Innovators	Oncology	Small molecules
Challengers	Genetic diseases	

Execution-Focused

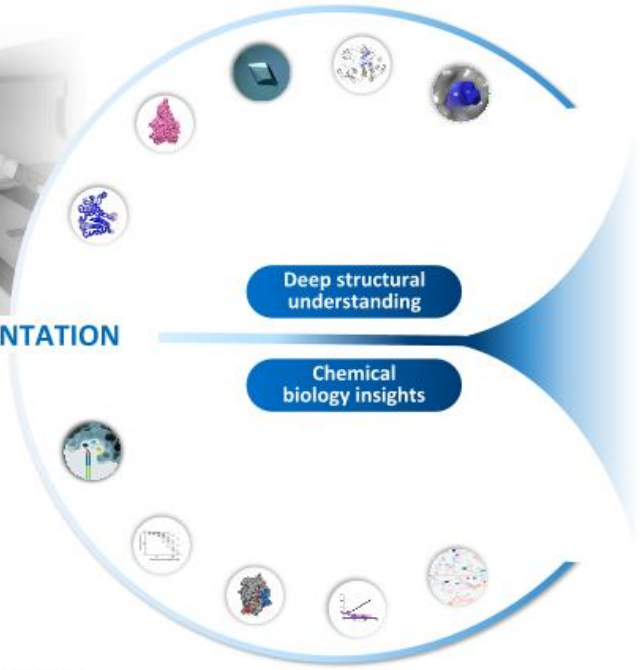
The more we do, the better we get

Relay Tx – Created by the Nexus of 3 Unstoppable Forces and Data



The Dynamo™ Platform – Integrating Experimentation with Computation

The Dynamo™ Platform – Experimentation



EXPERIMENTATION

Deep structural understanding

Chemical biology insights

Tools

Cryo-EM

Ambient Temp X-Ray Crystallo-graphy

People and Functions

- Target Mechanistics
- Time-resolved Biophysics
- Nanoscale Chemistry
- Protein Engineering
- Etc.

Experience

2016 → 3 clinical assets in 5 years → Today

The Dynamo™ Platform – Computation

Tools

Swimming Simulations

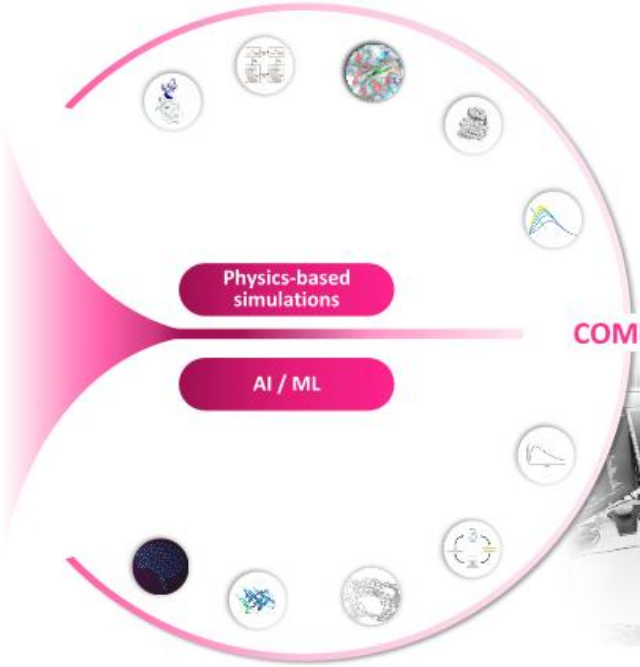
Virtual Screens

People and Functions

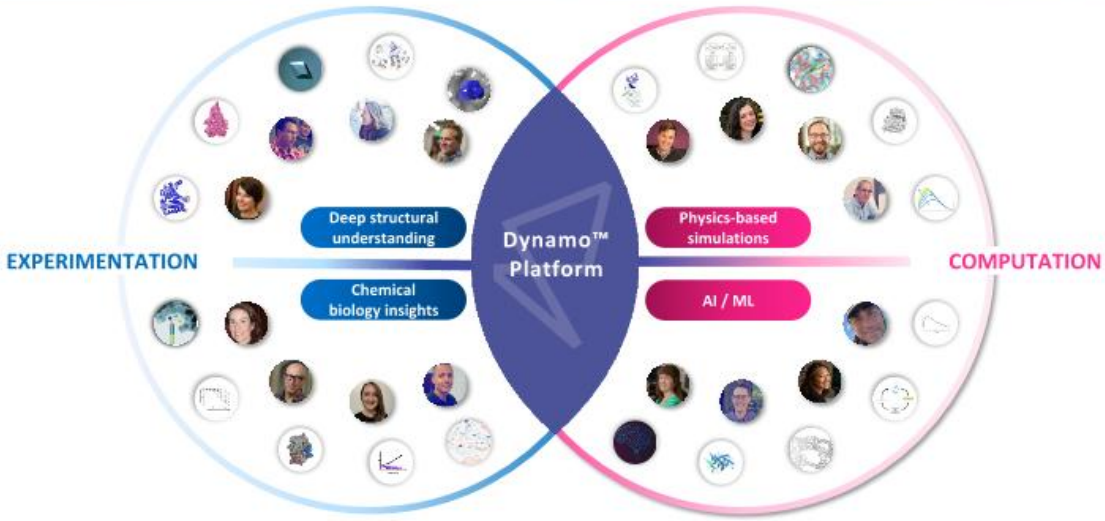
- Automated Chemical Design
- Force Field Development
- Quantum Mechanics
- Free Energy Methods
- Etc.

Experience

2016 → 3 clinical assets in 5 years → Today



The Dynamo™ Platform – The Power of Experimentation + Computation



2 therapeutic areas

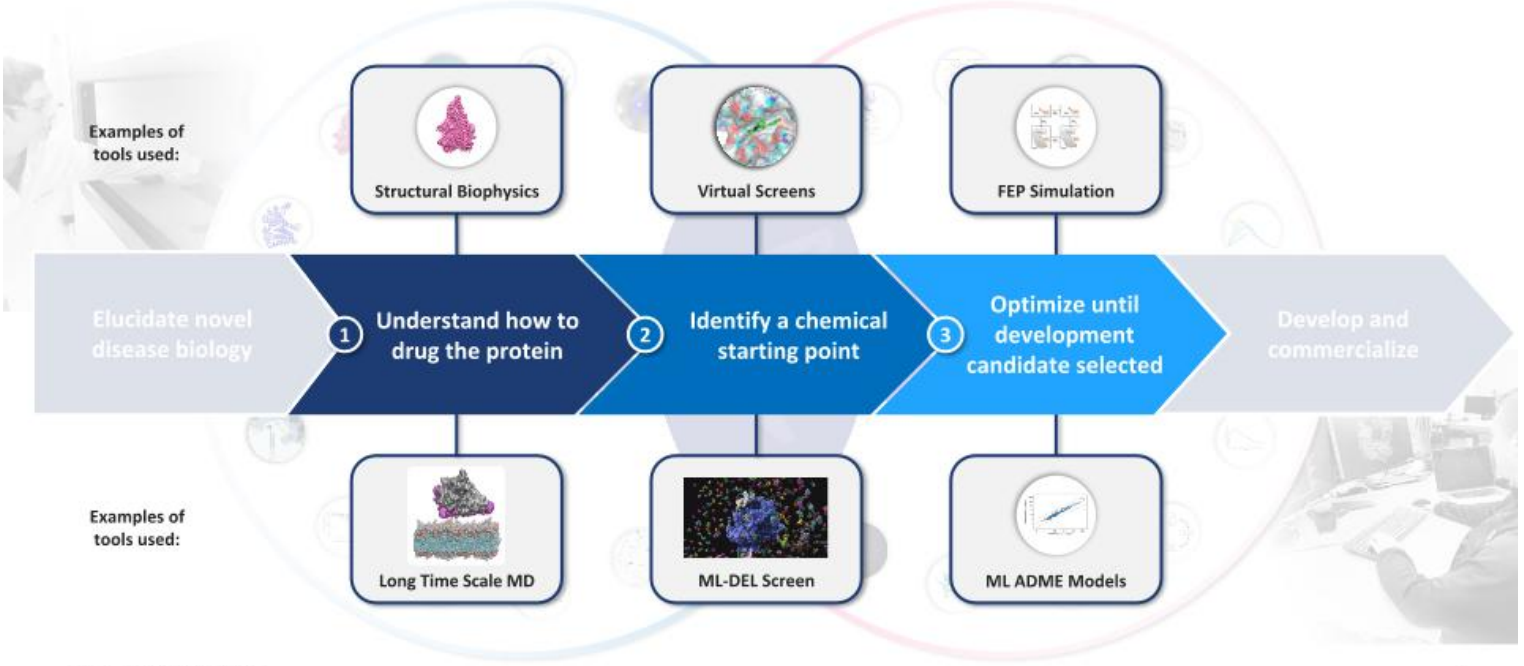
5+ earlier stage programs in pipeline

3 clinical assets

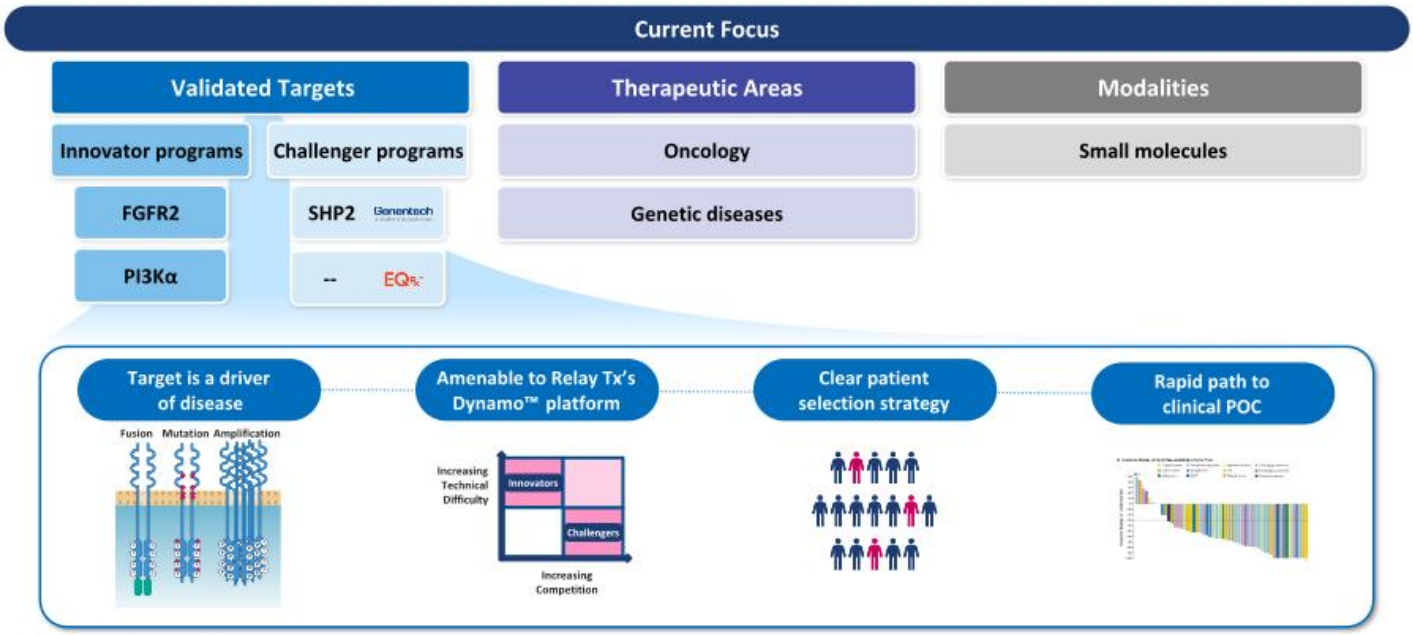
SHP2 *RLY-1971* | FGFR2 *RLY-4008* | PI3Kα^{H1047R} *RLY-2608*

The more we do, the better we get

Relay Tx – Our 3-Step Drug Discovery Process

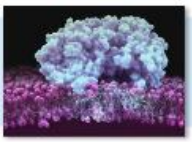
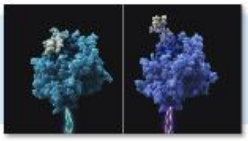
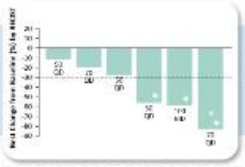
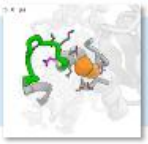


Relay Tx – Our Current Focus



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

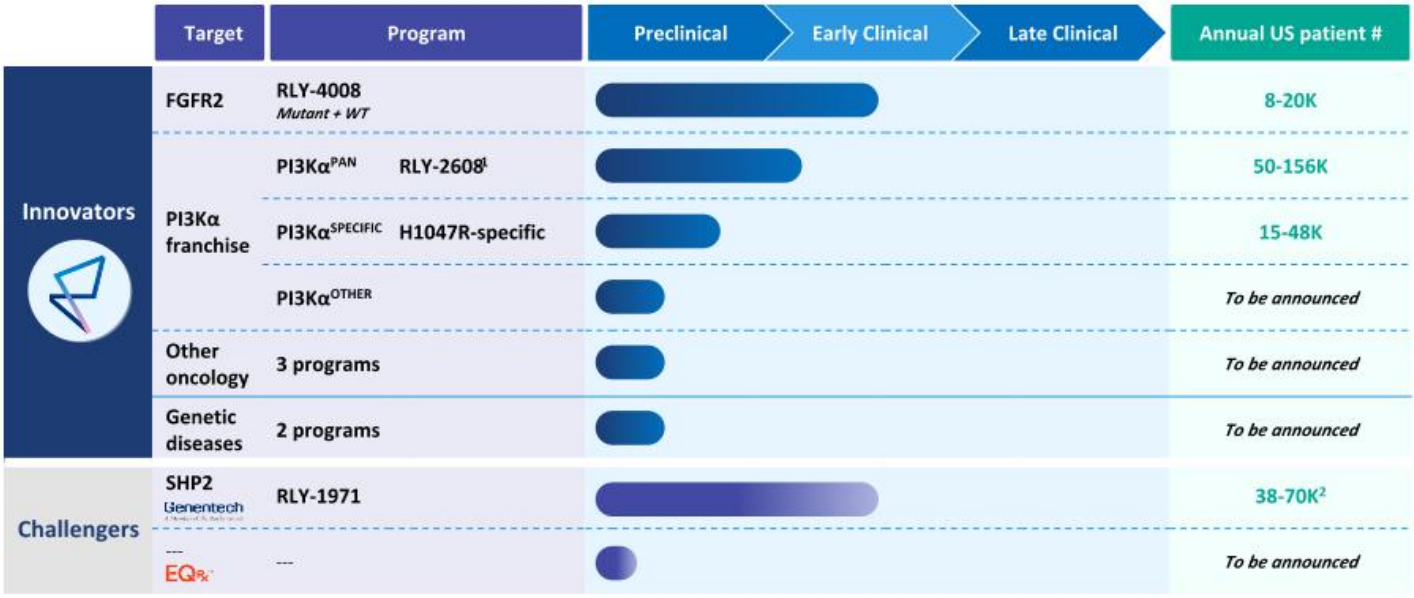
Relay Tx – We Have Validated Our Approach and Built Significant Advantage

	Motion-Based Hypothesis	Pre-Clinical Validation	Clinical Progress	Opportunity Size Annual US patient #
PI3Kα^{PAN} RLY-2608		✓	First patient dosed	50-156K H1047X, E542X, E545X
FGFR2 RLY-4008		✓		8-20K Fusions, Amps, Muts
SHP2 RLY-1971		✓	Genentech A Member of the Roche Group	38-70K Combo*

The more we do, the better we get

Note: Patient #'s refer to total annual number of US patients with late-line cancers compared to comprehensive annual incidence that may be amenable to treatment with our programs
*SHP2 combo only includes KRAS G12C in lung and CRC, EGFR mutations in lung, and ALK fusions in lung

Relay Tx – Our Extensive Precision Medicines Pipeline



Note: Patient #'s refer to total annual number of US patients with late-line cancers compared to comprehensive annual incidence that may be amenable to treatment with our programs
1. RLY-2608 covers H1047X, E542X, E545X hot spots; 2. SHP2 combo only includes KRAS G12C in lung and CRC, EGFR mutations in lung, and ALK fusions in lung

Relay Tx – What to Expect

RLY-4008 (FGFR2)

- Expansion cohorts open
- Additional data update expected in 2H 2022

RLY-2608 ($PI3K\alpha^{PAN}$)

- Clinical trial initiated

RLY-1971 (SHP2)

- GDC-6036 (KRAS G12C) combo trial initiated in July 2021

Next target in pipeline

- To be disclosed in 1H 2022

$617M
Cash, cash equivalents and investments as of the end of Q3 2021

$381M
Net proceeds from follow-on offering in October 2021

Execution focus underpins value creation

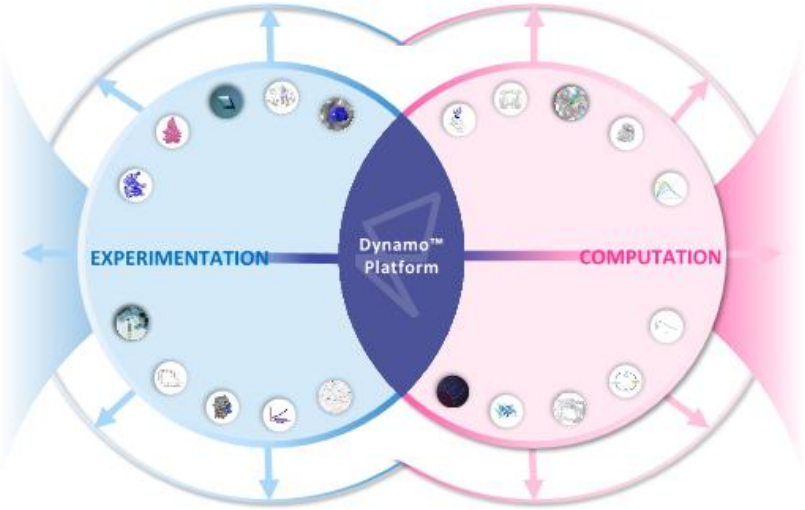
The Dynamo™ Platform – Evolving with Landscape of Leading Edge Techniques

Quantitative DEL

Generating data to build pharmacokinetic ML models

High-throughput and automated chemistry

Structural biology on difficult targets



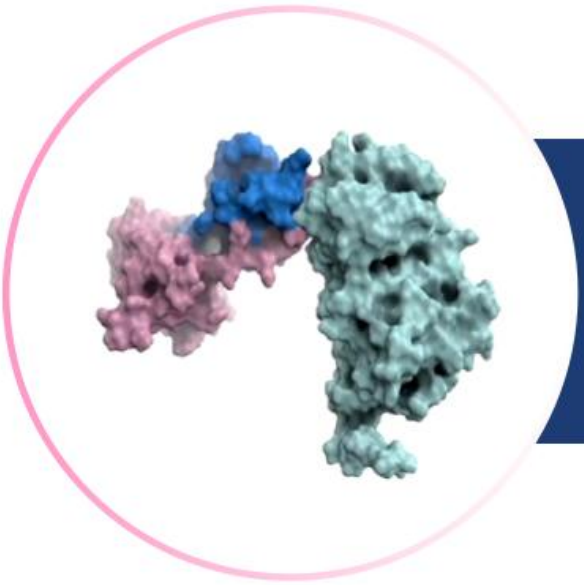
Automated chemical design

Protein structure prediction (AlphaFold)

ML directed free energy calculations

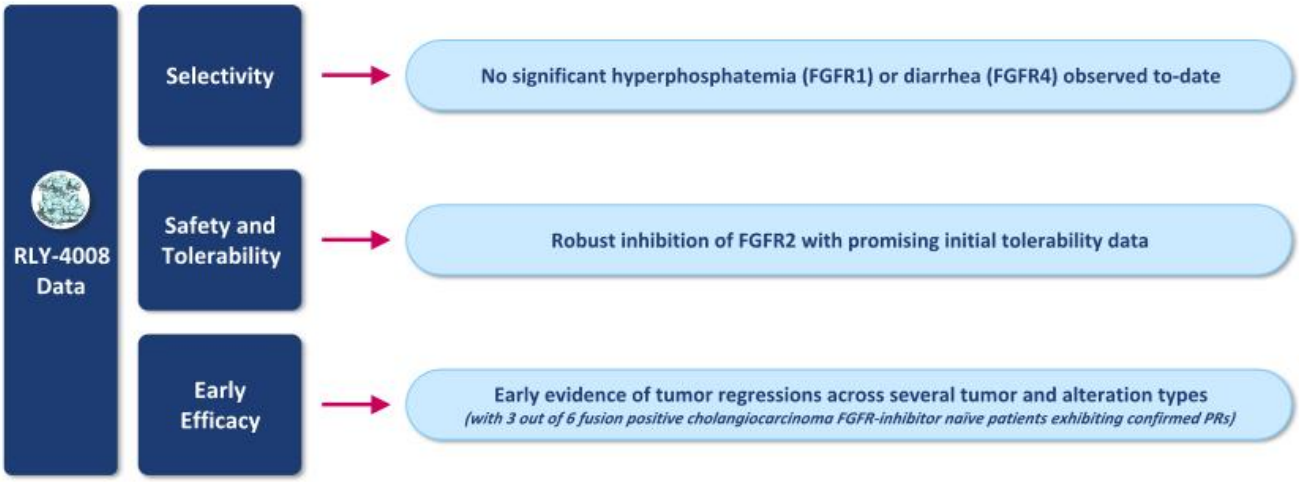
Active learning

Long-time scale MD



Relay Tx Programs

FGFR2 – Highlights from RLY-4008 Interim Clinical Data Disclosure (Oct 2021)

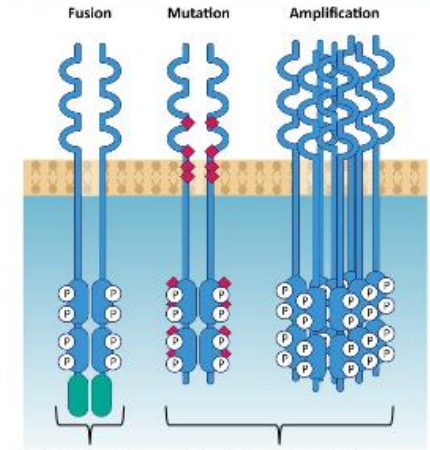


Source: RLY-4008 data as presented at 2021 AACR-NCI-EORTC Molecular Targets Conference

Preliminary data as of 09-Sept-2021

FGFR2 – Validated Target Present in Several Tumor Types

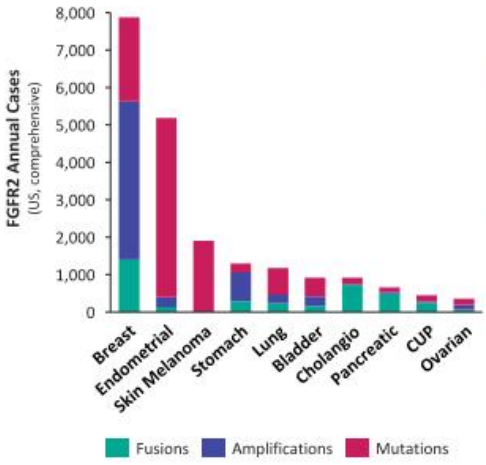
Three classes of driver alterations in FGFR2



~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

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%

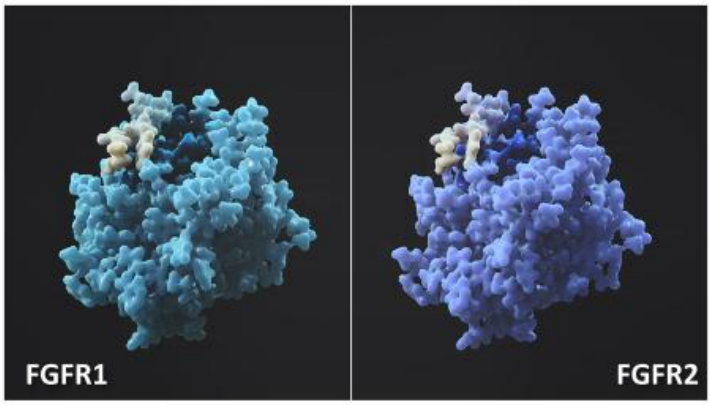
Late-line treatment with chemotherapy can be highly toxic and only results in incremental efficacy

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

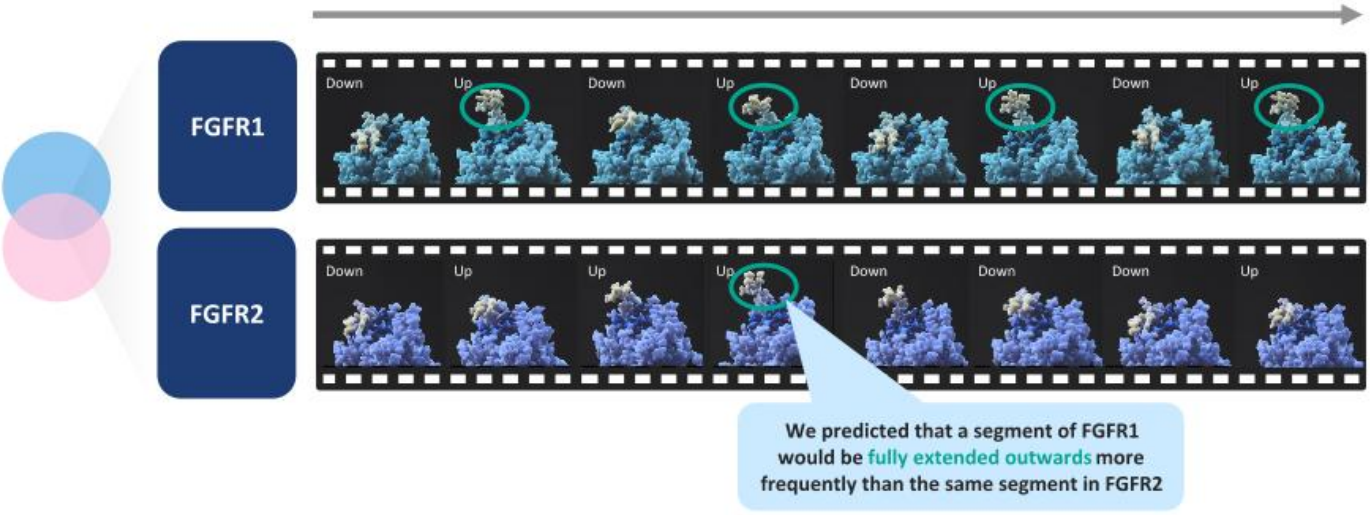
Sources: Pemigatinib – Prescribing information; Infigratinib – Prescribing information; Futibatinib/TAS-120 – AACR 2021 (diarrhea %s approximated from presentation); Erdafitinib – Prescribing information; FOLFOX – ABC-06 Publication in Lancet Oncology 2021

FGFR2 – Standard Approach to Discovery Has Had Limited Success

Standard Approach



FGFR2 – Increasing Experimental Resolution Reveals New Opportunities



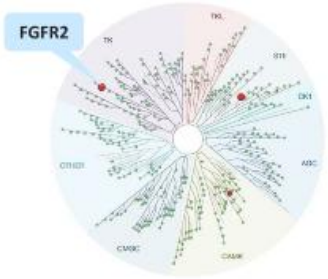
We predicted that a segment of FGFR1 would be fully extended outwards more frequently than the same segment in FGFR2

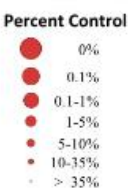
Exploiting the dynamic difference between FGFR1 and FGFR2 enabled Relay Tx to design a selective FGFR2 inhibitor

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

RELAY THERAPEUTICS

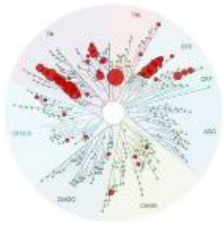
RLY-4008



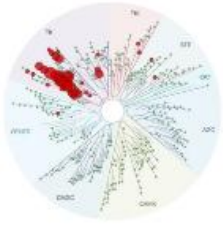


Pan-FGFR Inhibitors

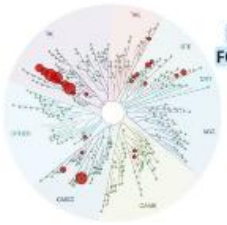
AZD4547



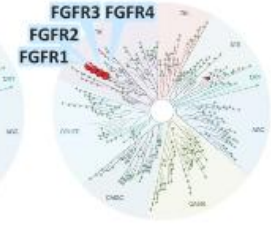
Erdafitinib

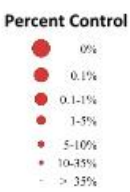


Pemigatinib



Futibatinib

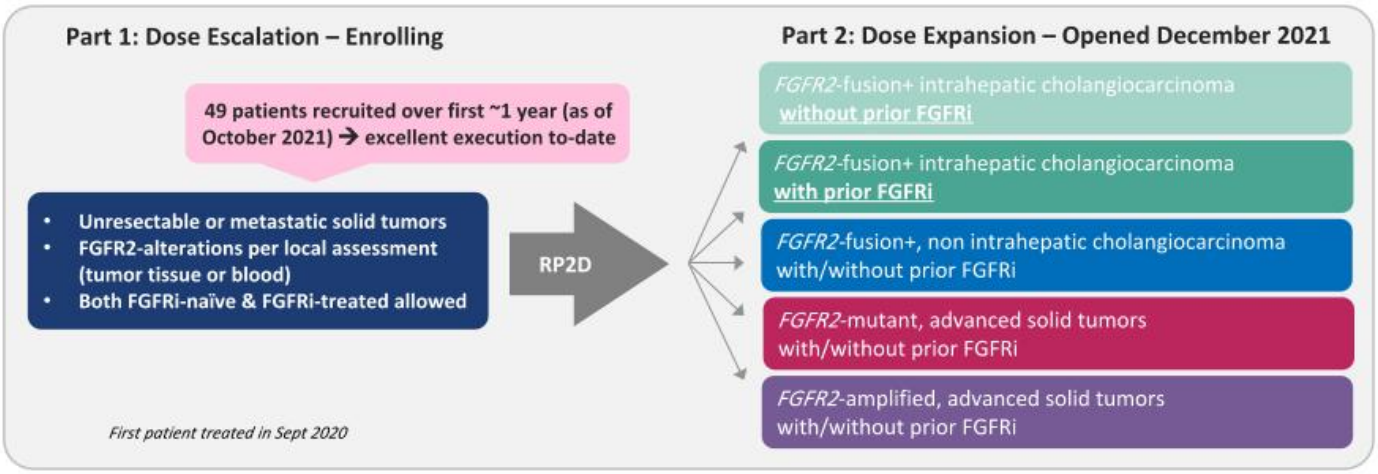




Note: Single experiment that tested each compound run at 500nM against 468 targets in the absence of ATP and without preincubation
Source: KINOMEscan™ by Eurofins DiscoverX

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

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

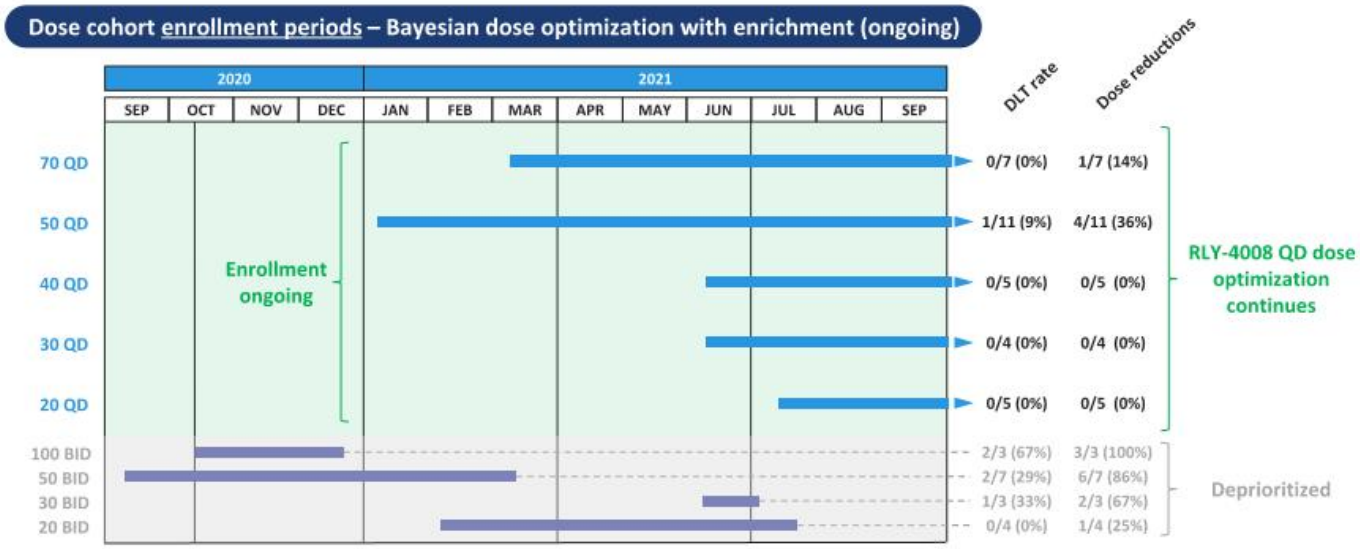


Orally dosed; BID and QD schedules explored using the Bayesian Optimal Interval Escalation (BOIN) design; Starting dose was 50 mg BID

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

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

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

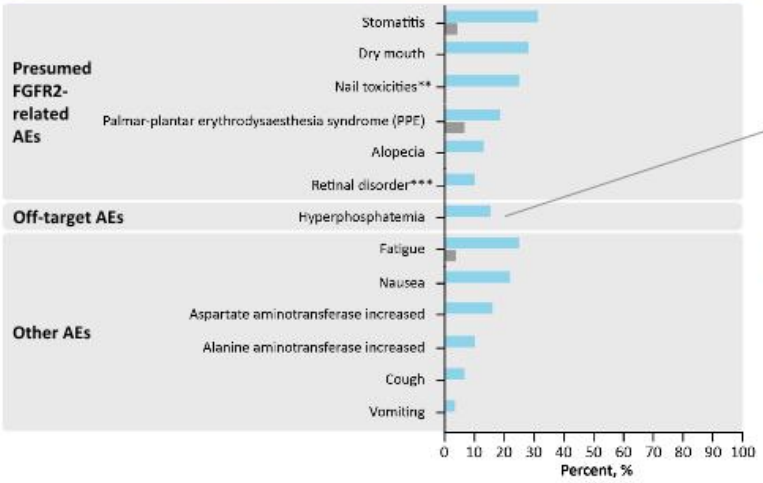


Source: RLY-4008 data as presented at 2021 AACR-NCI-EORTC Molecular Targets Conference

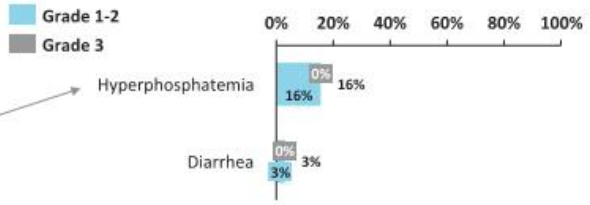
Preliminary data as of 09-Sept-2021

FGFR2 – RLY-4008 FIH Study: RLY-4008 QD Safety Profile

Treatment-Emergent Adverse Events*



Key Off-Target Safety (FGFR1 and FGFR 4)



Dry Eye and Corneal Details

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

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

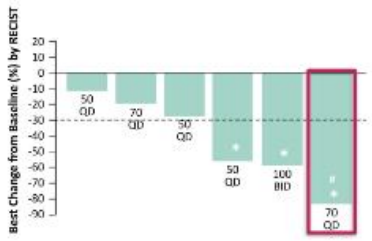
On-target AEs have been mostly low grade (no Gr 4/5, < 10% in the QD dosing regimen), and all of them have been reversible, manageable with dose modification or no intervention and monitorable

Source: RLY-4008 data as presented at 2021 AACR-NCI-EORTC Molecular Targets Conference (QD schedule n=32); Bemarituzumab ASCO 2021 Presentation – notes corneal AEs are defined by Standardised MedDRA Queries (SMQ) of corneal disorders, which includes dry eye
*Included if ≥ 20% based on both QD (n=32) and BID (n=17) schedules.
**Included preferred terms of nail disorder, nail discoloration, nail ridging, onychalgia, onychoclasis, onycholysis, onychomadesis, paronychia.
***Included preferred terms of retinal pigment epithelium detachment, retinopathy, blurred vision, subretinal fluid.

Preliminary data as of 09-Sept-2021

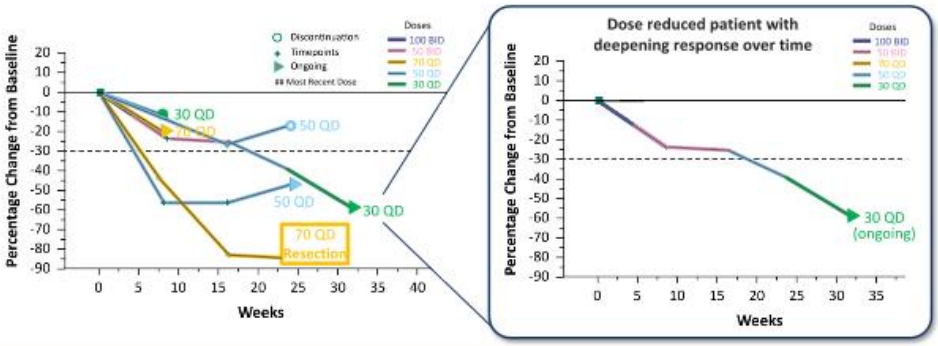
FGFR2 – RLY-4008 FIH Study: RLY-4008 Induced Radiographic Tumor Regression in FGFR Inhibitor-Naïve FGFR2-Fusion+ Cholangiocarcinoma

Best RECIST change from baseline



3/6 patients exhibit a confirmed PR

Relative change from baseline in tumor size



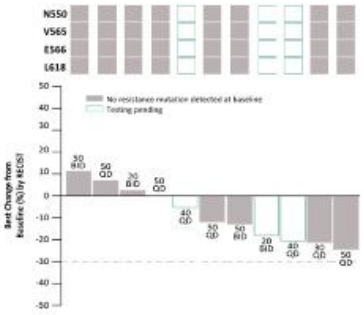
3/6 patients ongoing on treatment, and 1 patient had resection with curative intent

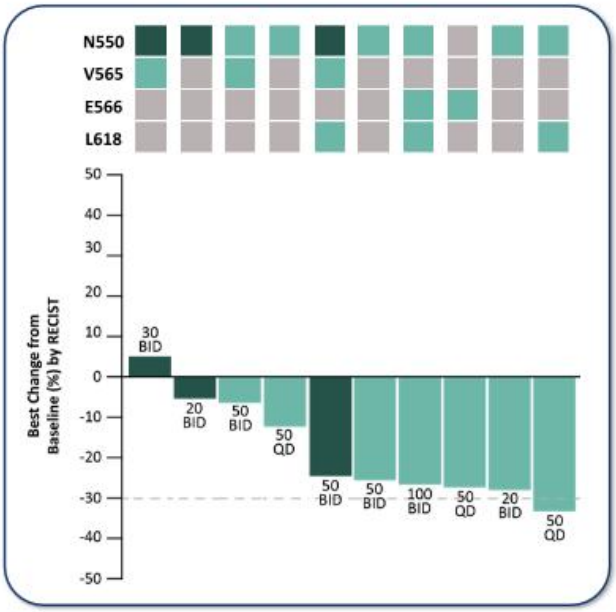
Pan-FGFR benchmark in this population is 23-36% ORR

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

Preliminary data as of 09-Sept-2021

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





Resistance mutation cleared at C2D1

Resistance mutation not cleared at C2D1

No resistance mutation at baseline

Testing pending

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

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

Clearance of resistance clones implies greater duration in earlier line patients

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

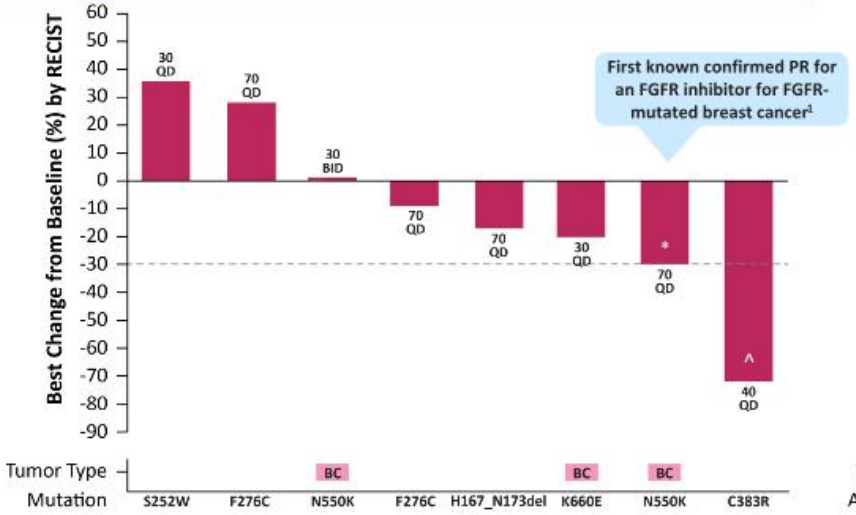
Note: (N550, N549), (V565, V564), (E566, E565), (L618, L617) are different terminology for the same mutated site; ctDNA, circulating DNA; FGFRi, fibroblast growth factor receptor inhibitor

Preliminary data as of 09-Sept-2021

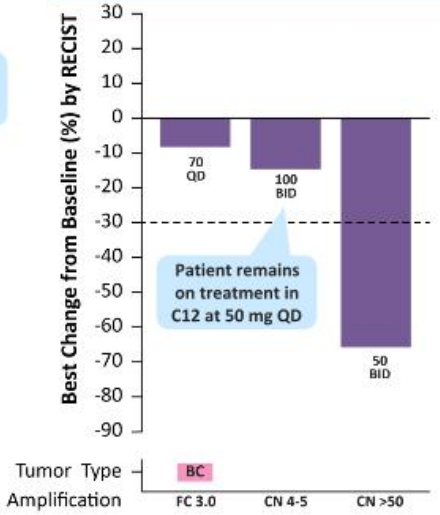
FGFR2 – RLY-4008 FIH Study: RLY-4008 Showed Radiographic Tumor Regression in FGFR2 Oncogenic Mutations and in FGFR2 Amplifications

RELAY THERAPEUTICS

FGFR2 Oncogenic Mutations



FGFR2 Amplifications



No FDA-approved FGFR targeted therapies for FGFR2 oncogenic mutations or amplifications

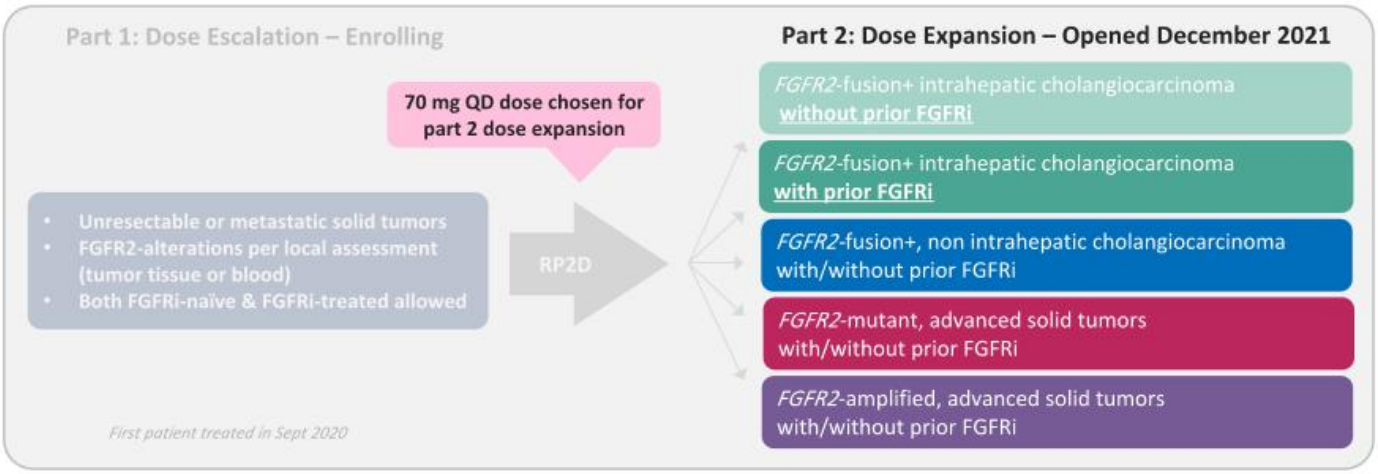
■ Breast cancer (BC)

*Confirmed PR with increased tumor reduction after data cut; ^PR pending confirmation.
1. Based on Company's review of presented meeting abstracts and published studies to-date.
Note: FC, fold change; CN, copy number.
Source: RLY-4008 data as presented at 2021 AACR-NCI-EORTC Molecular Targets Conference

Preliminary data as of 09-Sept-2021

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

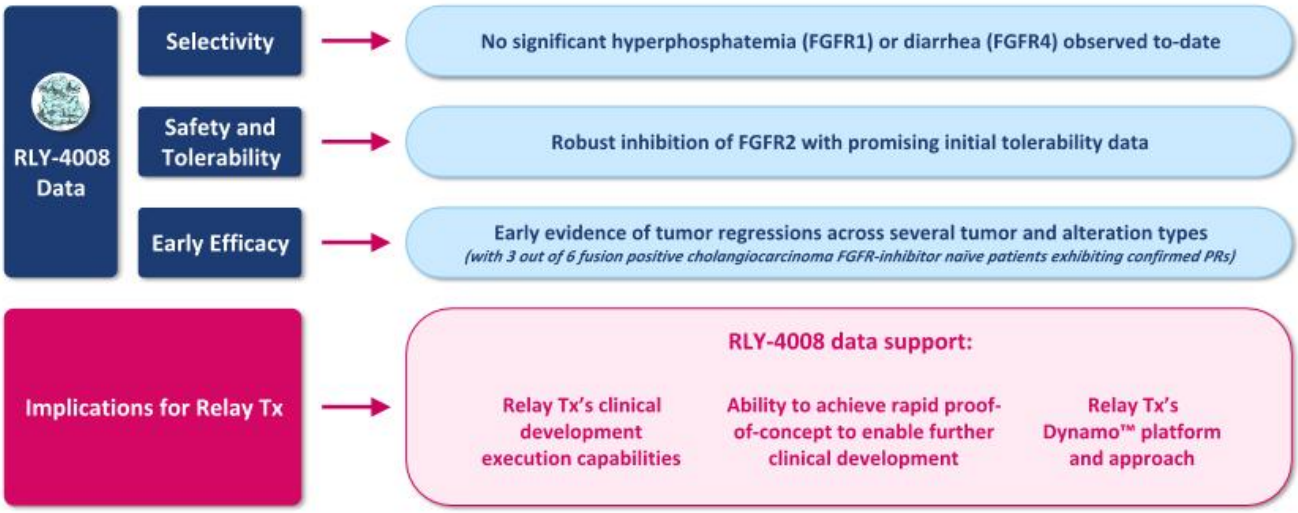
Key Objectives:
MTD/RP2D, safety, pharmacokinetics, biomarkers (ctDNA, tumor markers), preliminary anti-tumor activity



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

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

FGFR2 – Highlights from RLY-4008 Interim Clinical Data Disclosure (Oct 2021)

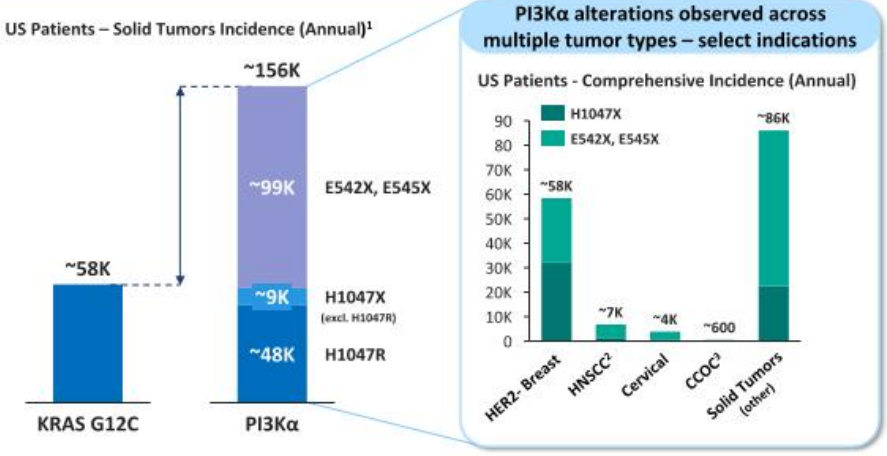


Source: RLY-4008 data as presented at 2021 AACR-NCI-EORTC Molecular Targets Conference

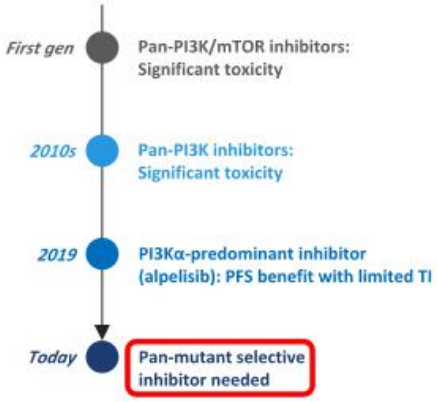
Preliminary data as of 09-Sept-2021

PI3Kα Opportunity Is Among the Largest Ever for Precision Oncology

Pan-mutant selective drug represents significant clinical opportunity



Evolution of PI3K inhibitors



Sources: FoundationInsights® database; SEER; Alpelisib – FDA prescribing label

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

PI3Kα – Existing Inhibitors Establish POC, but Have Limited Therapeutic Window

Hyperglycemia is on-target tox from PI3Kα WT

Breast Cancer

Monotherapy and Combo Data from Leading Competitors

Compound/ Company	Stage	Mutant Selective	Regimen	Response Rate	% of Patients with Hyperglycemia	% of Patients with GI Toxicity	% of Patients Discontinued or Dose Reduced
Alpelisib (NOVARTIS)	Approved	No	Monotherapy (Dose Escalation)	3% (1/36)	52% (24% Gr3-4)	40%	52%
			Combo (Fulvestrant) in mBC, CDKi pre-treated	19% mPFS 7.3mo	58% (28% Gr3-4)	60%	83%[1]
Inavolisib (Genentech)	Phase 3	No	Monotherapy (Dose Escalation)	20% (4/20)	70% (20% Gr3-4)	40%	30%[2]
			Triplet mBC Combo, no prior CDKi (CDK4/6 + Fulvestrant)	40% (6/15)	61% (23% Gr3-4)	48%	36%

1. Includes dose interruptions in addition to dose reductions and discontinuations
2. Dose reductions only; discontinuations not reported

Non-Breast Cancer

Monotherapy Anecdotal Responses Validate PIK3CA as a Tumor Driver Outside Breast Cancer

Compound	PI3K Isoform Selectivity	Mutant Selective	Tumor Types Where Monotherapy Objective Responses In PIK3CAm Patients Have Been Observed (# of Patients)
Alpelisib	Alpha-Predominant	No	Cervical (6), Breast (2), Endometrial (2), Colorectal (2), GIST (2), Head & Neck (1)
Inavolisib	Alpha-Predominant	No	Breast (4)
Taselisib	Alpha, Delta, Gamma	No	Head & Neck (4), Breast (3), Endometrial (2), Cervical (2), CCA (2), CRC (1), Pancreatic (2), Salivary Gland (1)
CYH33	Alpha-Predominant	No	Clear-Cell Ovarian (1), Other Ovarian (1), Breast (1), CRC (1), Gastric (1)

Sources: Alpelisib Monotherapy – Juric et al 2018; Alpelisib Combo – 2021 SABCS Presentation – BYLieve Cohort A; Inavolisib Monotherapy – SABCS 2019 Poster, Inavolisib Combo – SABCS 2020 Poster; Taselisib Monotherapy – Jhaveri et al 2020; CYH33 – ESMO-TAT 2020 Presentation

PI3Kα – Relay Tx Has a Unique Understanding of PI3Kα

KRAS experience teaches us pan-mutant coverage is required

Similarities between PI3K and KRAS:

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

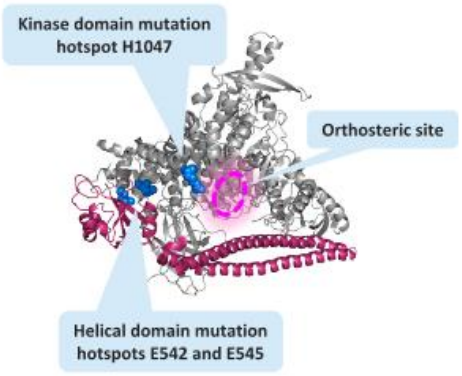
KRAS G12C

Examples of on-target resistance mechanisms

- KRAS G13D
- KRAS G12V
- KRAS Y96D

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

Relay Tx has a unique understanding of PI3Kα



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

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

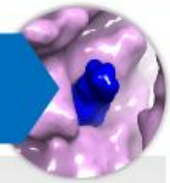
Source: Hata, Helst, & Corcoran et al, *Cancer Discovery* 2021
*RLY-2608 covers H1047X, E542X, E545X hot spots

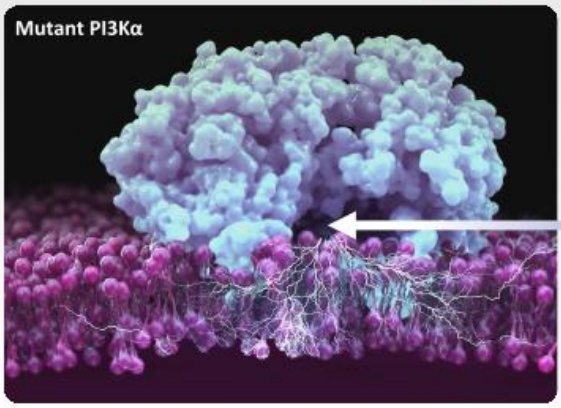
PI3Kα – Proprietary Insights Unlock Additional Approaches

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

Discovered novel allosteric pocket favored in mutant protein

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

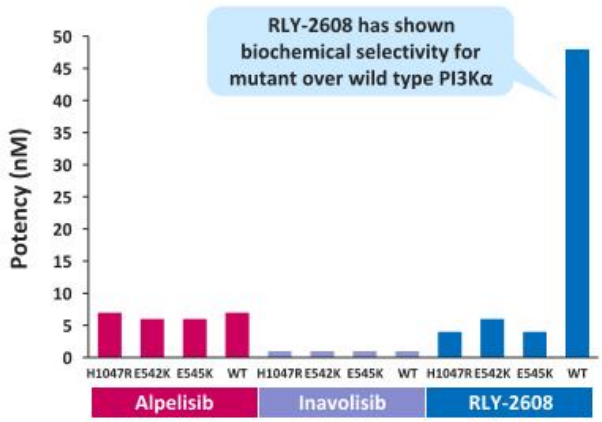




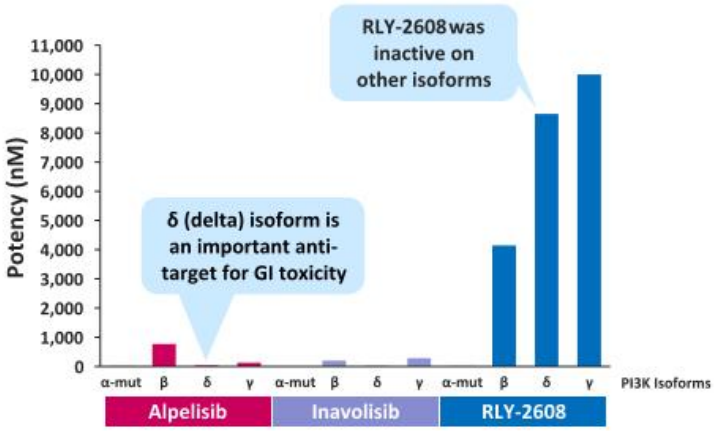
A differentiated understanding of the structure of PI3Kα and its relationship to function equips Relay Tx to design optimal mutant-selective inhibitors of PI3Kα

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

Mutant vs. WT PI3Kα potency

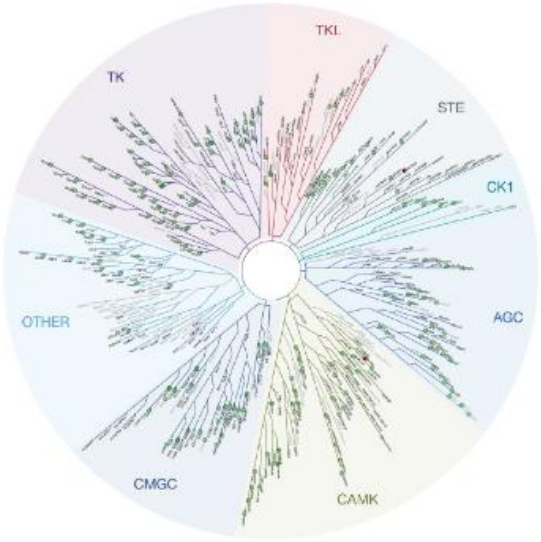


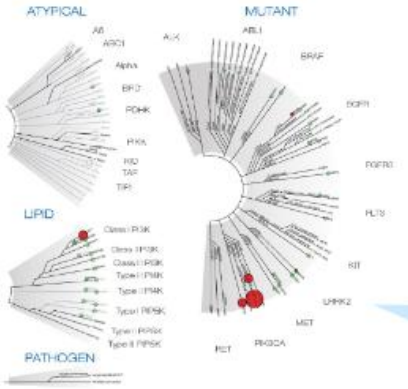
Mutant PI3Kα vs. other isoform potency



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

PI3Kα – RLY-2608 Is Selective Across the Kinome





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

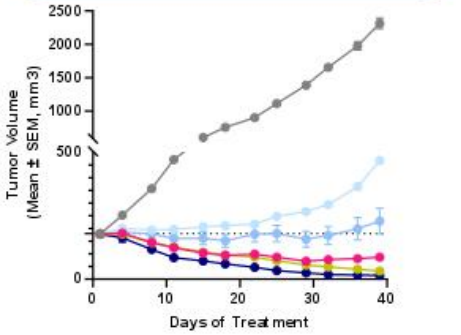
Kinase Inhibition @ 10 µM

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

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

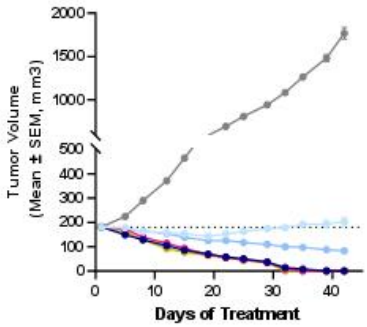
PI3Kα – In Vivo Tumor Regressions Across Both Mutation Hotspots (Mouse Study)

H1047R mutant (HCC1954) (mouse)



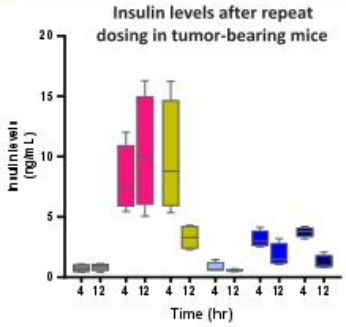
Vehicle
Alpelisib PO 50mpk QD
Inavolisib 25mg/kg QD
RLY-2608 25mg/kg BID
RLY-2608 50mg/kg QD
RLY-2608 100mg/kg BID

E545K mutant (MDAMB361) (mouse)[1]



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

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



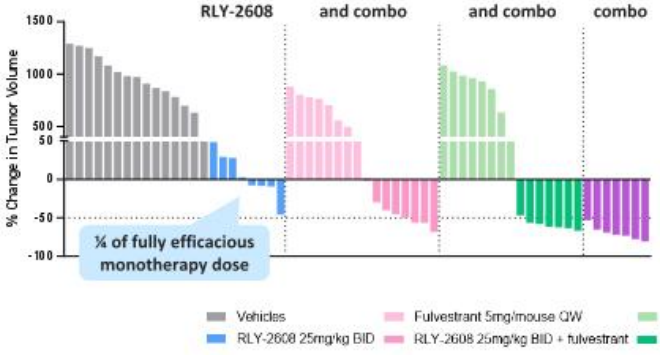
Vehicle
Alpelisib PO 50mpk QD
Inavolisib 25mg/kg QD
RLY-2608 25 mg/kg BID
RLY-2608 50mg/kg QD
RLY-2608 100mg/kg BID

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

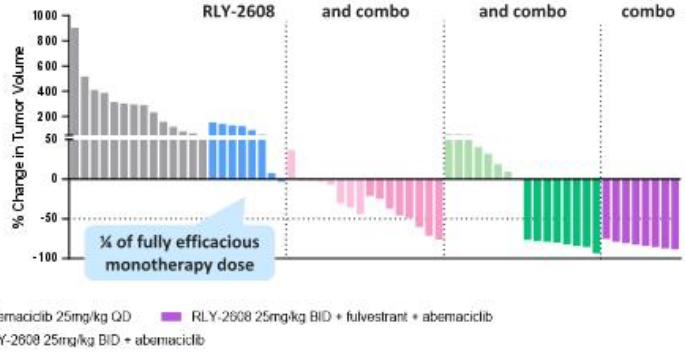
PI3Kα – RLY-2608 Combines with Standard of Care Therapies to Drive Regressions in ER+/HER2- Breast Cancer Models

ST1056 (ER+/HER2-; H1047R)



ST986 (ER+/HER2-; E542K)

Superior efficacy observed preclinically in the triple combination

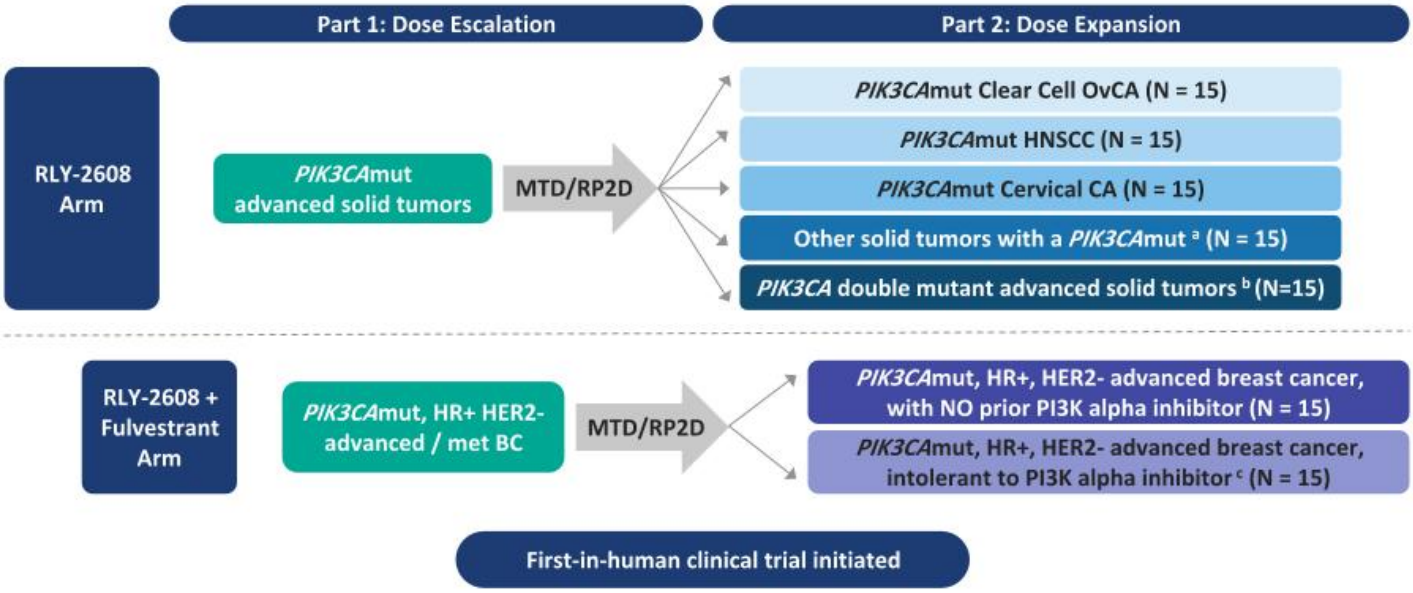


Vehicles
RLY-2608 25mg/kg BID
Fulvestrant 5mg/mouse QW
RLY-2608 25mg/kg BID + fulvestrant
Abemaciclib 25mg/kg QD
RLY-2608 25mg/kg BID + abemaciclib
RLY-2608 25mg/kg BID + fulvestrant + abemaciclib

Combination arms with similar tolerability to monotherapy arms

Source: RLY-2608 data as presented in 2021 SABCS poster presentation

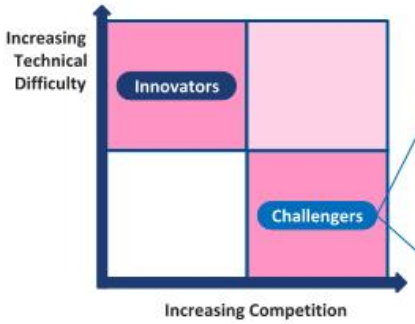
PI3Kα – RLY-2608 Trial Design



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.

Challengers – Supporting the Build of Our Dynamo™ Platform

Challengers Have Lower Technical Risk



Challengers Solve Problems with "Known" Answers

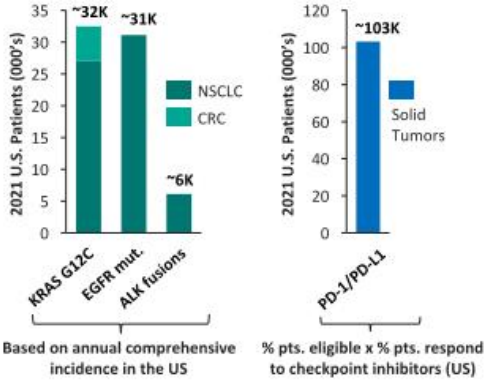
Enable higher volume of programs → Serve as a data factory and increase experience

Our challengers: SHP2 RLY-1971 Genentech; -- EQRx

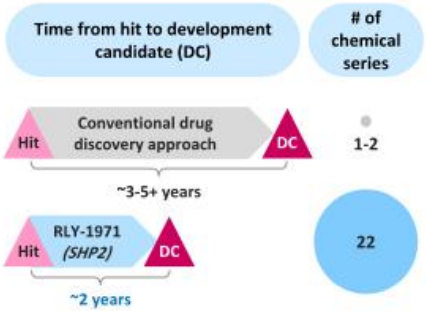
The more we do, the better we get

SHP2 – RLY-1971 Is Potent and Selective with Potential for Multiple Therapeutic Uses

Potential Patient Populations



RLY-1971 Discovery



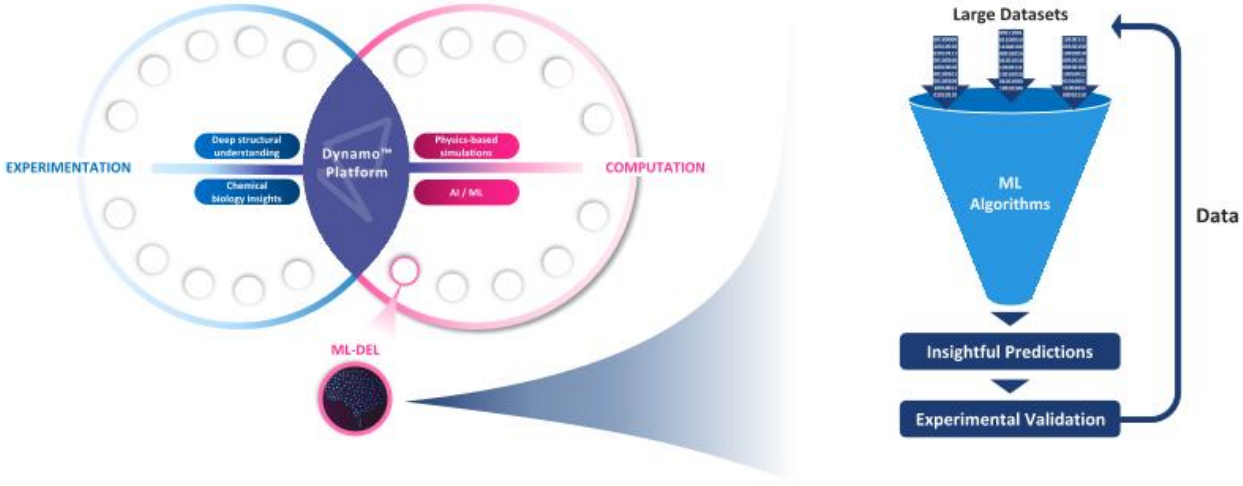
Key Differentiating Features of RLY-1971

Dosing potential	Projected to be continuous once daily dosing
Potency	Demonstrated 750pM IC50 inhibition of SHP2 in biochemical assays
Novel chemistry	Chemically distinct from other SHP2 inhibitors

RLY-1971 and GDC-6036 (KRAS G12C) combination trial initiated in July 2021

Sources: SEER; Foundation Medicine Insights; *JAMA Netw Open.* 2019;2(5):e192535. doi:10.1001/jamanetworkopen.2019.2535

Challengers – Creating a Data Factory



The acquisition of our ML-DEL capabilities unlocks our ability to be a data factory

Relay Tx – What to Expect

RLY-4008 (FGFR2)

- Expansion cohorts open
- Additional data update expected in 2H 2022

RLY-2608 ($PI3K\alpha^{PAN}$)

- Clinical trial initiated

RLY-1971 (SHP2)

- GDC-6036 (KRAS G12C) combo trial initiated in July 2021

Next target in pipeline

- To be disclosed in 1H 2022

$617M
Cash, cash equivalents and investments as of the end of Q3 2021

$381M
Net proceeds from follow-on offering in October 2021

Execution focus underpins value creation


RELAY®
THERAPEUTICS