RELAY®
THERAPEUTICS

Company Presentation

June 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 and initial clinical data for RLY-2608; the potential therapeutic benefits of our product candidates, including potential efficacy and tolerability, and combination potential of our product candidates; whether preliminary results from our preclinical or clinical trials will be predictive of the final results of the trials or any future clinical trials of our product candidates; the possibility that unconfirmed results from these trials will not be confirmed by additional data as the clinical trials progress; the competitive landscape and market opportunities for our product candidates; the expected strategic benefits under our collaborations; our ability to successfully establish or maintain collaborations or strategic relationships for our product candidates; expectations regarding current and future interactions with the U.S. Food and Drug Administration (FDA); our ability to manufacture our product candidates in conformity with the FDA's requirements; the capabilities and development of our Dynamo™ platform; our financial performance; the effect of the COVID-19 pandemic, including mitigation efforts and economic effects, on any of the foregoing or other aspects of our business operations, including but not limited to our preclinical studies and future clinical trials; our plans to develop, manufacture and commercialize our current product candidates and any future product candidates; and the implementation of our business model and strategic plans for our business, current product candidates and any future product candidates.

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

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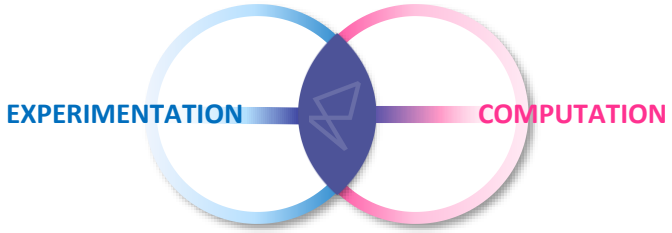
Relay Tx – Patient-Driven & Execution Focused

New Breed of Biotech



Clear Focus

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

Validated Approach

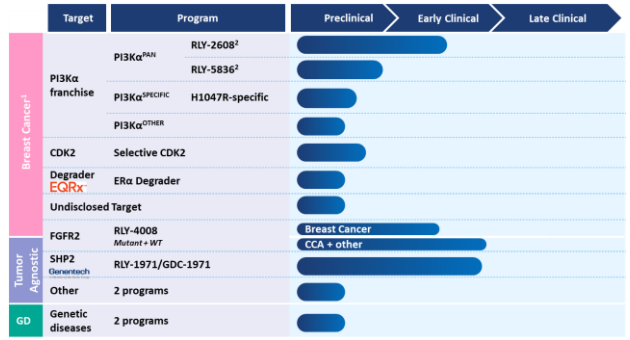
Clinical

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

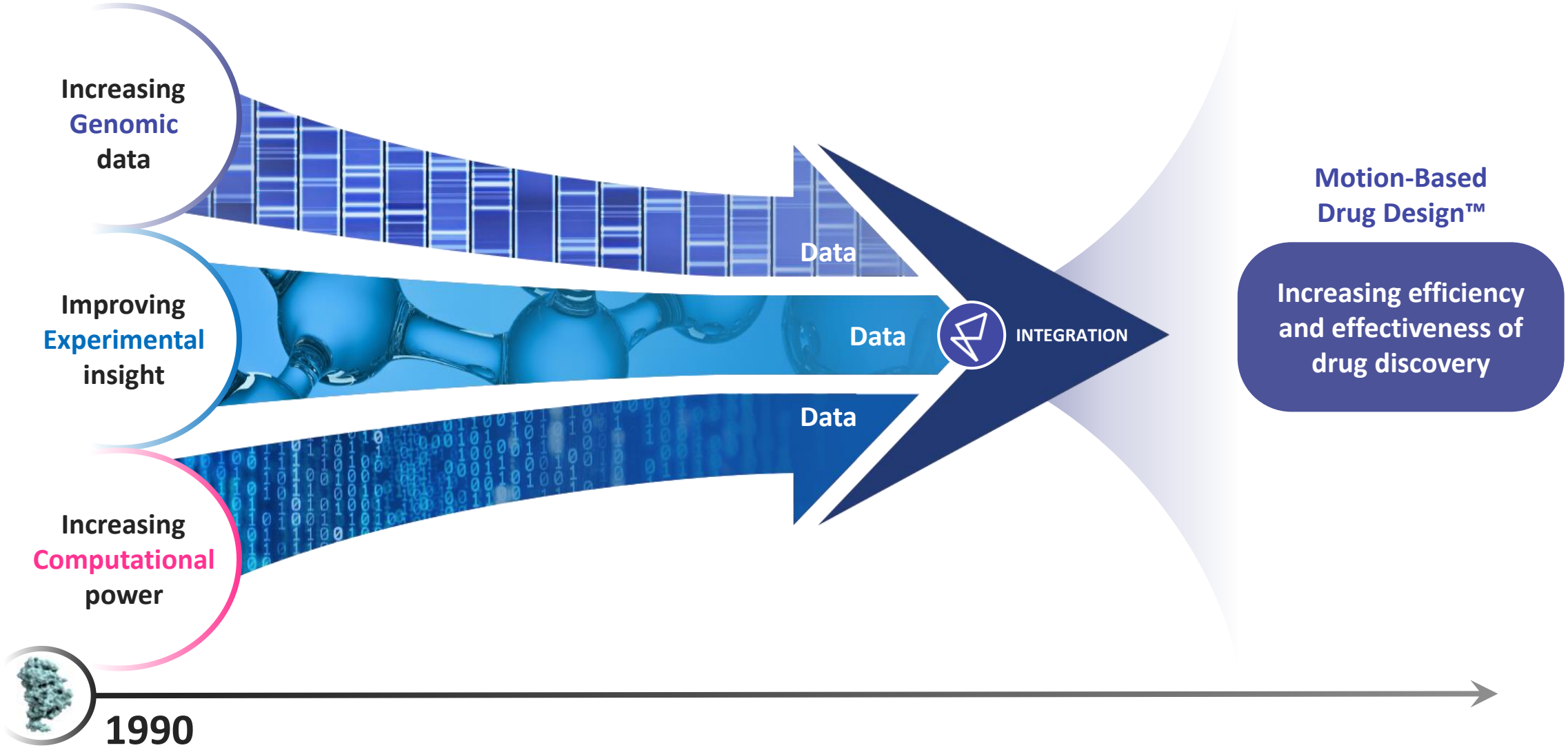
Pre-clinical

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

Execution-Focused



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



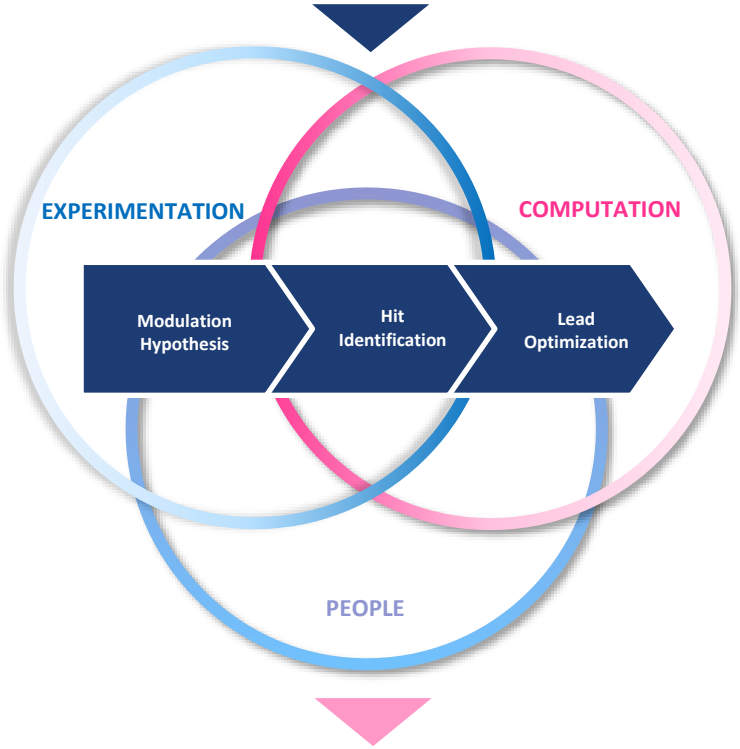
Relay Tx – Understanding Next Generation Drug Discovery: 4 Questions

The "What"

What problems do we work on?

The "Where"

Where do we focus?



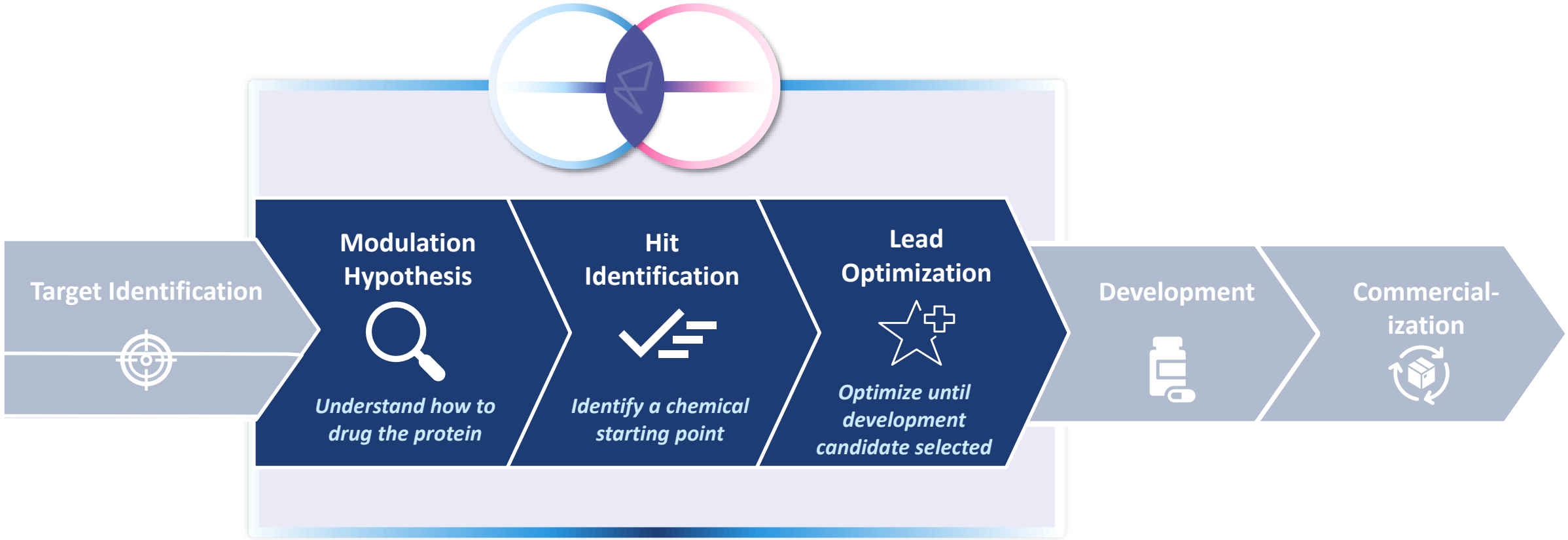
The "How"

How do we work to solve problems?

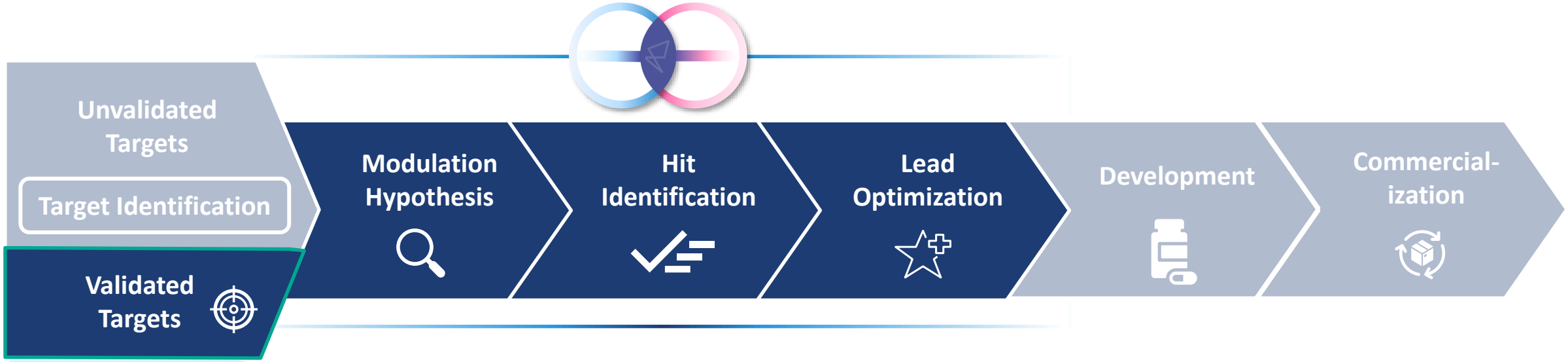
The Impact

How do we measure output?

Relay Tx – Where We Focus Our Dynamo™ Platform Today



Relay Tx – What Problems We Tackle



- Target is known driver of disease
- Amenable to Dynamo platform
- Clear patient selection strategy
- Anticipated rapid path to clinical POC

Relay Tx – How Our Team Solves Problems – The Dynamo™ Platform

EXPERIMENTATION

Deep structural understanding

Chemical biology insights

Physics-based simulations

AI / ML

COMPUTATION

PEOPLE

Relay Tx – How Our Team Solves Problems – Our 3-Step Drug Discovery Process

RELAY THERAPEUTICS

Experimental tool examples:

Structural Biophysics

Nanoscale Chemistry

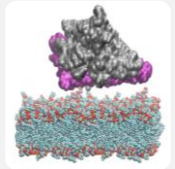
Library Synthesis

1 **Modulation Hypothesis** — ***Proteins***

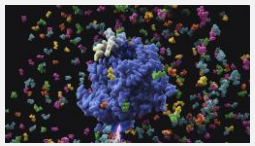
2 **Hit Identification** — ***Small Molecules***

3 **Lead Optimization** — ***Oral Administration***

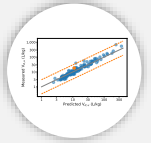
Computational tool examples:



Long Time Scale MD[1]



ML-DEL Screen[2]

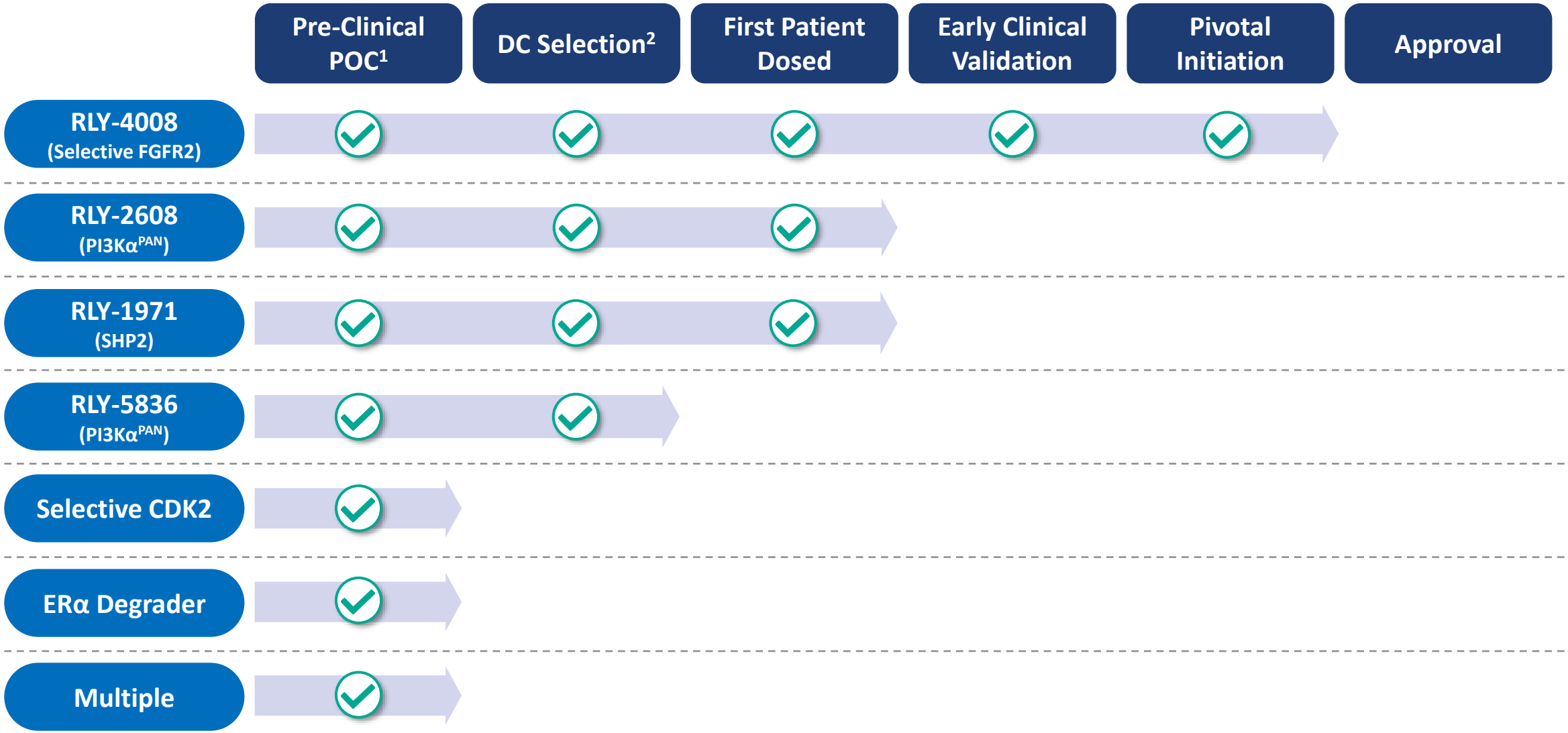


ML ADME Models[3]

PEOPLE

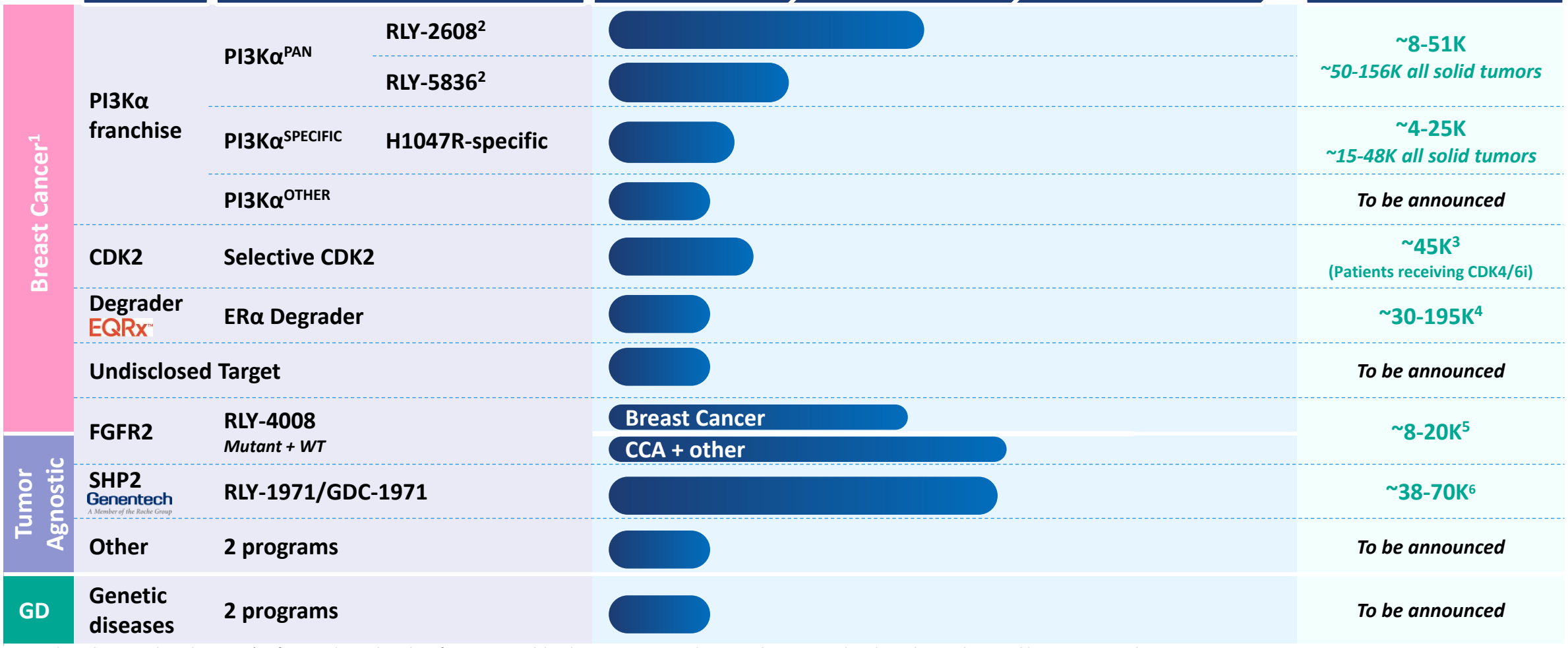
[1]MD - molecular dynamics. [2]ML-DEL - machine-learning DNA-encoded small-molecule libraries. [3]ML ADME - machine learning adsorption, distribution, metabolism and excretion.

Relay Tx – Measuring our Impact



[1]POC - proof-of-concept. [2]DC - development candidate.

Relay Tx – Extensive Precision Medicine Focused Pipeline

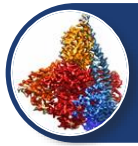


Note: Unless otherwise indicated, patient #'s refer to total annual number of US patients with late-line cancers compared to comprehensive annual incidence that may be amenable to treatment with our programs

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

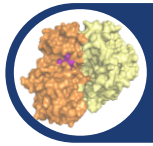
Relay Tx – Capital, Team & Execution Focus to Deliver on Anticipated Milestones

Breast Cancer Franchise



RLY-2608
(PI3Kα^{PAN})

Initial data
in 1H 2023



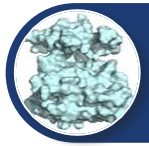
Selective CDK2

Clinical start in
Q4 2023 or Q1 2024

ERα Degrader

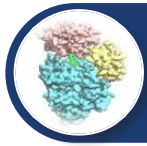
Development candidate
nomination
in 2023

Tumor Agnostic



RLY-4008
(Selective FGFR2)

Additional
data updates
in 2H 2022 & 2023



RLY-1971
(SHP2)

Atezolizumab combo
trial to be initiated
in 2H 2022

$898M

Cash, cash equivalents and investments
as of the end of Q1 2022

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

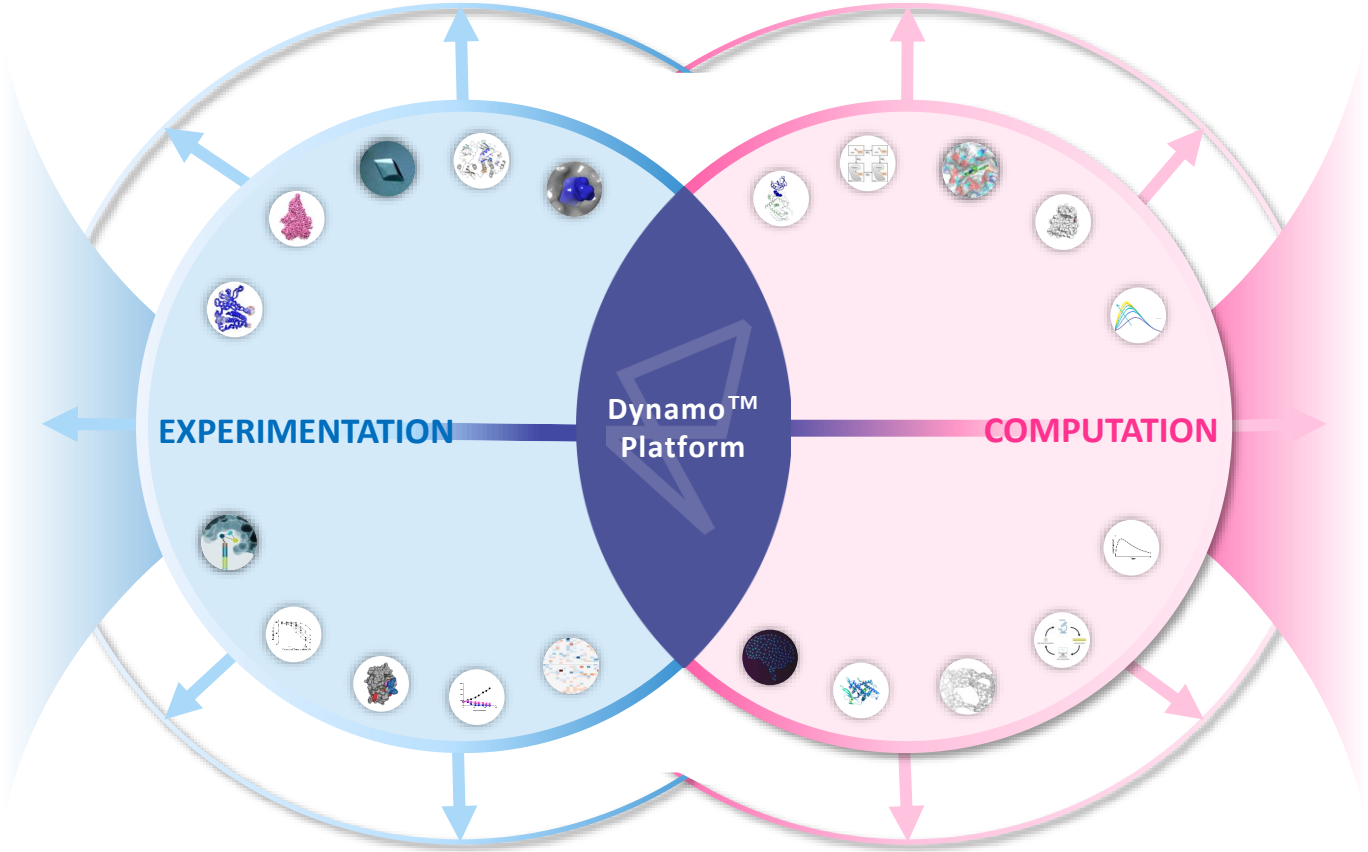
The Dynamo™ Platform – Evolving with Landscape of Leading Edge Techniques

Quantitative DEL

Generating data to build pharmacokinetic ML models

High-throughput and automated chemistry

Structural biology on difficult targets



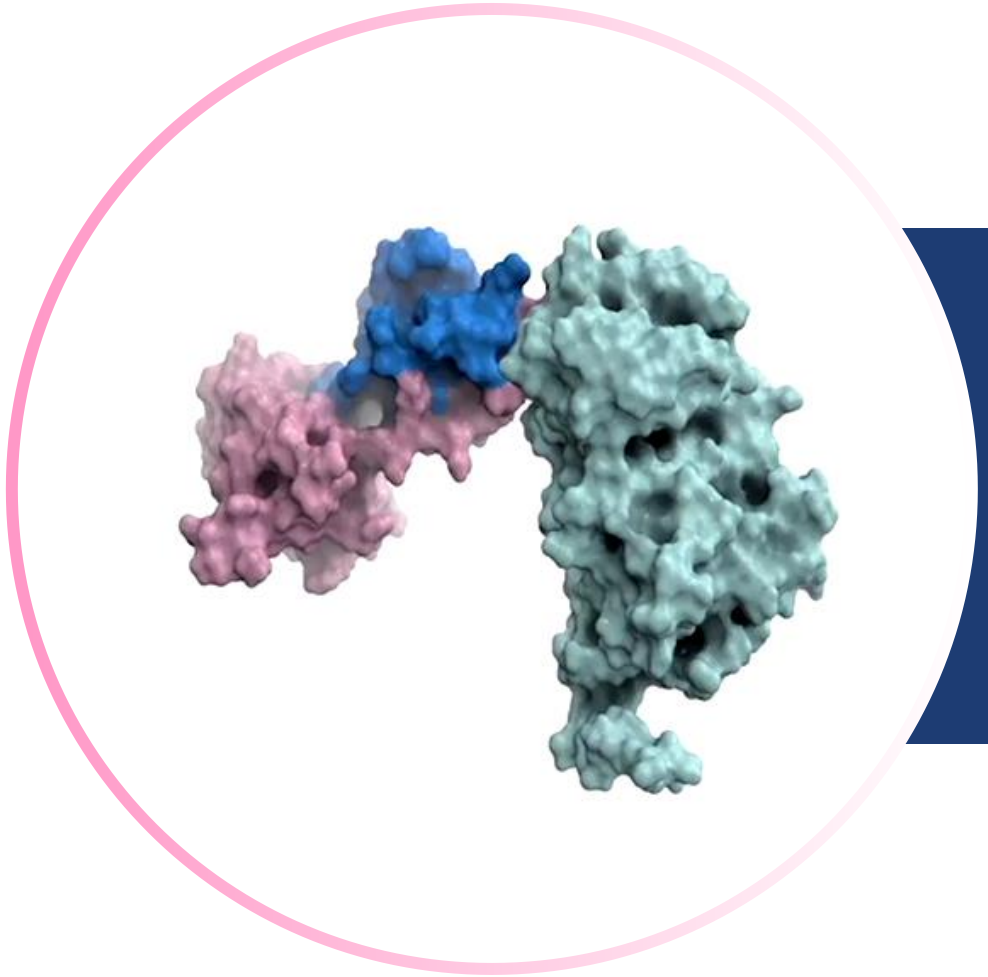
Automated chemical design

Protein structure prediction (AlphaFold)

ML directed free energy calculations

Active learning

Long-time scale MD



Relay Tx

Programs

RLY-4008 – Alignment on Registrational Trial Design

Extensive Dose Finding Completed

Dose Escalation (Opened Sep 2020)
Twice-daily, intermittent, & once daily schedules explored
70 mg QD selected

Dose Expansion (Opened Dec 2021)
70 mg QD ongoing

Pivotal Expansion (Commenced)
70 mg QD selected

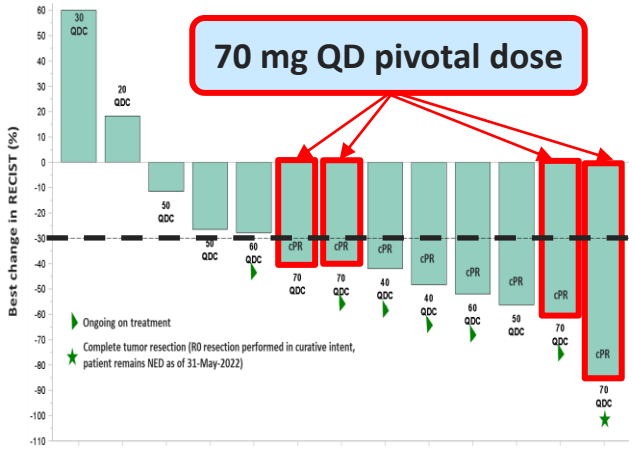
Pivotal Study Aligned with FDA

Pivotal Expansion
FGFR2-fusion+ cholangiocarcinoma (CCA) **without prior FGFRi** (n=100)

Supportive cohorts
- FGFR2-fusion+ CCA **with prior FGFRi** (n=50)
- FGFR2-fusion+ CCA **with no prior treatment** (n=20)
- FGFR2 amps/mut CCA (n=20)

Encouraging Efficacy

***FGFR2*-fusion+ cholangiocarcinoma (CCA) without prior FGFRi**



Project Optimus shaped trial design

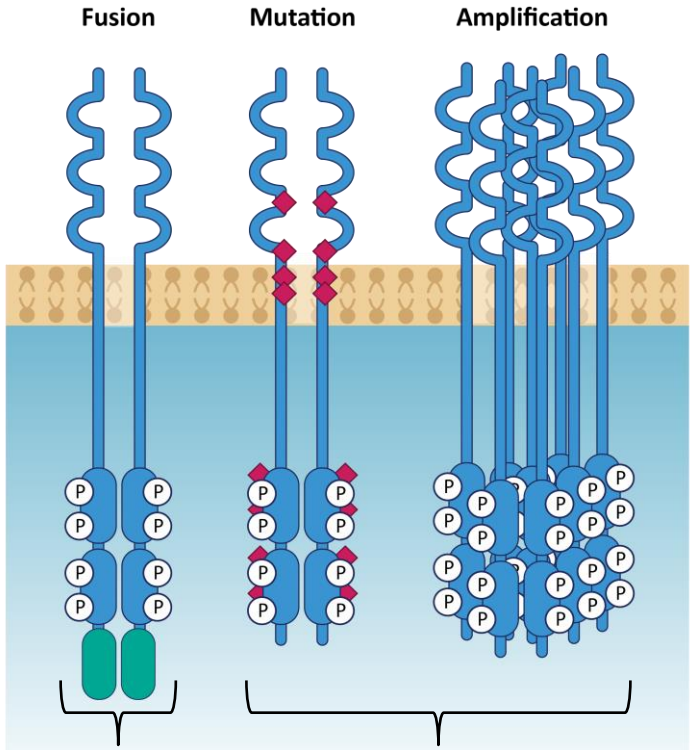
Alignment with FDA on single arm, trial design for FGFRi-naïve FGFR2-fusion CCA to potentially support accelerated approval

Potential for RLY-4008 as an important treatment option for patients

Preliminary data as of 19-April-2022

FGFR2 – Validated Target Present in Several Tumor Types

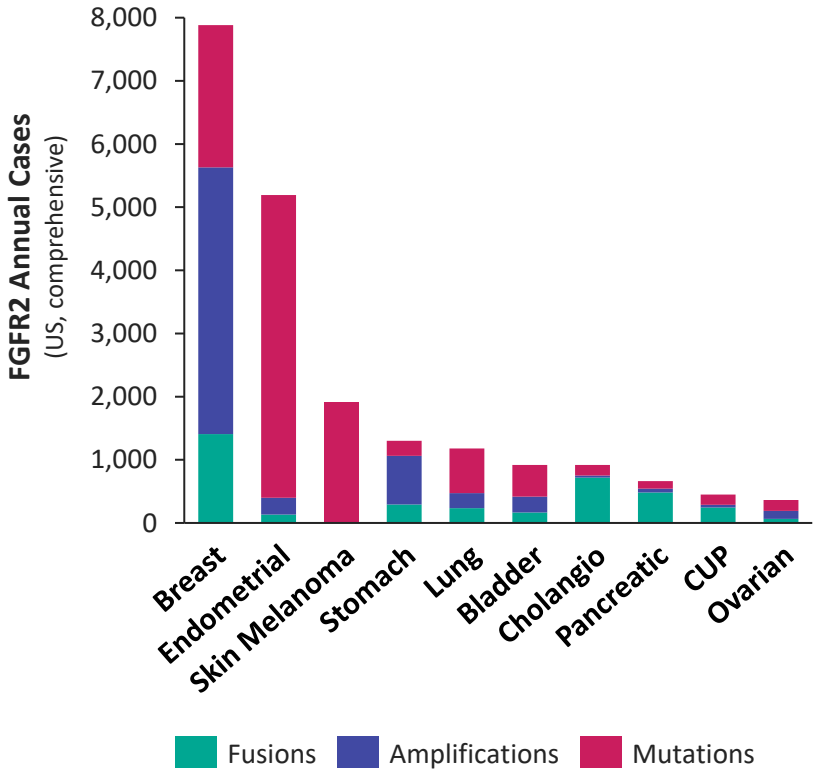
Three classes of driver alterations in FGFR2



~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 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%

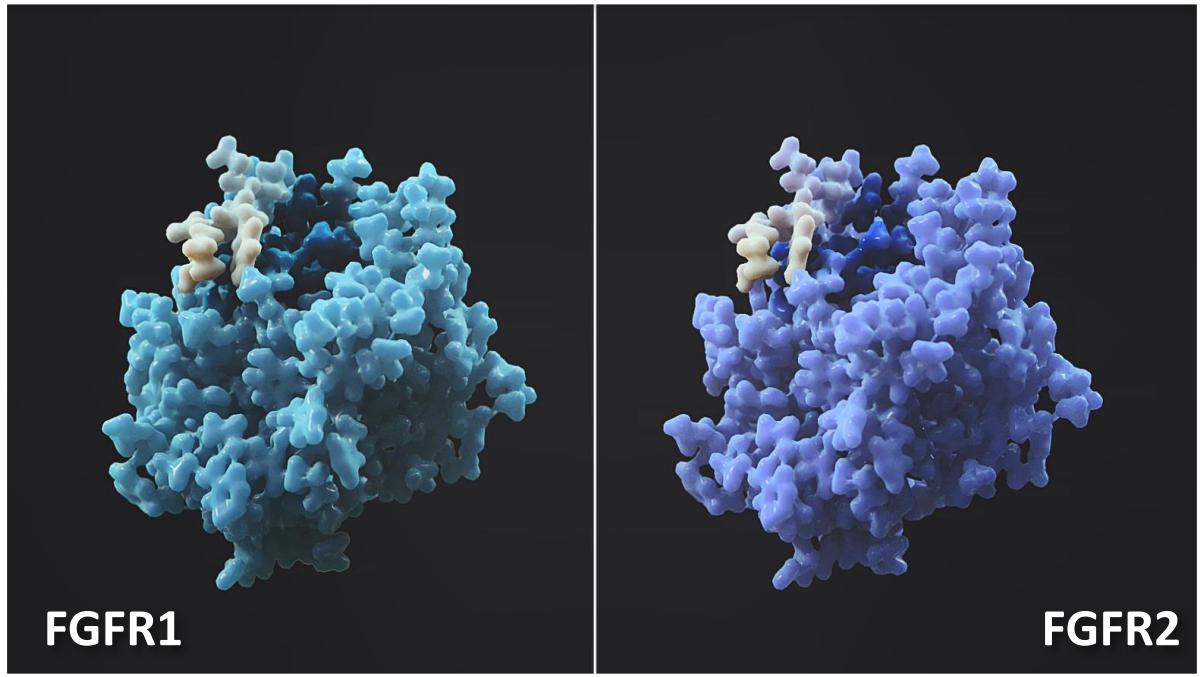
Late-line treatment with chemotherapy can be highly toxic and only results in incremental efficacy

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

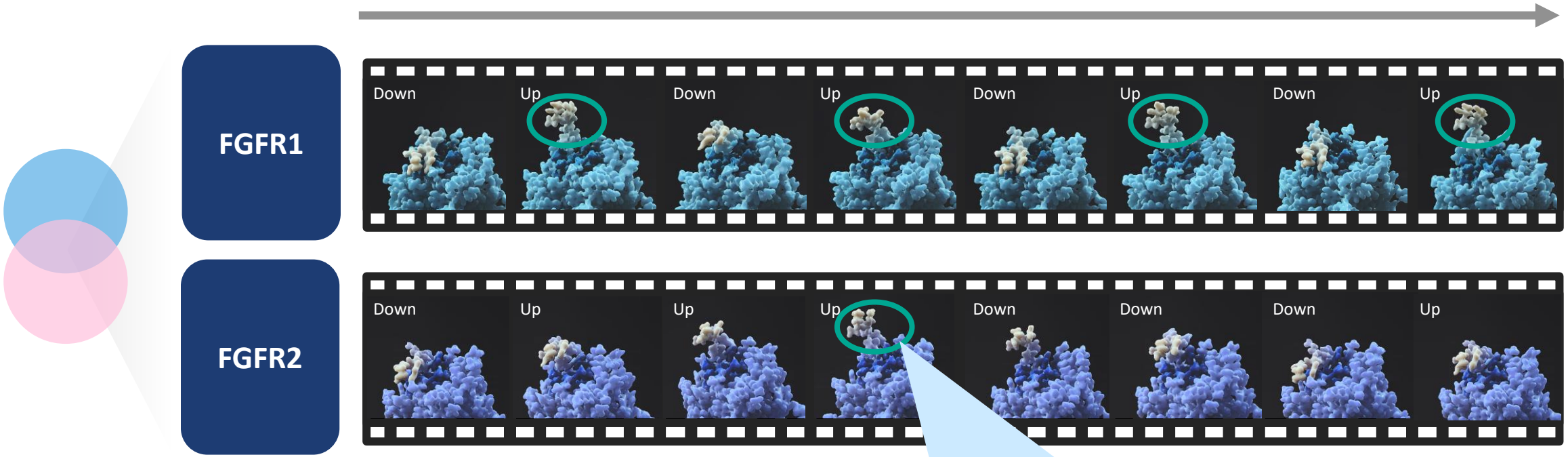
Sources: Pemigatinib – Prescribing information; Infigratinib – Prescribing information; Futibatinib/TAS-120 – AACR 2021 (diarrhea %s approximated from presentation); Erdafitinib – Prescribing information; FOLFOX – ABC-06 Publication in Lancet Oncology 2021

FGFR2 – Standard Approach to Discovery Has Had Limited Success

Standard Approach



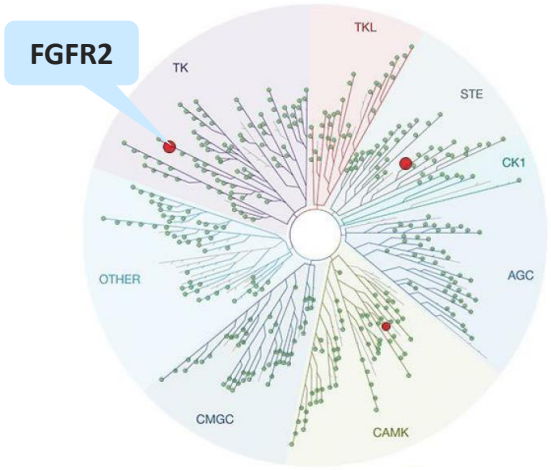
FGFR2 – Increasing Experimental Resolution Reveals New Opportunities



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

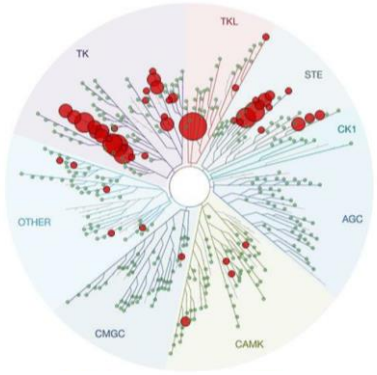
RLY-4008 – Is A Highly Selective and Irreversible Inhibitor

RLY-4008

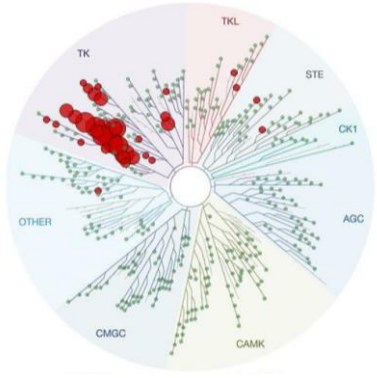


Pan-FGFR Inhibitors

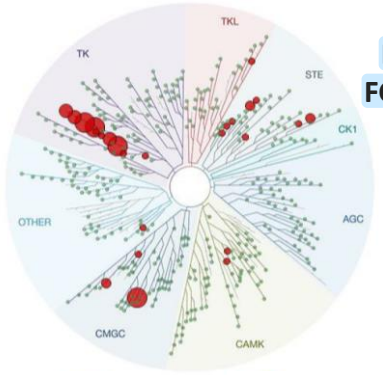
AZD4547



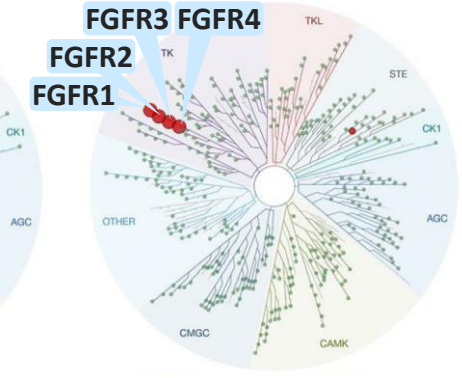
Erdafitinib



Pemigatinib

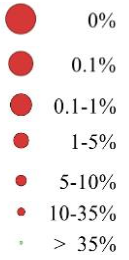


Futibatinib



Percent Control

Percent Control



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

RLY-4008 – Context: October 2021 Clinical Data Disclosure - Dose Escalation

Dose Escalation
(Opened September 2020)

Bayesian Optimal Interval Escalation (BOIN) design

Unresectable or metastatic solid tumors

FGFR2-alterations per local assessment (tumor tissue or blood)

Both FGFRi-naïve & FGFRi-treated allowed

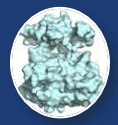
Once & twice daily schedules explored across 6 different doses

October 2021 Disclosure

Data from 2021 AACR-NCI-EORTC Molecule Targets Presentation (October 2021, n = 49 patients)

Execution → **49** patients (through October 2021)

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** → 3 out of 6 fusion+ CCA FGFRi naïve patients with confirmed PRs

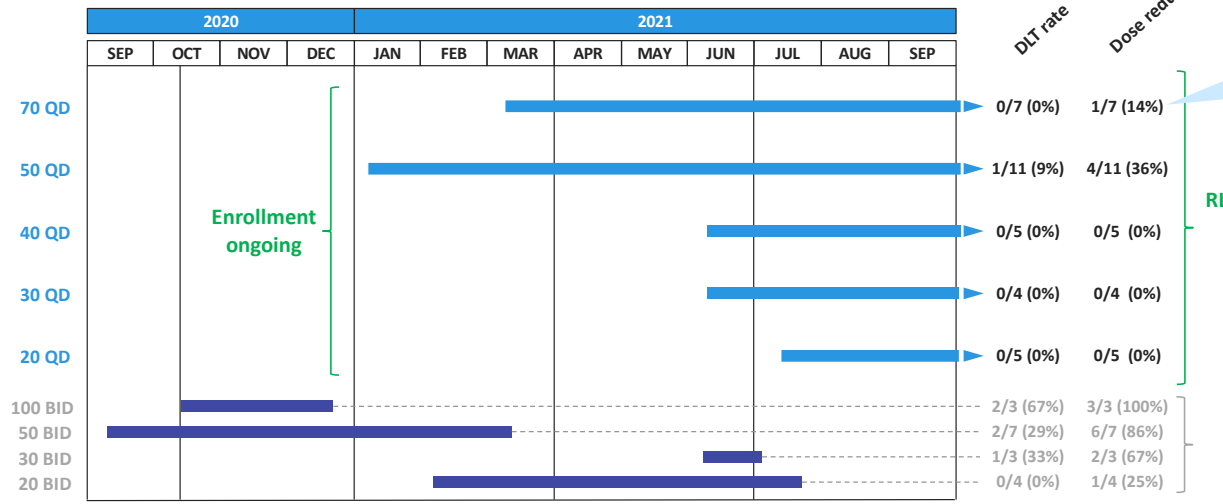
Source: RLY-4008 data as presented at 2021 AACR-NCI-EORTC Molecular Targets Conference

RLY-4008 - Dose Escalation
BID Schedule De-Prioritized & 70 mg QD Selected For Expansion Cohorts

Data from 2021 AACR-NCI-EORTC Molecule Targets Presentation (October 2021)

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

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



70 mg QD selected for expansion cohorts with goal to optimize efficacy given sustained 95% target engagement

BID schedule de-prioritized

In addition, intermittent dose schedule explored and deprioritized

Doses at ≥40mg resulted in 90%+ target inhibition

RLY-4008 – Continued Clinical Execution

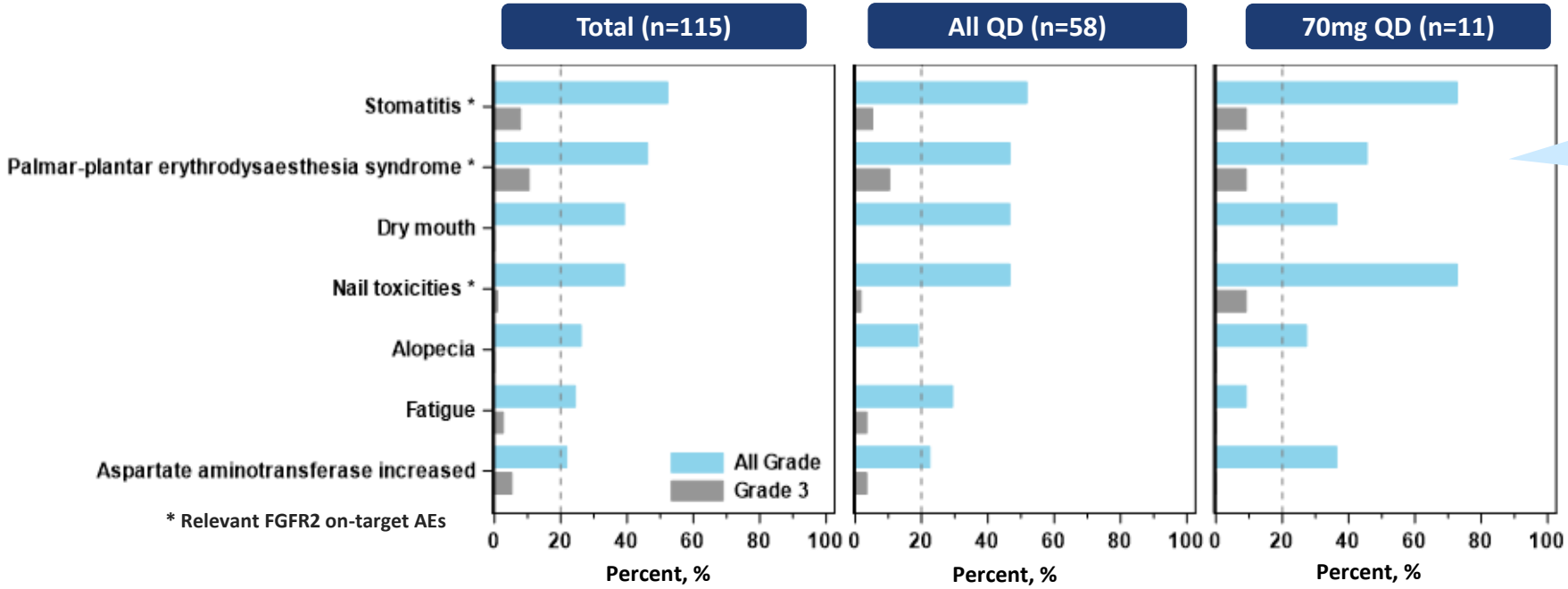
	Presentation at EORTC NCI AACR in Oct 2021 (as of 9 Sept 2021)	Relay Tx Analyst and Investor Event in June 2022 (as of 19 April 2022)		
	Total	Total	QD (once daily)	70 mg QD
Total Patients Dosed	49	115	58	11
Cholangiocarcinoma (CCA) Patients				
FGFRi pre-treated				
Fusion	25	49	25	1
Other FGFR2 alteration	3	6	2	1
FGFRi naïve				
Fusion	7*	24	13	4
Other FGFR2 alteration	5	11	6	2
Non-Cholangiocarcinoma				
Fusion	0	7	2	1
Mutation	6	13	7	1
Amplification	1	3	2	0
Other FGFR2 driven tumor	2	2	1	1
Countries Open	1	11		
Sites	11	35		

*6 evaluable

Continued robust clinical execution since the October disclosure

RLY-4008 – Treatment Emergent Adverse Events (TEAEs) Profile

TEAEs ≥20%



Most TEAEs are expected FGFR2-on target, low grade, monitorable, manageable and largely reversible

	Total (n=115)	All QD (n=58)	70mg QD (n=11)
Median time on treatment (wks)	16	18	16
Dose modification due to related TEAEs			
Dose interruption (%)	38	38	55
Dose reduction (%)	21	19	36
Dose discontinuation (%)	0	0	0

70 mg QD actual dose intensity of 65 mg/day

No drug related dose discontinuation

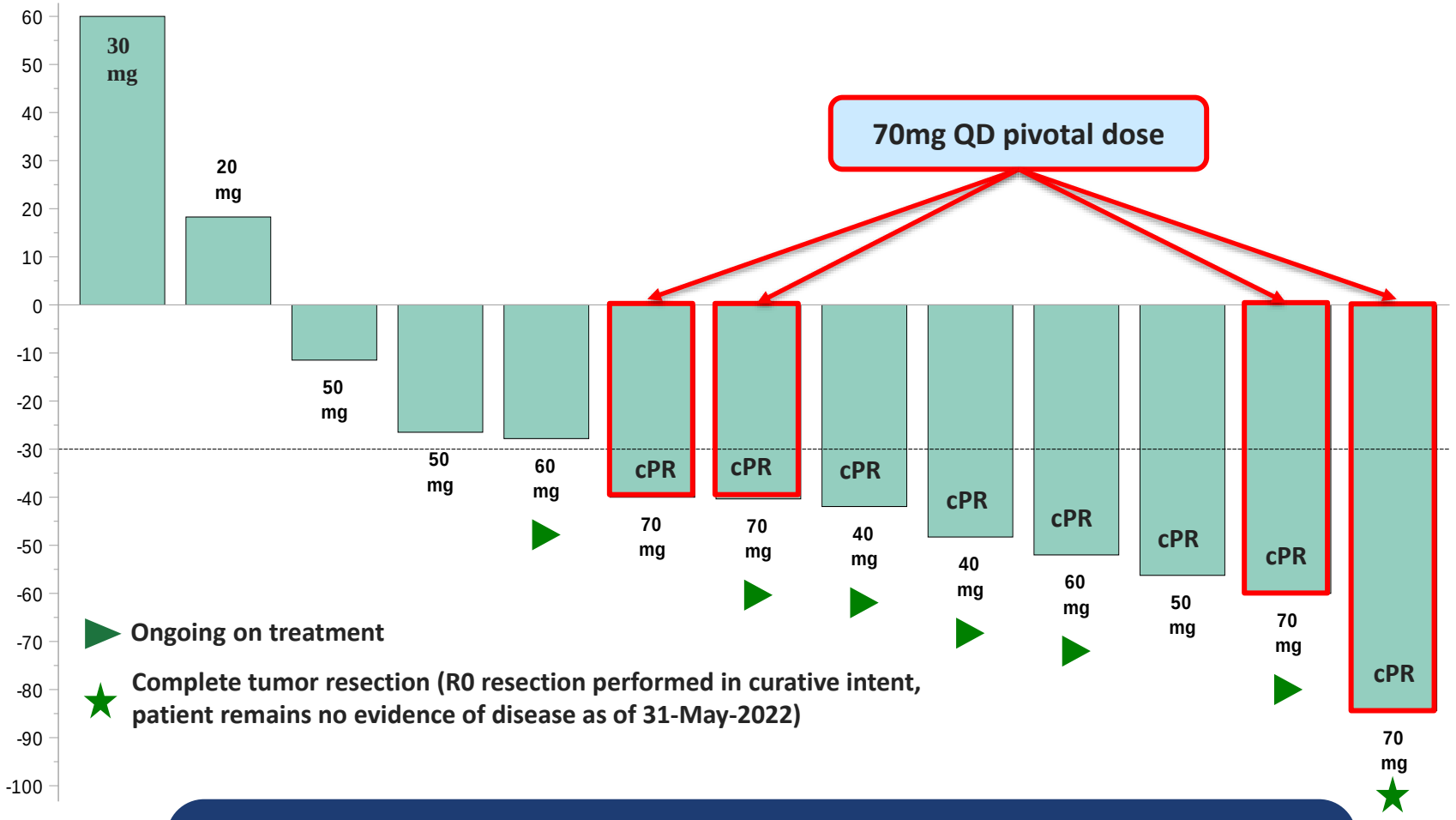
Clinically insignificant off-target hyperphosphatemia (14%, all Gr 1-2) and diarrhea (10%, all Gr 1-2) allow for optimization of FGFR2 inhibition

Note: Treatment-emergent adverse events (TEAEs) ≥ 20% in total population

Preliminary data as of 19-April-2022

RLY-4008 – Radiographic Tumor Regression Data Continue to Show Promise for FGFRi-Naïve Cholangiocarcinoma QD Patients

Best RECIST Change (%) from Baseline Based on Investigator Evaluated Response for FGFRi-Naïve Cholangiocarcinoma Patients



In October 2021 disclosure:

- 3 out of 6 fusion+ CCA FGFRi naïve patients with confirmed PRs

In June 2022 disclosure:

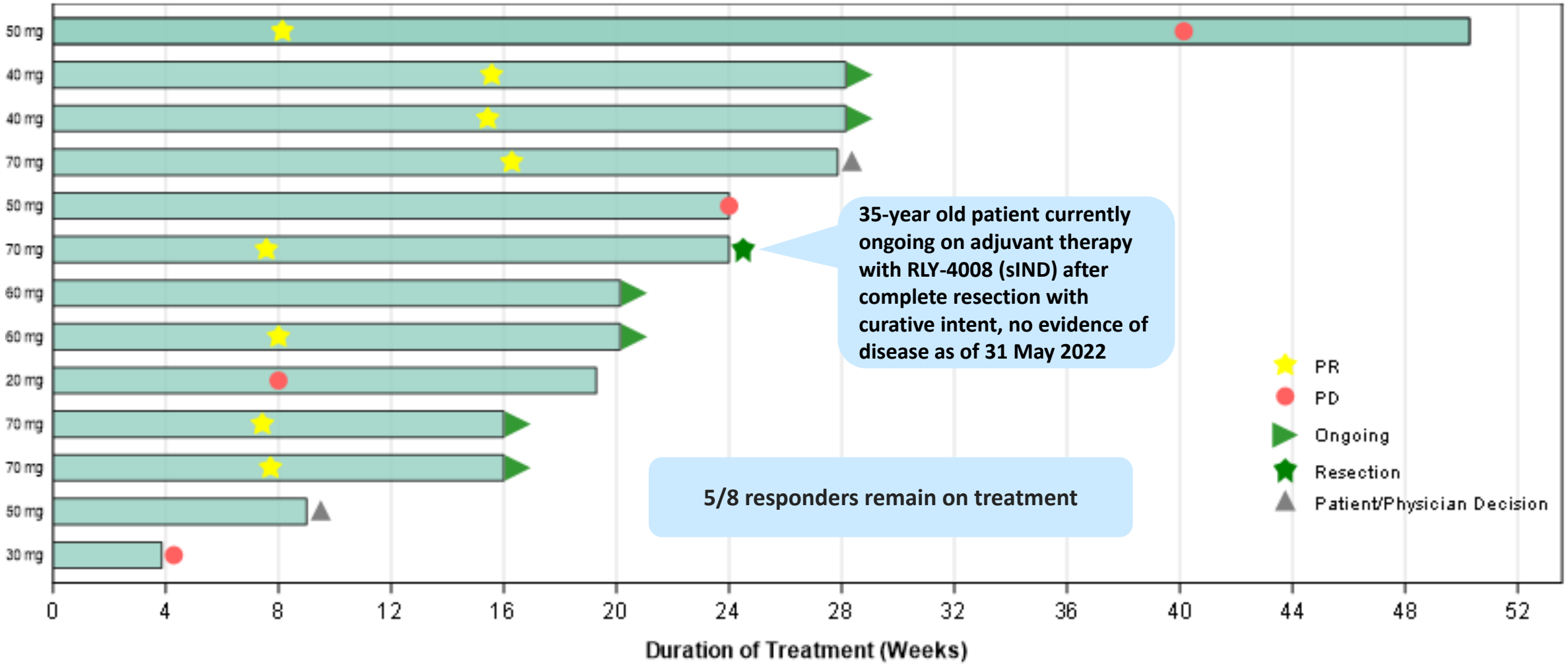
- 8/13 pts with confirmed PRs, 6 pts ongoing (62% ORR) across all once daily doses

Approved Pan-FGFR inhibitors demonstrate 23-36% ORR in this population

cPR = confirmed partial response; ORR = overall response rate

Preliminary data as of 19-April-2022

RLY-4008 – Time on Treatment for FGFRi-Naïve Cholangiocarcinoma QD Patients

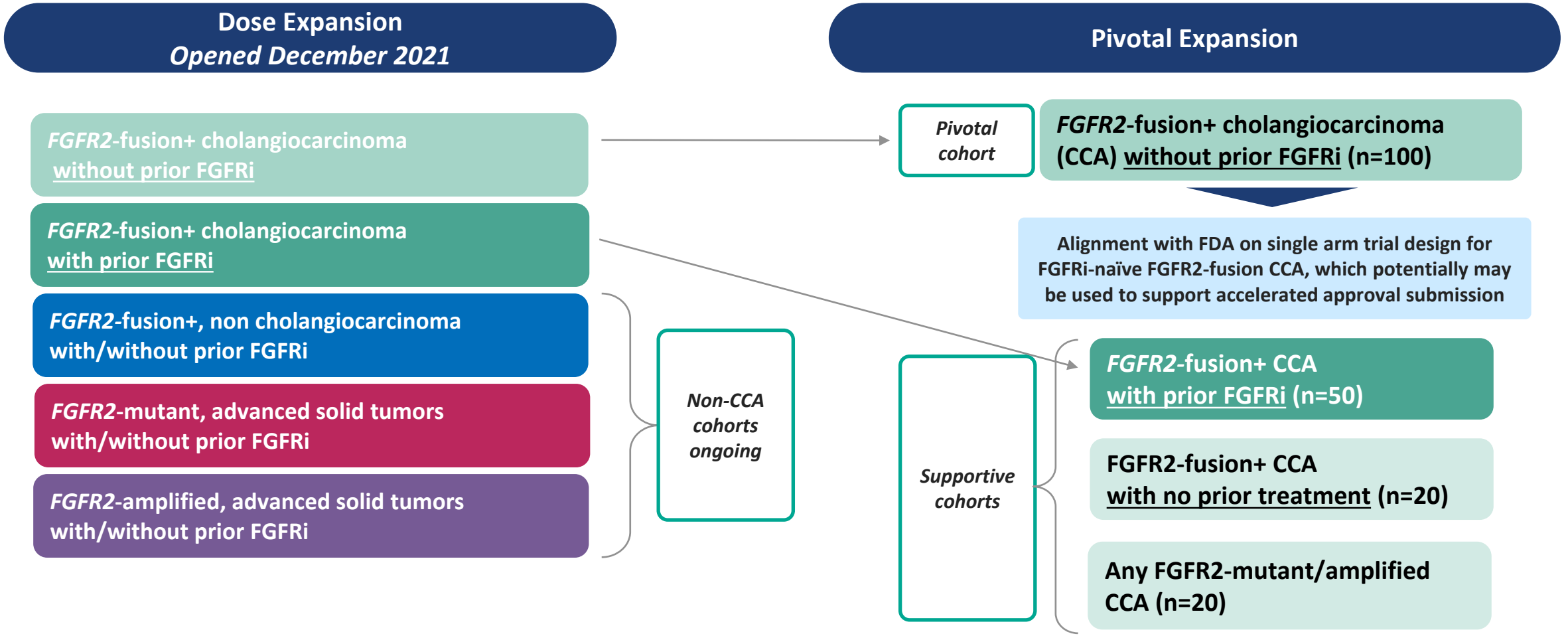


Note: All PRs in this cohort have been confirmed.

PR = partial response; PD = progressive disease

Preliminary data as of 19-April-2022

RLY-4008 – Pivotal Study Design



RLY-4008 – Exemplary Clinical Execution

Completed extensive dose exploration

Twice Daily (BID) *n = 17*	Intermittent *n = 40*	Once Daily (QD) *n = 58*
100 mg	100 mg	70 mg (Pivotal dose)
50 mg	90 mg	60 mg
30 mg	70 mg	50 mg
20 mg	60 mg	40 mg
	50 mg	30 mg
		20 mg

115 patients enrolled across **39** sites and **11** countries over **19** months

- Continued promising safety and tolerability profile
- Signs of promising efficacy
- Defined regulatory plan

QD: once daily, Intermittent: 3 wks on – 1 wk off, BID: twice daily

Relay Tx's Emerging Breast Cancer Franchise

Goals: Greater selectivity → Better combinability → Increased efficacy

Relay Tx's PI3Kα Franchise

PI3Kα^{PAN}

- **RLY-2608*** Pan-mutant selective allosteric inhibitor
- **RLY-5836*** Pan-mutant selective allosteric inhibitor
- Additional chemically distinct programs

PI3Kα^{SPECIFIC}

- H1047R-specific allosteric inhibitor
- Additional chemically distinct programs

PI3Kα^{OTHER}

- Other mutant-selective mechanisms

Relay Tx Rational Combination Partners

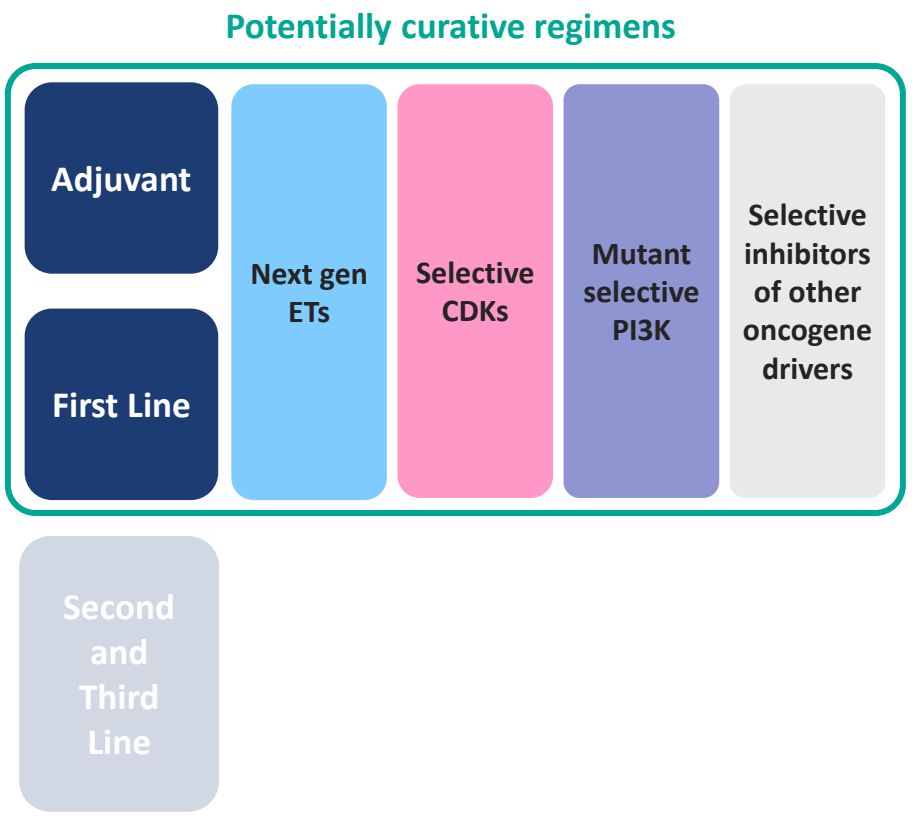
- Selective CDK2 Inhibitor
- ERα Degrader
- RLY-4008 (Selective FGFR2)
  - Demonstrated activity in FGFR2-mutant BC patient (Oct 2021 disclosure)
- Pan-mutant + Mutant Specific PI3Kα Combinations
- RLY-1971 (SHP2)
- Undisclosed Target

*Covers H1047X, E542X, E545X hot spots

Seeking to Transform the Breast Cancer Treatment Paradigm

Potential near-term augmentation of standard of care*

Aspirational future standard of care

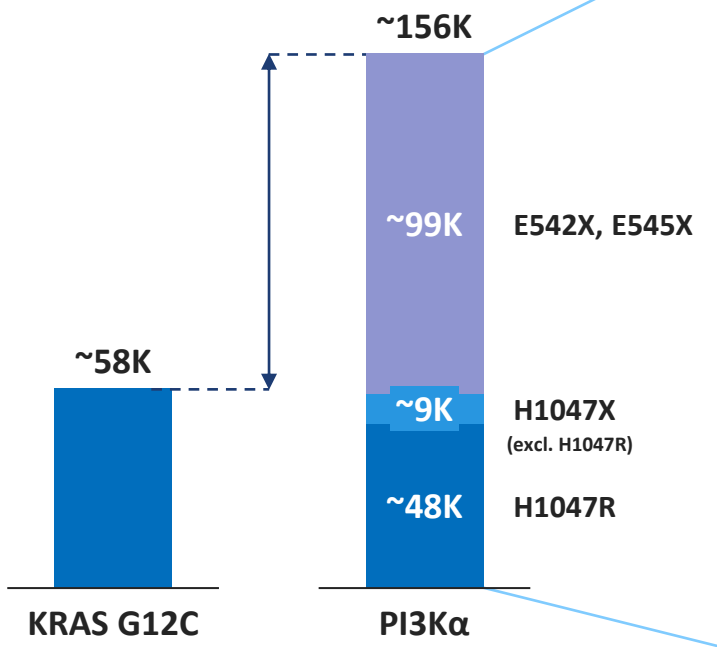


*If approved

PI3Kα Opportunity Is Among the Largest Ever for Precision Oncology

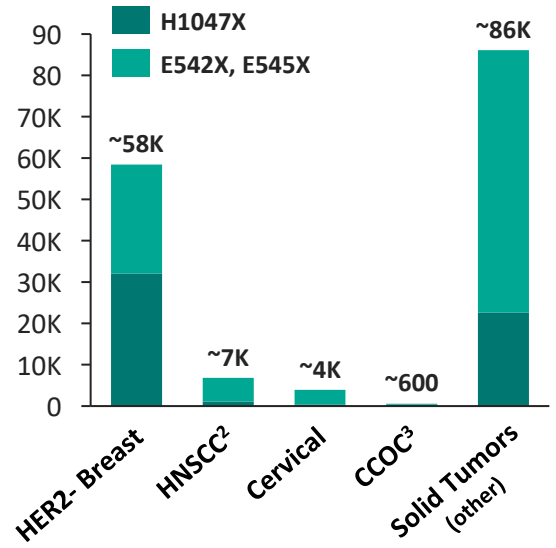
Pan-mutant selective drug represents significant clinical opportunity

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



PI3Kα alterations observed across multiple tumor types – select indications

US Patients - Comprehensive Incidence (Annual)



Evolution of PI3K inhibitors

- ***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; 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)	4% (1/27)	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, A Member of the Roche Group)	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

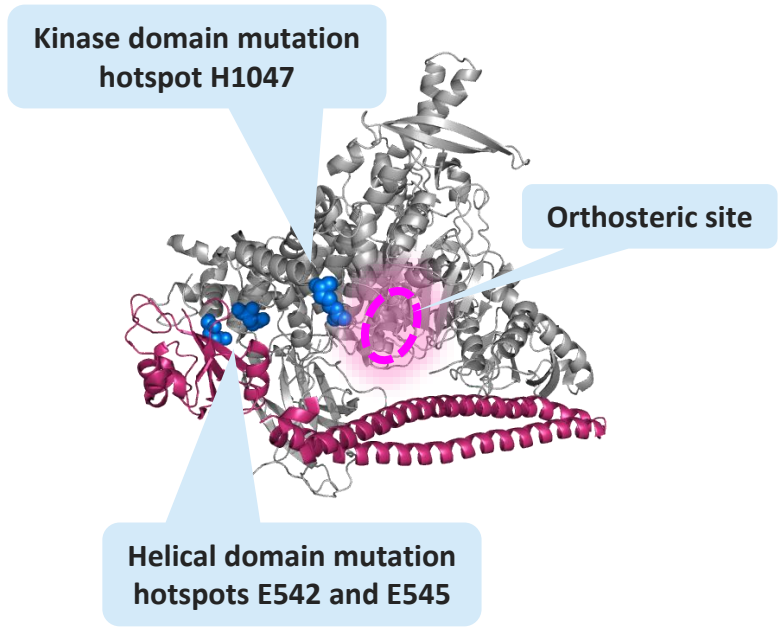
KRAS G12C

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

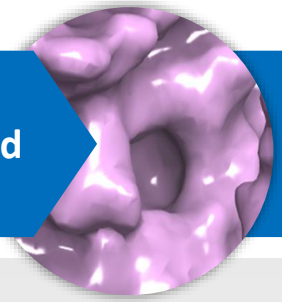
PI3Kα Franchise		
	PI3Kα^{PAN}	**RLY-2608*** *Pan-mutant selective allosteric inhibitor*
	PI3Kα^{SPECIFIC}	*H1047R-specific allosteric inhibitor*
	PI3Kα^{OTHER}	*Other PI3Kα allosteric programs*

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

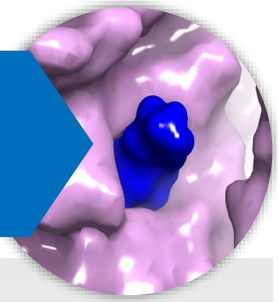
PI3Kα – Proprietary Insights Unlock Additional Approaches

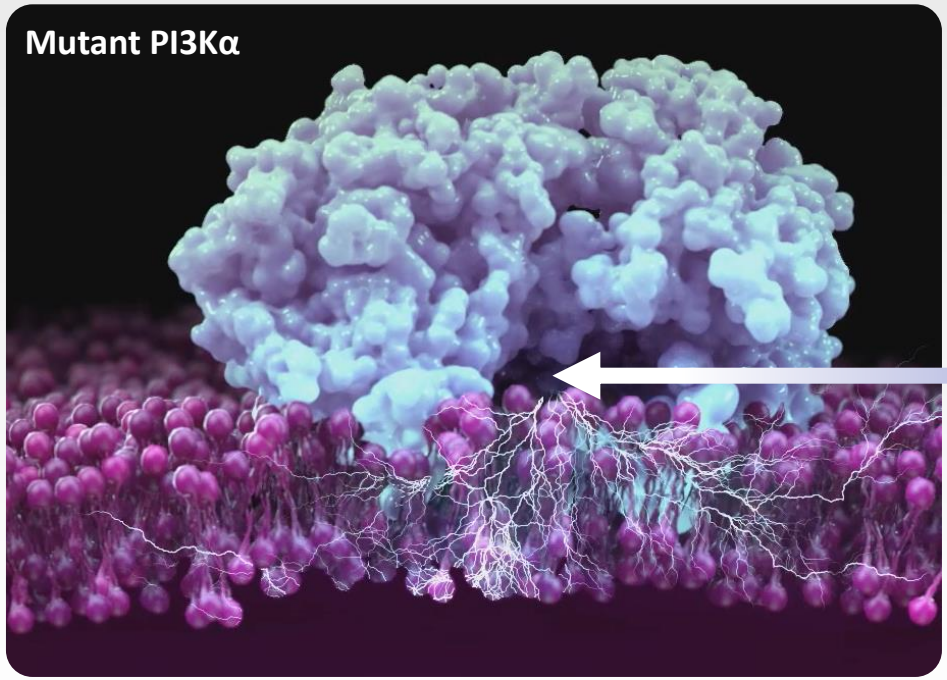
Solved first full-length structures of PI3Kα (mutant and wild-type)

Discovered novel allosteric pocket favored in mutant protein



Designed pan-mutant selective PI3Kα inhibitor (PI3Kα^{PAN})

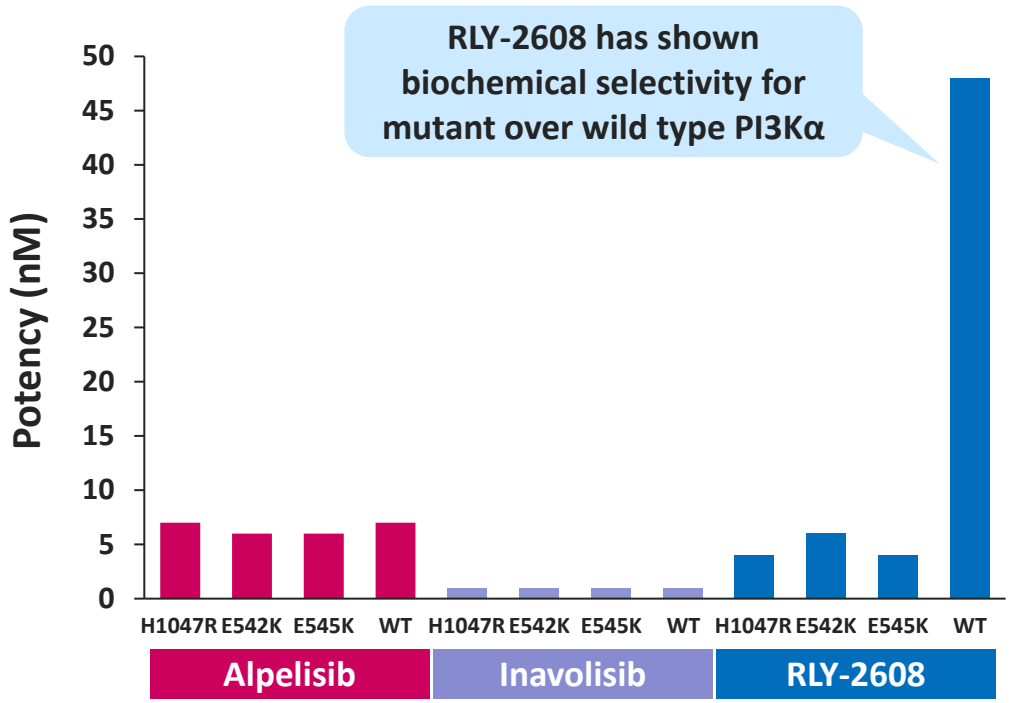




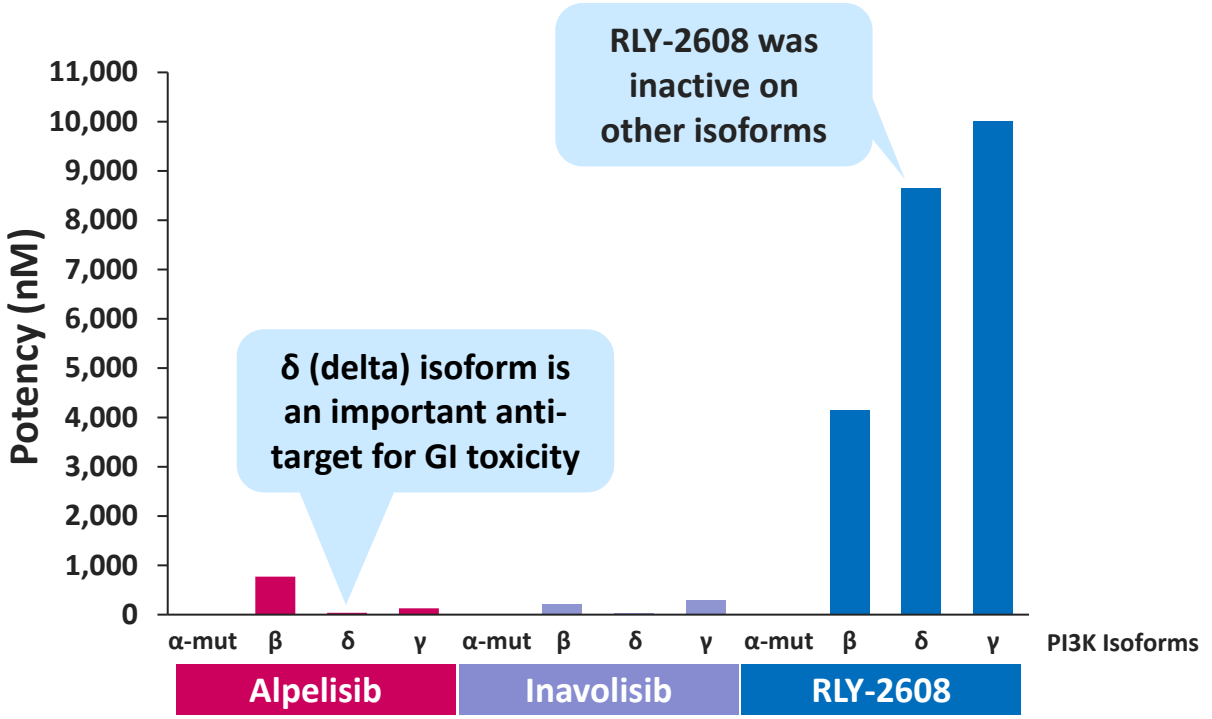
A differentiated understanding of the structure of PI3Kα and its relationship to function equips Relay Tx to design optimal mutant-selective inhibitors of PI3Kα

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

Mutant vs. WT PI3Kα potency

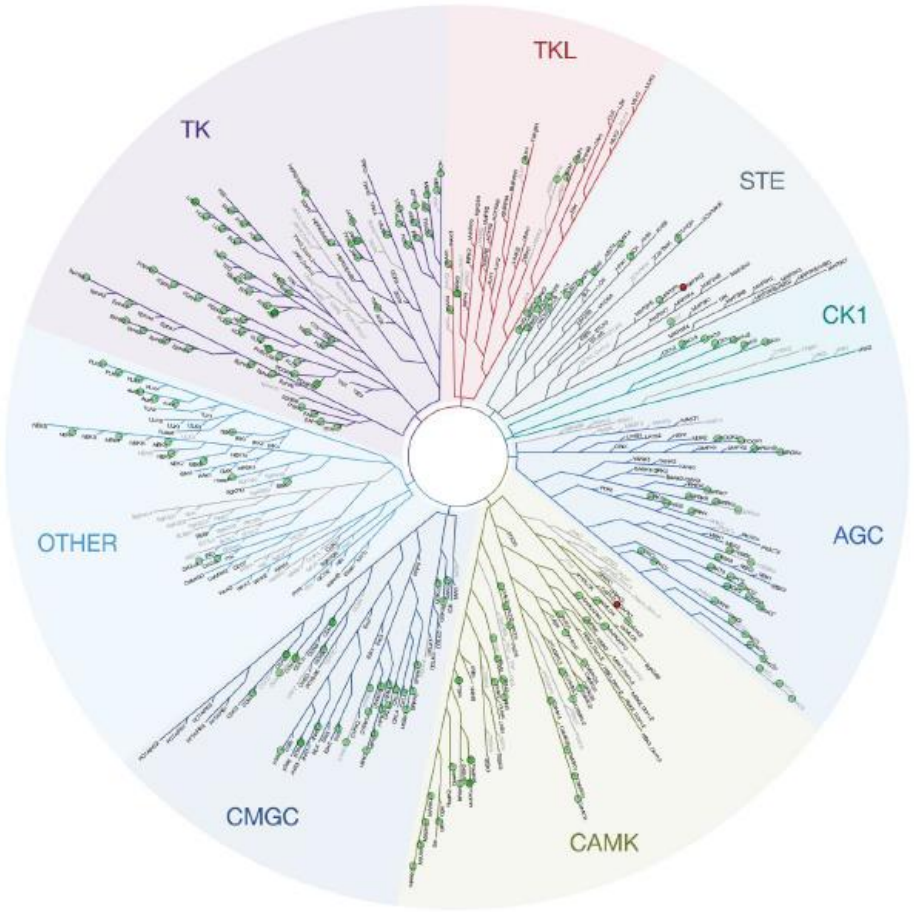


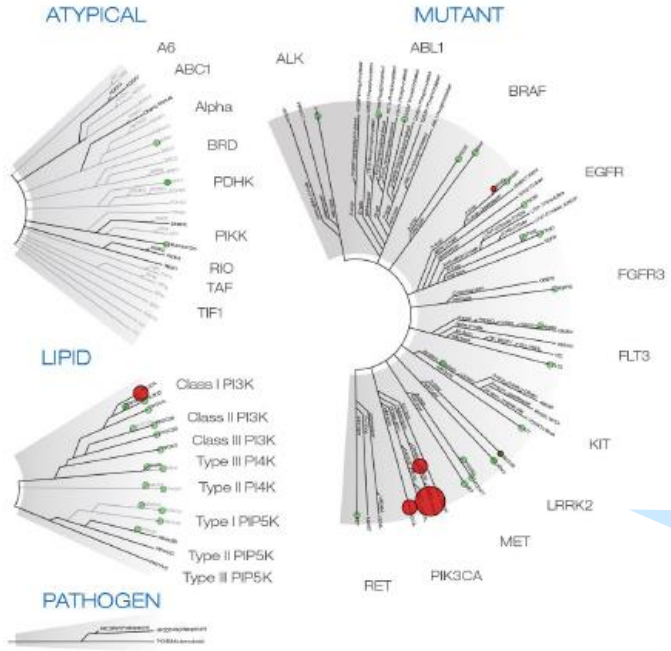
Mutant PI3Kα vs. other isoform potency



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

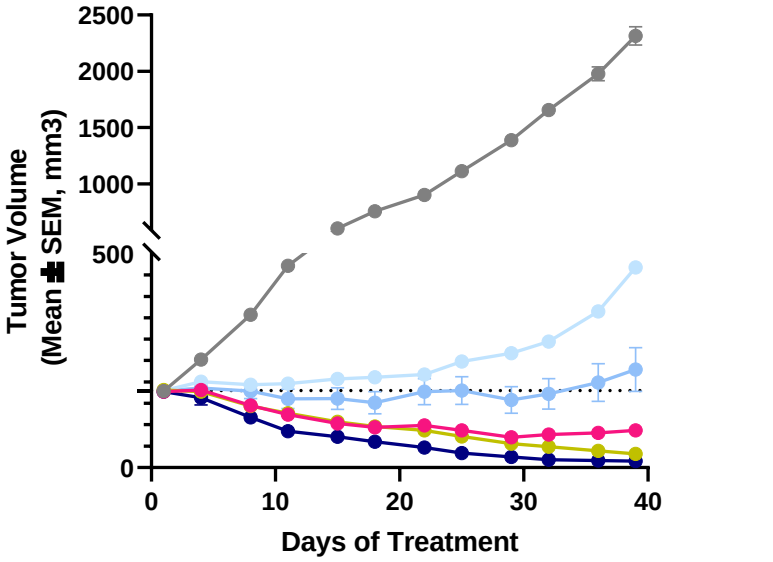
Kinase Inhibition @ 10 µM

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

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

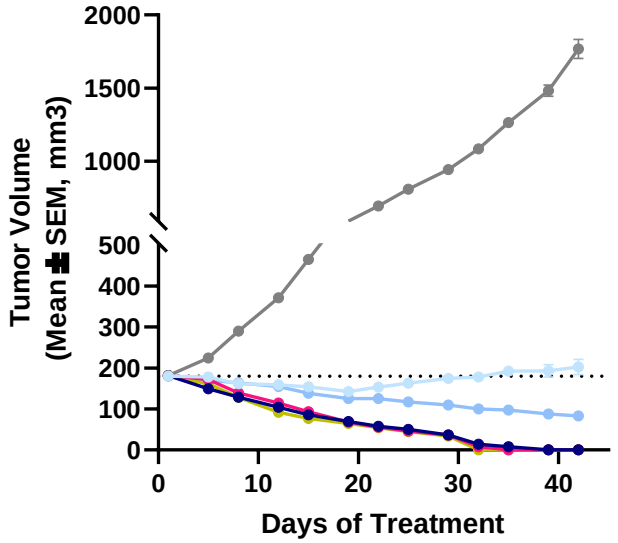
PI3Kα – In Vivo Tumor Regressions Across Both Mutation Hotspots (Mouse Study)

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]



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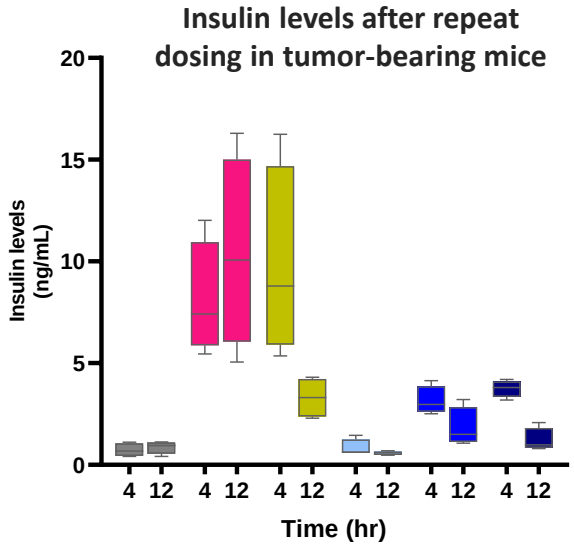
RLY-2608 50mg/kg QD
RLY-2608 100mg/kg BID

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
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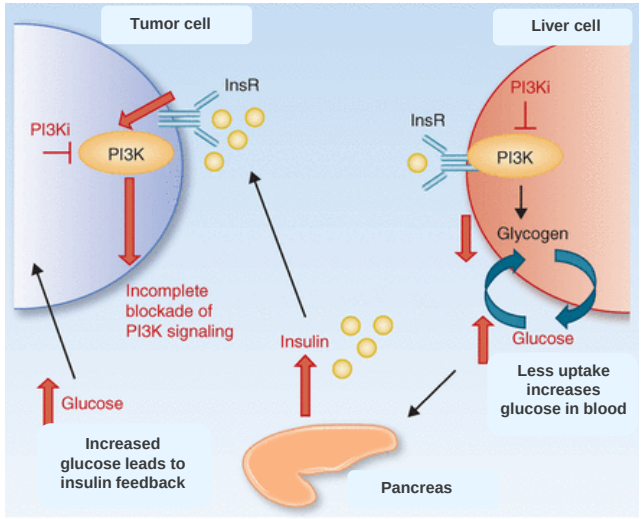
RLY-2608 100mg/kg BID

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

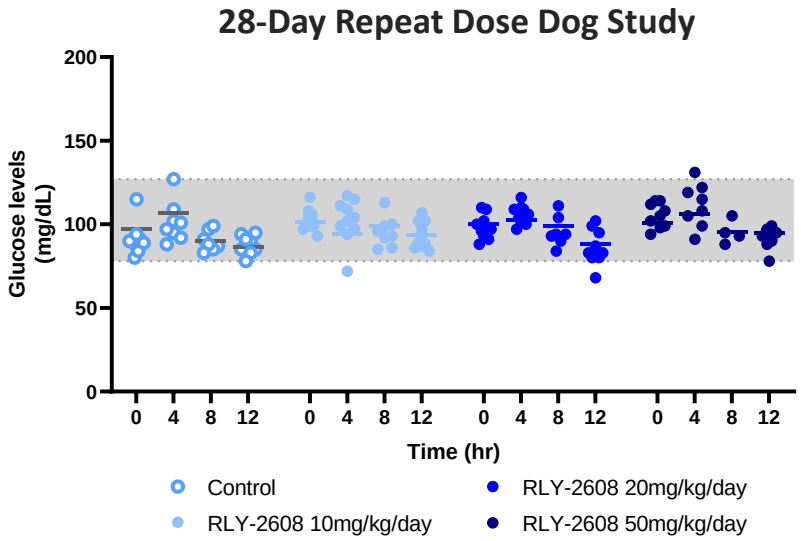
PI3Kα – RLY-2608 Had Reduced Impact on Glucose Homeostasis (28-Day Dog Study)

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

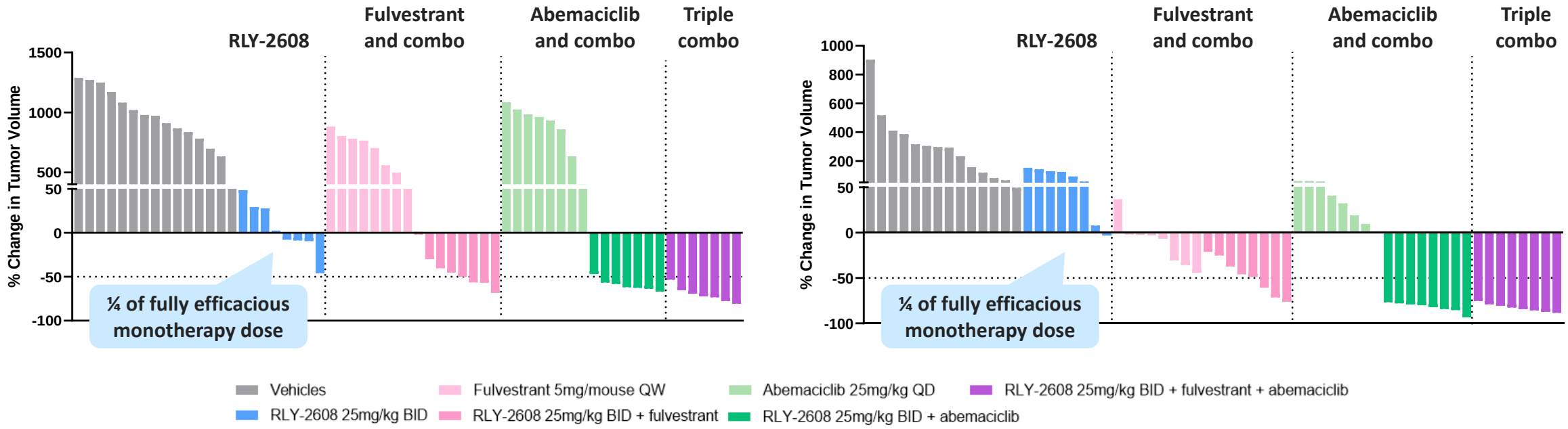
In higher species, dosing of RLY-2608 for 28 days showed no histopathological or ophthalmic findings associated with hyperglycemia

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)

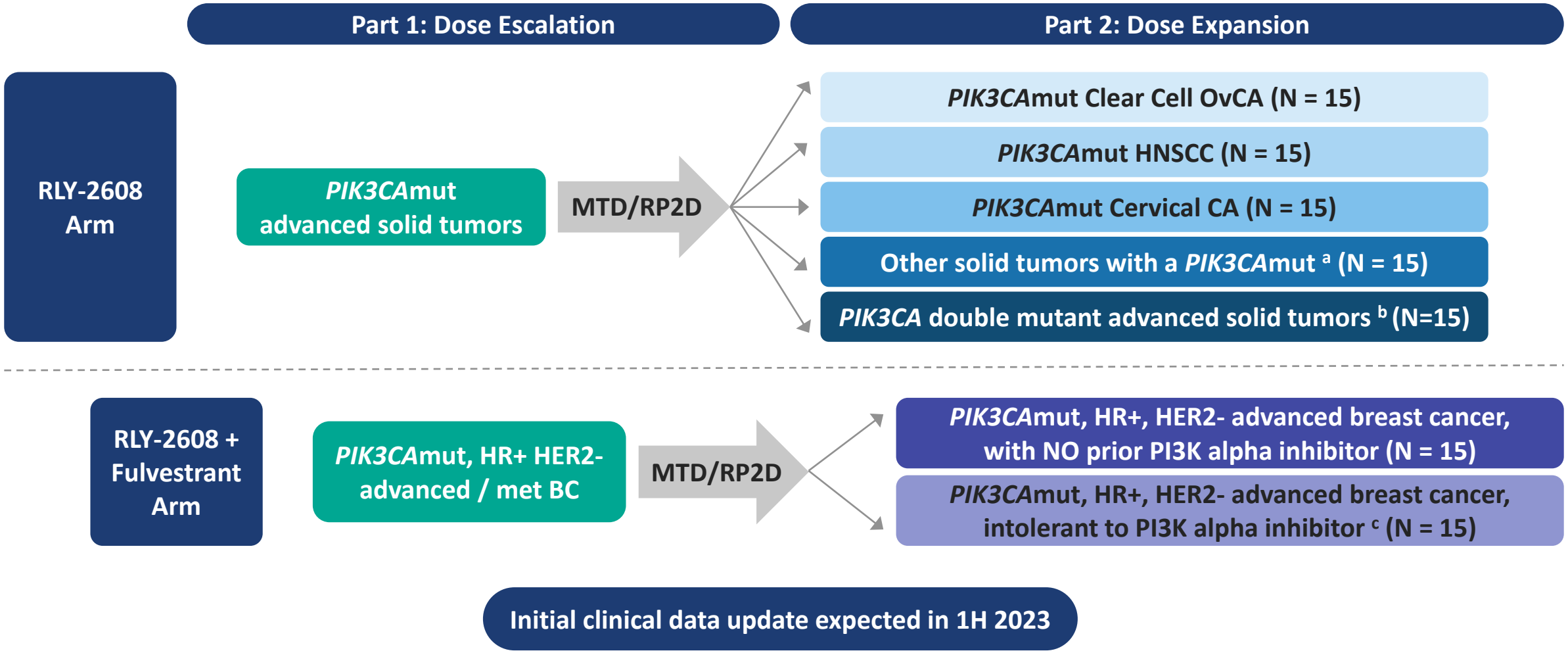
Superior efficacy observed preclinically in the triple combination



Combination arms with similar tolerability to monotherapy arms

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

PI3Kα – RLY-2608 Trial Design



Initial clinical data update expected in 1H 2023

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

Relay Tx's Emerging Breast Cancer Franchise

Goals: Greater selectivity → Better combinability → Increased efficacy

Relay Tx's PI3Kα Franchise

PI3Kα^{PAN}

- RLY-2608* Pan-mutant selective allosteric inhibitor
- **RLY-5836* Pan-mutant selective allosteric inhibitor**
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PI3Kα^{SPECIFIC}

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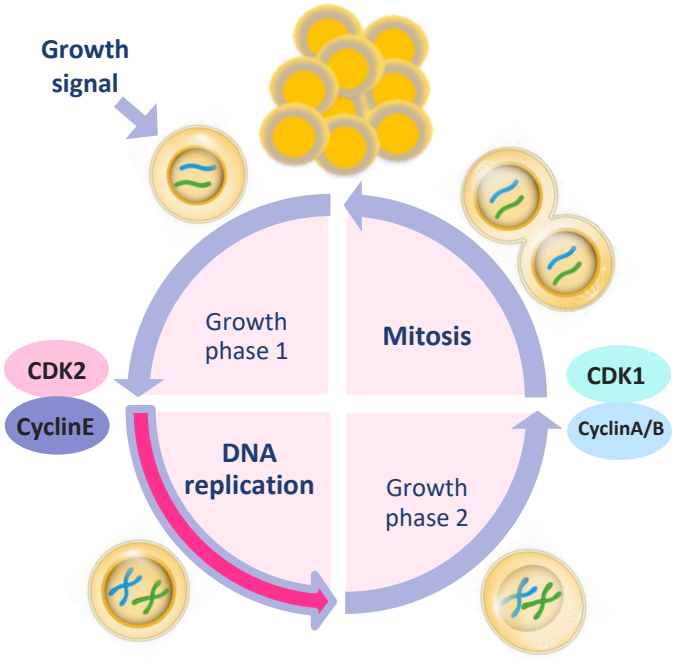
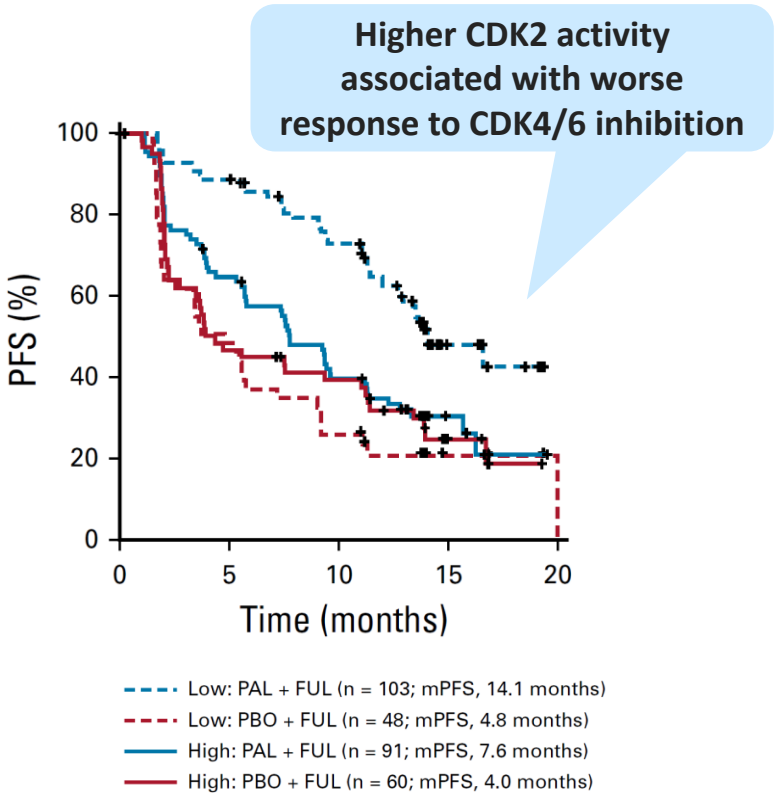
*Covers H1047X, E542X, E545X hot spots

CDK2 – A Validated Target in ER+ Breast Cancer

Cyclin E activates CDK2 to drive cancer



Clinical data demonstrate the importance of CDK2 in ER+ breast cancer



Turner, N.C., *et al*. JCO 2019

~45K patients receiving CDK4/6 inhibitors in the US

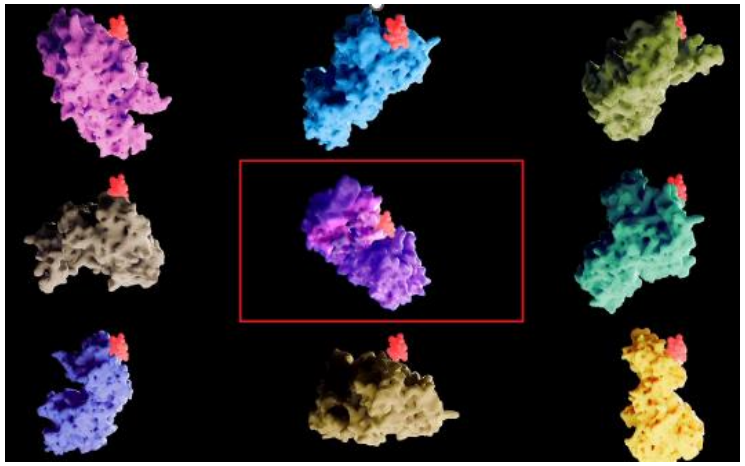
Patients receiving adjuvant CDK 4/6i	~23K
Patients receiving 1L CDK 4/6i	~18K
Patients receiving 2L CDK 4/6i	~5K

Source: Foundation Medicine Insights; SEER 2022; Decision Resources Group Breast Cancer Market Forecast, Feb 2022 (above corresponds to 2023 forecasted patient numbers); Scheidemann, 2021; Li, 2020

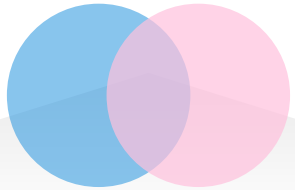
CDK2 – Relay Tx Unlocking Insights Into the Drivers of CDK2 Selectivity

Traditional approach

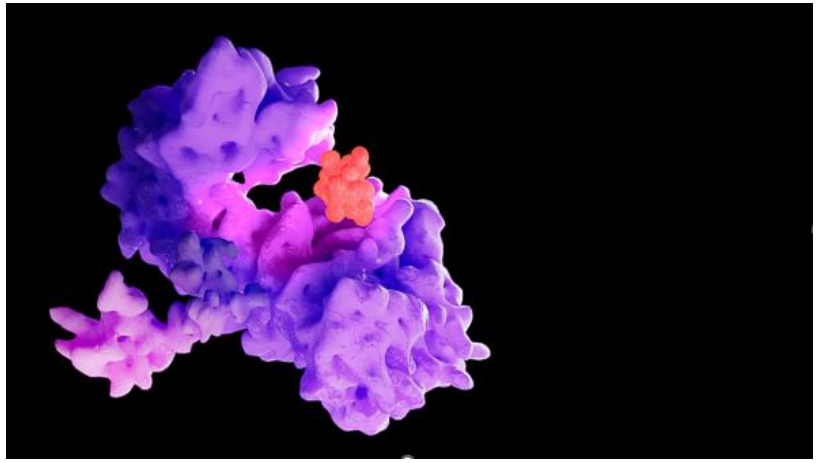
Non-selective CDK inhibitors



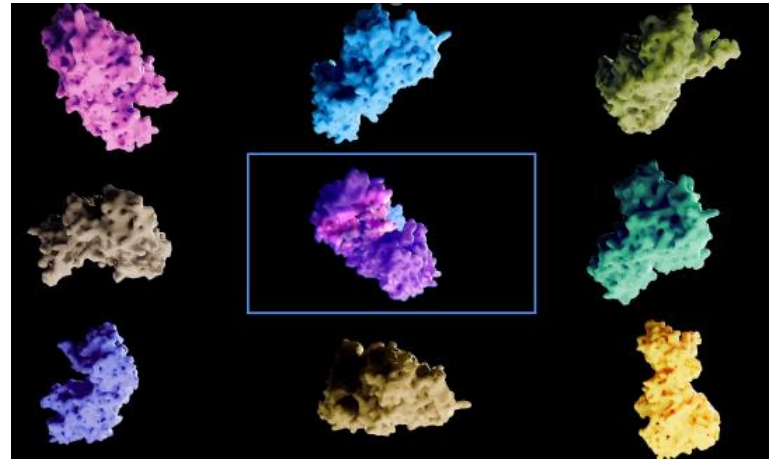
Relay Tx Approach



Motion-based insights into drivers of CDK2 selectivity…



…leveraged to design highly selective CDK2 inhibitors



CDK2 – Computational Modeling Designed to Enable Breakthrough Speed

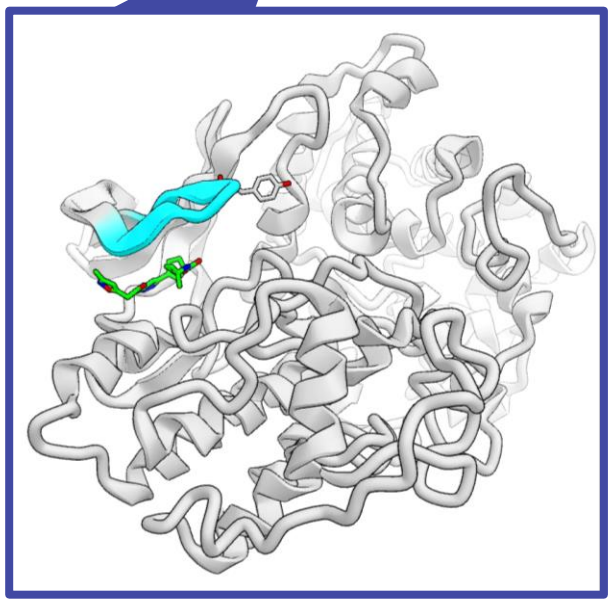
Collect MD frames
500 frames / MD
1000's of MDs

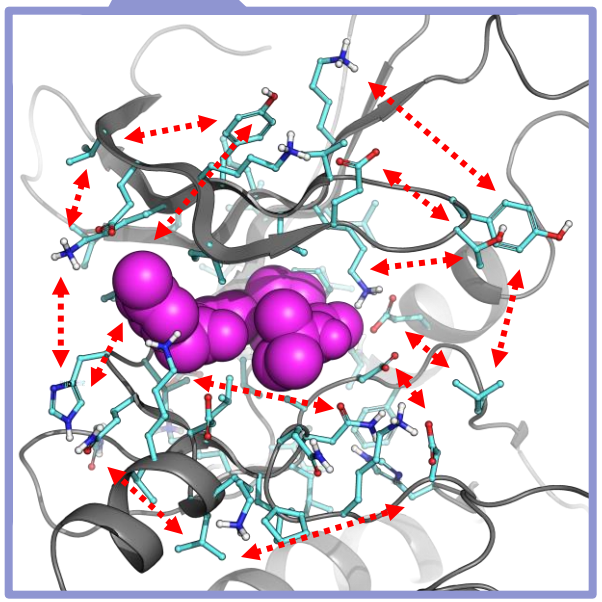
Extract features
~50,000 distances / frame

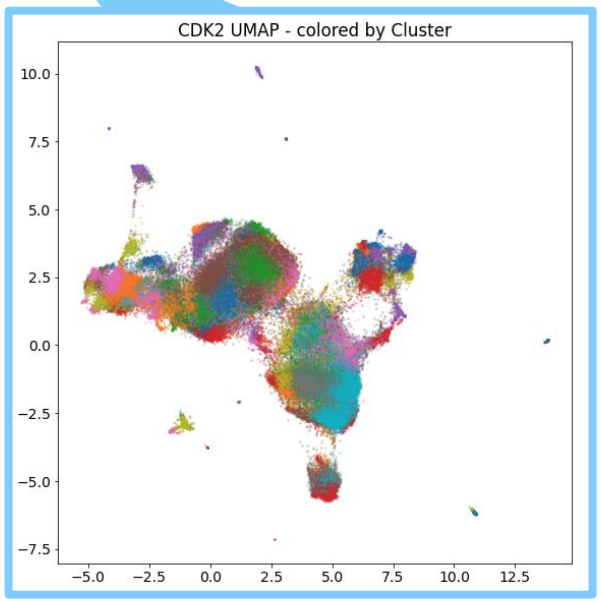
Cluster frames
100 clusters / CDK

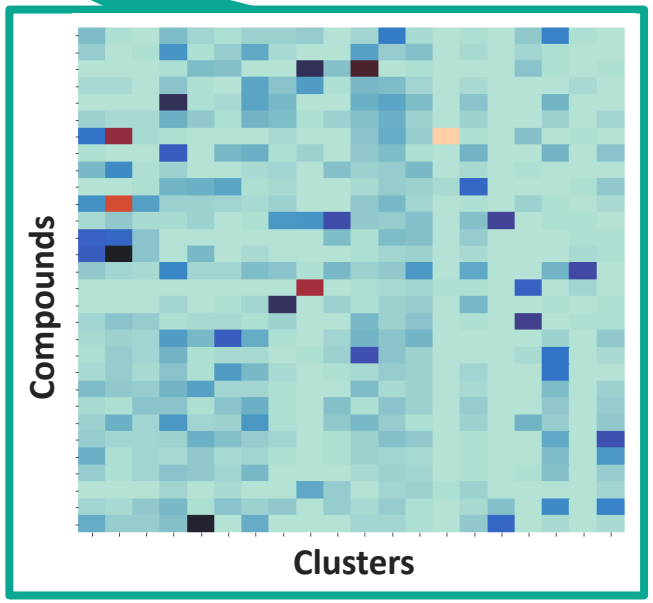
Assign cluster populations
200 cl. pops / ligand

Predict selectivity









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

CDK2 – Relay Tx's CDK2 Inhibitors Observed to be Highly Selective and Demonstrated Combination Potential with RLY-2608 in Breast Cancer

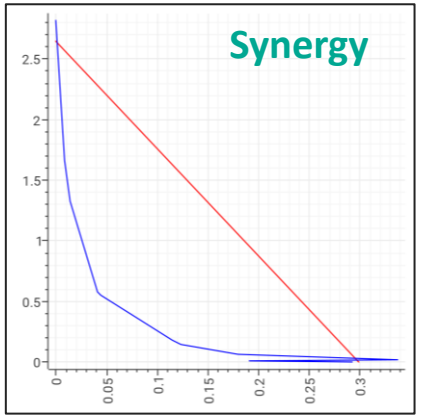
RTX-1 and RTX-2 achieved exquisite selectivity for a CDK2 inhibitor

		RTX-1	RTX-2
Biochemical Potency	CDK2/CycE IC_{50} (μM)	0.002	0.004
Biochemical Selectivity (fold over)	CDK1/CycB	300x	94x
	CDK4/CycD1	810x	270x
	CDK6/CycD3	830x	280x
	CDK9/CycT1	7900x	2400x
	GSK3β	59000x	68000x

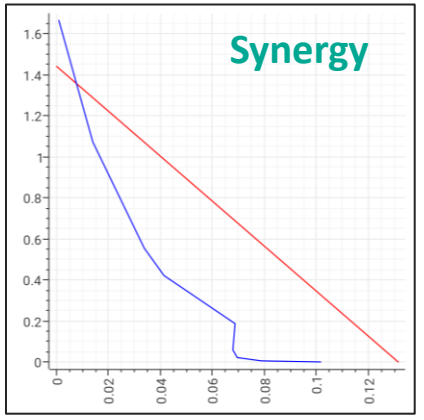
RTX-2 was synergistic with RLY-2608 (PI3Kα^{PAN}) in HR+ *PIK3CA*-mut breast cancer resistant to CDK4/6 inhibitors

RTX-2 (CDK2 inhibitor) + RLY-2608 (PI3Kα inhibitor)

CDK4/6i Sensitive



CDK4/6i Resistant



Clinical start expected in Q4 2023 or Q1 2024

Relay Tx's Emerging Breast Cancer Franchise

Goals: Greater selectivity → Better combinability → Increased efficacy

Relay Tx's PI3Kα Franchise

PI3Kα^{PAN}

- RLY-2608* Pan-mutant selective allosteric inhibitor
- RLY-5836* Pan-mutant selective allosteric inhibitor
- Additional chemically distinct programs

PI3Kα^{SPECIFIC}

- H1047R-specific allosteric inhibitor
- Additional chemically distinct programs

PI3Kα^{OTHER}

- Other mutant-selective mechanisms

Relay Tx Rational Combination Partners

- Selective CDK2 Inhibitor
- **ERα Degrader**
- RLY-4008 (Selective FGFR2)
- Pan-mutant + Mutant Specific PI3Kα Combinations
- RLY-1971 (SHP2)
- Undisclosed Target

*Covers H1047X, E542X, E545X hot spots

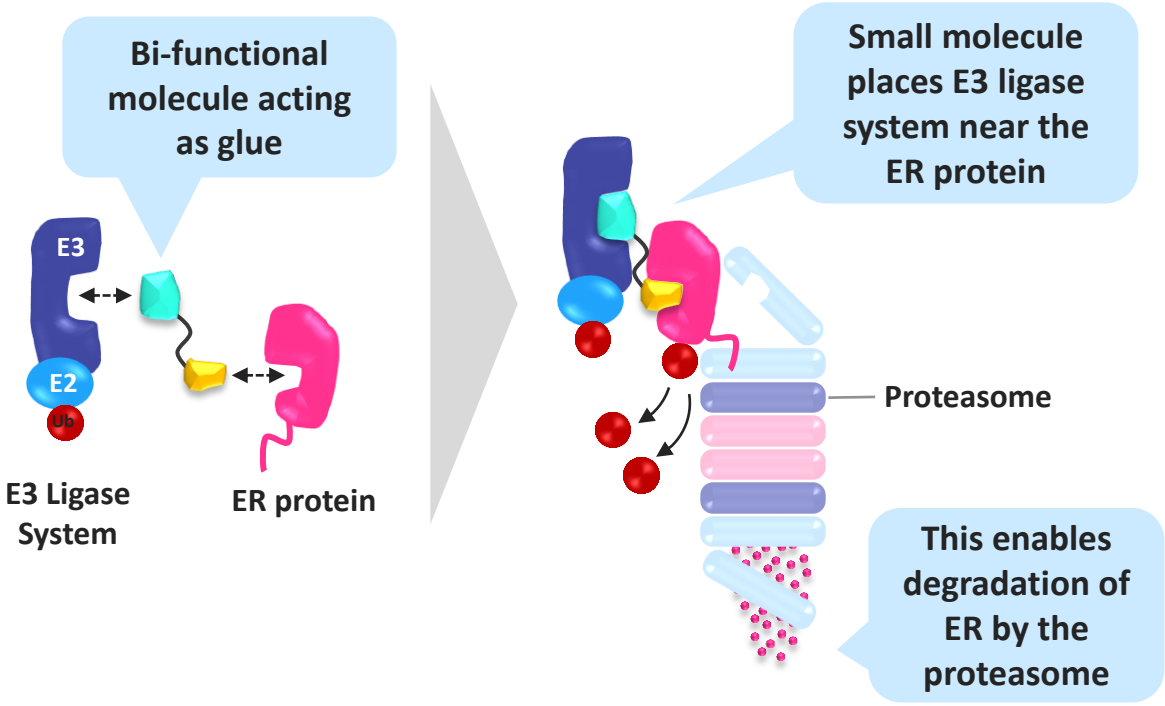
ERα Degrader – Endocrine Therapy is Central in the Treatment of HR+/HER2- Breast Cancer

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

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

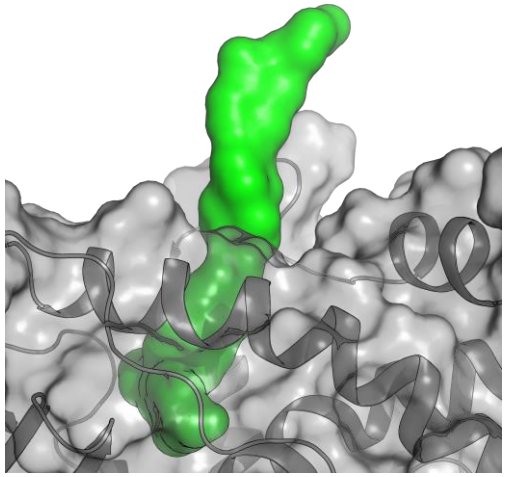
In-house ERα Degrader would further strengthen Relay Tx's Breast Cancer franchise

Enabling degradation of the estrogen receptor (ER) protein



ERα Degrader – Rational Design of Targeted Protein Degraders

Traditional Approach

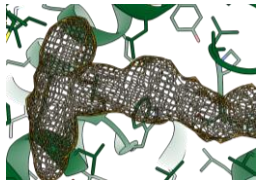


Relay Tx Approach

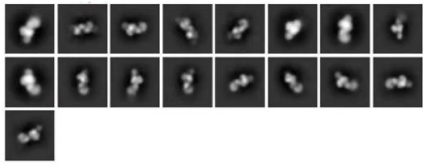
Multiple experimental tools deployed….

…to inform long-time scale MD models

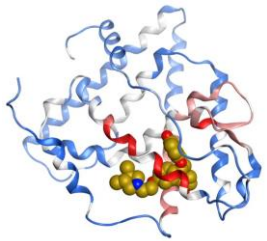
X-ray Crystallography

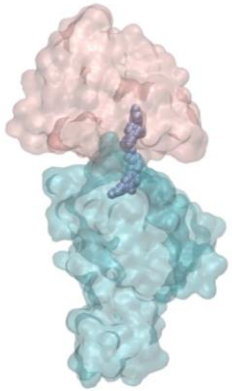


Cryo-EM



Binary complex HDX-MS

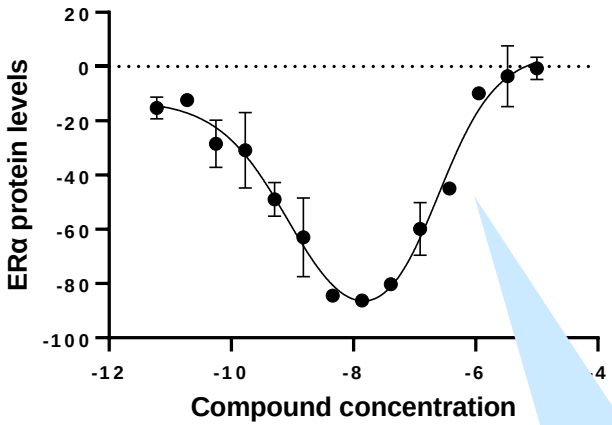




Conformational models enable effective triage of degrader design ideas

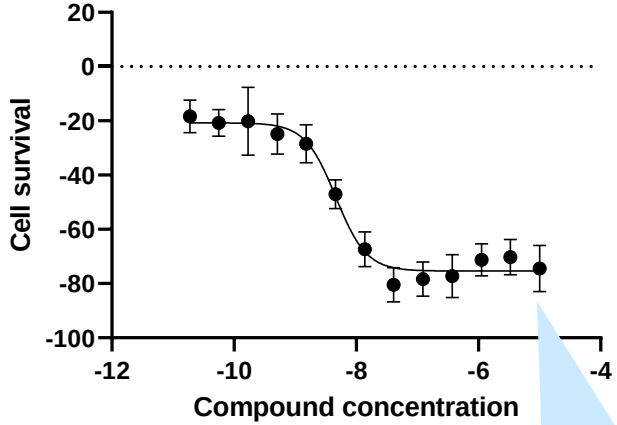
ERα Degrader – Relay Tx has Rapidly Obtained Potent Degraders of ERα

Protein degradation*



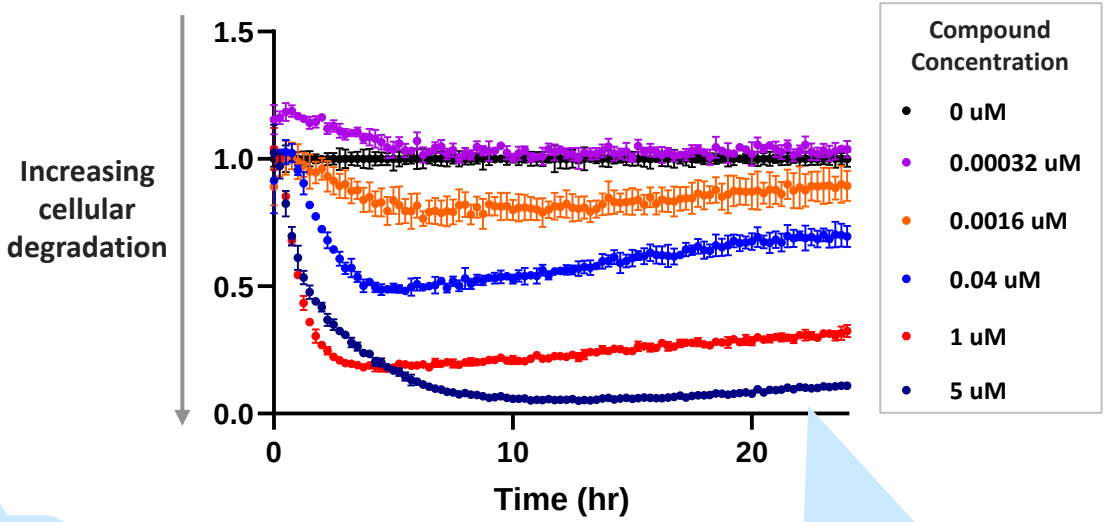
Hook effect characteristic of degraders observed with Relay Tx compound

Cellular proliferation*



Relay Tx compound potently inhibits cellular proliferation

Cellular degradation kinetics

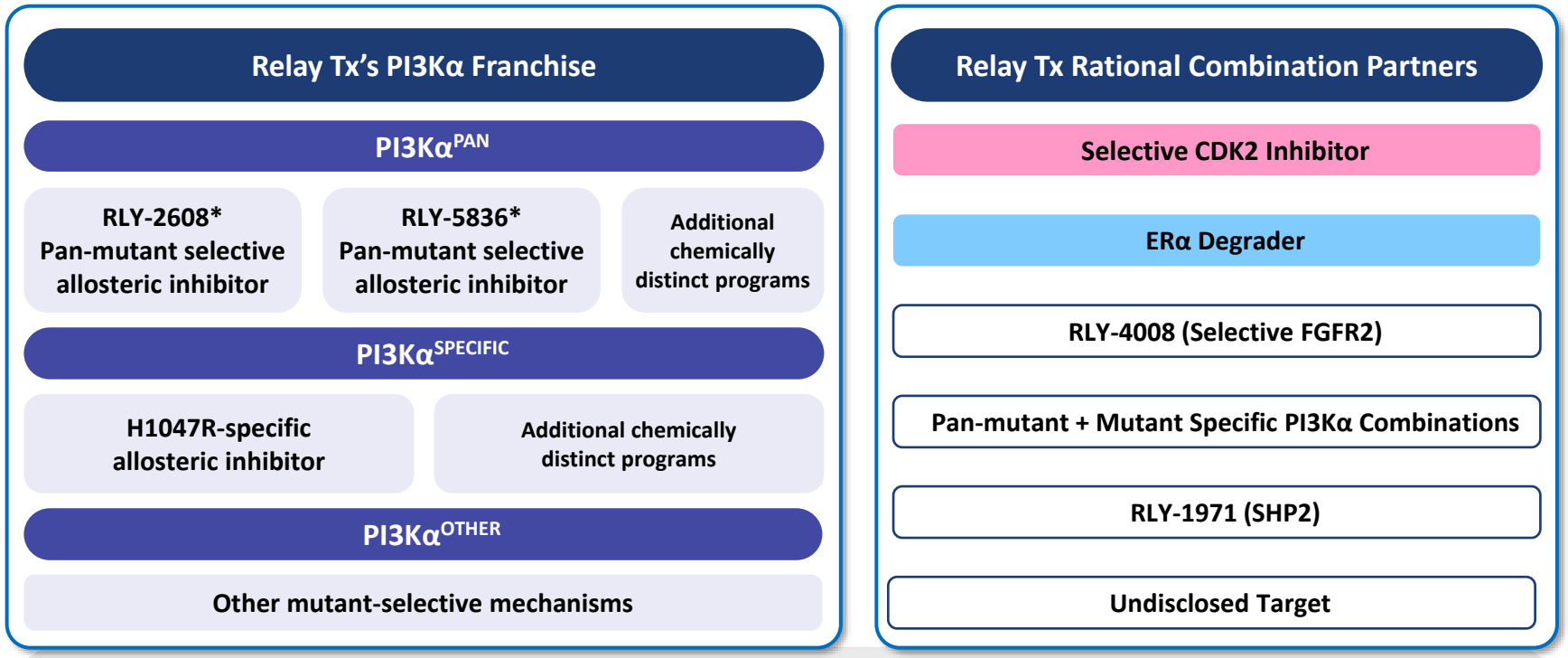


Increasing compound concentration yields faster and deeper protein degradation

Development candidate nomination expected in 2023

*MCF7-ERα -HiBiT cells

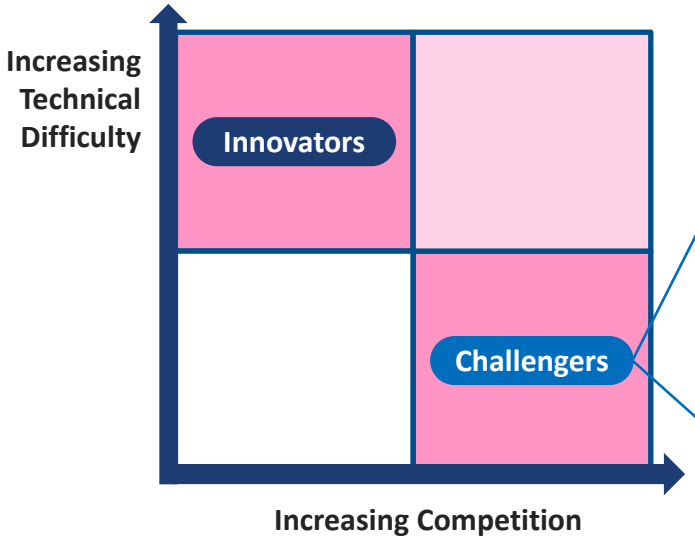
Large Breast Cancer Patient Population



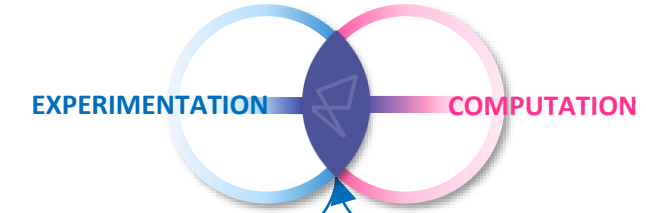
~195K patients diagnosed annually in the US with HR+, HER2- breast cancer

Challengers – Supporting the Build of Our Dynamo™ Platform

Challengers Have Lower Technical Risk



Challengers Solve Problems with "Known" Answers

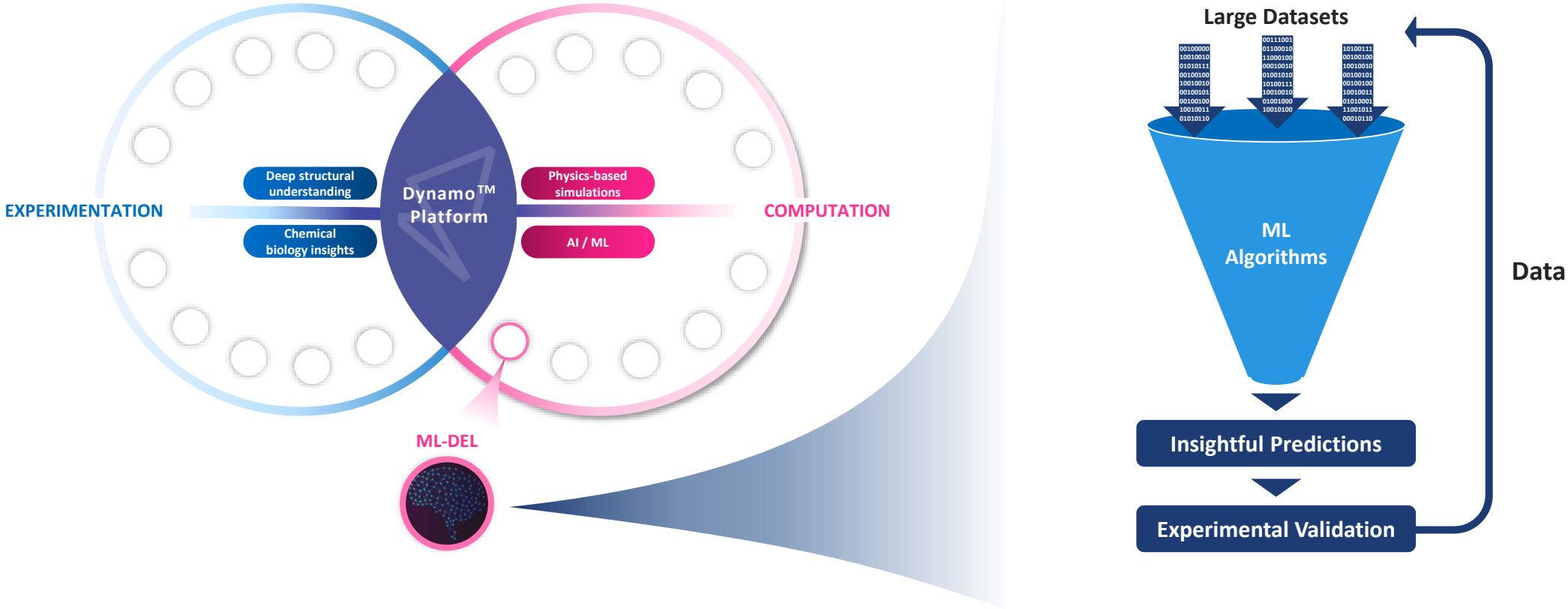


Enable higher volume of programs → **Serve as a data factory and increase experience**

Our challengers: SHP2 *RLY-1971* (Genentech) -- (EQRx)

The more we do, the better we get

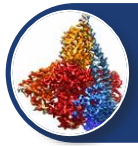
Challengers – Creating a Data Factory



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

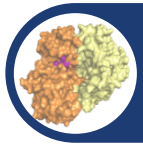
Relay Tx – Capital, Team & Execution Focus to Deliver on Anticipated Milestones

Breast Cancer Franchise



RLY-2608
(PI3Kα^{PAN})

Initial data
in 1H 2023



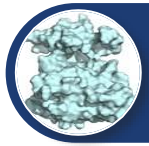
Selective CDK2

Clinical start in
Q4 2023 or Q1 2024

ERα Degrader

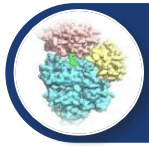
Development candidate
nomination
in 2023

Tumor Agnostic



RLY-4008
(Selective FGFR2)

Additional
data updates
in 2H 2022 & 2023



RLY-1971
(SHP2)

Atezolizumab combo
trial to be initiated
in 2H 2022

$898M

Cash, cash equivalents and investments
as of the end of Q1 2022

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

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