RELAY®
THERAPEUTICS

Company Presentation

November 2021

Disclaimer

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

Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make due to a number of risks and uncertainties. These and other risks, uncertainties and important factors are described in the section entitled "Risk Factors" in our Quarterly Report on Form 10-Q for the quarter ended September 30, 2021, as well as any subsequent filings with the Securities and Exchange Commission. Any forward-looking statements represent our views only as of the date of this presentation and we undertake no obligation to update or revise any forward-looking statements, whether as a result of new information, the occurrence of certain events or otherwise. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. No representations or warranties (expressed or implied) are made about the accuracy of any such forward-looking statements.

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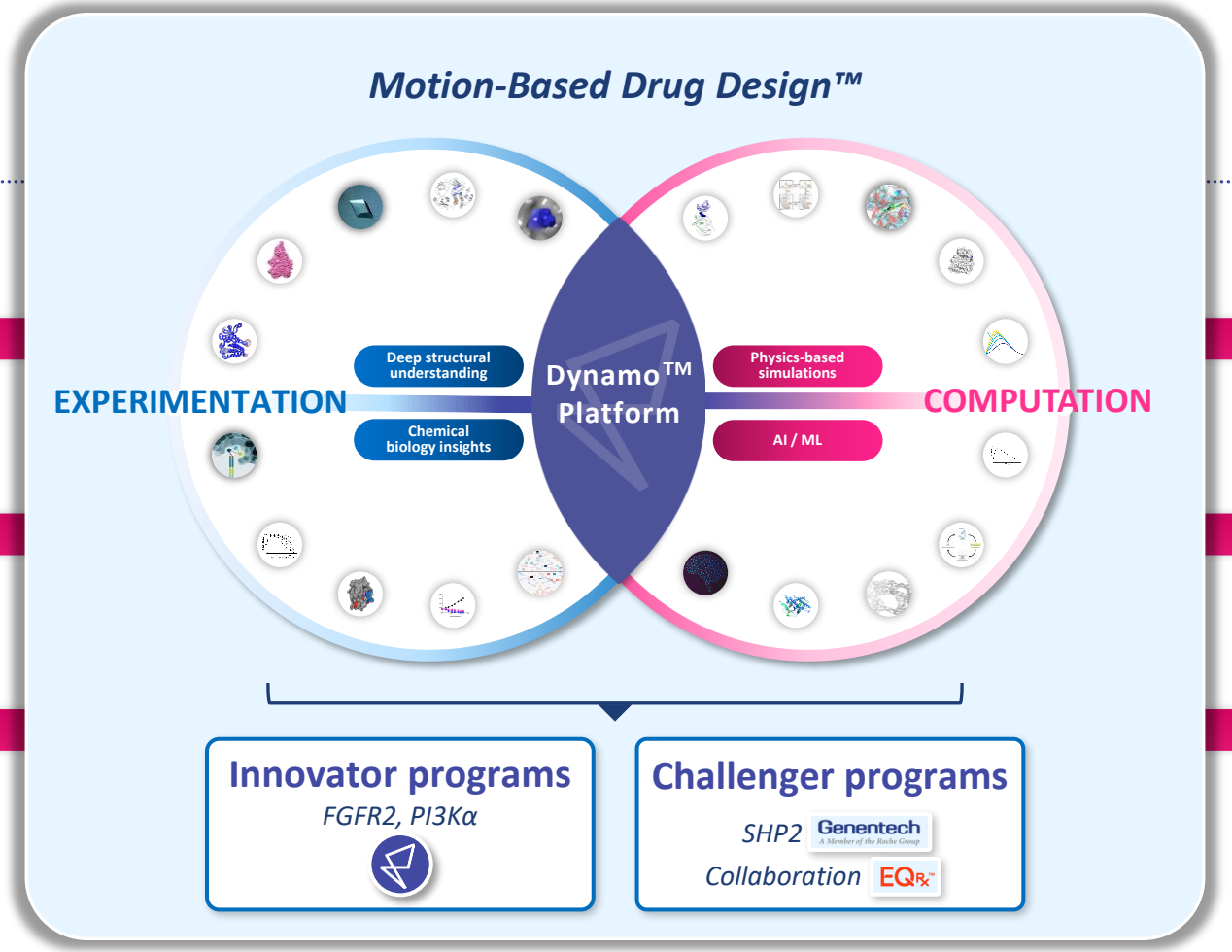
Relay Tx – Our Vision

Current focus

- **Oncology and genetic diseases**
- **Small molecule inhibitors**
- **Validated targets**



Future focus

- **Additional therapeutic areas**
- **Additional modalities**
- **Franchise expansion**

The more we do, the better we get

Relay Tx – Where We Operate Today

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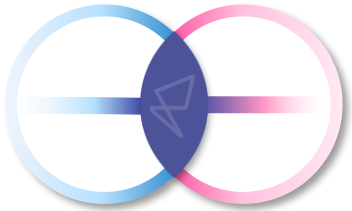
Elucidation of novel disease biology

Selection of validated targets

Creation of new medicines

Execution of precision medicines clinical trials

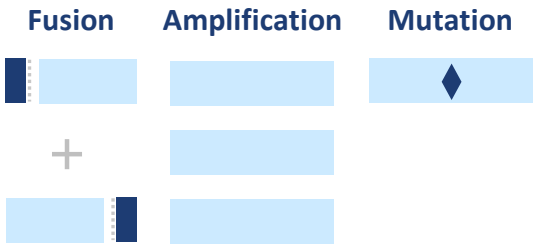
Commercialization and generation of real world data



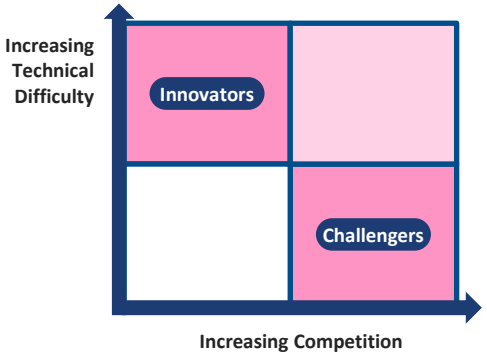
Relay Tx – Selection of Validated Targets

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

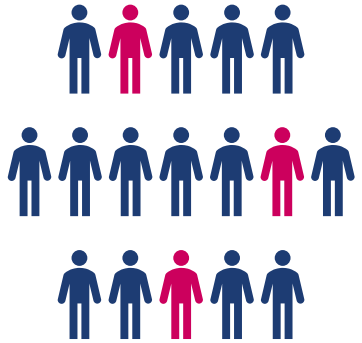
Target is a driver of disease



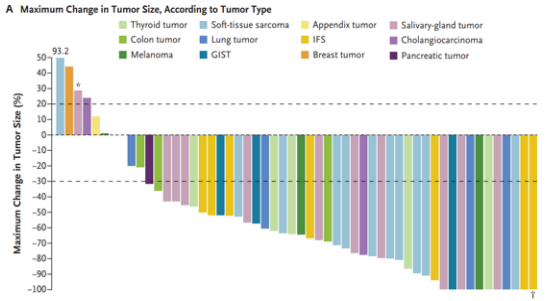
Amenable to Relay Tx's Dynamo™ platform



Clear patient selection strategy



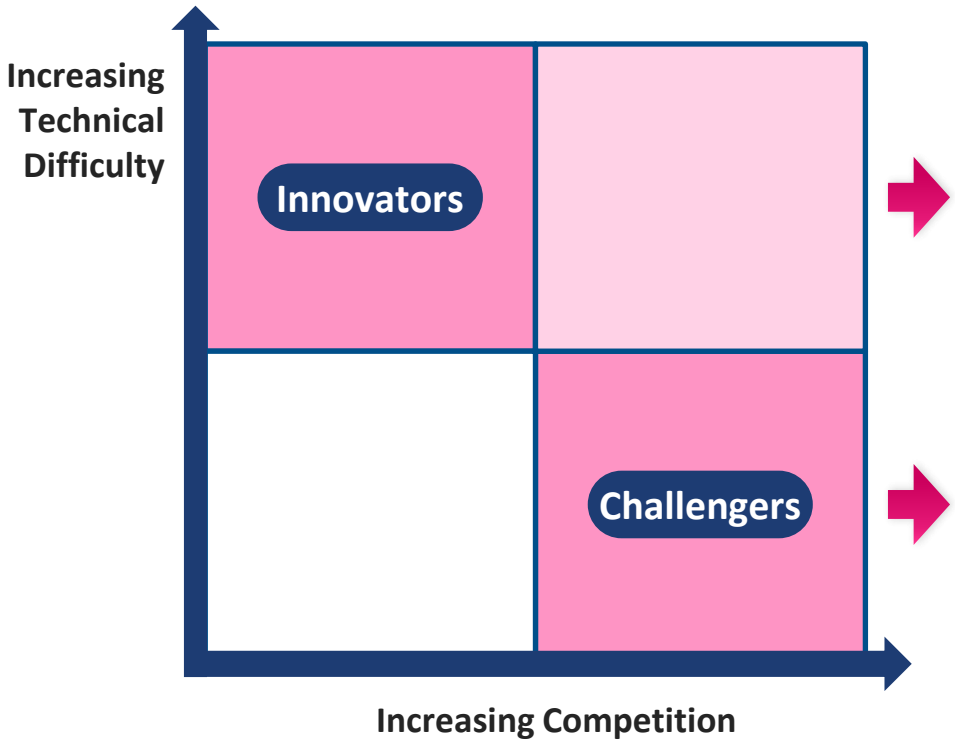
Rapid path to clinical POC



Initial focus on cancer then genetic diseases, with potential for additional therapeutic areas

Relay Tx – Validated Approach to Value Creation

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



Innovator programs *(Wholly-owned programs)*

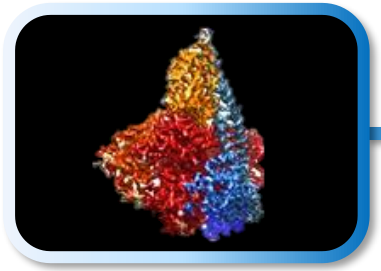
- **RLY-4008** — *FGFR2 (mutant + WT)*
- **RLY-2608** *+ Add'l programs* — *PI3Kα (mutant)*
- **Other oncology** *(3)*
- **Genetic diseases** *(2)*

Challenger programs *(Partnered programs)*

- **RLY-1971** (Genentech) — *SHP2*
- **Collaboration** (EQRx)

Relay Tx – Creation of New Medicines

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



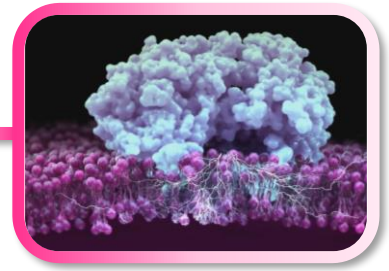
EXPERIMENTATION

- Deep structural understanding
- Chemical biology insights

Dynamo™ Platform

COMPUTATION

- Physics-based simulations
- AI / ML



1. Target modulation hypothesis → 2. Hit finding and lead generation → 3. Lead optimization

Relay Tx – Execution of Precision Medicines Clinical Trials

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

Clinical and regulatory paradigm

- Optimized precision medicine trials
- Sophisticated patient finding
- Streamlined clinical trials execution
- Robust and interpretable data disclosures
- Rapid path to regulatory filings

Relay Tx achievements to-date

3

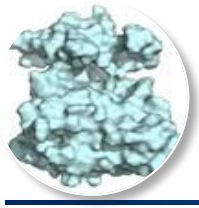
# of assets for which development has been initiated
RLY-1971 | RLY-4008 | RLY-2608

40+

# of FTEs in development organization

2

# of pharma partners
RLY-1971 Genentech partnership
Collaboration with EQRx



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

RLY-4008 Data

Selectivity	**No significant hyperphosphatemia (FGFR1) or diarrhea (FGFR4) observed to-date**
Safety and Tolerability	**Robust inhibition of FGFR2 with promising initial tolerability data**
Early Efficacy	**Early evidence of tumor regressions across several tumor and alteration types** *(with 3 out of 6 fusion positive cholangiocarcinoma FGFR-inhibitor naïve patients exhibiting confirmed PRs)*

Implications for Relay Tx

RLY-4008 data support:

- **Relay Tx's clinical development execution capabilities**
- **Ability to achieve rapid proof-of-concept to enable further clinical development**
- **Relay Tx's Dynamo™ platform and approach**

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

PI3Kα Opportunity Is Among the Largest Ever for Precision Oncology

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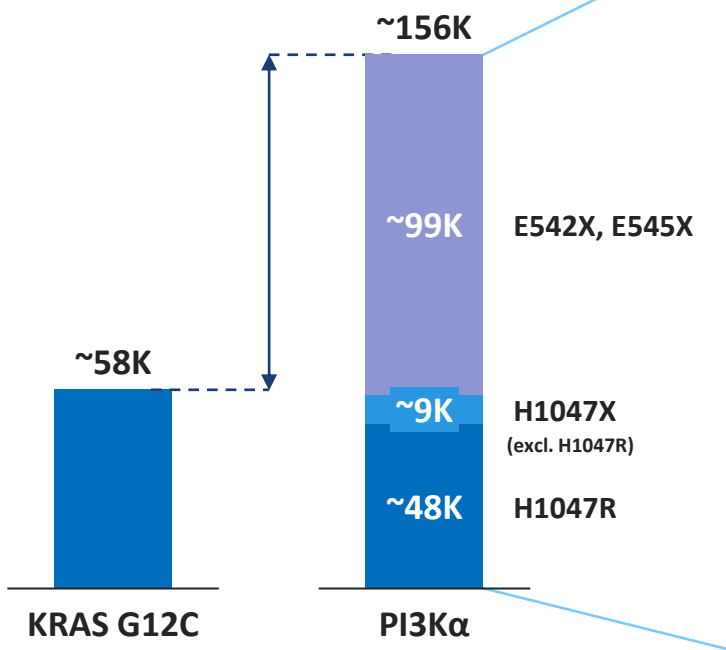
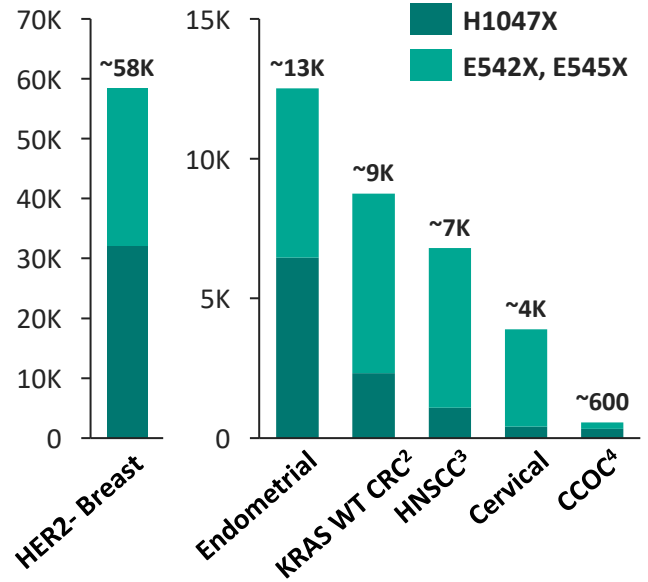
Pan-mutant selective drug represents significant clinical opportunity

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

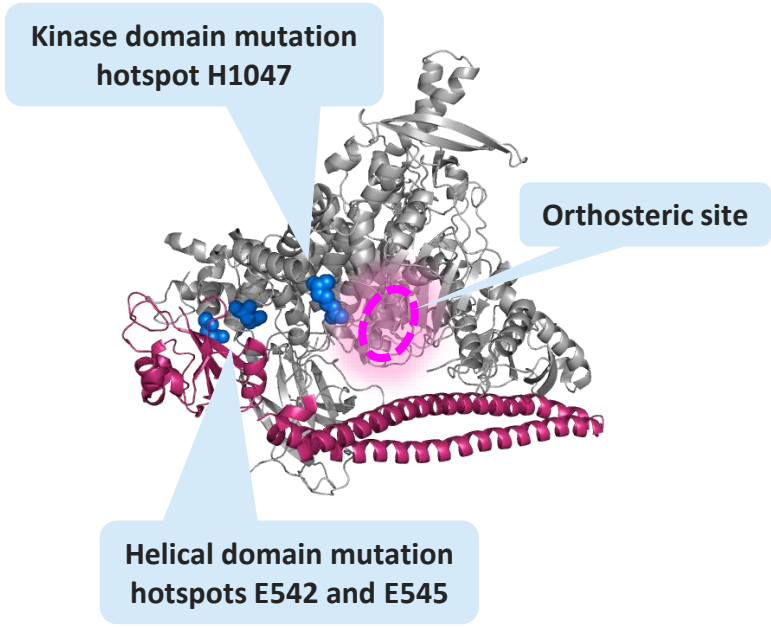


PI3Kα alterations observed across multiple tumor types – select indications

US Patients - Comprehensive Incidence (Annual)



Relay Tx has a unique understanding of PI3Kα



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

2010s — Pan-PI3K inhibitors: Significant toxicity

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

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

Sources: FoundationInsights® database; SEER

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

PI3Kα – Highlights from Recent RLY-2608 Preclinical Data Disclosure

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RLY-2608 Data

Novel Mechanism	**Mutant-selective binding to novel allosteric site discovered by Dynamo™ platform**
Pan-Mutant Selectivity	**Inhibited not only H1047X, but also E542X and E545X, potentially doubling the addressable population, while sparing WT PI3Kα**
Tolerability	**Achieved tumor regressions in vivo at doses projected to be clinically relevant with significantly reduced impact on glucose metabolism compared to non-mutant selective inhibitors**
Approaching Clinic	**First-in-human study anticipated to start in 1H22***
Implications for Relay Tx	**RLY-2608 represents the start of Relay Tx's emerging PI3Kα franchise**

*Subject to submission and acceptance of IND by the FDA

Relay Tx Has Delivered Against All Key Objectives

Programs

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

Dynamo™ Platform and Capabilities

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

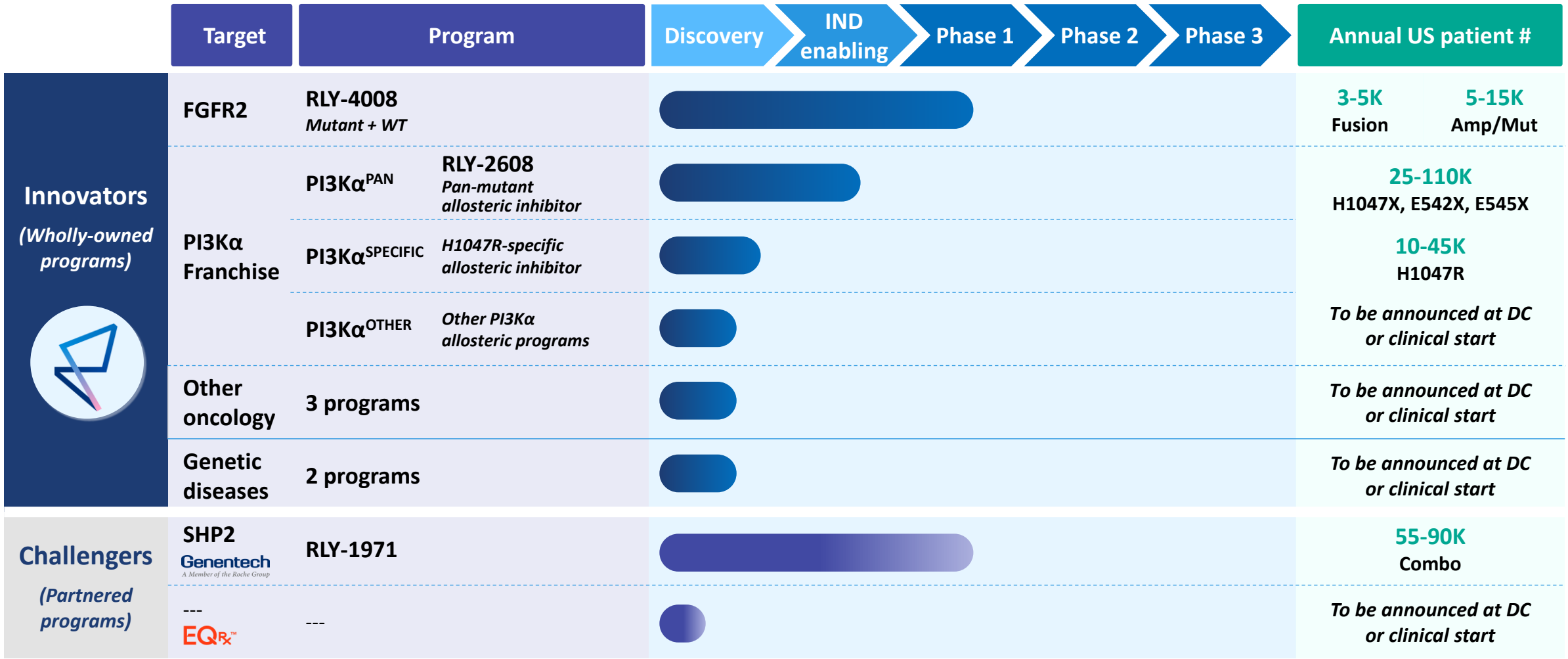
Clear focus on execution

Relay Tx – We Have Validated Our Approach

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

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

Extensive Precision Medicines Pipeline

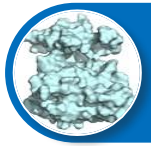


Note: Patient #'s refer to total annual number of US patients with late-line cancers compared to comprehensive annual incidence that may be amenable to treatment with our programs

What To Expect From Relay Tx

Nearer-term milestones

Innovators

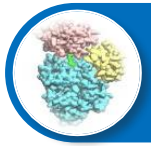


RLY-4008 (FGFR2) — Expansion cohorts open by 2021 year end; Additional data update expected in 2022

RLY-2608 (PI3Kα^{PAN}) — Clinical start expected in 1H 2022*; Add'l preclinical data at SABCS (Dec 2021)

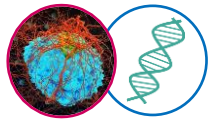
Next target in pipeline — Next target to be disclosed in 1H 2022

Challengers



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

Medium-term drivers

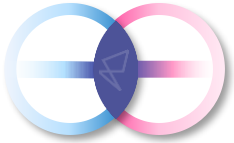


5 additional innovator programs

Genentech — A Member of the Roche Group

EQRx™

Pursuit of challenger targets through partnerships



Continued evolution of our Dynamo™ platform

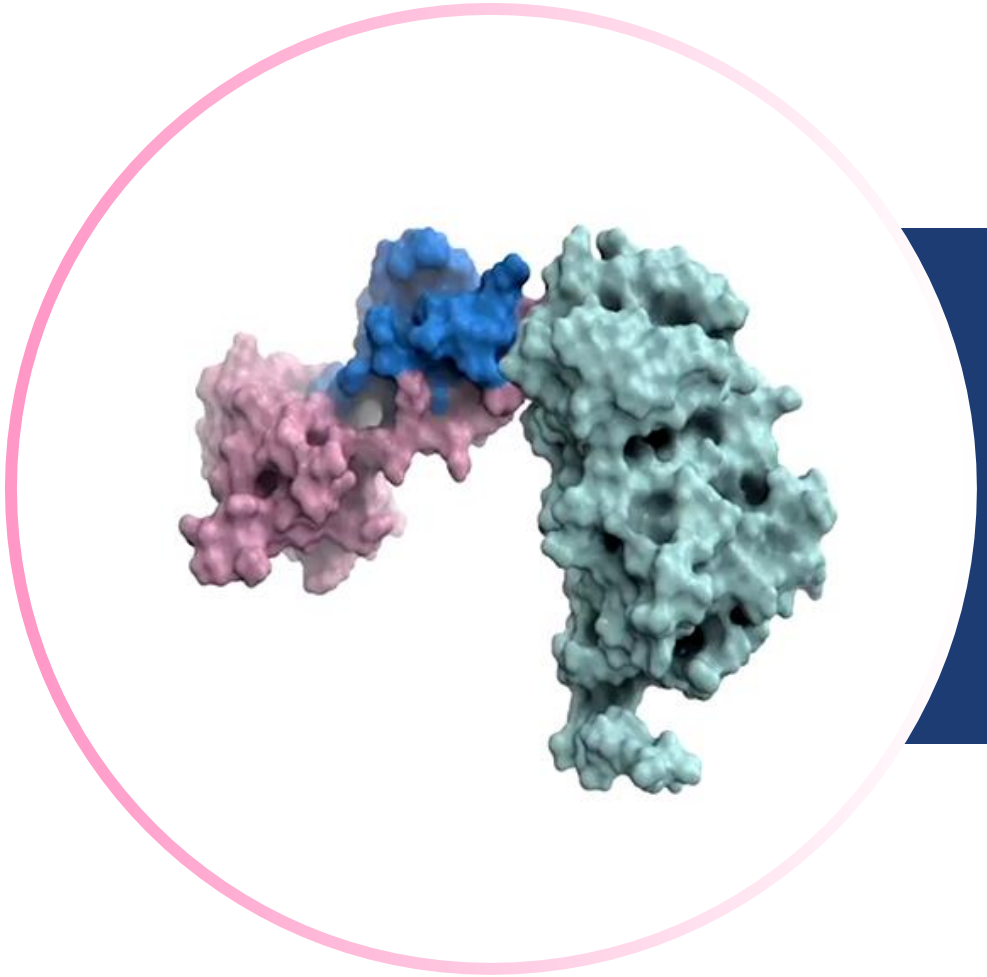
Continued expansion of pipeline scope and scale

$617M

Cash, cash equivalents and investments as of the end of Q3 2021
Not inclusive of ~$380M net proceeds from October 2021 follow-on public offering

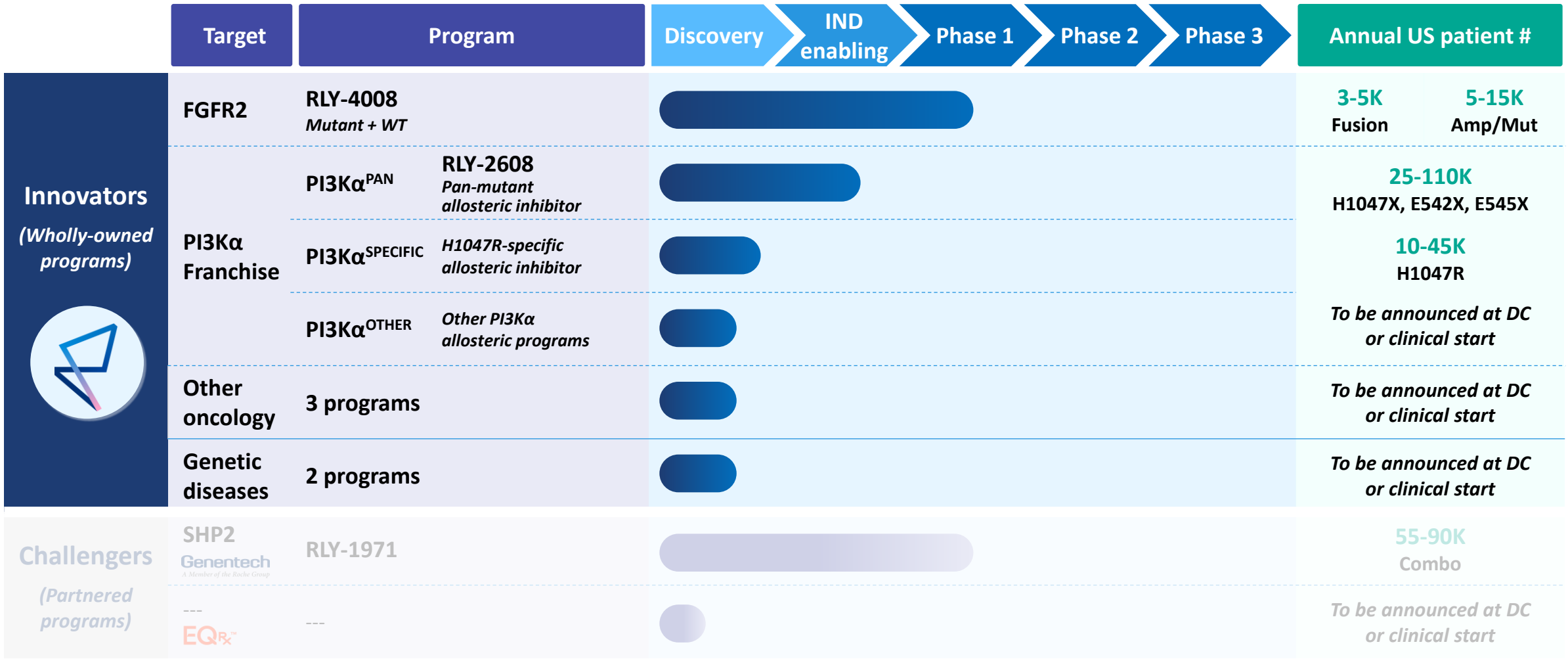
Execution focus underpins value creation

*Subject to submission and acceptance of IND by the FDA

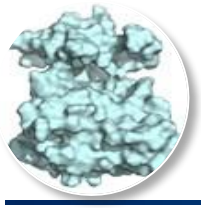


Relay Tx Programs

Extensive Precision Medicines Pipeline – Innovators



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



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

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Early Efficacy	**Early evidence of tumor regressions across several tumor and alteration types** *(with 3 out of 6 fusion positive cholangiocarcinoma FGFR-inhibitor naïve patients exhibiting confirmed PRs)*

Implications for Relay Tx

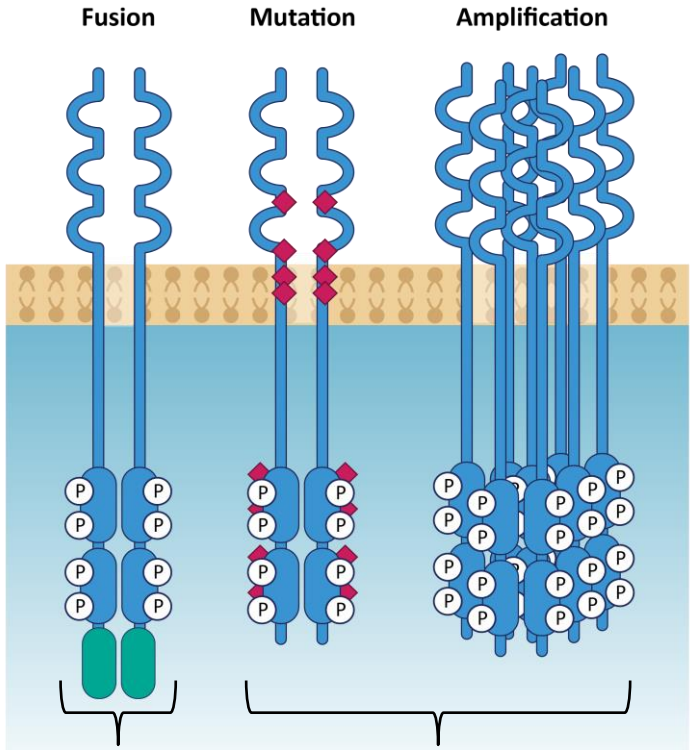
RLY-4008 data support:

- **Relay Tx's clinical development execution capabilities**
- **Ability to achieve rapid proof-of-concept to enable further clinical development**
- **Relay Tx's Dynamo™ platform and approach**

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

FGFR2 – Validated Target Present in Several Tumor Types

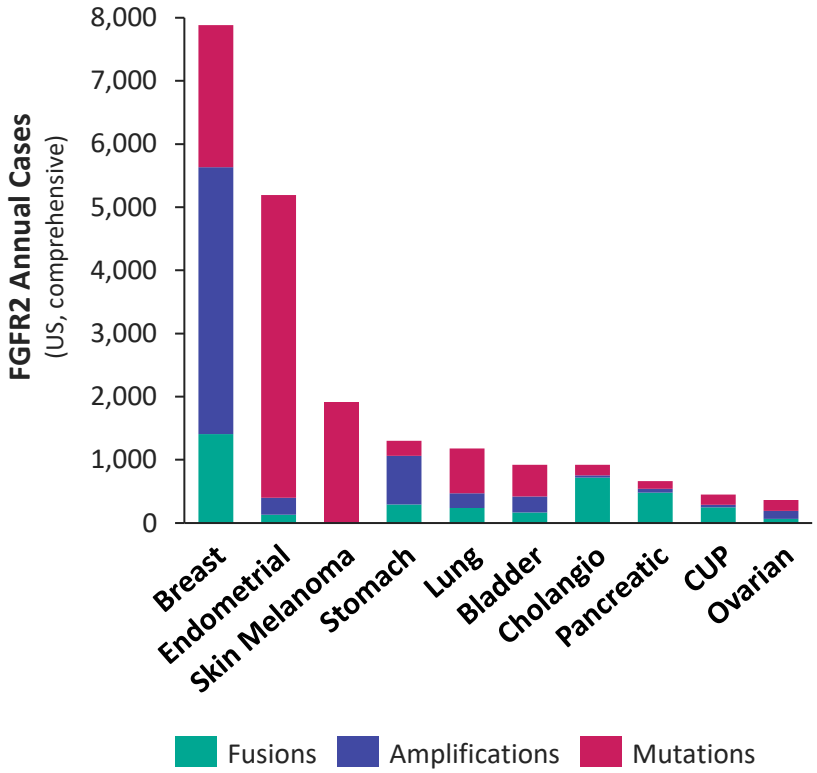
Three classes of driver alterations in FGFR2



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

Sources: FoundationInsights® database, using 8 copies as the threshold for amplification, and including only mutations with known or likely functional significance; SEER and ACS databases

1. Patient #'s refer to total annual number of US patients with late-line cancers vs. comprehensive annual incidence that may be amenable to treatment with our programs; 2. Cholangio, cholangiocarcinoma; CUP, carcinoma unknown primary

FGFR2 – Selective Inhibitor Required to Address Large Unmet Medical Need

Second Line:
FGFRi Treatment Naïve Precedent

FGFRi treatment naïve patient population

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

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

High toxicity limits efficacy of non-selective FGFR inhibitors

Late-Line:
Retreating with Chemo Precedent

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

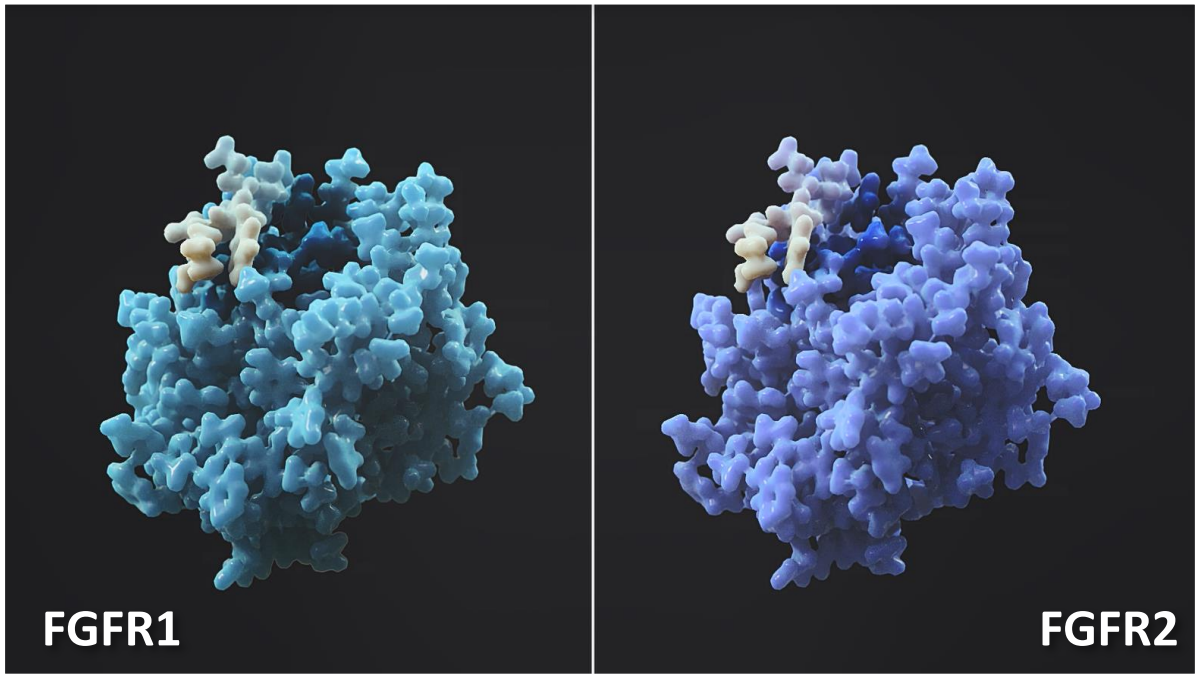
Late-line treatment with chemotherapy can be highly toxic and only results in incremental efficacy

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

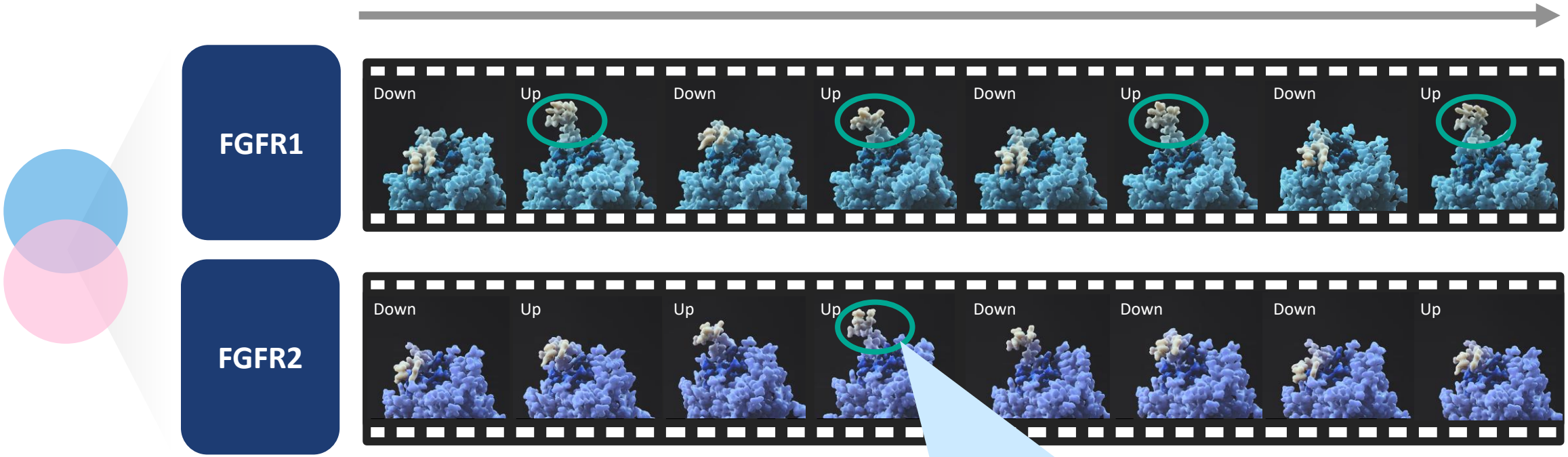
Sources: Pemigatinib – Prescribing information; Infigratinib – Prescribing information; Futibatinib/TAS-120 – AACR 2021 (diarrhea %s approximated from presentation); Erdafitinib – Prescribing information; N.R. = not reported; FOLFOX – ABC-06 Publication in Lancet Oncology 2021

FGFR2 – Standard Approach to Discovery Has Had Limited Success

Standard Approach



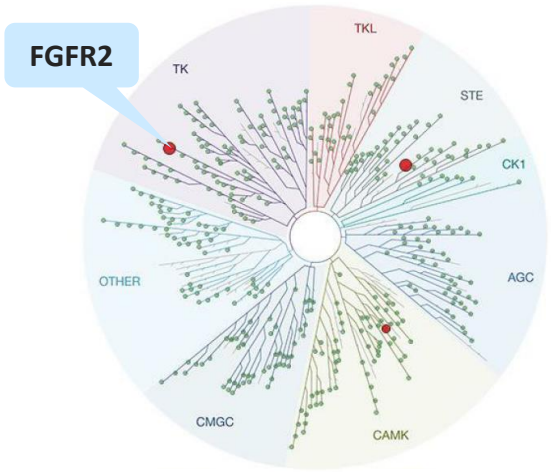
FGFR2 – Increasing Experimental Resolution Reveals New Opportunities



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

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

RLY-4008

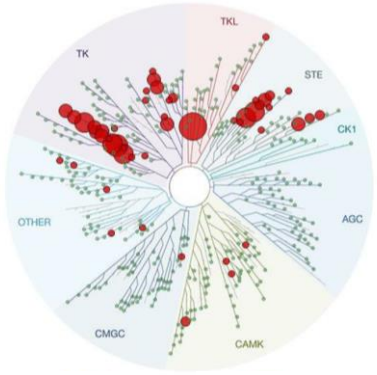


Percent Control

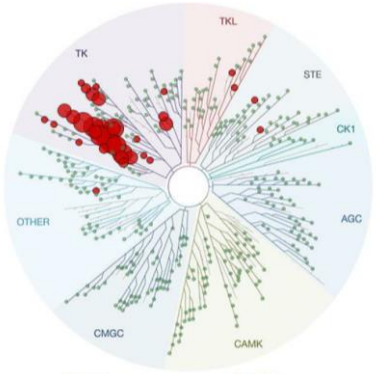
- 0%
- 0.1%
- 0.1-1%
- 1-5%
- 5-10%
- 10-35%
- > 35%

Pan-FGFR Inhibitors

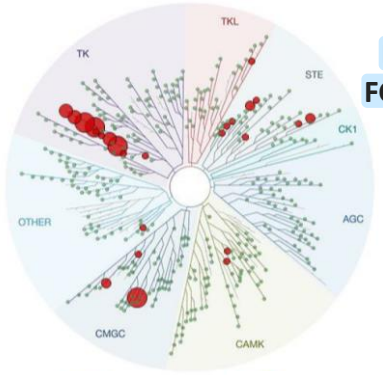
AZD4547



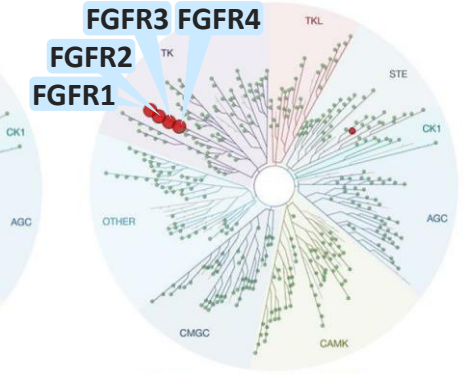
Erdafitinib



Pemigatinib



Futibatinib



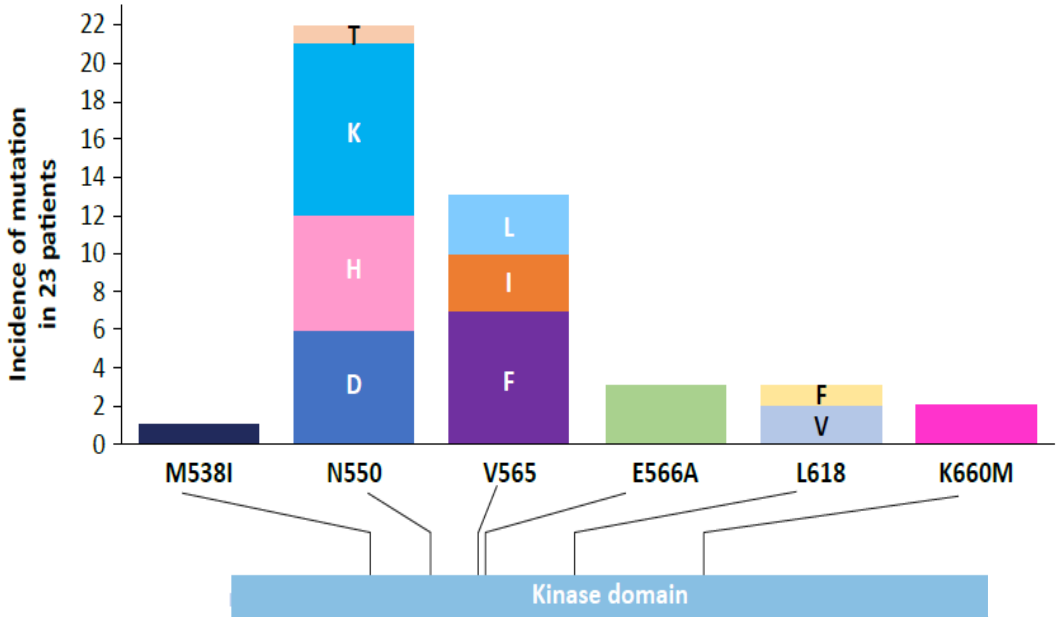
Percent Control

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

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

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

Reported on target resistance mutations for pan-FGFR inhibitors



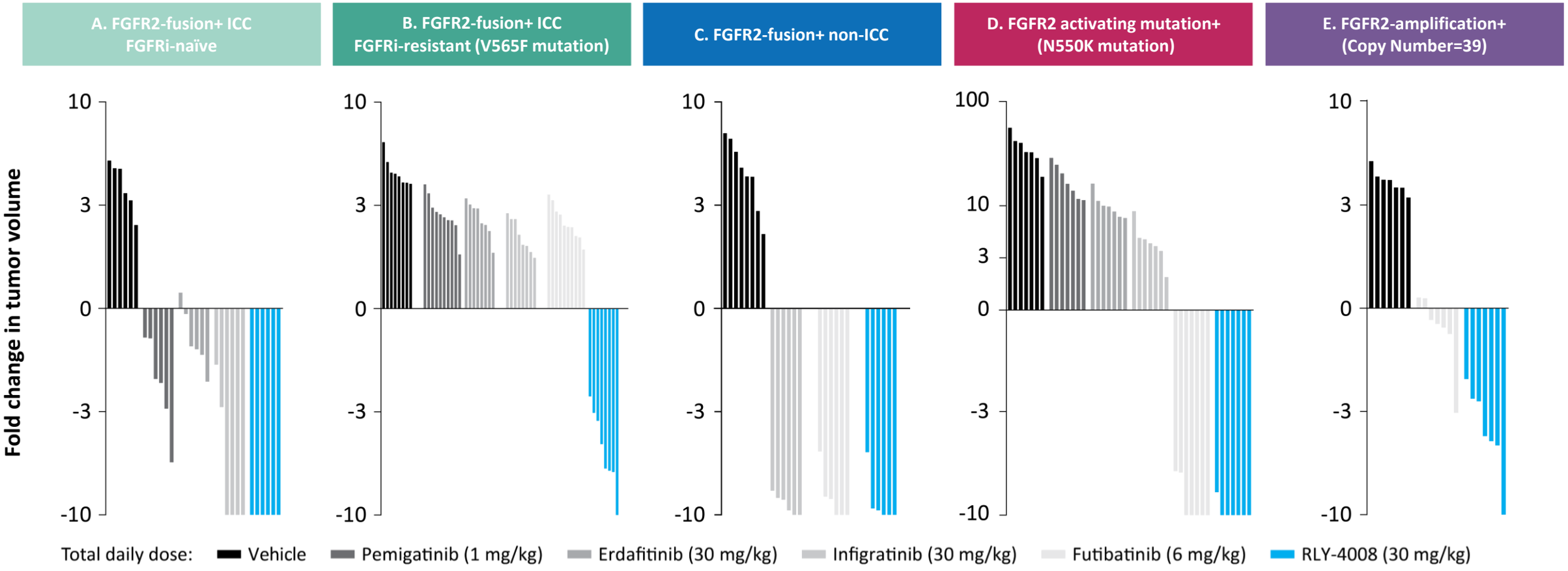
Activity against acquired resistance mutations

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

KEY:
Potency Fold Change
1 25 >50
Decreasing potency on resistance mutation

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

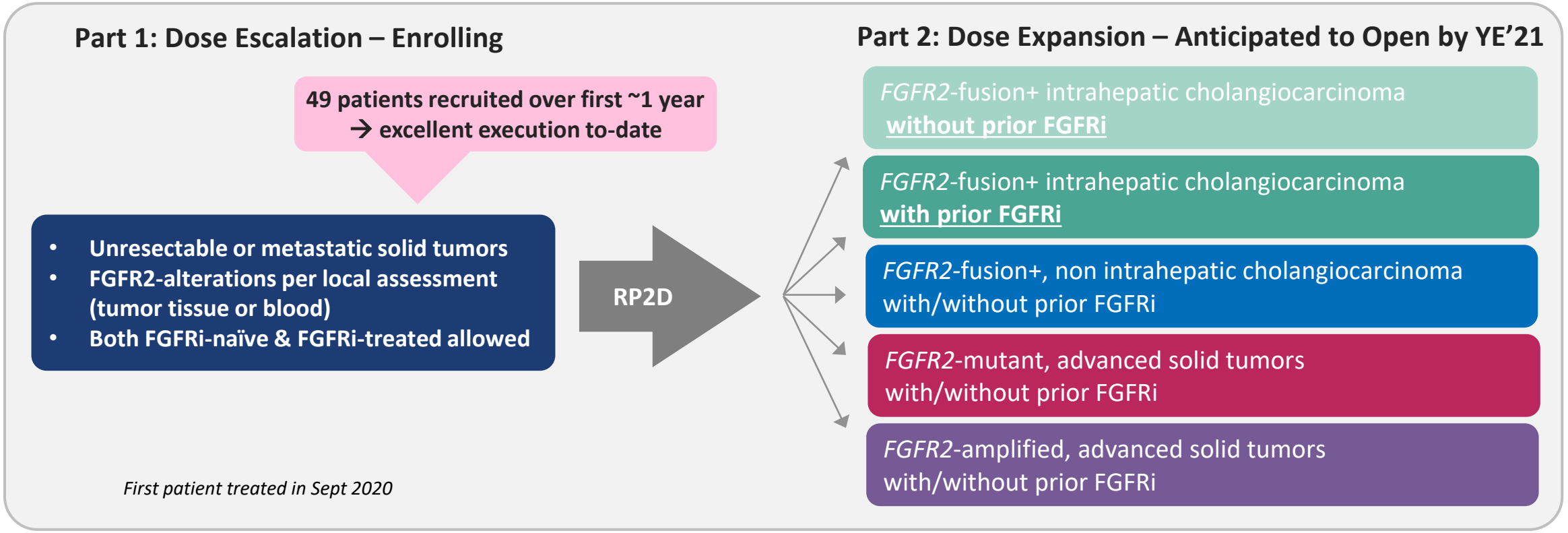
FGFR2 – RLY-4008 Has Potent *In Vivo* Antitumor Activity Against Primary FGFR2 Alterations and Common Resistance Mutations



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

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

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



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

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

FGFR2 – RLY-4008 FIH Study: Baseline Characteristics

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

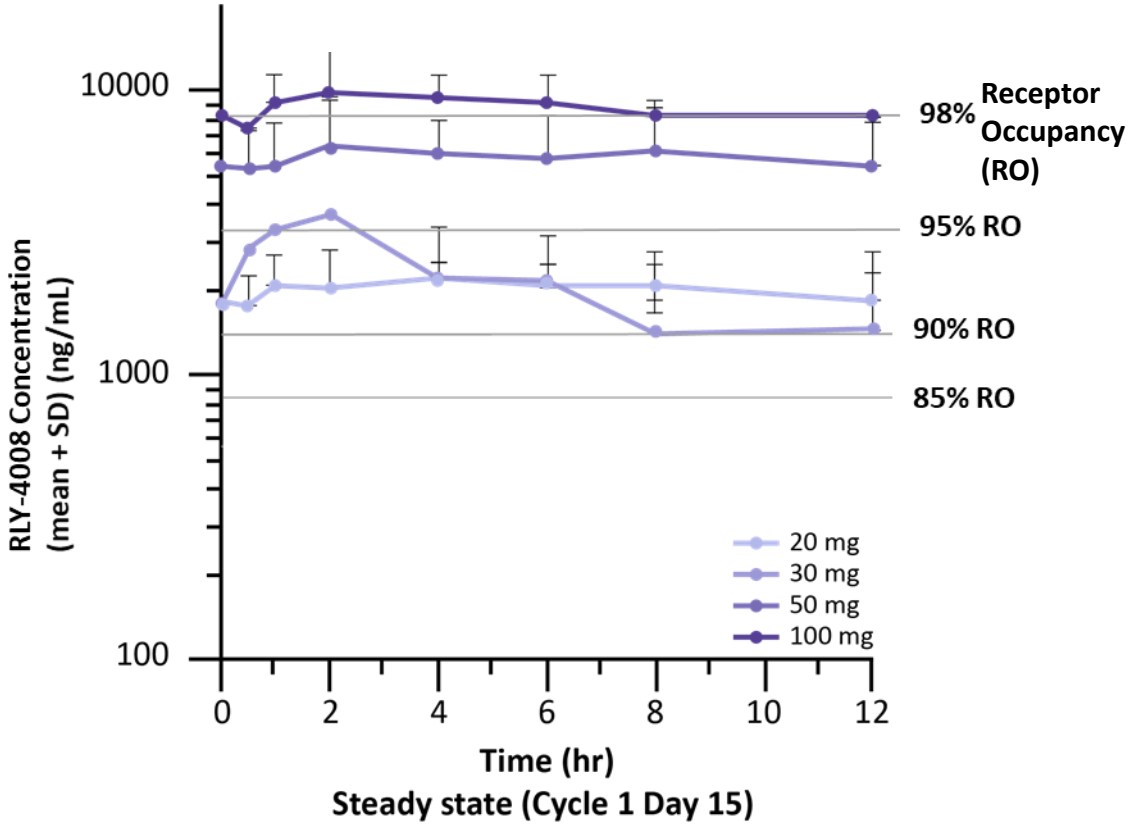
Parameter	Total (N=49)
Tumor types, n (%)	
Cholangiocarcinoma (CCA)	40 (82%)
Breast cancer	4 (8%)
Endometrial cancer	1 (2%)
Prostate adenocarcinoma	1 (2%)
Soft-tissue sarcoma*	1 (2%)
Uterus	1 (2%)
Melanoma (rectum)	1 (2%)
Baseline sum of target lesions (RECIST v1.1, cm), median (range)	**9.3 cm (1.4-22.0)**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

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

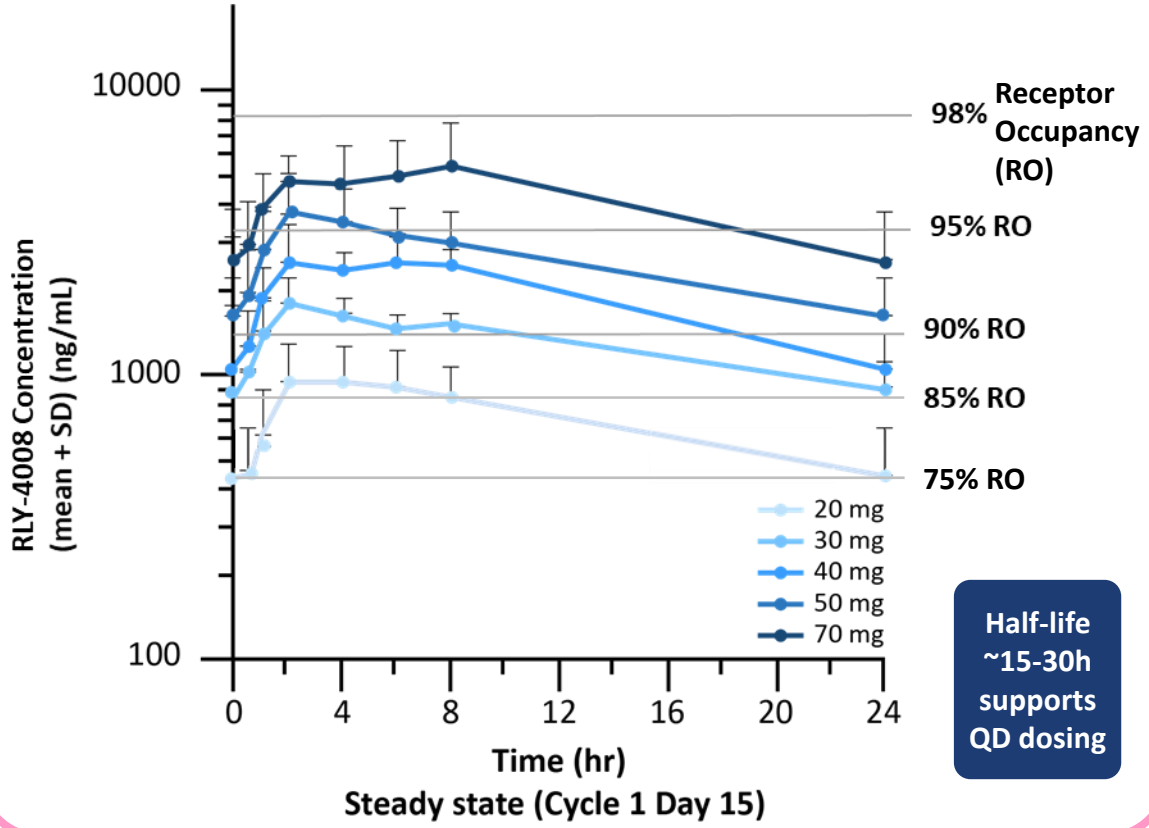
Preliminary data as of 09-Sept-2021

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

RLY-4008 BID Schedule



RLY-4008 QD Schedule



Half-life ~15-30h supports QD dosing

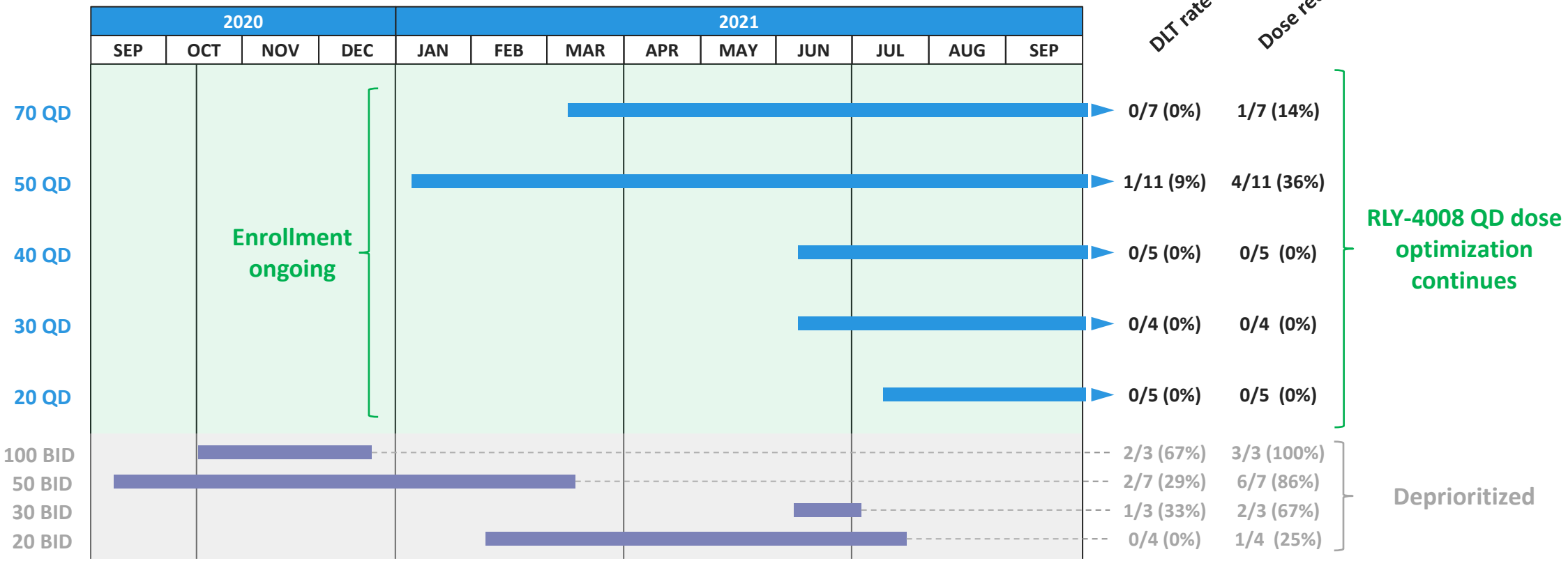
RLY-4008 showed ≥85 % predicted median receptor occupancy (based on modeling) across all dose levels
Pemigatinib 13.5mg QD achieves 76% inhibition of FGFR2 at trough*

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

Preliminary data as of 09-Sept-2021

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

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



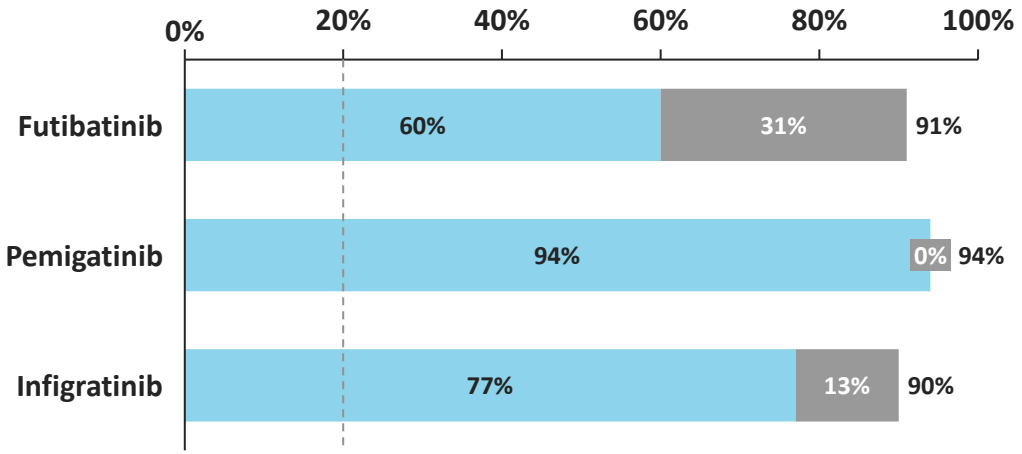
MTD not defined per protocol, RP2D selection is ongoing with the QD dosing schedule

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

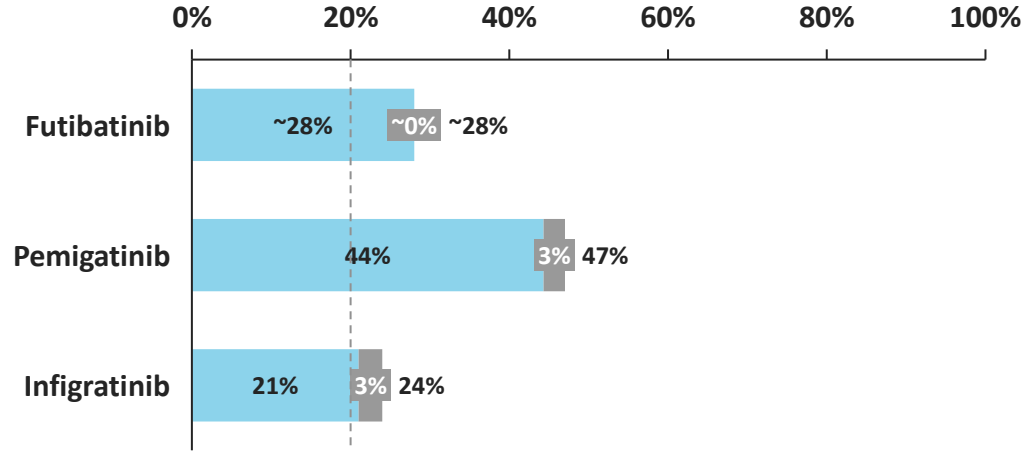
Preliminary data as of 09-Sept-2021

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

Hyperphosphatemia



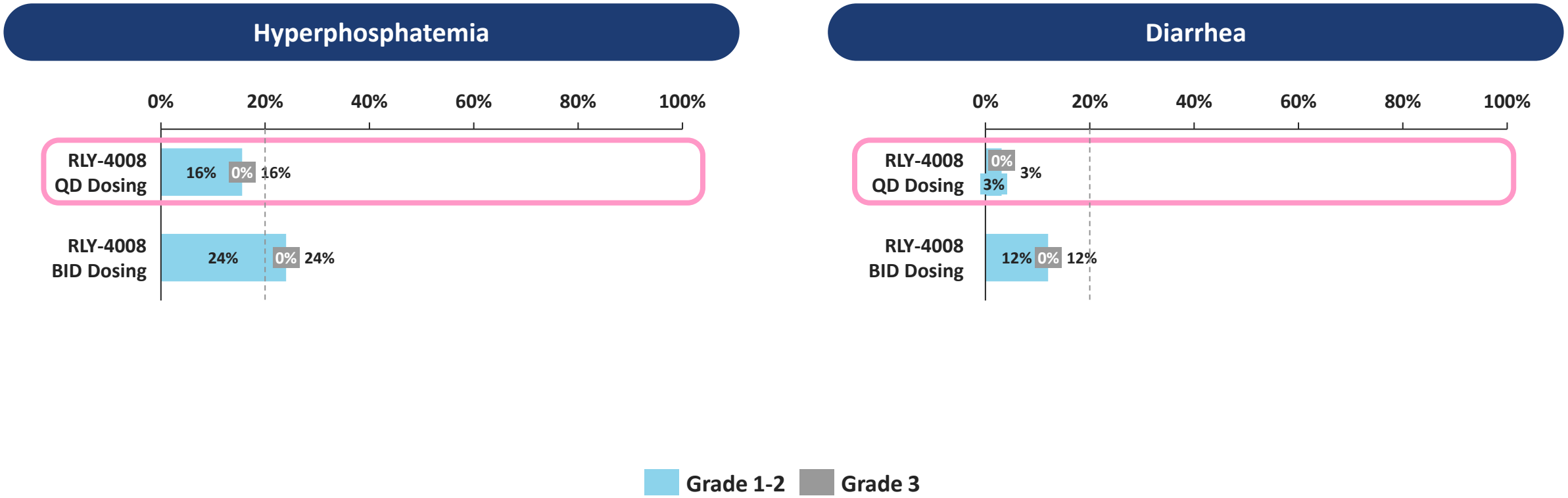
Diarrhea



Grade 1-2 Grade 3+

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

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

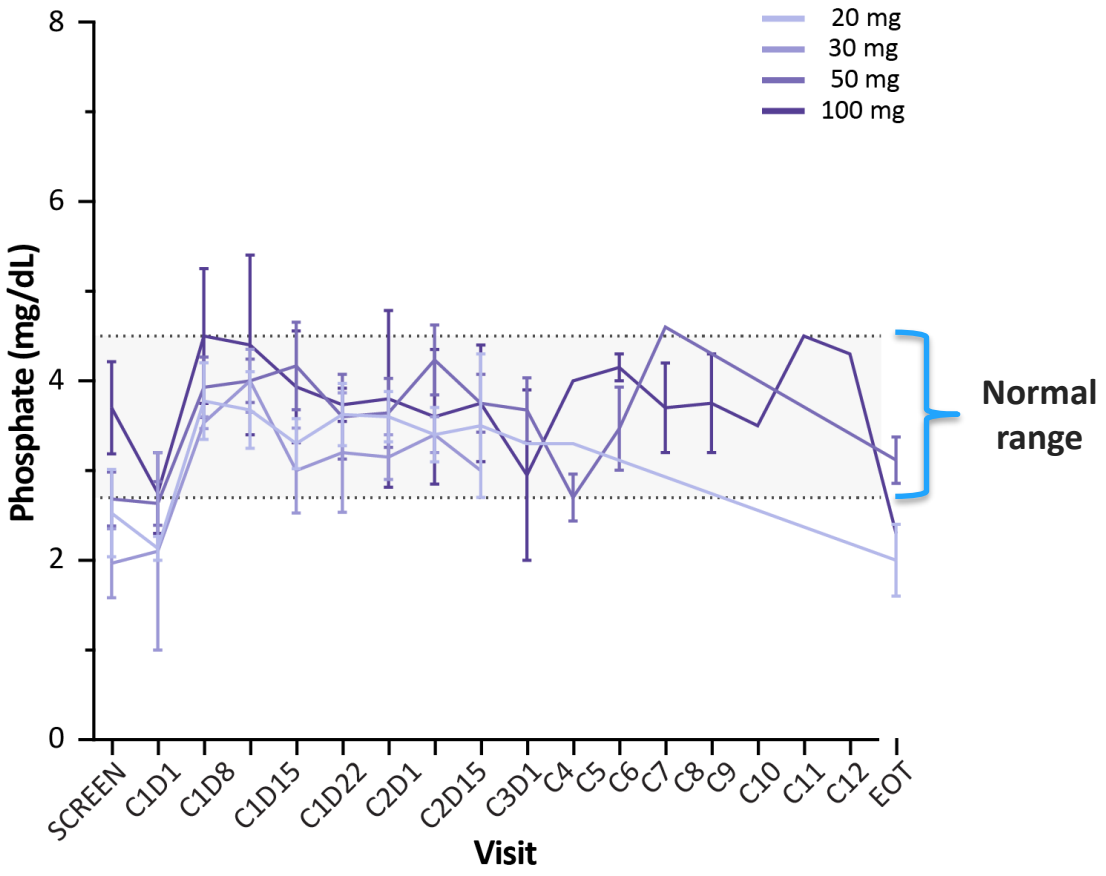


Source: RLY-4008 data as presented at 2021 AACR-NCI-EORTC Molecular Targets Conference

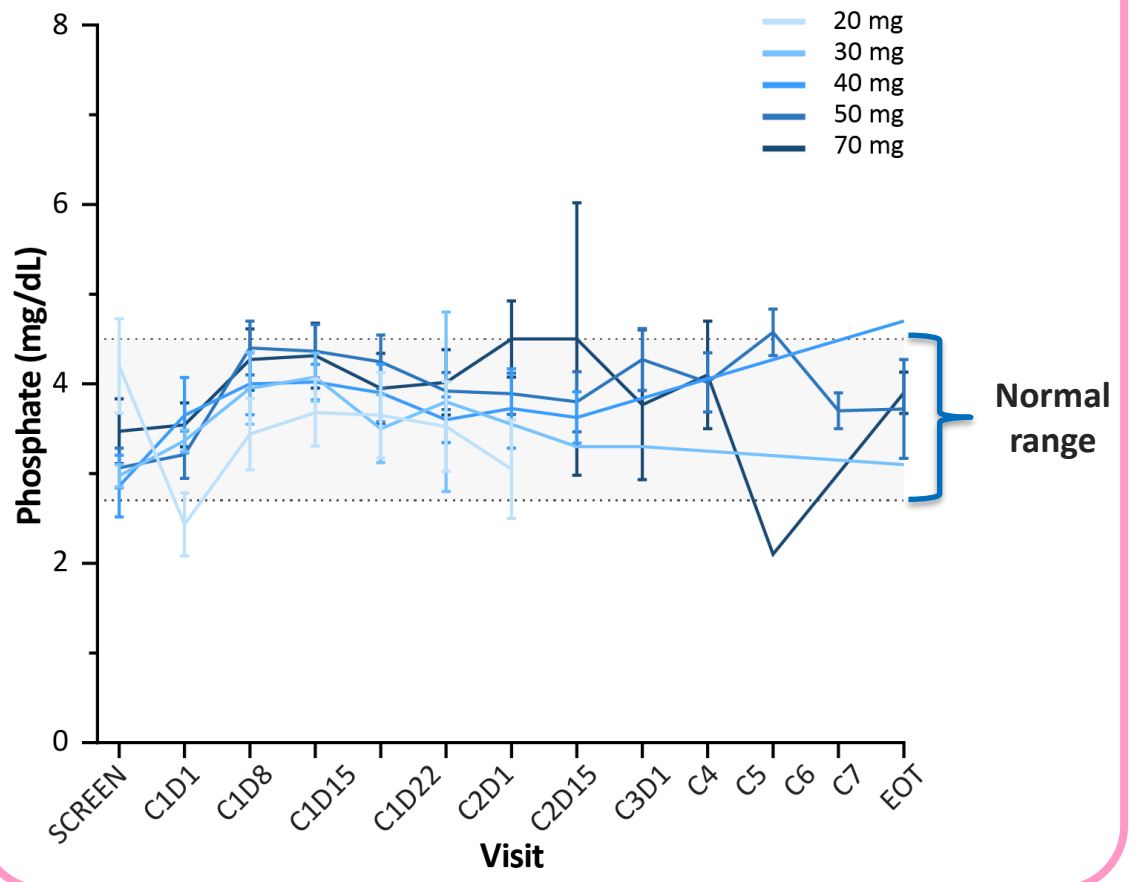
Preliminary data as of 09-Sept-2021

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

BID Schedule



QD Schedule

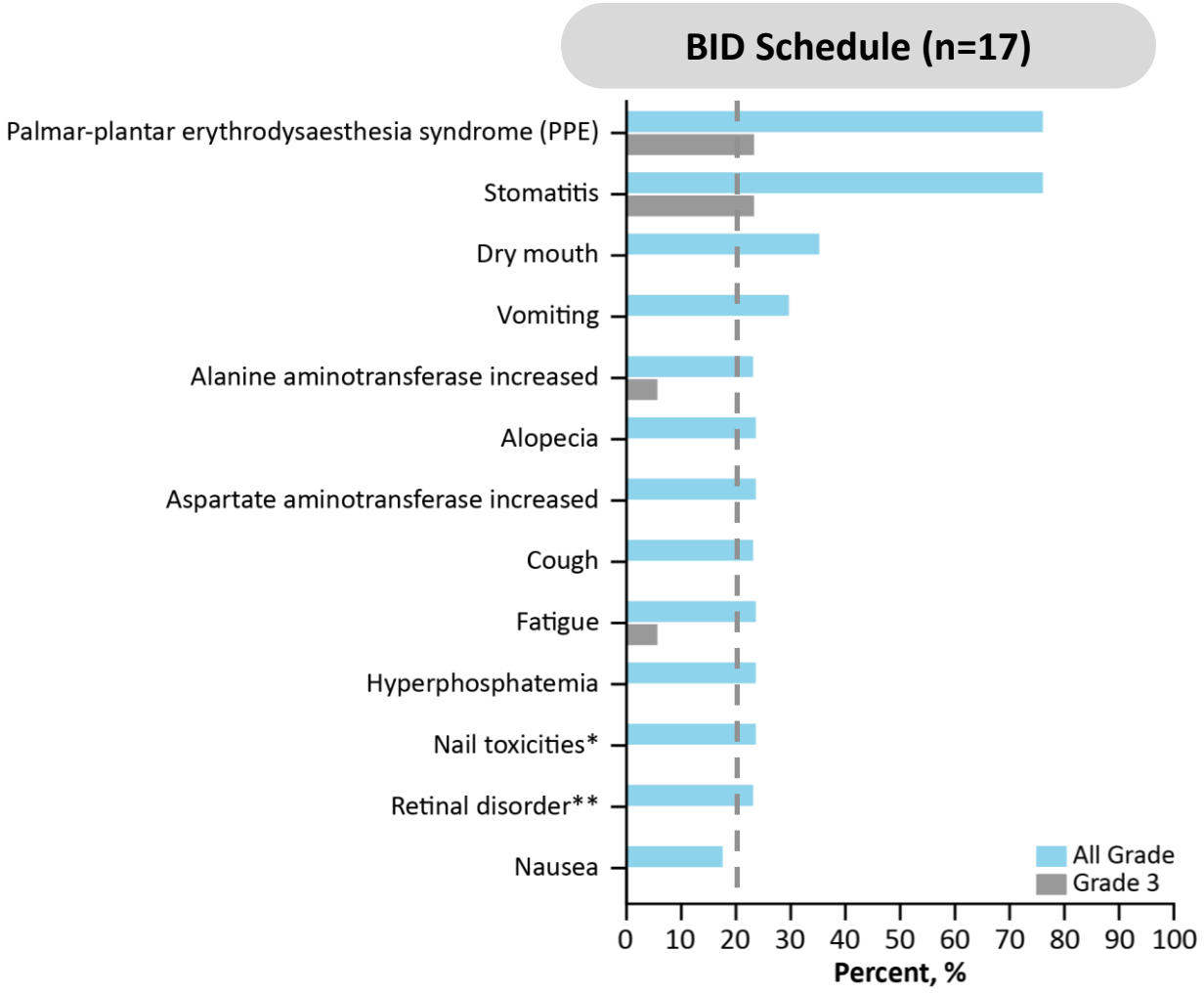


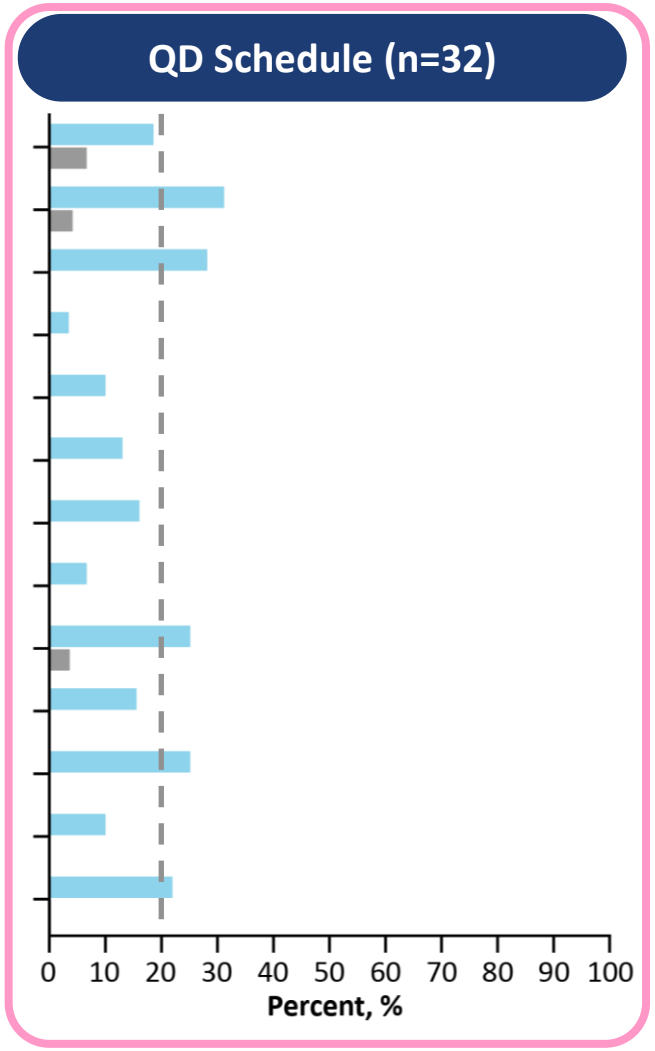
FGFR1 sparing: Hyperphosphatemia: n=9/49 (18%) patients, all low grade (Grade 1-2). Only 1/49 (2%) patients was prescribed phosphate binders.
FGFR4 sparing: Diarrhea: n=3/49 (6%) patients, all low grade (Grade 1-2) and unrelated.

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

Preliminary data as of 09-Sept-2021

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





No Grade 4-5 AE

Most AEs are low-grade, including hyperphosphatemia and diarrhea

- **TEAEs profile consistent with FGFR1- and FGFR4-sparing**

Retinopathy/Retinal Pigment Epithelial Detachment (RPED):

- **7 cases**
- **BID n=4/17 (24%)**
- **QD n=3/32 (9%)**
- **All events were Gr 1-2, self-limiting or resolved upon treatment interruption**

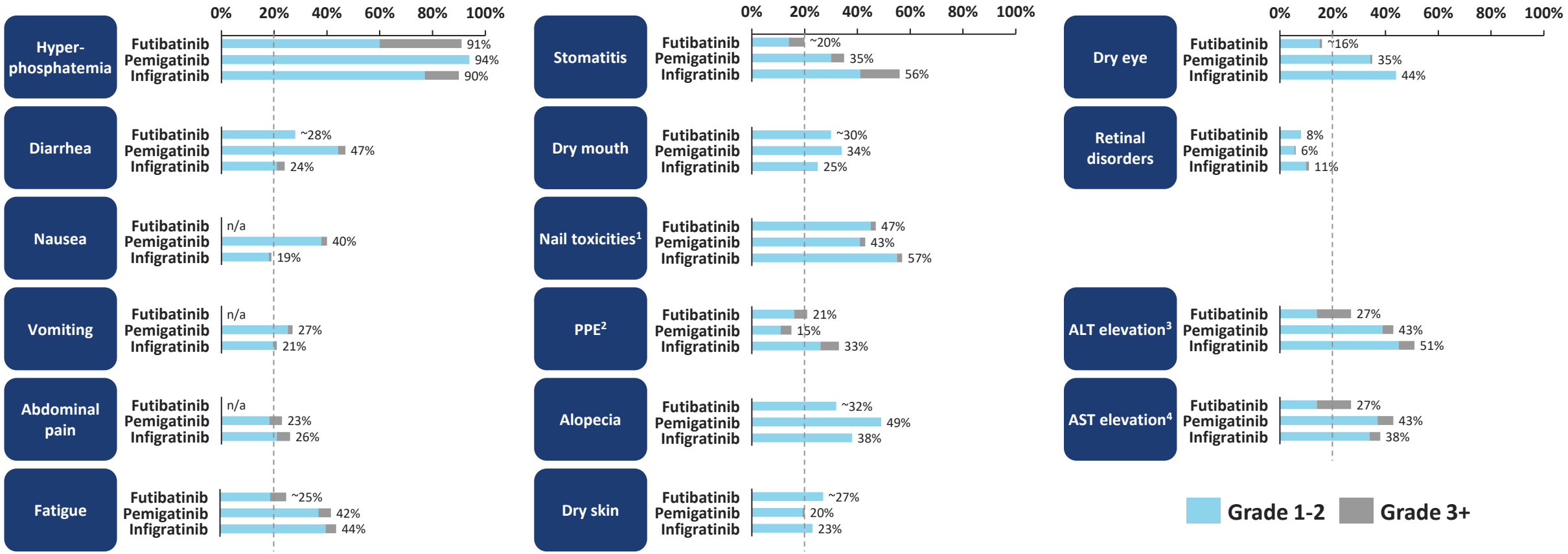
RLY-4008 QD dosing
Dry eye: 9% all grades, 0% grade 3+
Corneal AEs: 13% all grades, 0% grade 3+

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

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

Preliminary data as of 09-Sept-2021

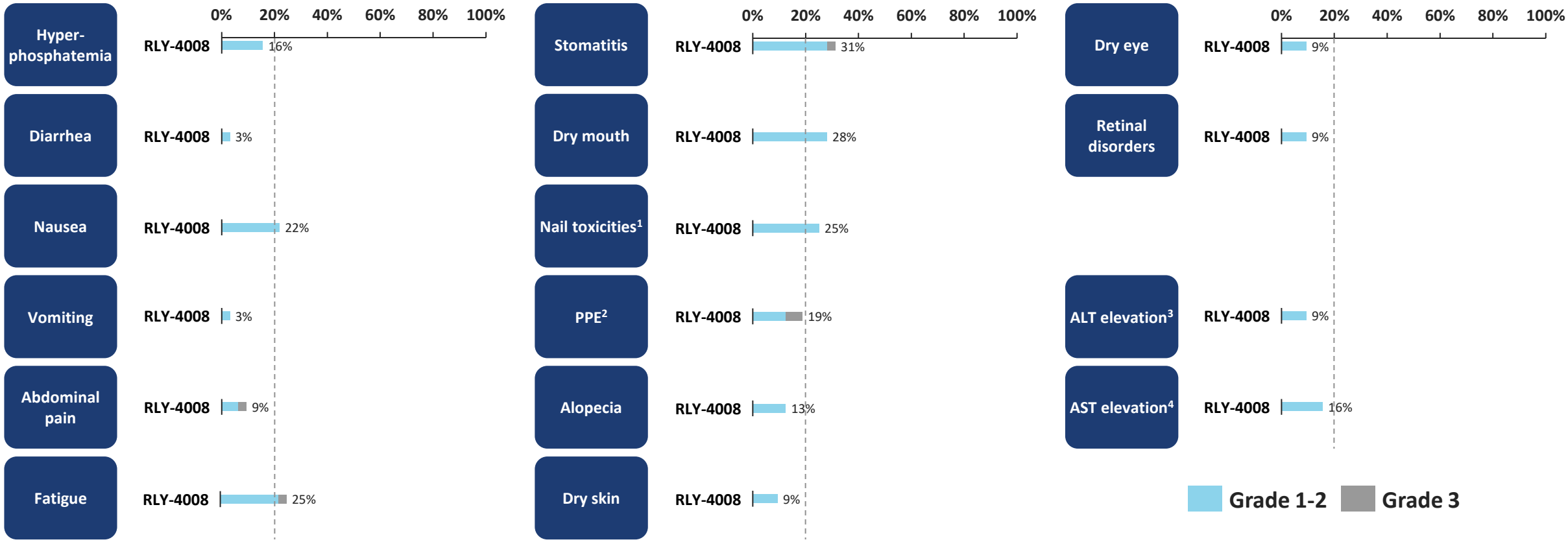
Tolerability Profile of Pan-FGFR Inhibitors



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

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

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



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

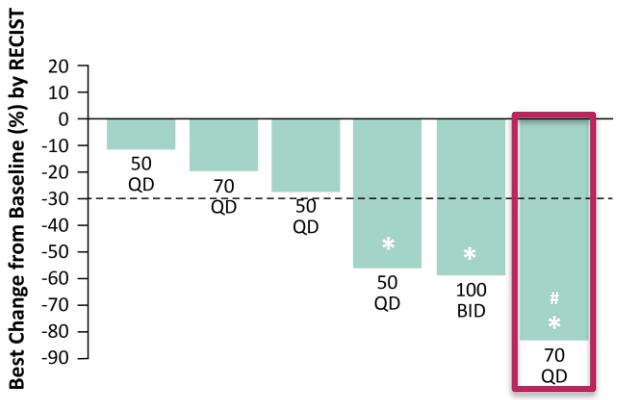
Source: RLY-4008 data as presented at 2021 AACR-NCI-EORTC Molecular Targets Conference

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

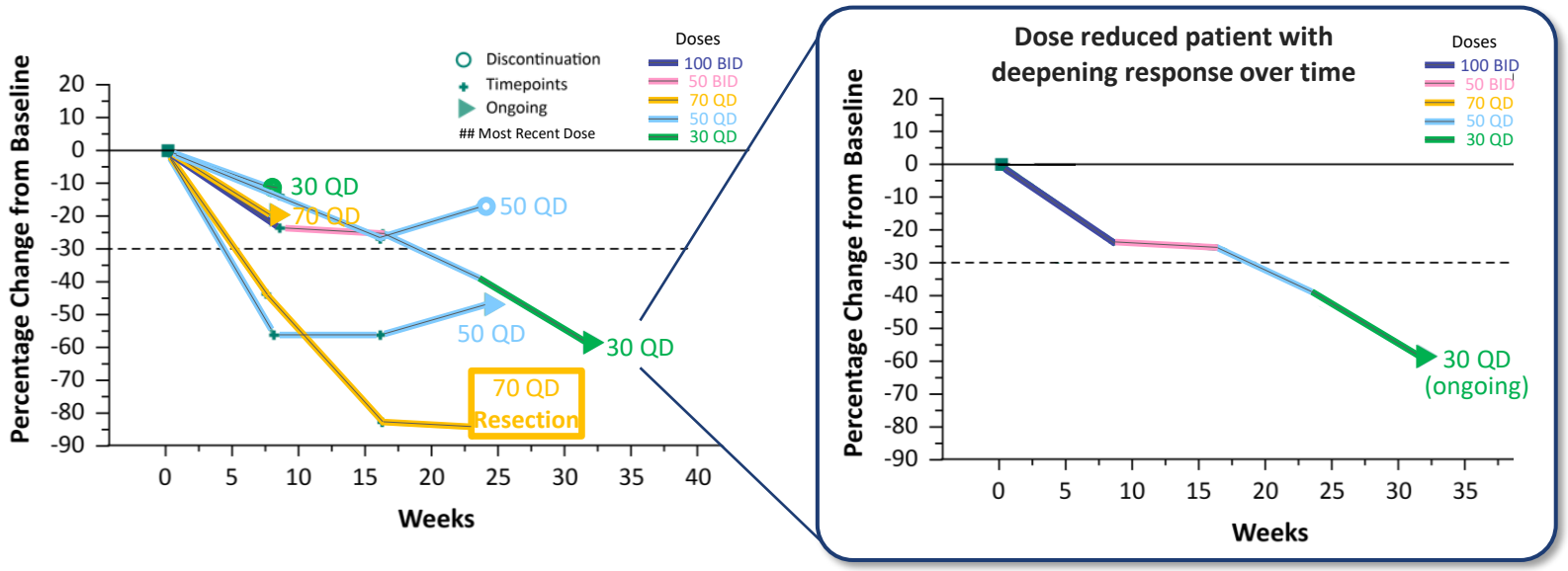
Preliminary data as of 09-Sept-2021

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

Best RECIST change from baseline



Relative change from baseline in tumor size



3/6 patients exhibit a confirmed PR

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

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

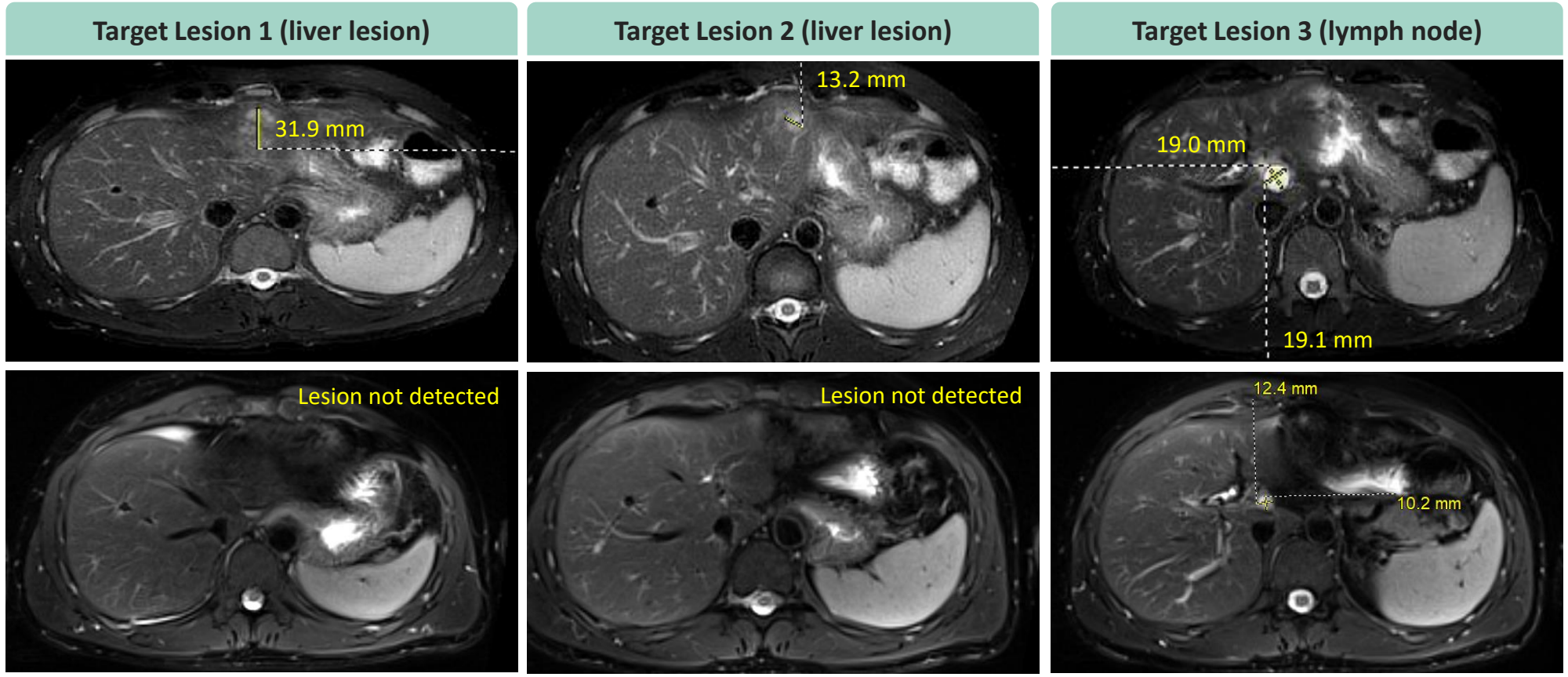
Source: RLY-4008 data as presented at 2021 AACR-NCI-EORTC Molecular Targets Conference
*Confirmed PR; #Tumor resection after data cut off.
FGFRi, fibroblast growth factor receptor inhibitor PR, partial response.

Preliminary data as of 09-Sept-2021

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

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

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



31.9 mm → Not detected

13.2 mm → Not detected

19.0 mm → 10.2 mm

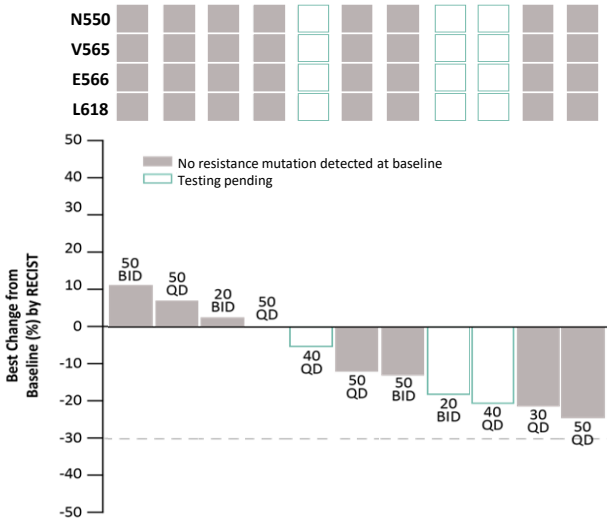
Confirmed PR (near CR) -83% by RECIST v1.1

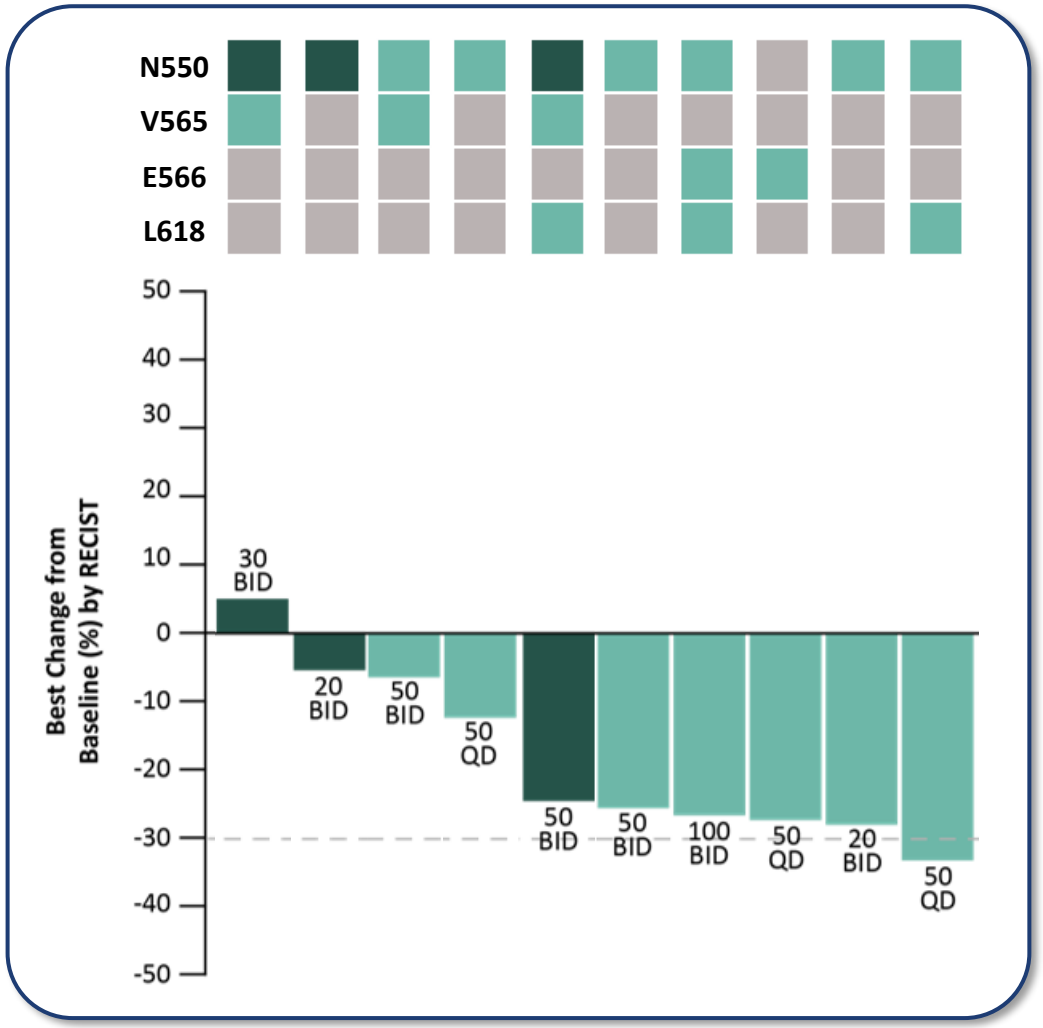
Patient underwent resection with curative intent

Source: RLY-4008 data as presented at 2021 AACR-NCI-EORTC Molecular Targets Conference
Courtesy: Dr. V. Sahai (U Michigan)

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

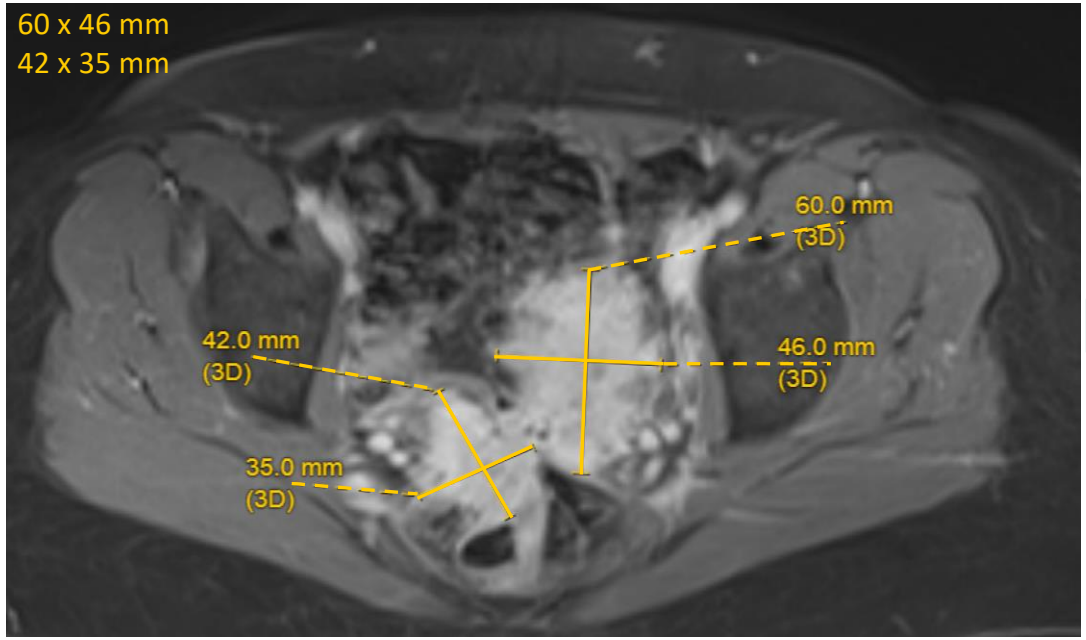
Preliminary data as of 09-Sept-2021

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

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

Baseline

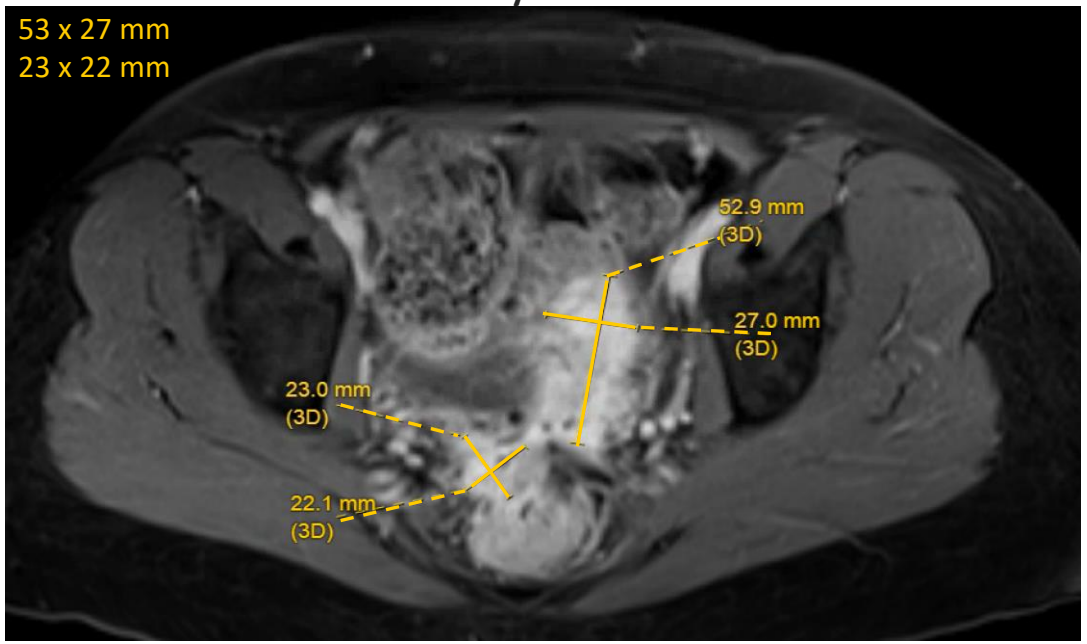
Pelvic lesions



Sustained tumor reduction at Cycle 7

- 21% by RECIST v1.1

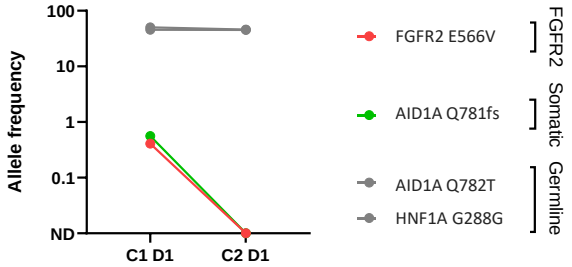
Cycle 7



<u>Antitumor activity:</u>
Sustained tumor reduction at C7 (-21% per RECIST v1.1)

<u>Safety and tolerability:</u>
No dose interruption or modification
RLY-4008 treatment is ongoing (50 mg QD)

<u>ctDNA:</u>
Baseline FGFR2-E566V mutation is undetectable at C2D1



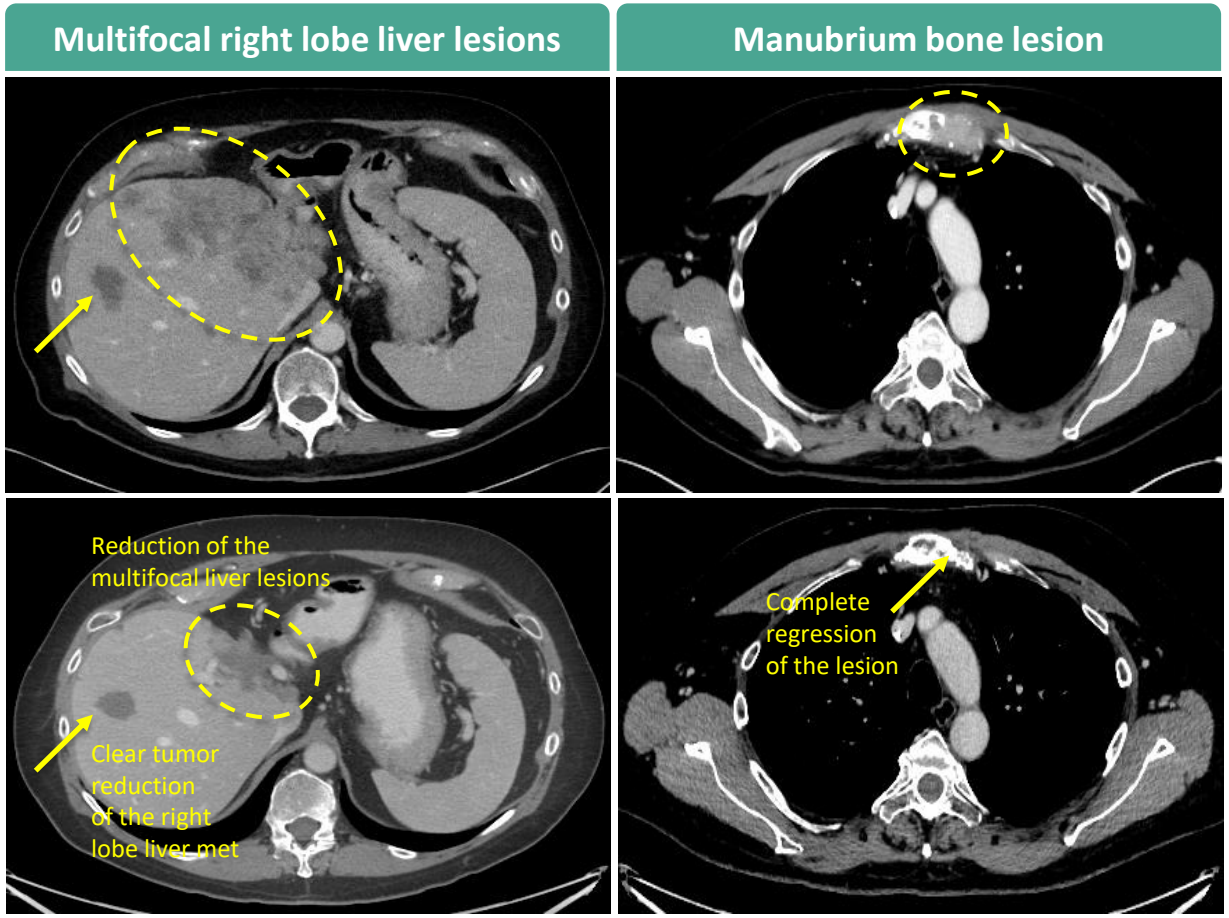
Source: RLY-4008 data as presented at 2021 AACR-NCI-EORTC Molecular Targets Conference
Note: E566 and E565 are different terminology for the same mutated site
Courtesy: Dr. L. Goyal (Mass. General Hospital)

Preliminary data as of 09-Sept-2021

Unconfirmed PR

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

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



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

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

No dose interruption
No dose reduction

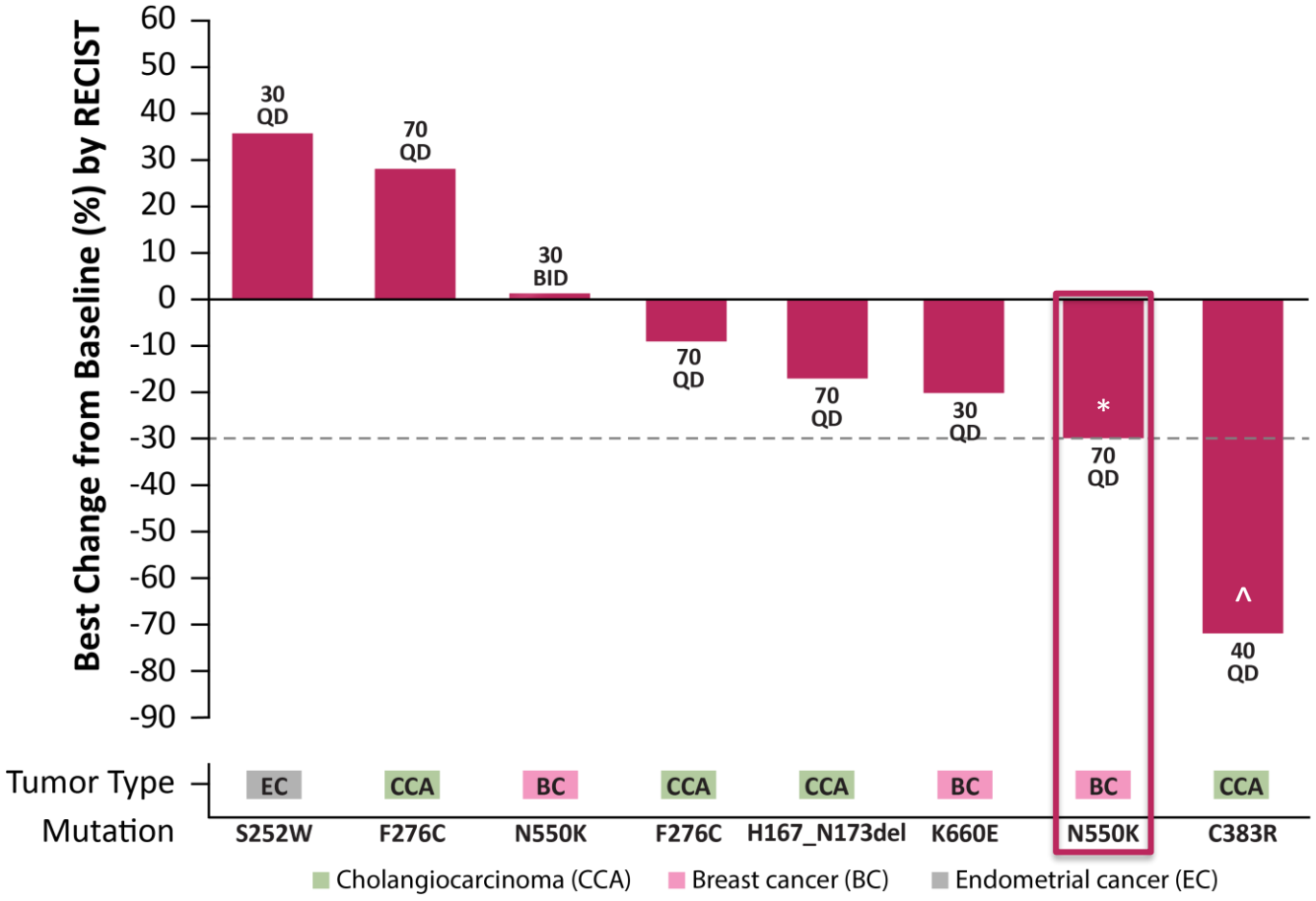
Efficacy data received after data lock and not included in the October 8 AACR-NCI-EORTC Molecular Targets Conference presentation data

Note: (N550, N549), (V565, V564) are different terminology for the same mutated site
Courtesy: Dr. V. Subbiah (MD Anderson)

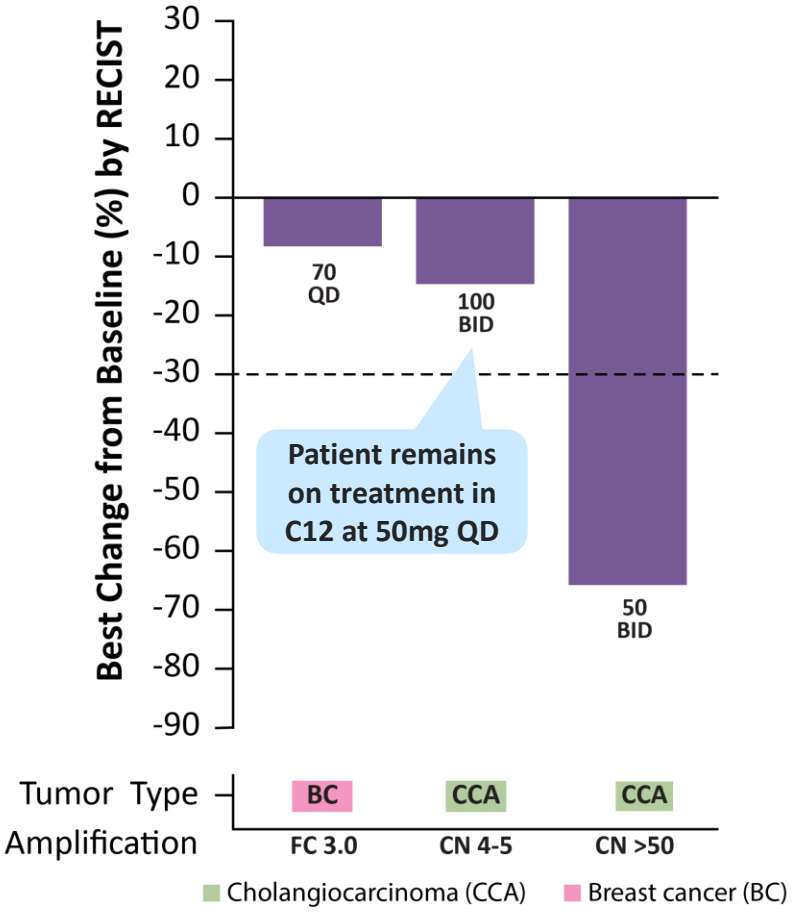
Data as of 01OCT21- post data lock

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

FGFR2 Oncogenic Mutations



FGFR2 Amplifications



No FDA-approved FGFR targeted therapies

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

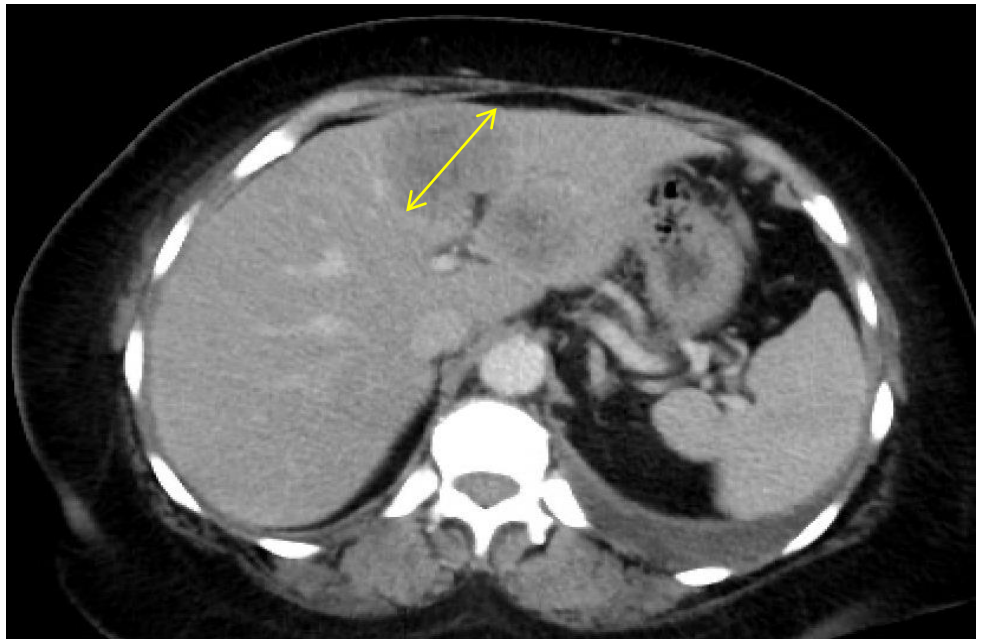
Preliminary data as of 09-Sept-2021

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

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

Liver lesion

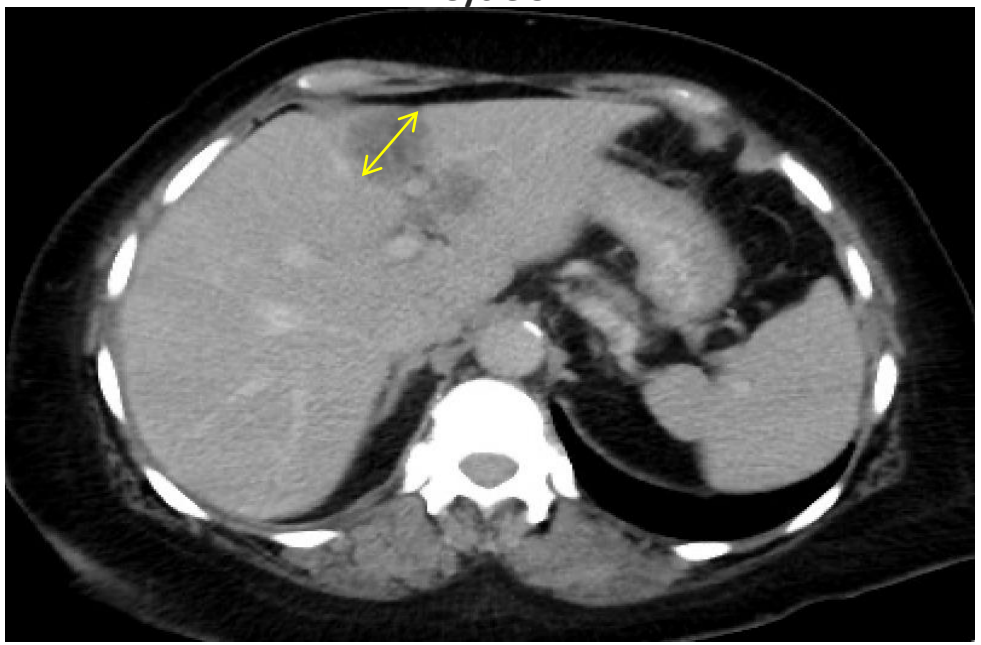
Baseline



Confirmed PR at Cycle 5

- 41% by RECIST v1.1

Cycle 5



Antitumor activity:

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

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

Safety and tolerability

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

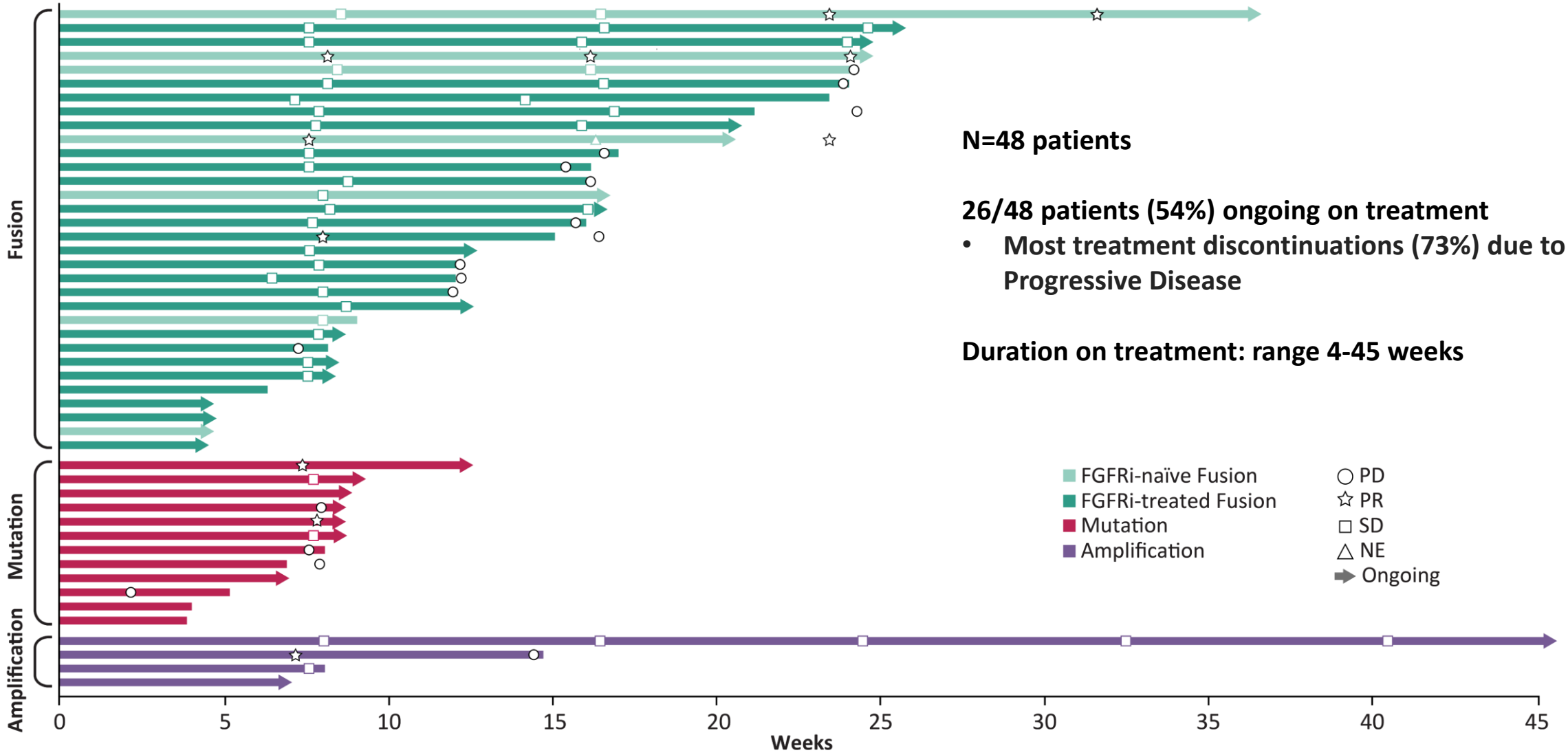
No dose reduction; RLY-4008 treatment is ongoing (70 mg QD)

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

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

Preliminary data as of 09-Sept-2021

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



N=48 patients

26/48 patients (54%) ongoing on treatment

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

Duration on treatment: range 4-45 weeks

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

FGFRi, fibroblast growth factor receptor inhibitor; NE, not evaluable; PR, partial response; PD, progressive disease; SD, stable disease.

Preliminary data as of 09-Sept-2021

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

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

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

Preliminary data as of 09-Sept-2021

PI3Kα – Highlights from Recent RLY-2608 Preclinical Data Disclosure

RELAY THERAPEUTICS

RLY-2608 Data

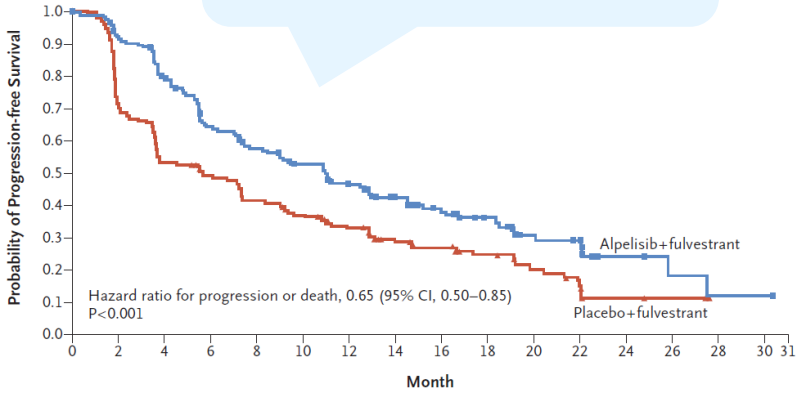
Novel Mechanism	**Mutant-selective binding to novel allosteric site discovered by Dynamo™ platform**
Pan-Mutant Selectivity	**Inhibited not only H1047X, but also E542X and E545X, potentially doubling the addressable population, while sparing WT PI3Kα**
Tolerability	**Achieved tumor regressions in vivo at doses projected to be clinically relevant with significantly reduced impact on glucose metabolism compared to non-mutant selective inhibitors**
Approaching Clinic	**First-in-human study anticipated to start in 1H22***
Implications for Relay Tx	**RLY-2608 represents the start of Relay Tx's emerging PI3Kα franchise**

*Subject to submission and acceptance of IND by the FDA

PI3Kα – Existing Inhibitors Establish POC but Have Limited Therapeutic Window

Alpelisib + fulvestrant vs. placebo + fulvestrant

Confirmed response rate:
Alpelisib + Fulvestrant 26.6%
Placebo + Fulvestrant 12.8%

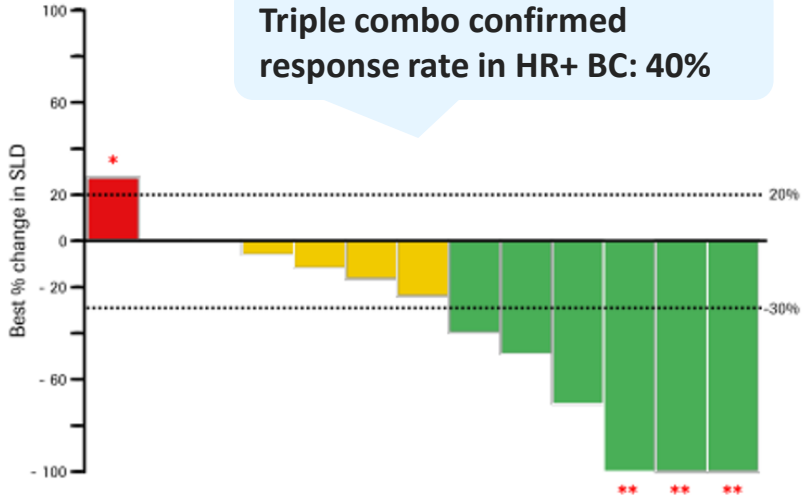


- **Dose modifications: 64%**
- **Hyperglycemia: 64% (36% Grade 3/4)**
- **GI toxicity: 58%**
- **Rash: 36%**

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

GDC-0077 + fulvestrant + palbociclib

Triple combo confirmed response rate in HR+ BC: 40%



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

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

PI3Kα – Relay Tx Has a Unique Understanding of PI3Kα

KRAS experience teaches us pan-mutant coverage is required

Similarities between PI3K and KRAS:

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

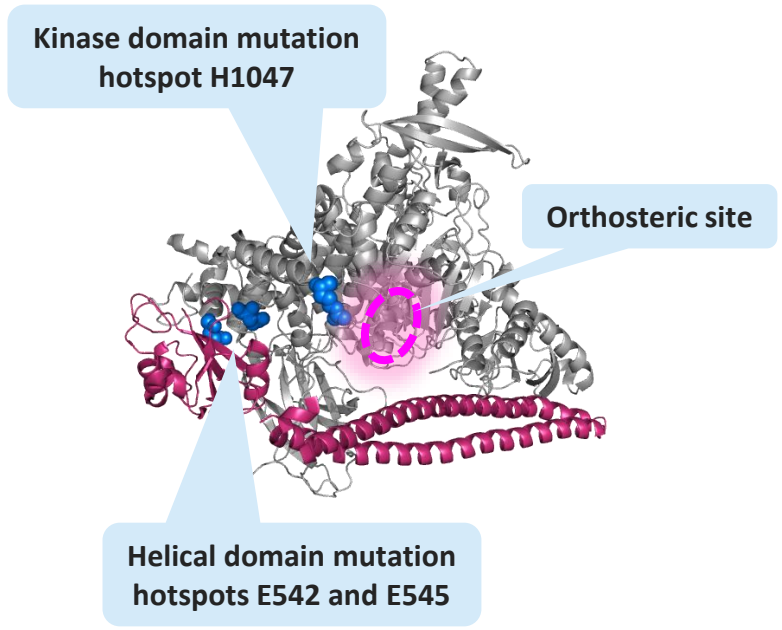
KRAS G12C

Examples of on-target resistance mechanisms

- KRAS G13D
- KRAS G12V
- KRAS Y96D

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

Relay Tx has a unique understanding of PI3Kα



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

PI3Kα Franchise

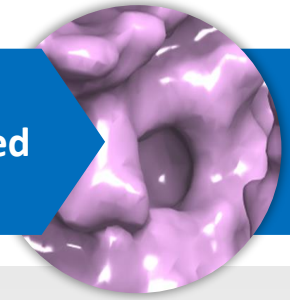
PI3Kα^{PAN}	**RLY-2608** *Pan-mutant allosteric inhibitor*
PI3Kα^{SPECIFIC}	*H1047R-specific allosteric inhibitor*
PI3Kα^{OTHER}	*Other PI3Kα allosteric programs*

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

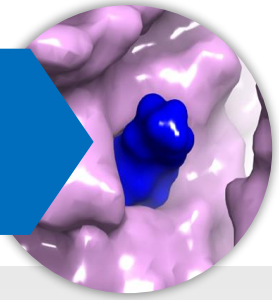
PI3Kα – Proprietary Insights Unlock Additional Approaches

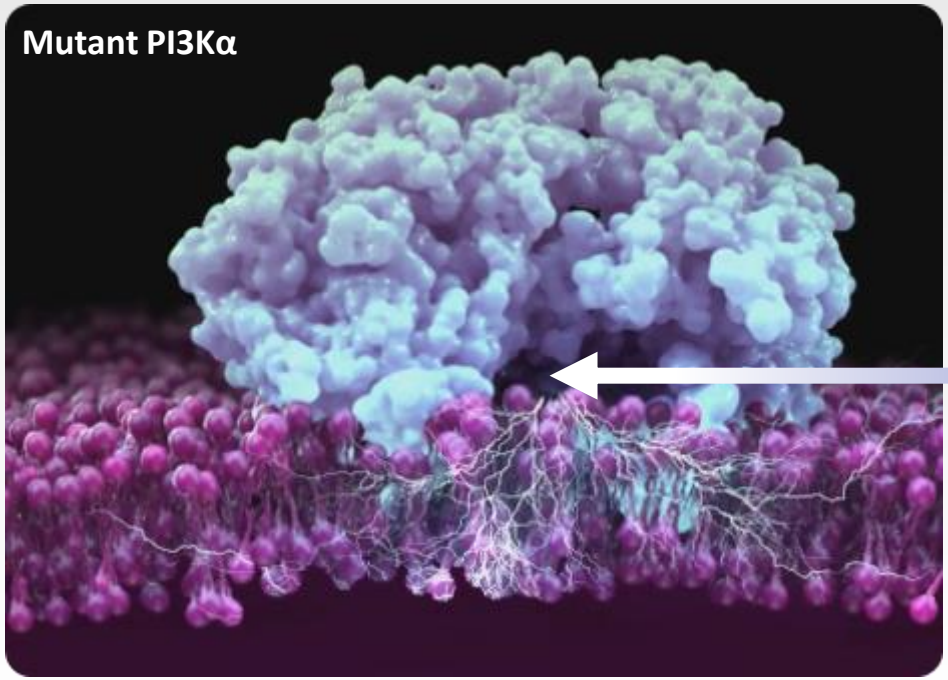
Solved first full-length structures of PI3Kα (mutant and wild-type)

Discovered novel allosteric pocket favored in mutant protein



Designed mutant selective PI3Kα inhibitor

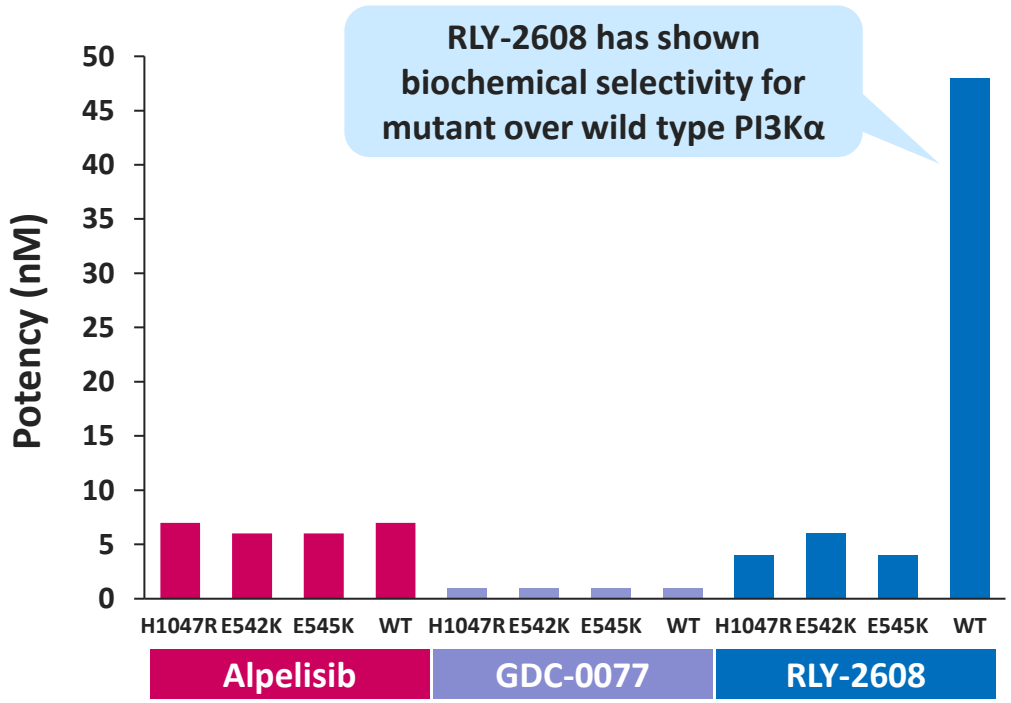




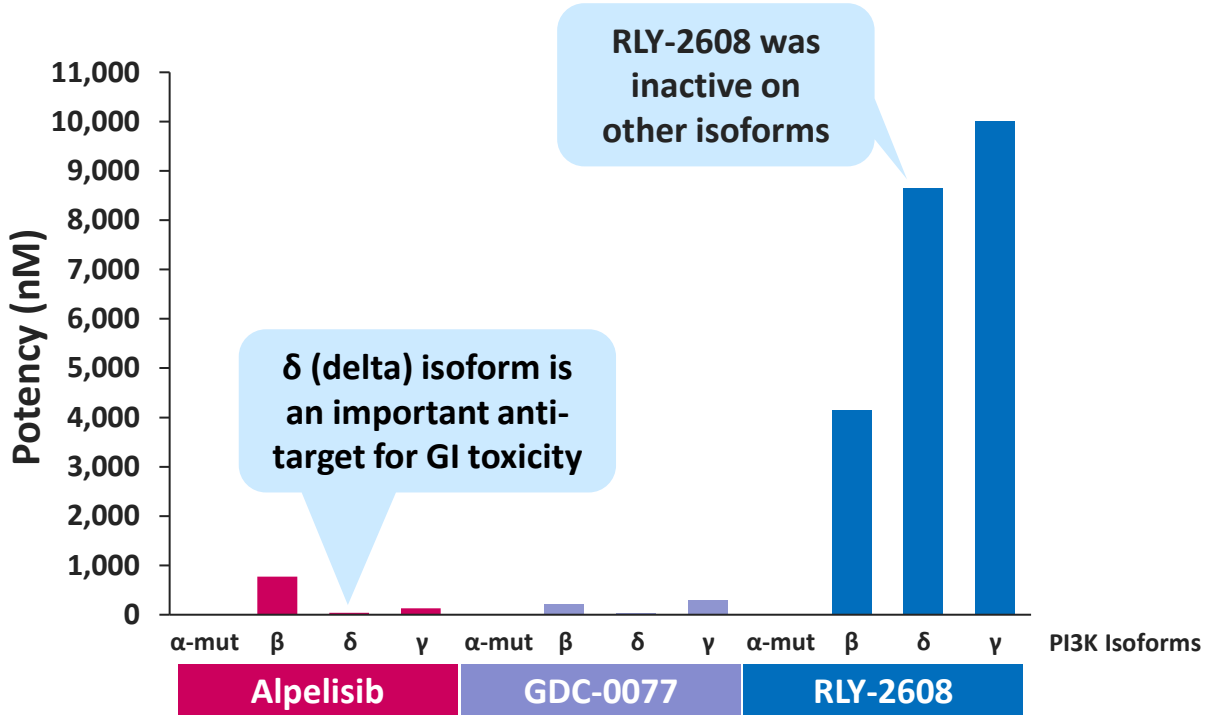
A differentiated understanding of the structure of PI3Kα and its relationship to function equips Relay Tx to design optimal mutant-selective inhibitors of PI3Kα

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

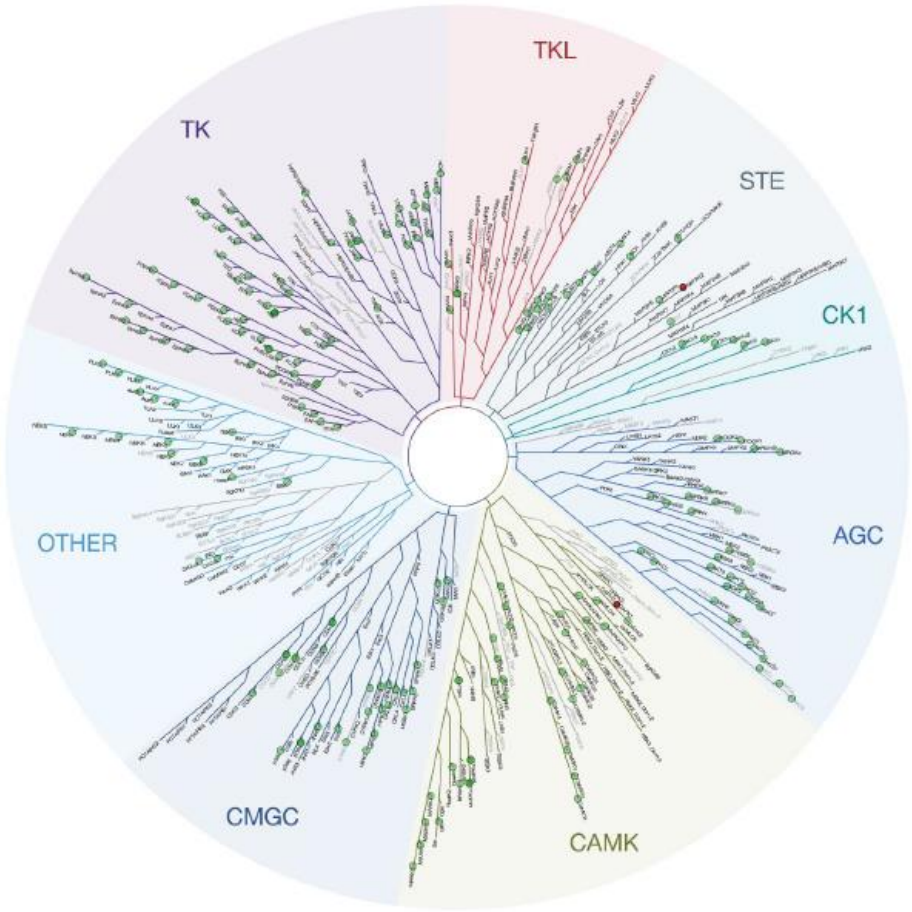
Mutant vs. WT PI3Kα potency

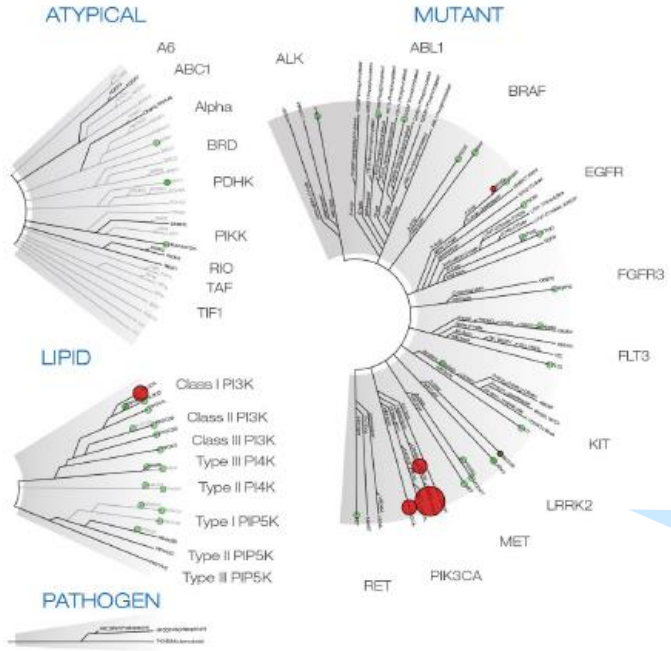


Mutant PI3Kα vs. other isoform potency



PI3Kα – RLY-2608 Is Selective Across the Kinome





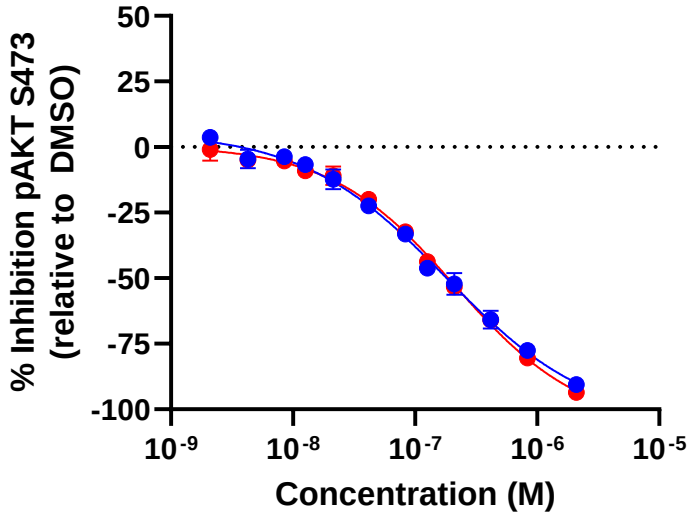
RLY-2608 inhibited only PI3Kα, with preferential inhibition of mutant

Kinase Inhibition @ 10 µM R

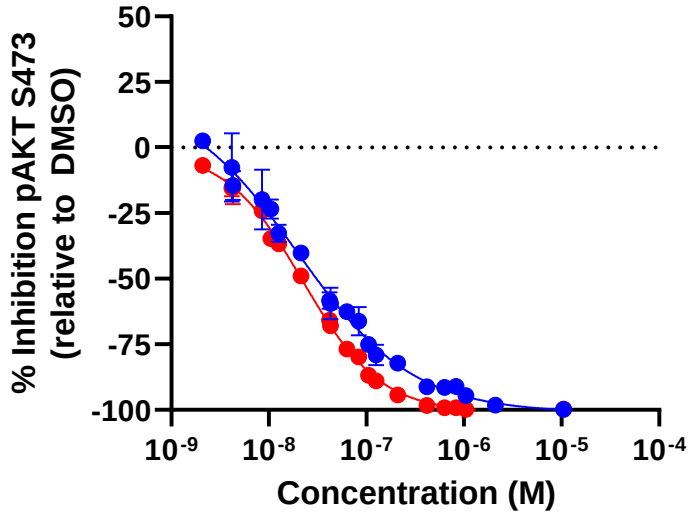
- **>80% inhibition**
- **20-80% inhibition**
- **< 20 % inhibition**

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

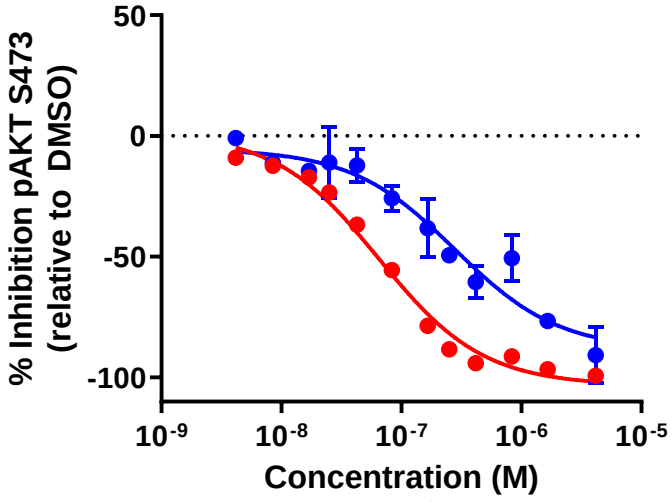
Alpelisib



GDC-0077



RLY-2608



Orthosteric binders were equipotent between WT and mutant

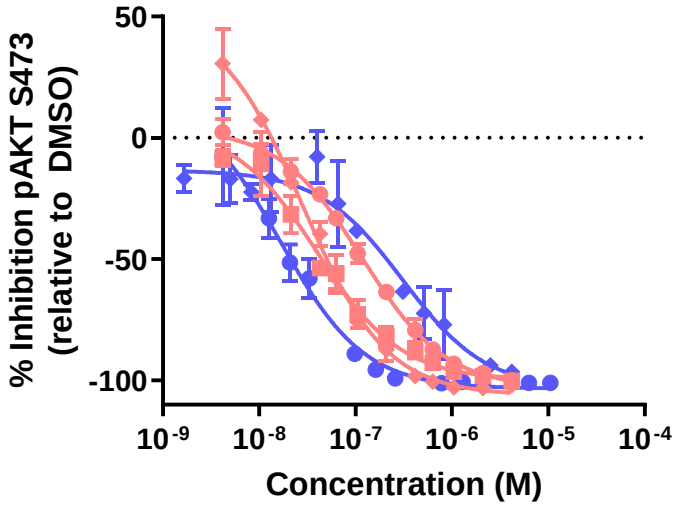
MCF10A Parental

MCF10A *PIK3CA* mutant

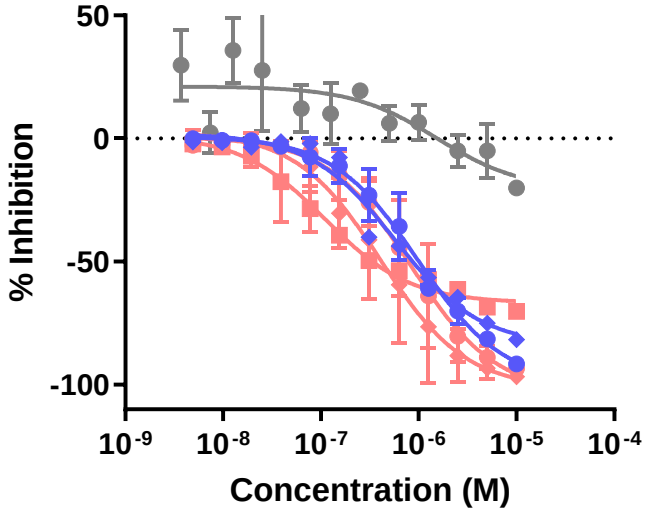
RLY-2608 was more potent against mutant cells

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

pAKT



Viability

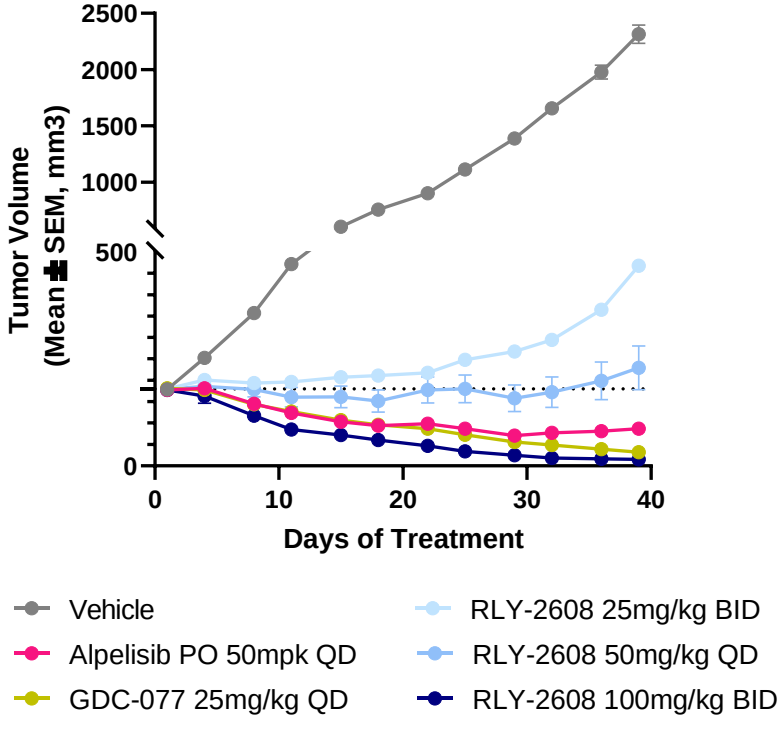


Activity observed in both kinase and helical domain mutant cell lines

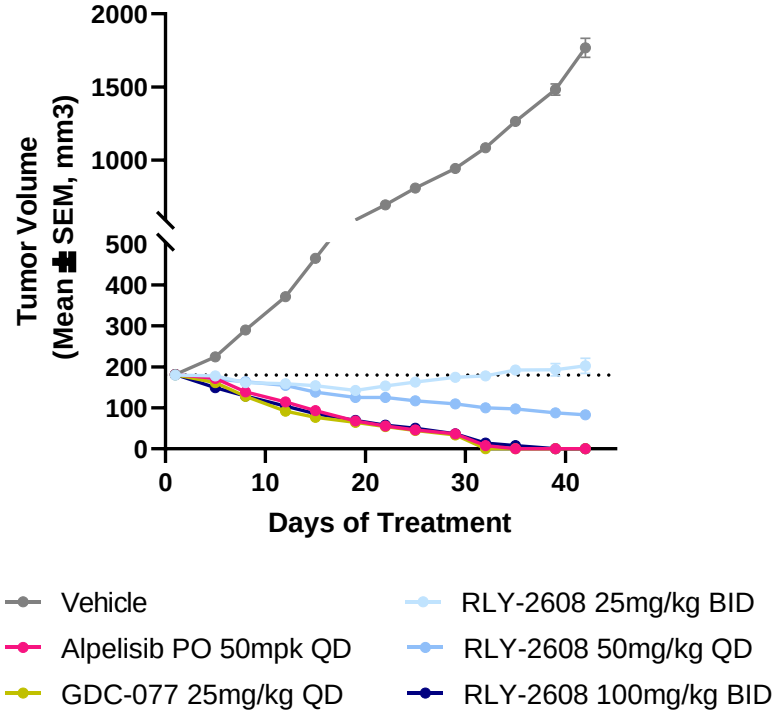
HCC1954 (H1047R)
T47D (H1047R)
CAL33 (H1047R)
MDAMB361 (E545K;K567R)
MCF7 (E545K)
HCC1428 (WT)

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

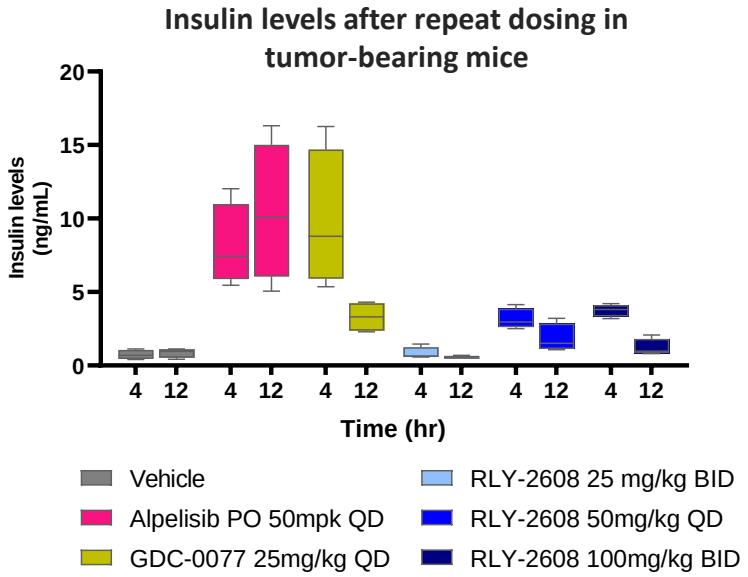
H1047R mutant (HCC1954) (mouse)



E545K mutant (MDAMB361) (mouse)[1]



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



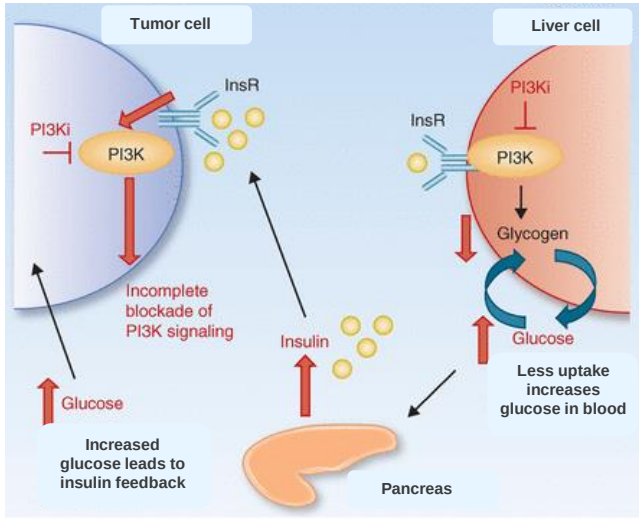
Consistent results for 1-hour time point[3]

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

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

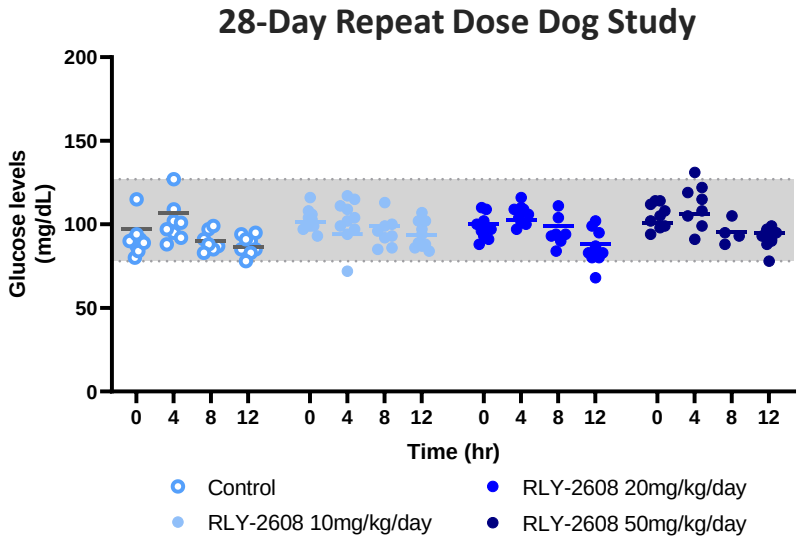
PI3Kα – RLY-2608 Had Reduced Impact on Glucose Homeostasis (28-Day Dog Study)

Inhibition of WT PI3Kα leads to hyperglycemia



Adapted from Hanker Cancer Disc 2019

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

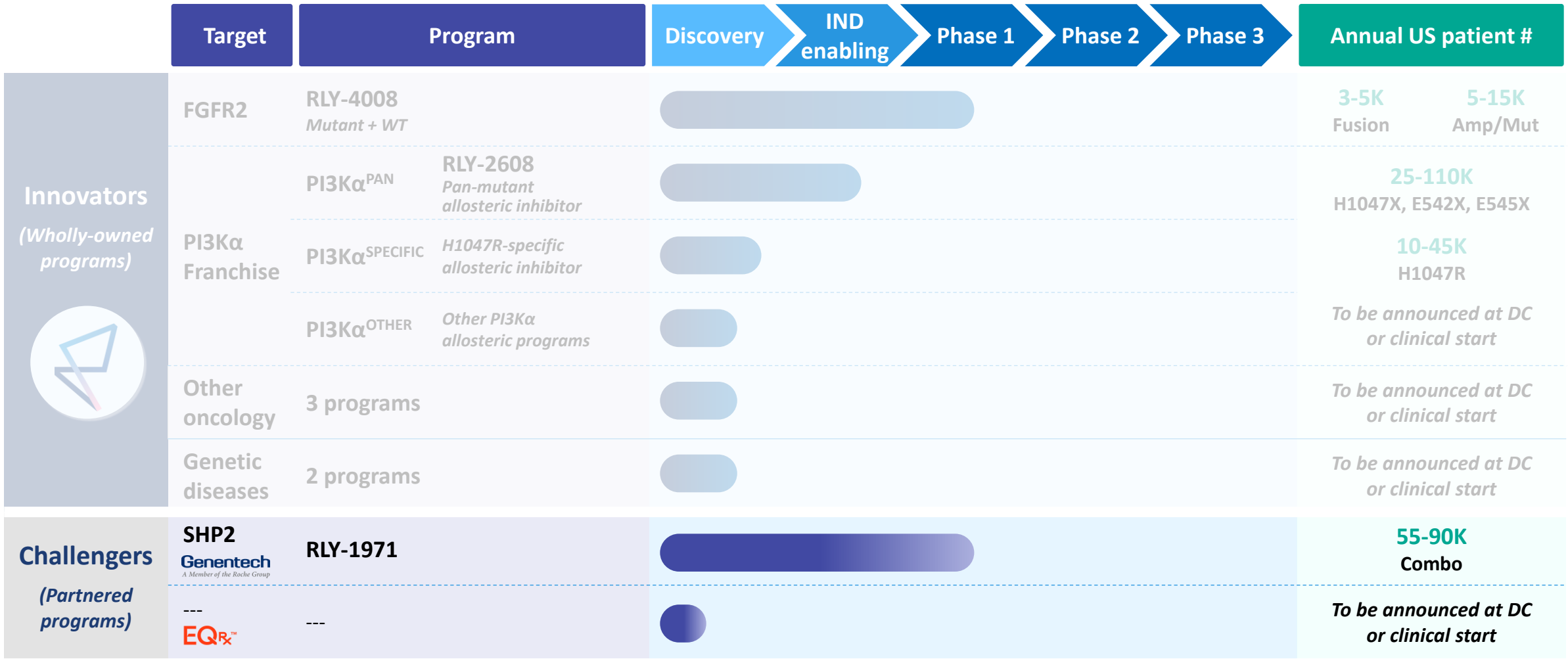


Equivalent exposures to efficacious mouse doses

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

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

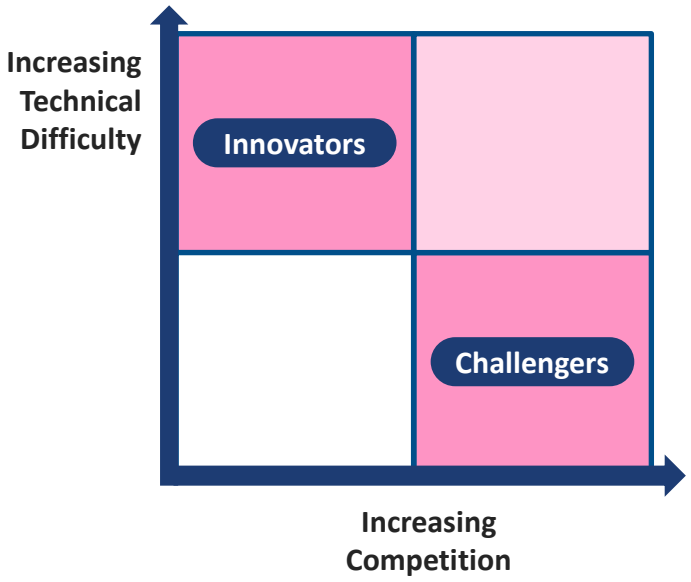
Extensive Precision Medicines Pipeline – Challengers



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

Challengers – Assisting in Further Building Out Our Dynamo™ Platform

Challengers have lower technical risk



The more we do, the better we get

Time from hit to development candidate (DC)	# of chemical series
Hit → Conventional drug discovery approach → DC: ~3-5+ years	1-2
Hit → RLY-1971 (*SHP2*) → DC: ~2 years	22
Hit → RLY-4008 (*FGFR2*) → DC: ~18 months	10

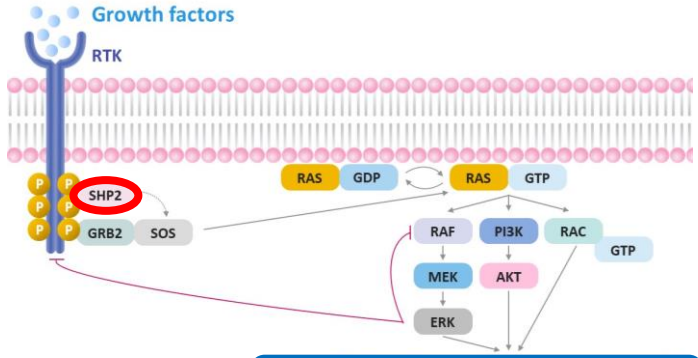
EQRx deal highlights

- Working on challenger targets makes Relay Tx's AI capabilities more effective against innovator targets
- Share 50% of costs with EQRx, with the ability to opt-out
- Retain significant economic upside (50% of profits)

The EQRx deal helps Relay Tx to be able to increase our volume of programs, strengthening our Dynamo platform feedback loop and continually making us better

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

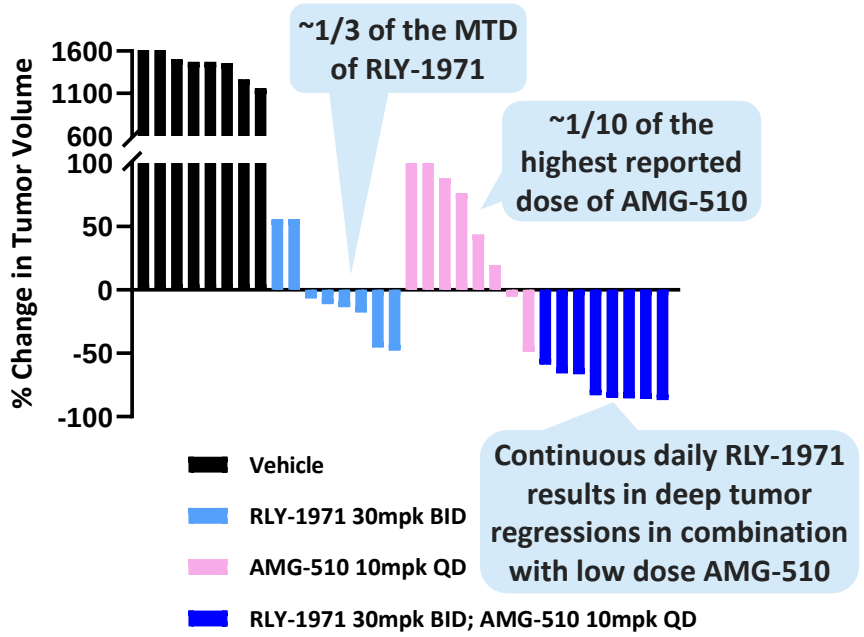
SHP2 is a rational combination partner for a number of therapies



Growth, proliferation, survival, migration, metabolic adaptation

KRAS G12C xenograft + KRAS G12Ci

NCI-H358 cell line



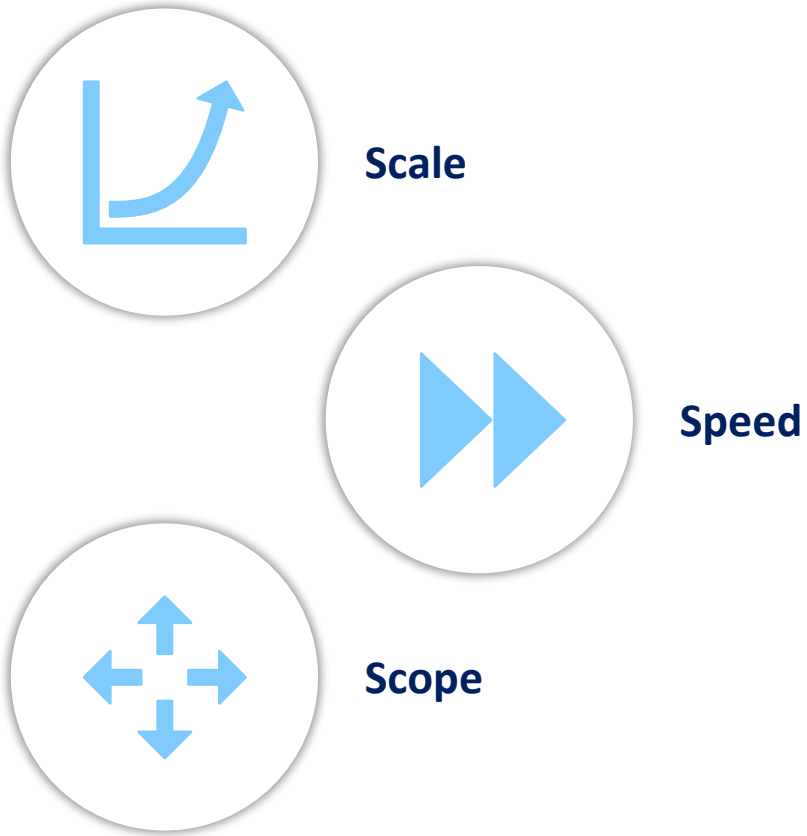
Key differentiating features of RLY-1971

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

SHP2 – Genentech Global Collaboration for RLY-1971

For the development and commercialization of RLY-1971, the collaboration increases…



Collaboration also provides meaningful economics to Relay Tx

Exclusive license*

$75M upfront + $25M in potential near-term payments

Up to $695M in additional total milestones

Low-to-mid teen royalties on global net sales

Eligible to receive additional royalties upon approval of RLY-1971 and GDC-6036 in combination

Opt-in option

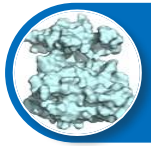
50-50 US profit share

*Agreed upon terms at signing in December 2020

What To Expect From Relay Tx

Nearer-term milestones

Innovators

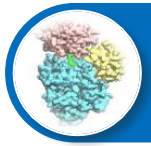


RLY-4008 (FGFR2) — Expansion cohorts open by 2021 year end; Additional data update expected in 2022

RLY-2608 (PI3Kα^{PAN}) — Clinical start expected in 1H 2022*; Add'l preclinical data at SABCS (Dec 2021)

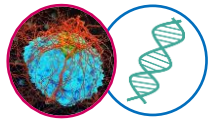
Next target in pipeline — Next target to be disclosed in 1H 2022

Challengers



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

Medium-term drivers

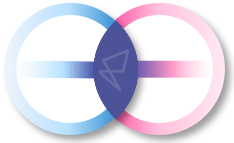


5 additional innovator programs

Genentech — A Member of the Roche Group

EQRx™

Pursuit of challenger targets through partnerships



Continued evolution of our Dynamo™ platform

Continued expansion of pipeline scope and scale

$617M

Cash, cash equivalents and investments as of the end of Q3 2021
Not inclusive of ~$380M net proceeds from October 2021 follow-on public offering

Execution focus underpins value creation

*Subject to submission and acceptance of IND by the FDA

Relay Tx 2020 ESG Summary – Beginning Our ESG Journey

Relay Tx's First ESG Disclosures

VALUE REPORTING FOUNDATION
SASB STANDARDS

SUSTAINABLE DEVELOPMENT GOALS

Patients

- 2 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% agree/strongly agree they would recommend Relay Tx as a great place to work
- Turnover below industry average rates
- Diversity & inclusion advisory group
- Training and development opportunities
- Equitable compensation

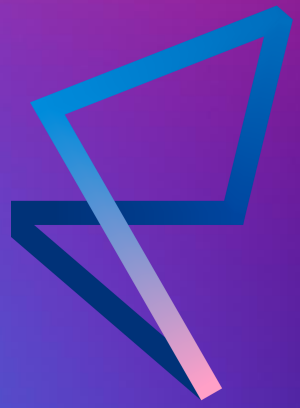
Environment

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

Governance

57 Average Age	Board Composition* (8 Directors Total)	38% Gender Diversity
38% Racial/Ethnic Diversity	3yrs Average Tenure	75% Independence (Separate CEO and Chair Role)

*As of August 2021



RELAY®

THERAPEUTICS