RELAY®
THERAPEUTICS

JPM Presentation

January 2023

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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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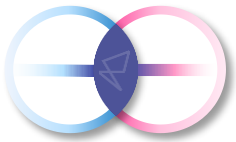
Relay Tx – Patient-Driven

New Breed of Biotech

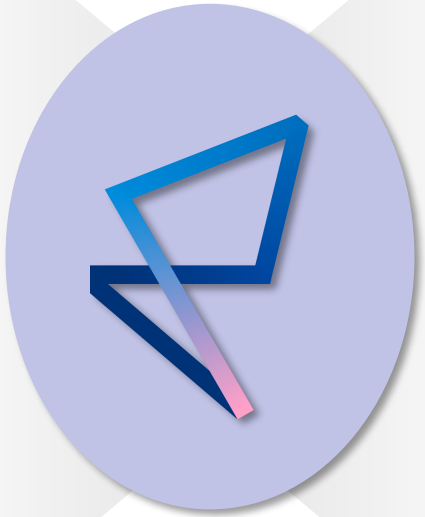
EXPERIMENTATION



COMPUTATION

Clear Focus

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



$1.1B

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

Validated Approach

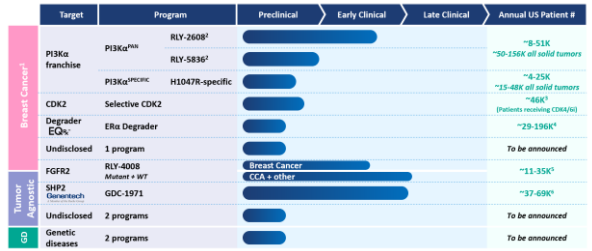
Clinical

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

Pre-clinical

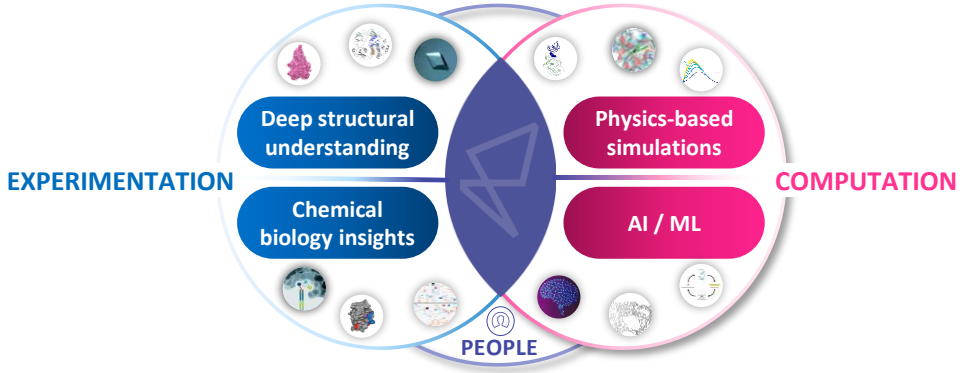
- PI3Kα^{PAN} *RLY-5836*
- Selective CDK2
- ERα Degrader

Execution-Focused

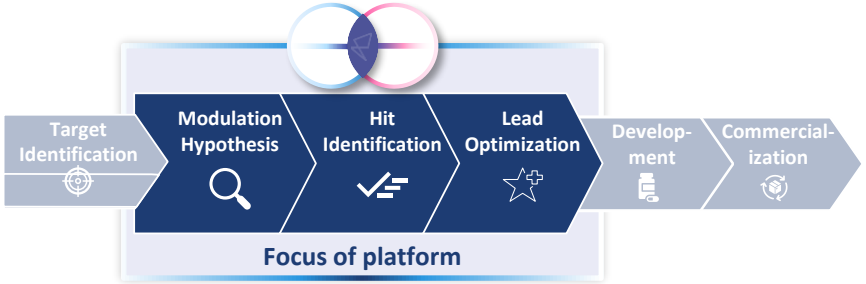


Relay Tx – Dynamo™ Platform

1 Dynamo™ Platform…



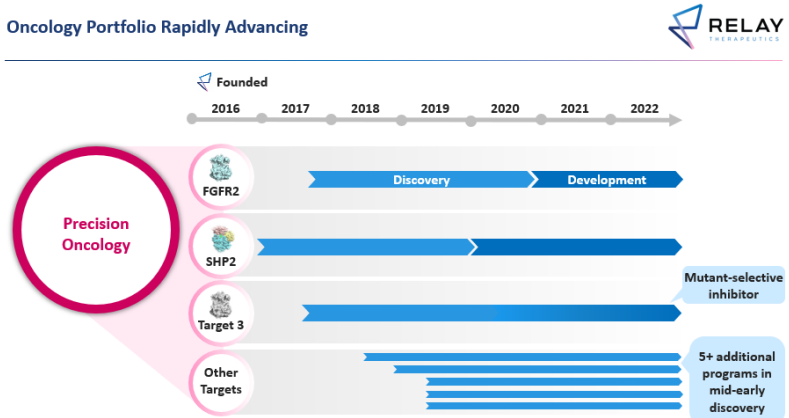
2 …is focused on making medicines



3 …aims to address selectivity on validated targets

Relay Tx – Execution Focused

Jan 2020



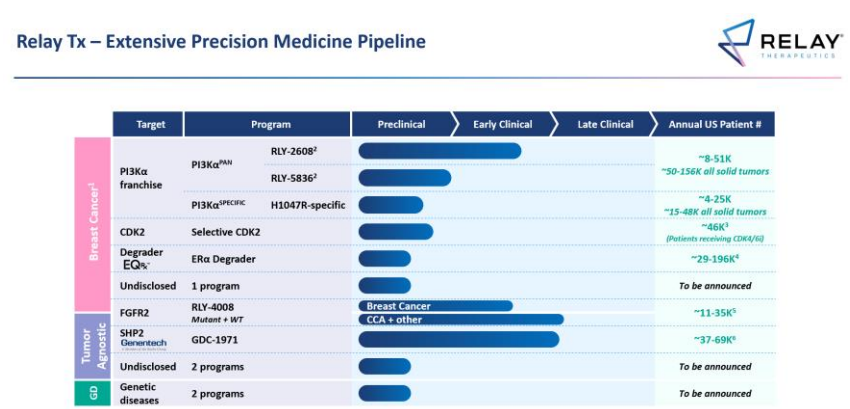
Company

- Private
- Preclinical
- Purely research

Programs

- 2 disclosed targets
- 6+ unnamed programs

Jan 2023



Company

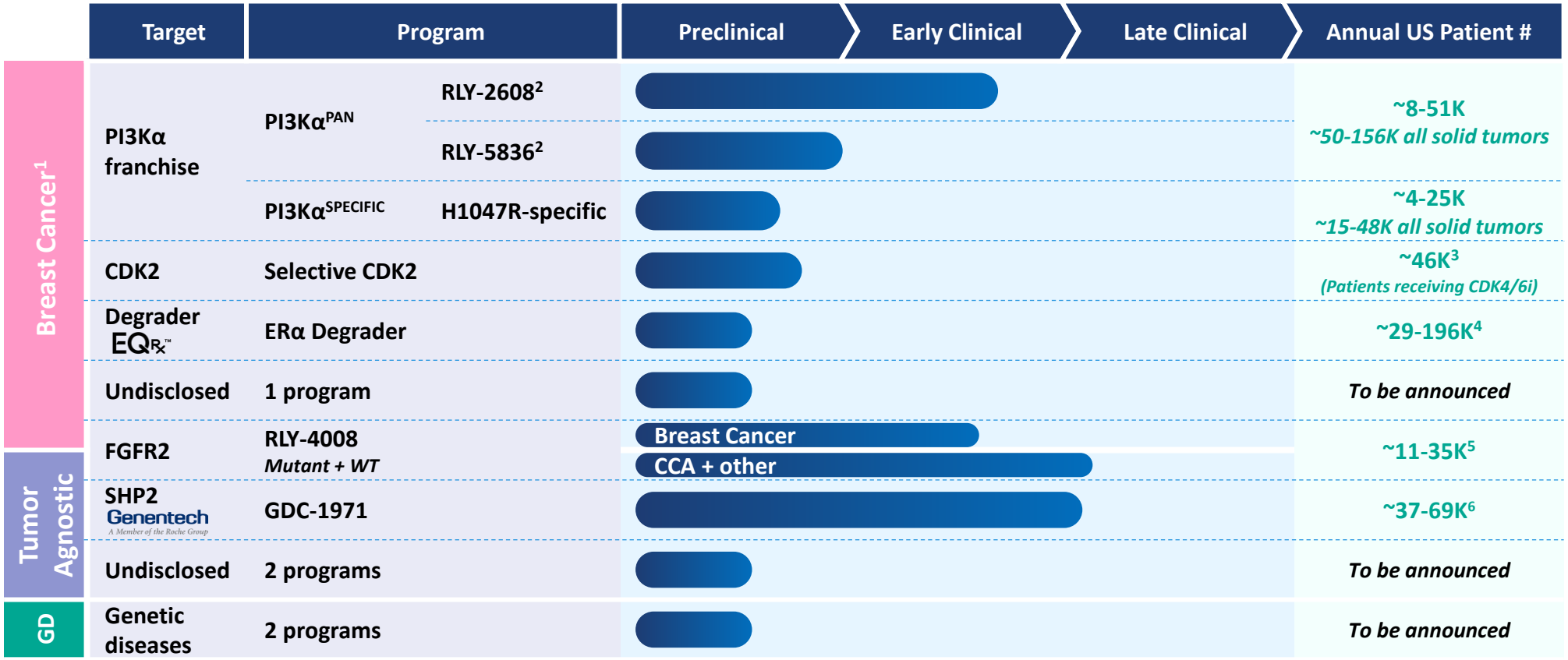
- Public, clinical org
- Cash runway into 2025
- Presented clinical data at ESMO & Triple Meeting

Programs

- 3 assets in clinic
- 5 disclosed programs
- 5+ unnamed programs
- Platform: + ML-DEL and Automation

Source: Relay Tx presentation at JPM conference Jan 2020

Relay Tx – Extensive Precision Medicine Pipeline



Note: Unless otherwise indicated, patient #'s refer to total annual number of US patients with late-line cancers compared to comprehensive annual incidence that may be amenable to treatment with our programs
1. Unless otherwise indicated, all breast cancer patient numbers refer to HR+/HER2- breast cancer tumors 2. RLY-2608 covers H1047X, E542X, E545X hot spots, and breast cancer patient range assumes HR+/HER2- population 3. ~46k HR+/HER2- breast cancer patients expected to receive CDK 4/6 inhibitors in adjuvant setting, first-line setting, and second-line setting in 2023, per Decision Resources Breast Cancer Market Forecast, report dated June 2022 4. HR+/HER2- US late-line breast cancer patients compared to HR+/HER2- US incident breast cancer patients 5. FGFR2 altered late-line solid tumors compared to comprehensive annual FGFR2 altered incident solid tumors including additional FGFR gene fusions and rearrangements resulting from truncation of the protein at exon 18 6. SHP2 combo only includes KRAS G12C in lung and CRC, EGFR mutations in lung, and ALK fusions in lung

Relay Tx – Capital, Team & Execution Focus to Deliver

Breast Cancer Franchise

PI3Kα^{PAN}

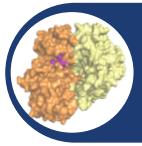
RLY-2608

Initial data in 1H 2023

RLY-5836

Clinical start in 2Q 2023

Selective CDK2



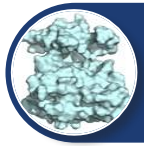
Clinical start in early 2024

ERα Degrader

Development candidate nomination in 2023

Tumor Agnostic

RLY-4008 (Selective FGFR2)

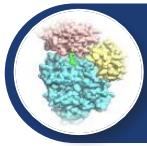


Full dose escalation data in 1H 2023

Non-CCA expansion cohorts data in 2H 2023

Pivotal cohort full enrollment in 2H 2023

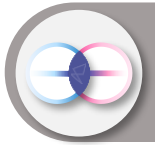
GDC-1971 (SHP2)



Ongoing combo trials; Genentech controls data disclosures

Undisclosed

To be announced



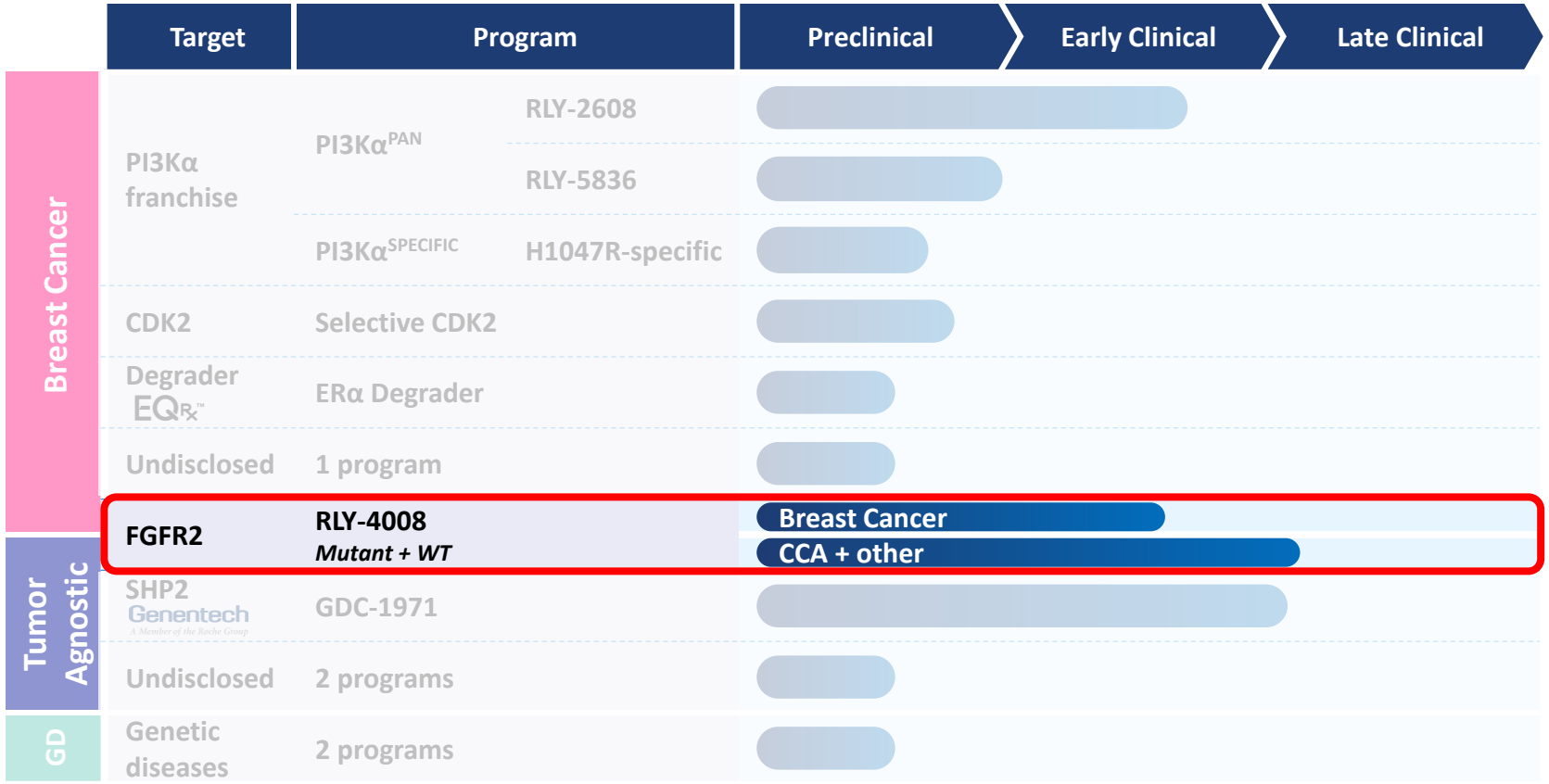
5+ undisclosed programs in preclinical development and additional early-stage efforts across platform

$1.1B

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

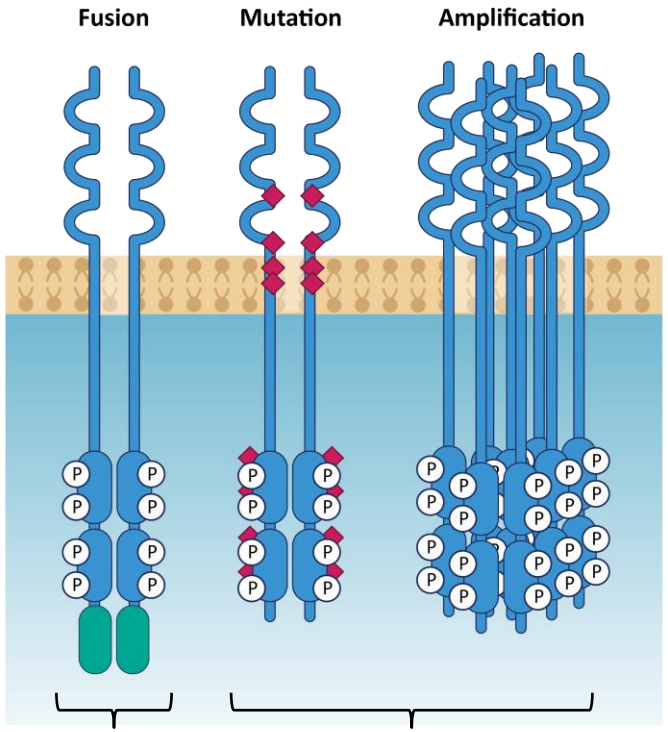
Current cash, cash equivalents and investments are expected to be sufficient to fund current operating plan into 2025

Relay Tx – Extensive Precision Medicine Pipeline



FGFR2 – Validated Target Present in Several Tumor Types

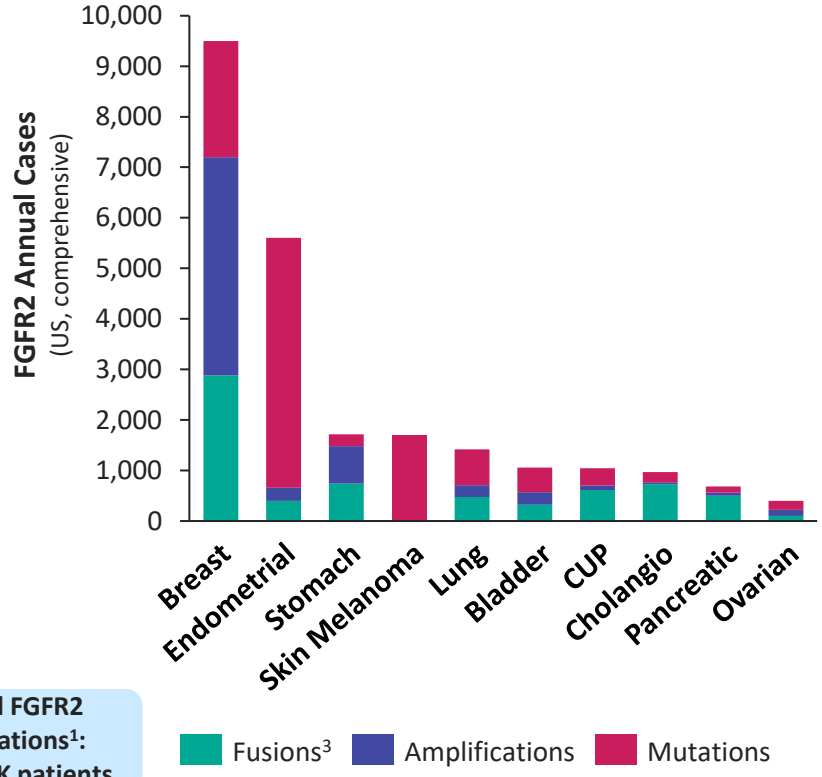
Three classes of driver alterations in FGFR2



Annual US Patient Count[1]

Total FGFR2 alterations[1]: ~11-35K patients

FGFR2 alterations are observed across multiple tumor types[2]



FGFR2-altered cancers remain a high unmet medical need

FDA approvals only in fusion+ CCA FGFRi-naïve patients

36-42% **Objective Response Rate[4]**

Limited treatment options for other FGFR2 driven cancers[5]

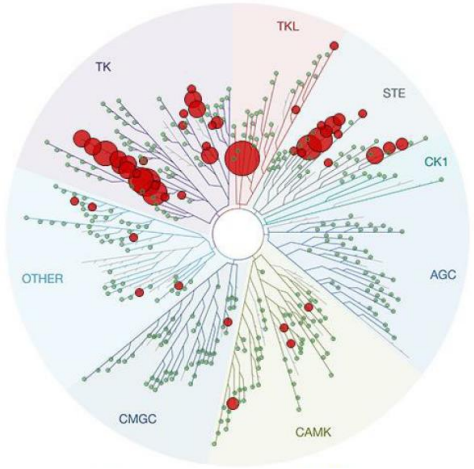
Sources: Image adapted from Babina IS, Turner NC. Nat Rev Cancer 2017;17: 318-332; Internal analysis based on third party industry data

1. All patient #'s refer to total annual number of US patients with late-line cancers vs. comprehensive annual incidence that may be amenable to treatment with our programs including additional FGFR gene fusions and rearrangements resulting from truncation of the protein at exon 18; 2. Cholangio, cholangiocarcinoma (CCA); CUP, carcinoma unknown primary; 3. FGFR2 fusion estimates include del18 truncations; 4. Based on pemigatinib, erdafitinib, and futibatinib prescribing information; 5. Erdafitinib is approved for urothelial carcinoma with FGFR2/3 alterations

FGFR2 – Limitations of Current FGFR Inhibitor Landscape

Limited Selectivity

Approved Pan-FGFRis are non-specific across FGFR family



Limited Target Inhibition

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

Limited Tolerability

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

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

Limited Efficacy

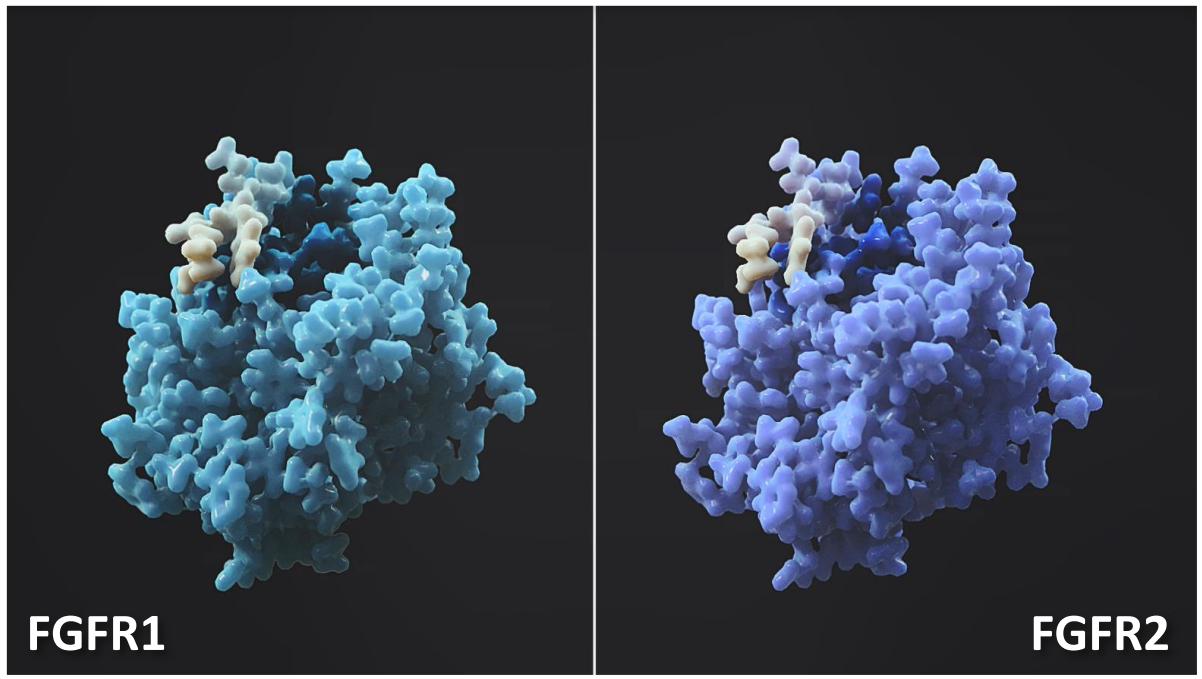
36-42% Objective Response Rate in Fusion+ CCA FGFRi-naïve pts

Sources: Pemigatinib – prescribing information; futibatinib – prescribing Information; erdafitinib – prescribing information

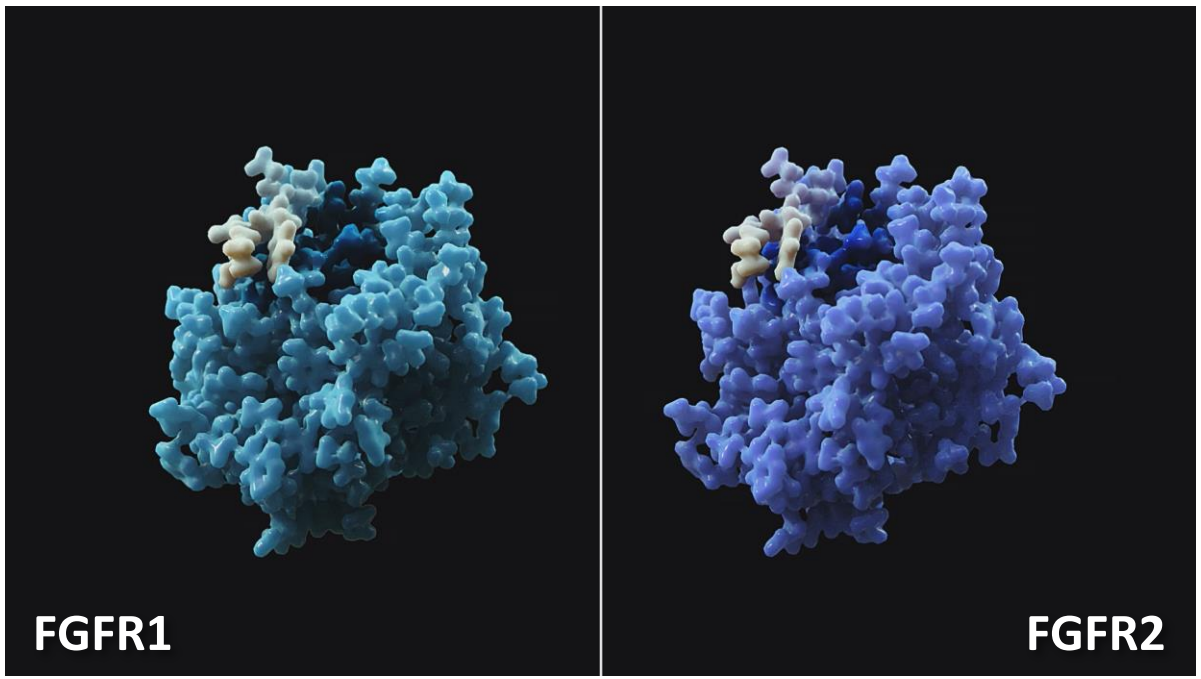
1. From pemigatinib NDA review documents: "Pemigatinib 13.5 mg daily provided 76% inhibition of ex vivo phosphorylated FGFR2α at trough"

FGFR2 – Increasing Resolution Reveals New Opportunities

Standard approach



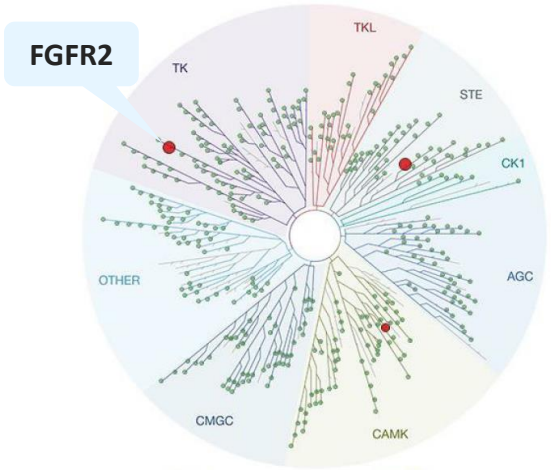
Relay Tx approach



Relay Tx Solution – Addressing Unmet Need Through Greater Selectivity

Favorable Selectivity[1]

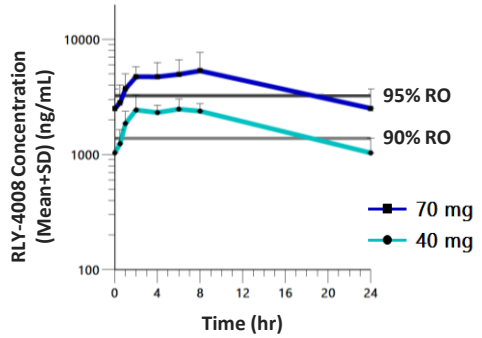
~200x selective for FGFR2 over FGFR1,
~5000x selective over FGFR4[2]



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

Favorable Target Inhibition[1]

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



Favorable Interim Tolerability[1]

Minimized key off-target toxicities[3]

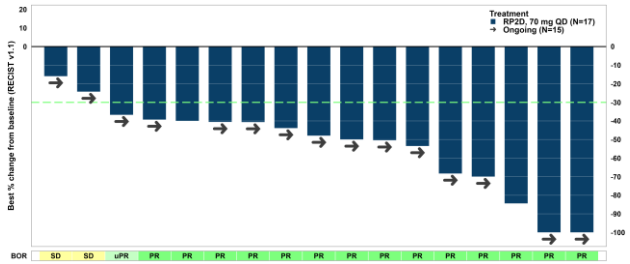
Hyper-phosphatemia[1]	Diarrhea	Discontinuation
12%	4%	1%

All Gr1-2

Favorable Interim Efficacy[1]

FGFR2 driven tumor shrinkage:

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



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

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

RLY-4008 – ReFocus Trial

Part 1: Dose Escalation
Demonstrate clinical proof of mechanism

Advanced solid tumors with FGFR2 alterations per local assessment; Both FGFRi-naïve & FGFRi-treated allowed

RP2D

Part 2: Dose Expansion and Pivotal Cohort
Confirm dose and establish efficacy

- Pivotal: Fusion+ CCA, FGFRi-naïve
- FGFR2-altered, non-CCA tumors
- Other FGFR2-altered CCA

Focus of Disclosure

- Selectivity
- Target Inhibition
- Tolerability
- Early Signals of Efficacy
- Interpretable Efficacy

4Q 2021: Triple Meeting

- Validated hypothesis with target inhibition and acute tolerability
- Provided early efficacy signals in heterogeneous populations

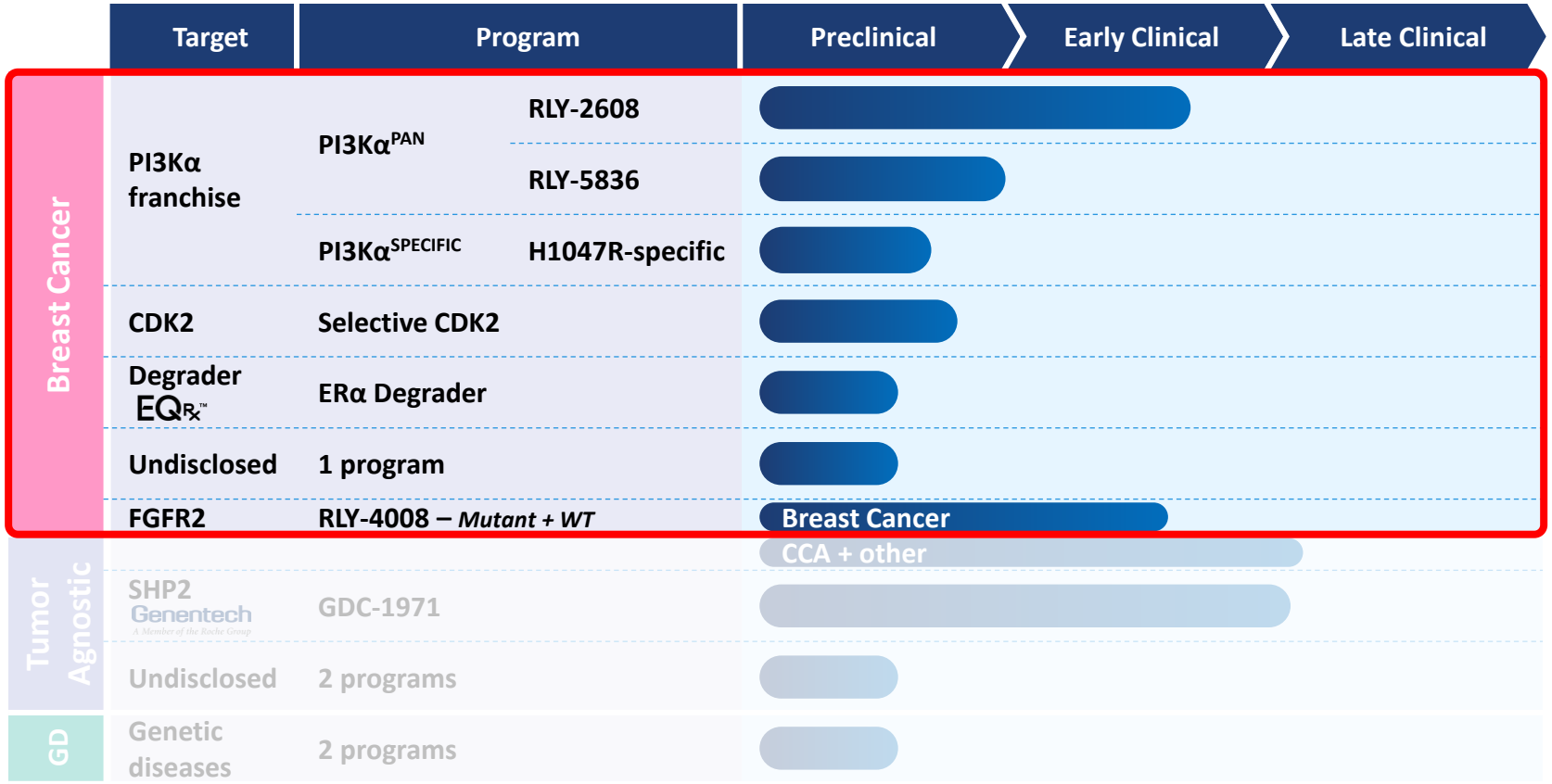
3Q 2022: ESMO

- Confirmed longer term safety and tolerability
- Established stronger support for FGFR2 fusion+ CCA, FGFRi-naïve efficacy

2023: Anticipated Milestones

- 1H 2023: Full dose escalation data
- 2H 2023: Pivotal cohort full enrollment
- 2H 2023: Non-CCA expansion cohorts data

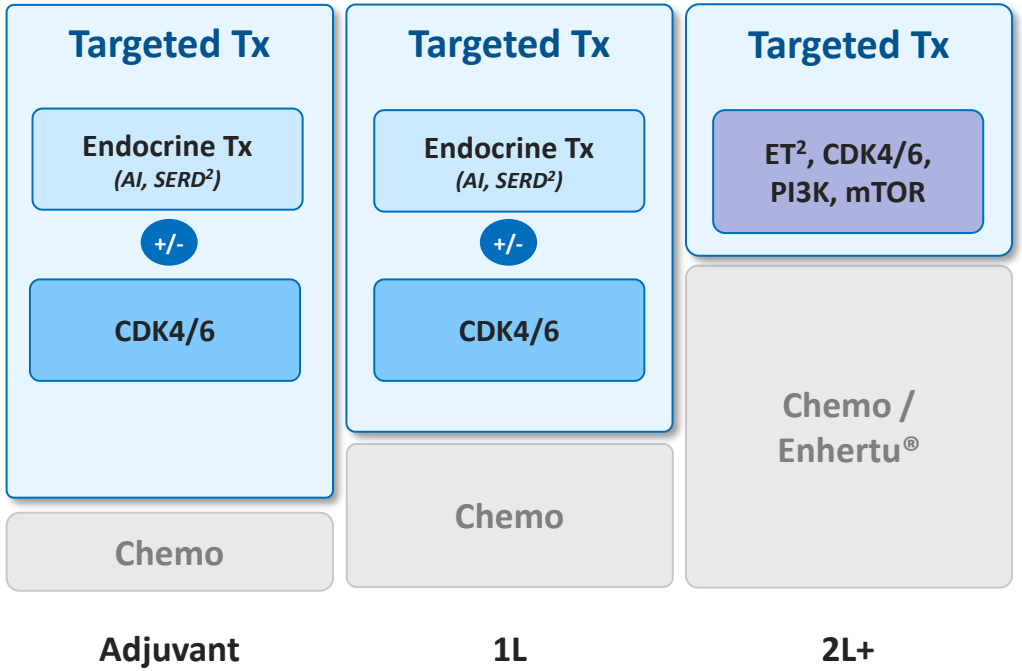
Relay Tx – Emerging Breast Cancer Franchise



Breast Cancer – Limitations of Current Standard of Care

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

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



…is limited by efficacy of available treatments

Source: Internal analysis based on third party industry data

1. Standard of care for HR+/HER2- breast cancer is illustrative; 2. AI = Aromatase Inhibitor; SERD: Selective Estrogen Receptor Degrader; ET = Endocrine Therapy

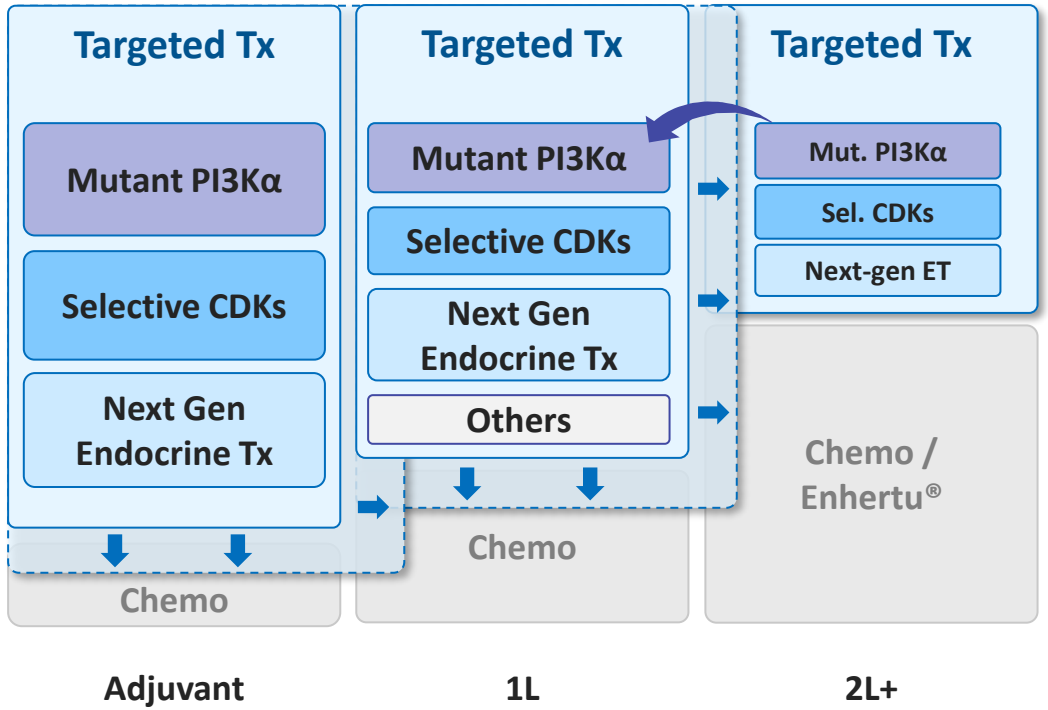
Relay Tx Solution – Highly Selective Breast Cancer Franchise

Relay Tx Solution

Relay Tx Breast Cancer Portfolio

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

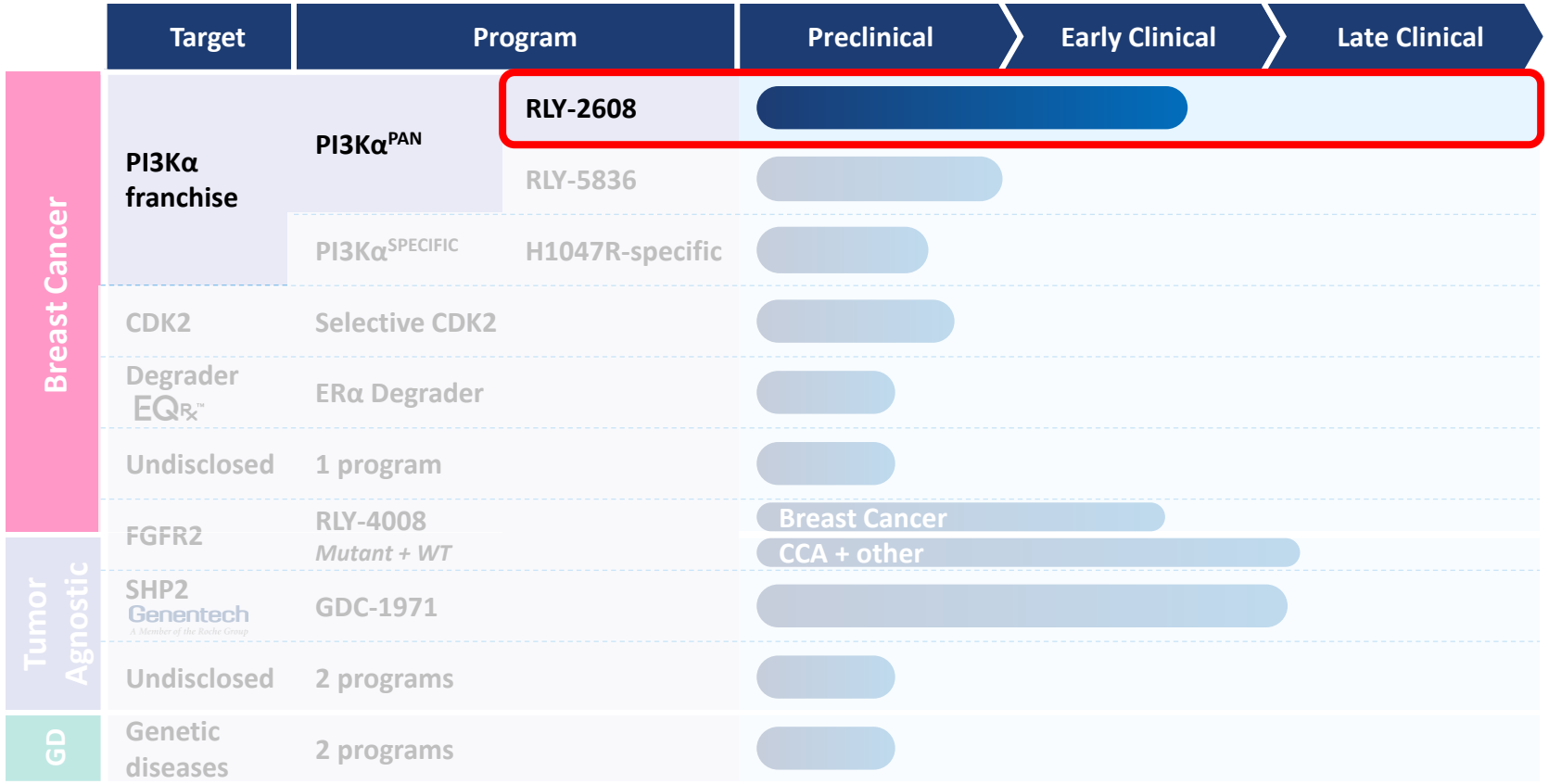
Aspirational future state standard of care (HR+/HER2- BC)[1]



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

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

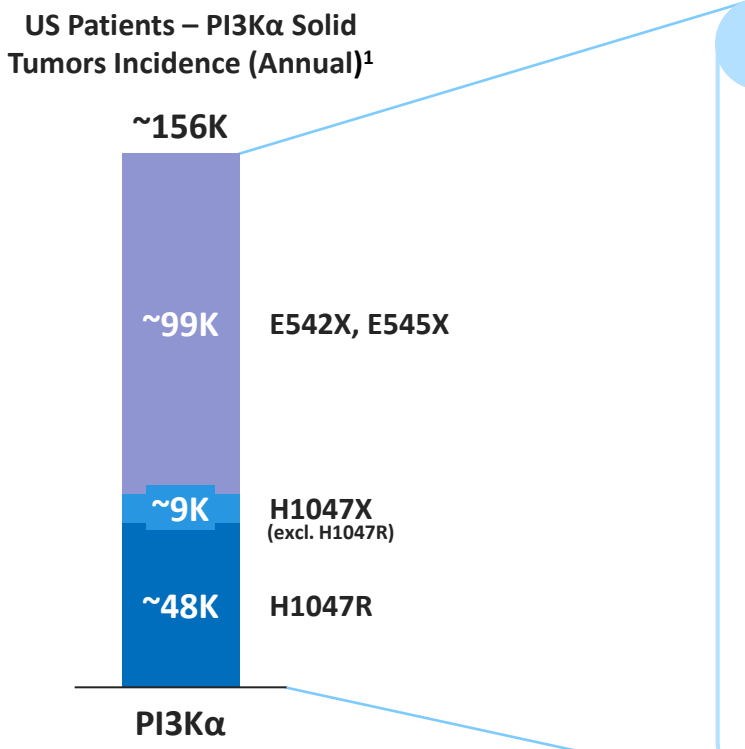
Relay Tx – Extensive Precision Medicine Pipeline



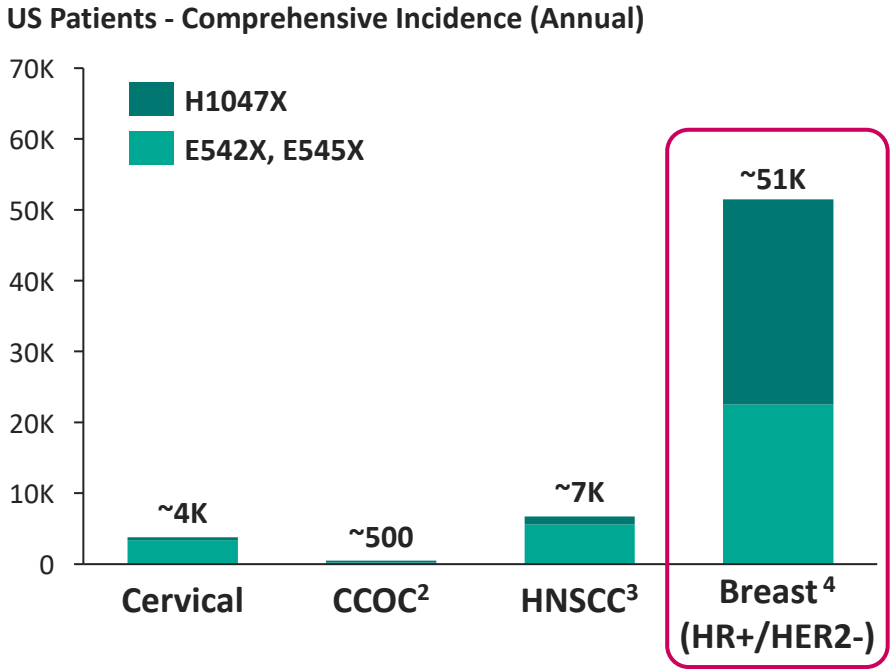
PI3Kα – Large Precision Oncology Opportunity

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

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



PI3Kα alterations observed across multiple tumor types – select indications



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

~30%

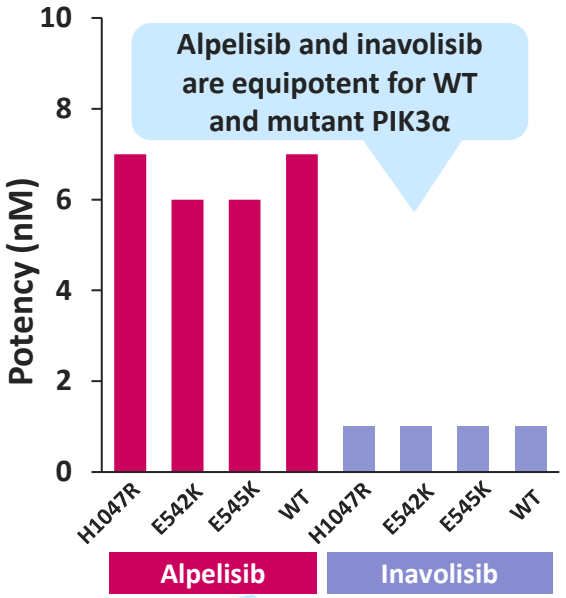
Of HR+/HER2- breast cancer patients harbor a hotspot PI3Kα mutation[4]

Sources: Internal analysis based on third party industry data

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

PI3Kα – Existing Inhibitors Have Limited Therapeutic Window

Limited Selectivity



Alpelisib and inavolisib are equipotent for WT and mutant PIK3α

Both also retain nM potency against other PI3K isoforms

Limited Target Inhibition

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

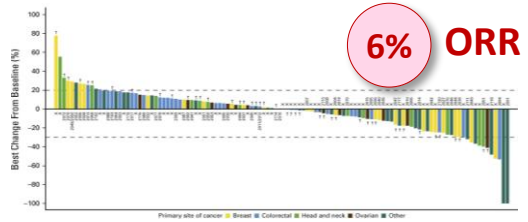
Alpelisib: Observed coverage (based on IC_{80}) at average clinical dose 9-13hr[7]

Limited Tolerability

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

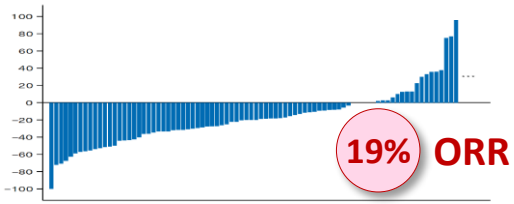
Limited Efficacy

Alpelisib Monotherapy Ph 1a[7]



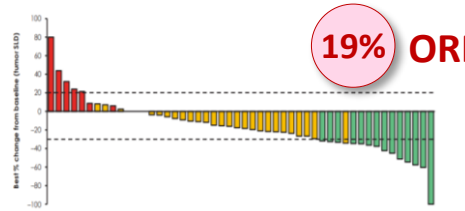
6% ORR

Alpelisib + fulvestrant Ph 2[4]



19% ORR

Inavolisib + fulvestrant Ph 1b[13]



19% ORR

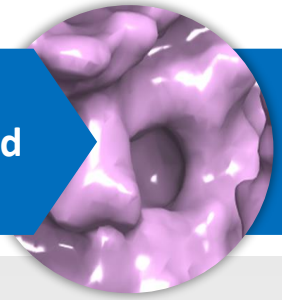
Note: fulv = fulvestrant; BC= breast cancer; all referenced studies are for their patient populations which are analogous to ongoing patient populations within RLY-2608 clinical trials; Alpelisib and fulvestrant are FDA approved, Inavolisib is in Phase 3 clinical trials

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

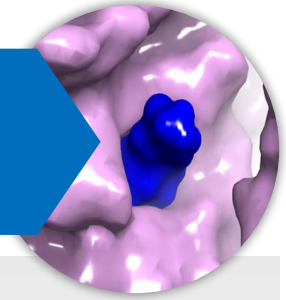
PI3Kα – Proprietary Insights Unlock Novel Approaches

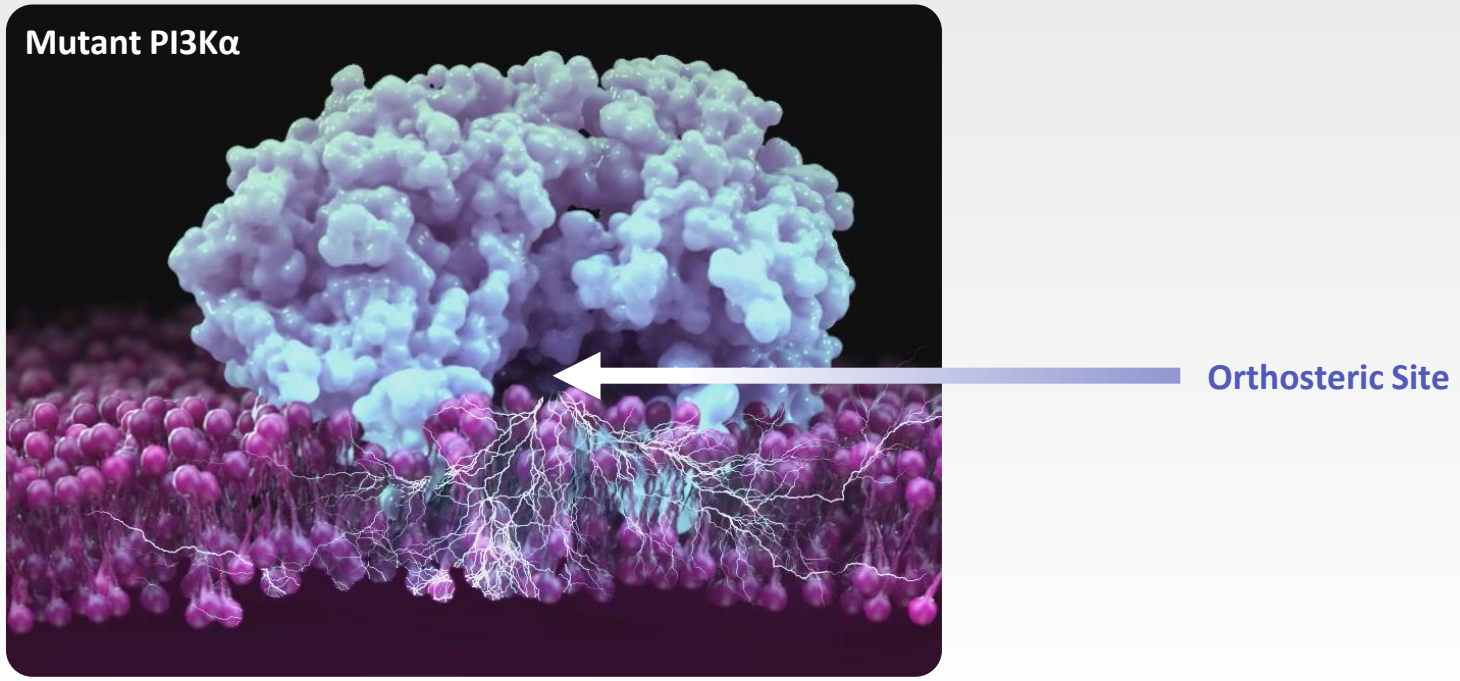
Solved first full-length structures of PI3Kα (mutant and wild-type)

Discovered novel allosteric pocket favored in mutant protein



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





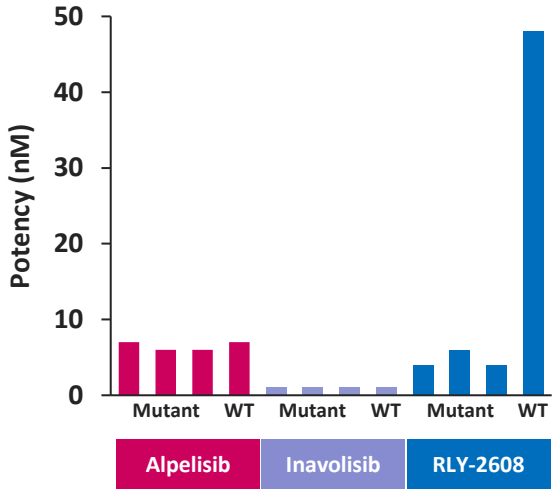
A differentiated understanding of the structure of PI3Kα and its relationship to function equips Relay Tx to design optimal mutant-selective inhibitors of PI3Kα

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

All Data Shown is Preclinical

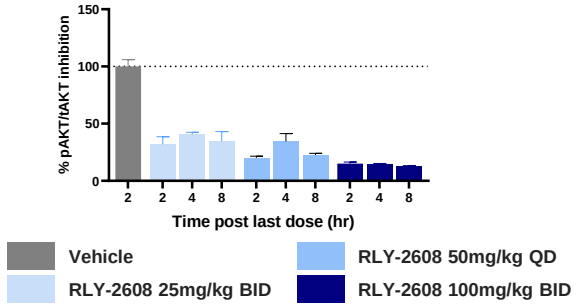
Favorable Selectivity

Limited potency against WT PI3Kα and other PI3K isoforms



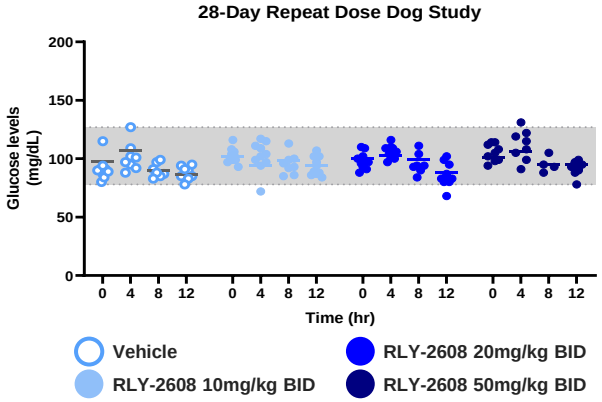
Favorable Target Inhibition

Maintains approx. 80% mutant PI3Kα inhibition in mouse model



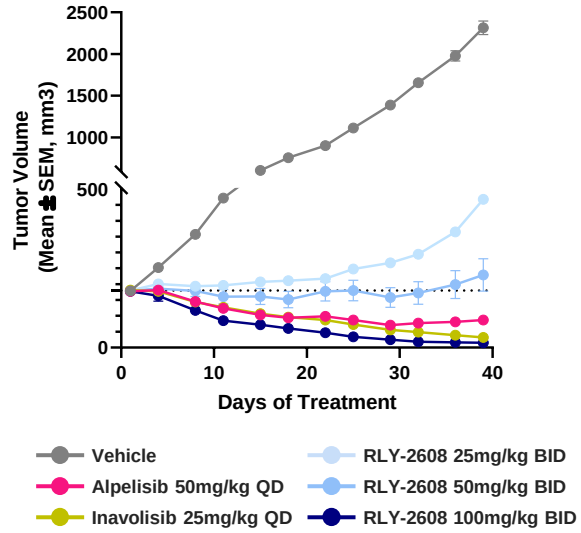
Favorable Tolerability

Manageable key toxicities, especially hyperglycemia shown in dog study

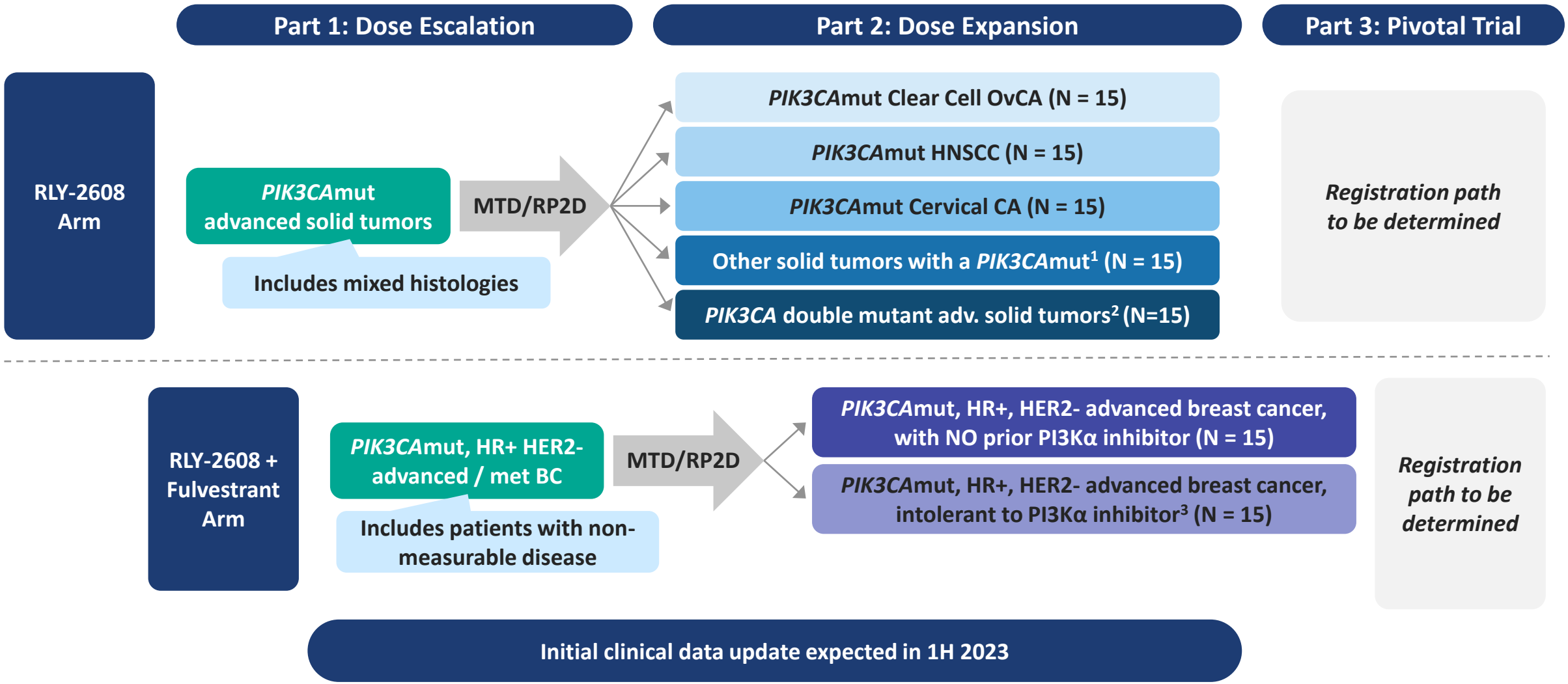


Favorable Efficacy

Robust tumor regression at tolerable doses in mouse model



RLY-2608 – Trial Design



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

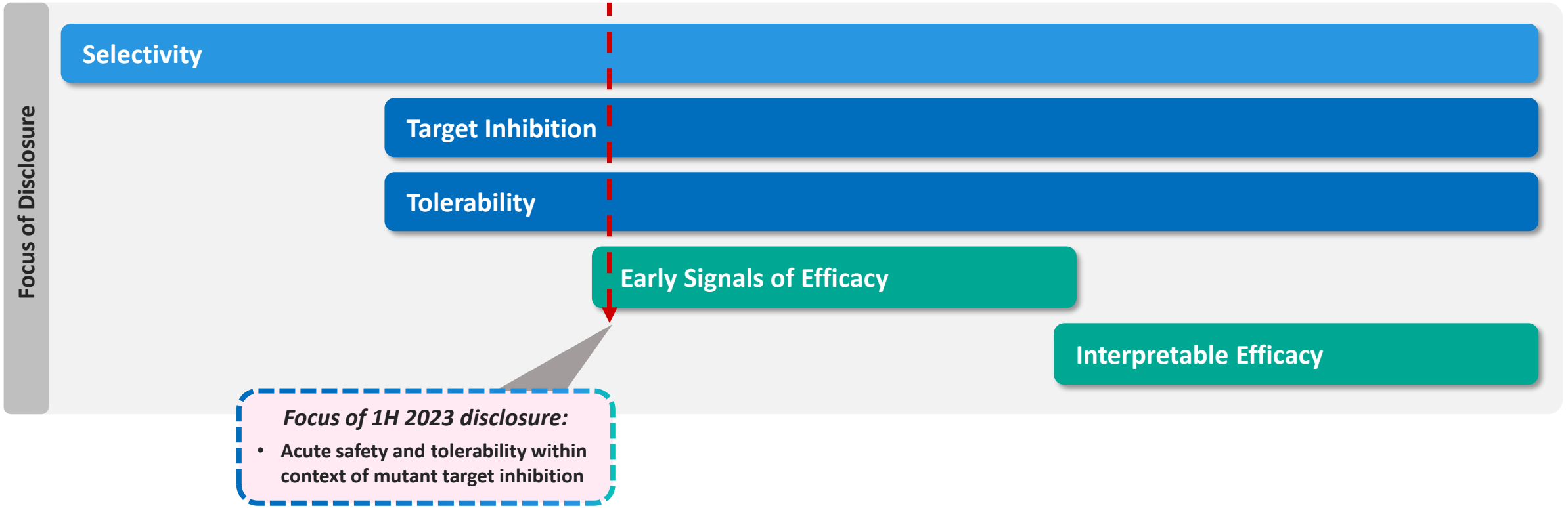
RLY-2608 – Data Disclosure

Part 1: Dose Escalation
Demonstrate clinical proof of mechanism

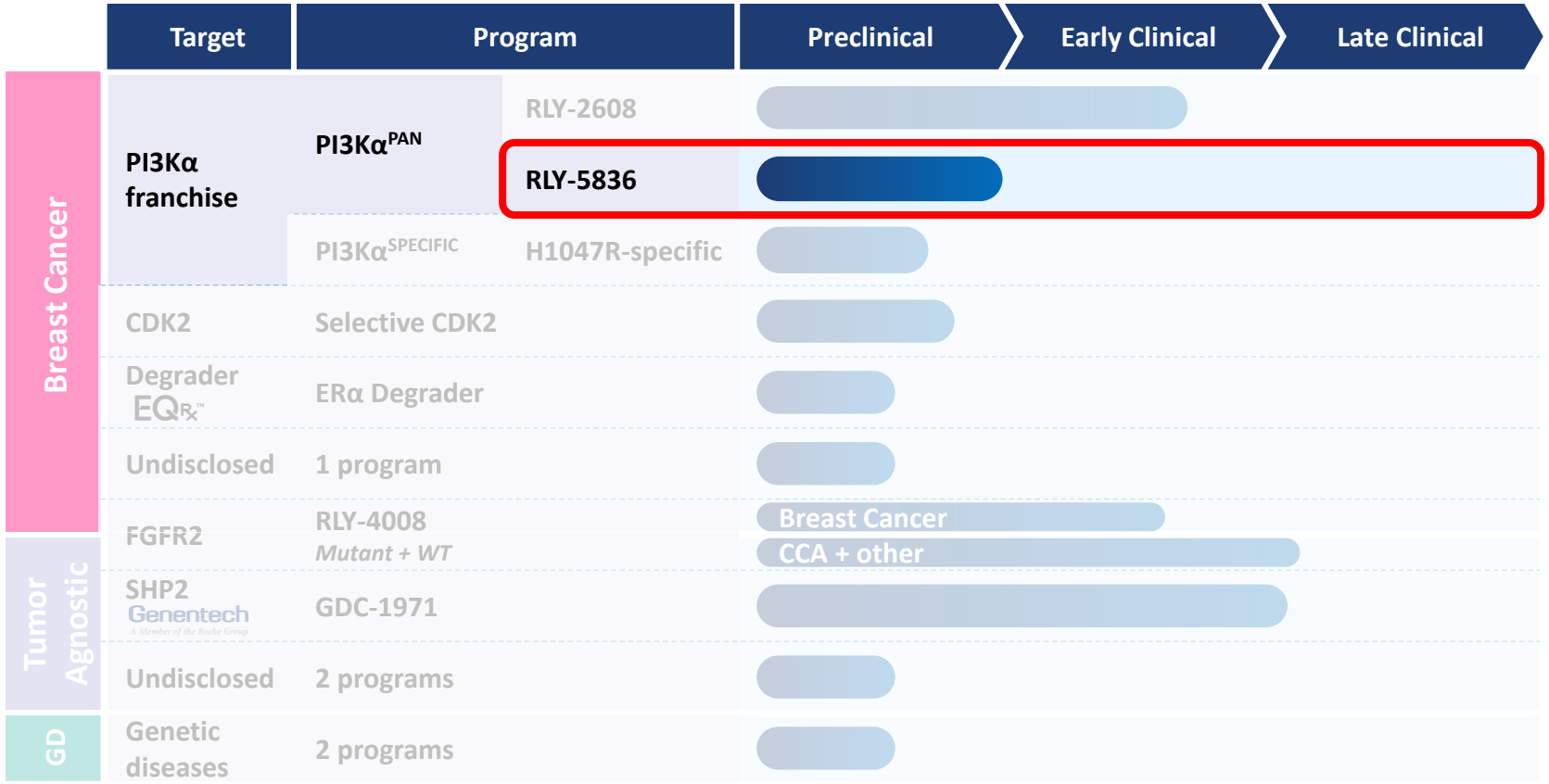
RP2D

Part 2: Dose Expansion
Establish early efficacy & confirm dose

Part 3: Pivotal Trial
Establish definitive efficacy

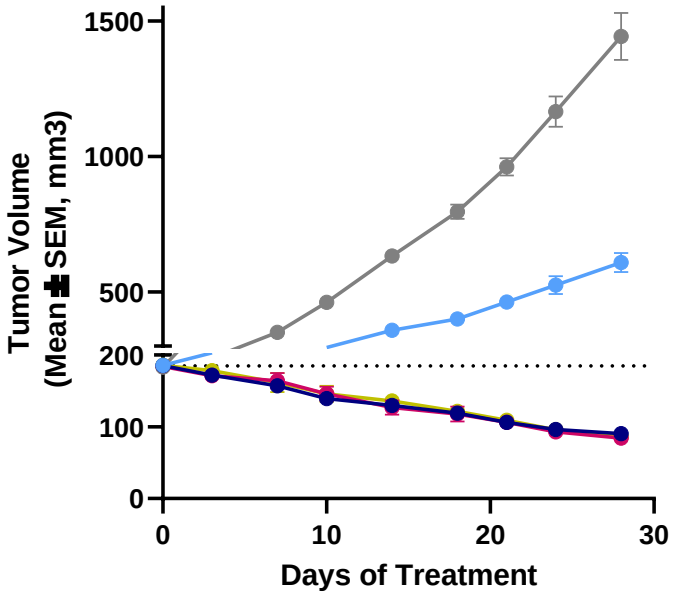


Relay Tx – Extensive Precision Medicine Pipeline



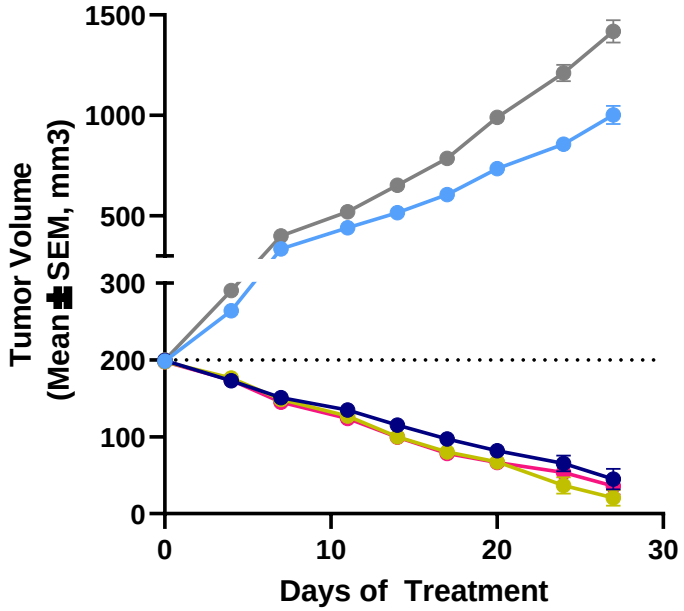
RLY-5836 – Similar Pre-clinical Profile, Different Chemical Properties from RLY-2608

H1047R mutant (HCC1954) (mouse)



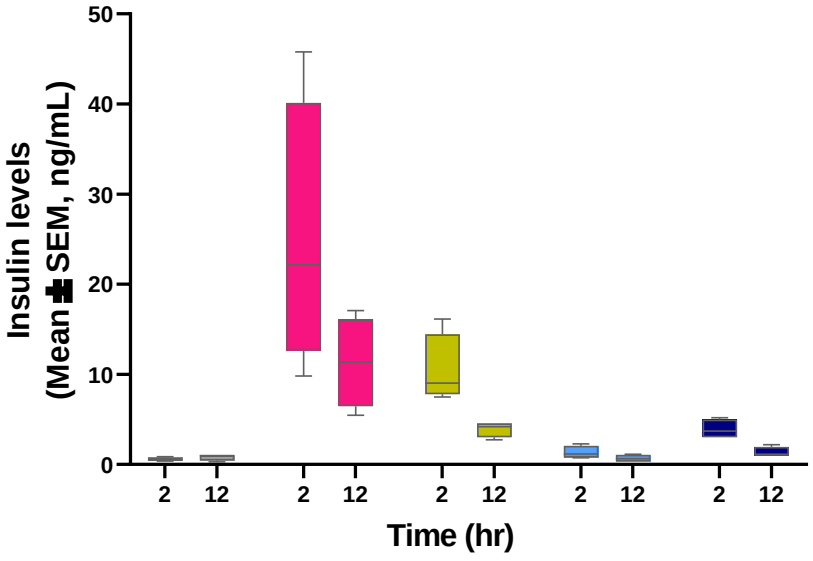
Vehicle
Alpelisib 50mg/kg QD
Inavolisib 25mg/kg QD
RLY-5836 30mg/kg BID
RLY-5836 150mg/kg BID

E545K mutant (MDAMB361) (mouse)[1]



Vehicle
Alpelisib 50mg/kg QD
Inavolisib 25mg/kg QD
RLY-5836 30mg/kg BID
RLY-5836 150mg/kg BID

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

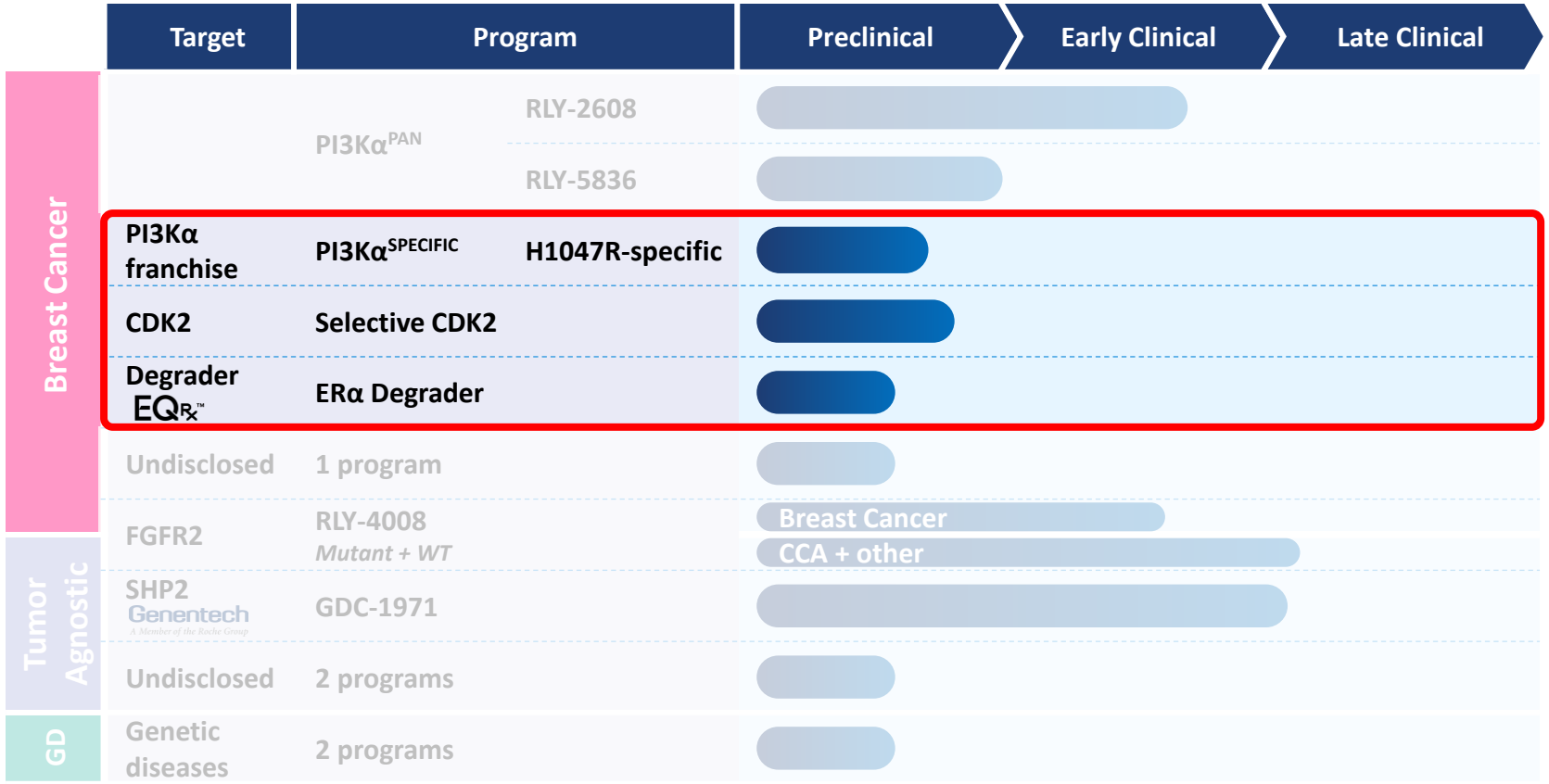


Vehicle
Alpelisib 50mg/kg QD
GDC-0077 25mg/kg QD
RLY-5836 30mg/kg BID
RLY-5836 150mg/kg BID

Clinical start anticipated in 2Q 2023

Source: Internal RLY-5836 data
1. This model also carries a second mutation at K567R

Relay Tx – Extensive Precision Medicine Pipeline



CDK2 – Highly Selective Inhibitors Identified

CDK2 is important in ER+ breast cancer

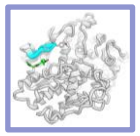
Patients receiving adjuvant CDK 4/6i — ~23K

Patients receiving 1L CDK 4/6i — ~18K

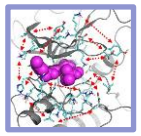
Patients receiving 2L CDK 4/6i — ~5K

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

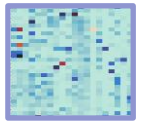
Computational modeling enabled breakthrough speed



Collect MD frames



Extract features



Cluster frames & assign cluster populations

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

Predict selectivity

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

Relay Tx's CDK2 inhibitors observed to be highly selective

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

Clinical start expected in early 2024

Source: Internal analysis based on third party industry data

ERα Degrader – Rapidly Obtained Potent Compounds

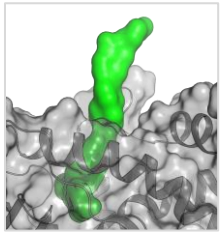
Endocrine therapies are used in every line of therapy in HR+/HER2- Breast Cancer

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

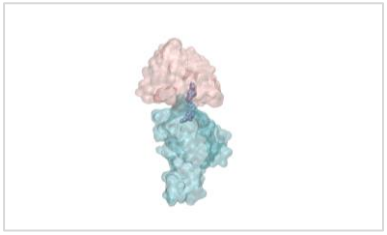
195k annual US patients with HR+/HER2- breast cancer

Relay Tx is leveraging rational design…

Traditional Approach



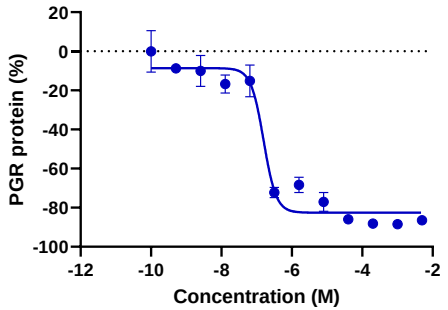
Relay Tx Approach



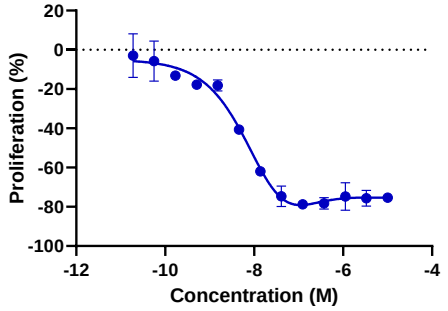
Multiple experimental tools deployed to develop conformational models that enable effective triage of degrader design ideas

…to obtain potent ERα degraders

Pathway suppression



Cellular proliferation

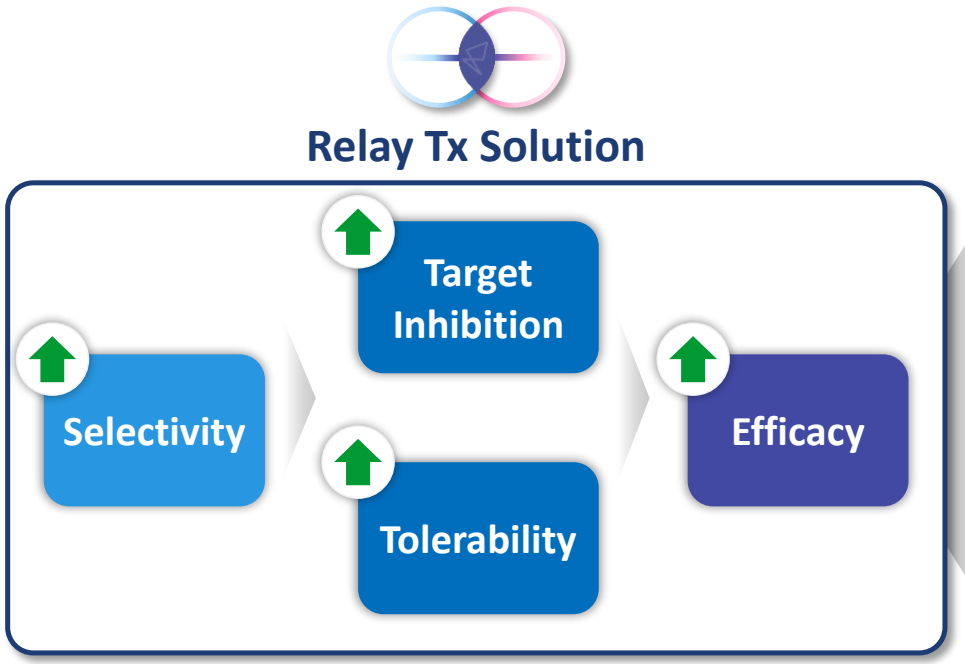


Development Candidate nomination expected in 2023

Source: Internal analysis based on third party industry data

Relay Tx Solution – Highly Selective Breast Cancer Franchise

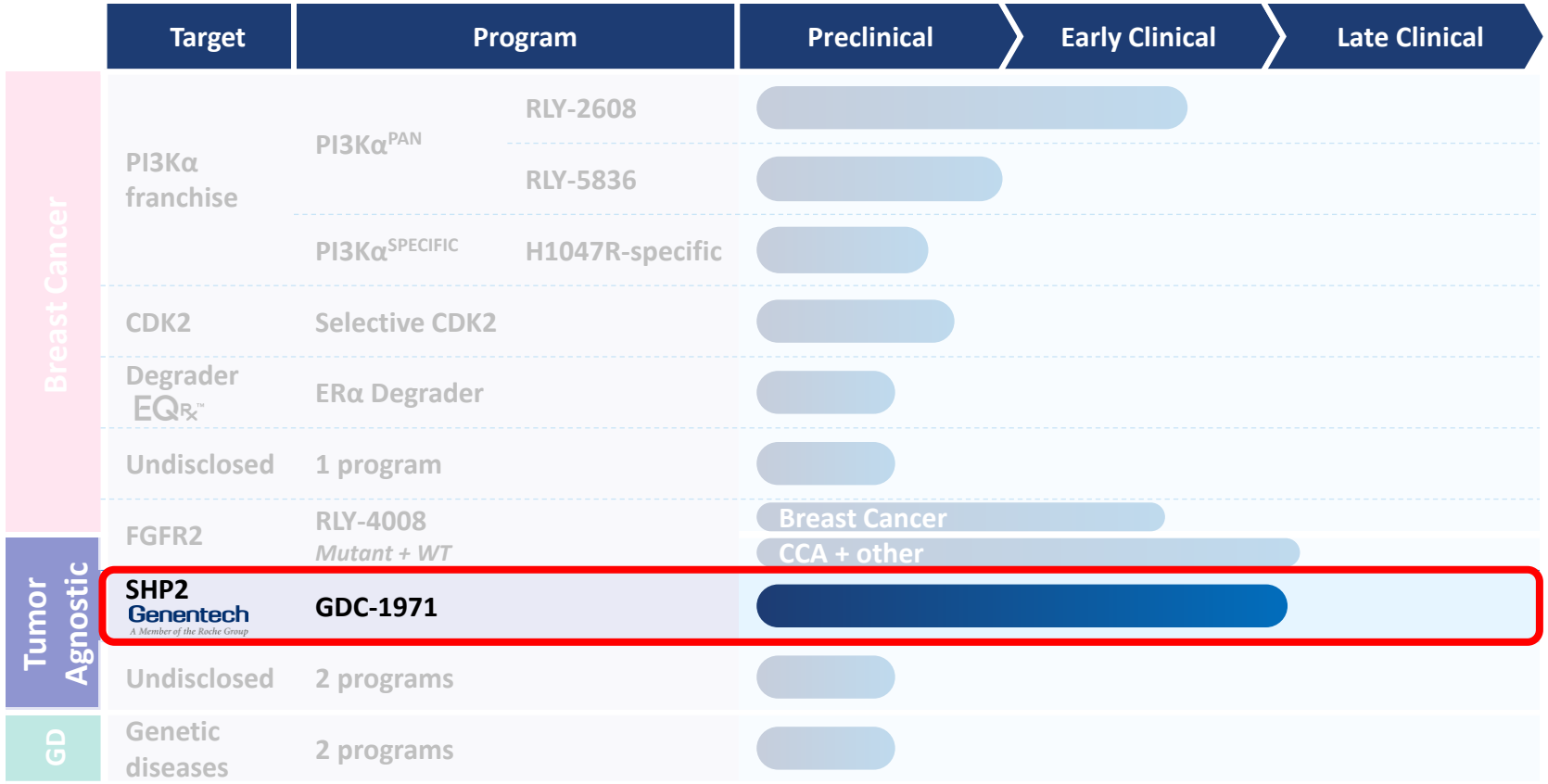
The Relay Tx Solution…



…aims to address selectivity on validated targets for breast cancer

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

Relay Tx – Extensive Precision Medicine Pipeline



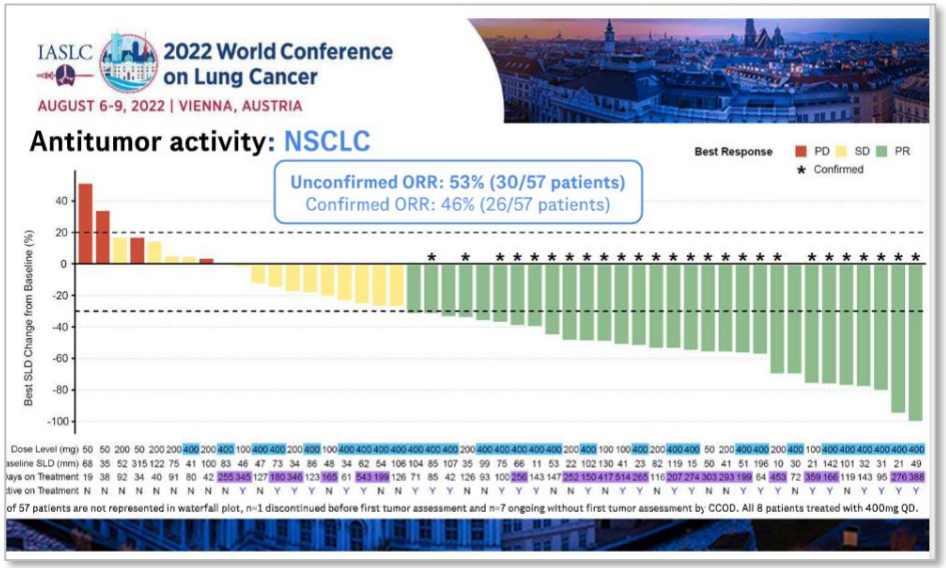
SHP2 – Genentech Global Collaboration for GDC-1971 (Formerly RLY-1971)

Two ongoing trials with GDC-1971:

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

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

Clinical Update for GDC-6036 Monotherapy at World Lung 2022



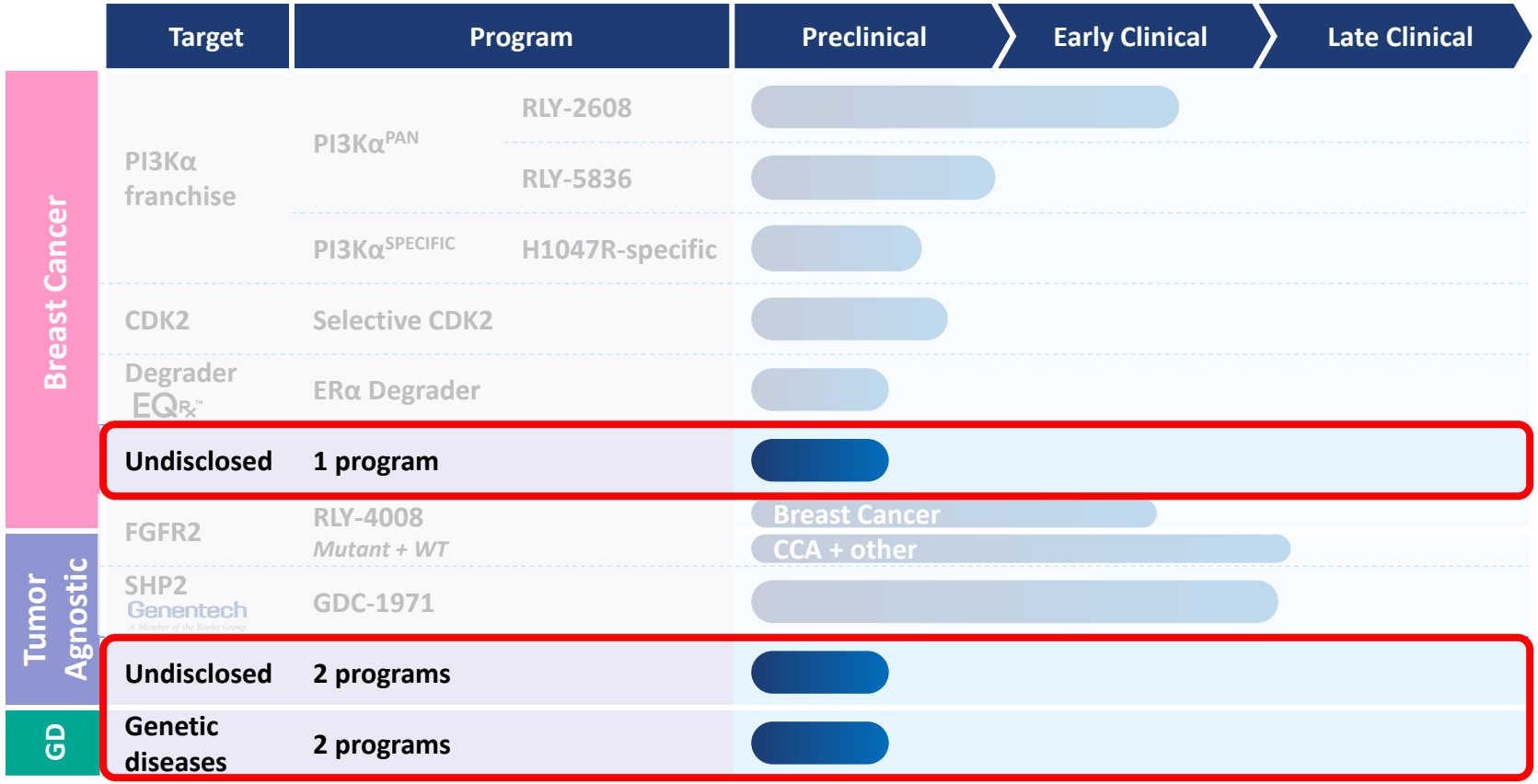
Unconfirmed ORR: 53% (30/57 patients)
Confirmed ORR: 46% (26/57 patients)

Collaboration provides meaningful economics to Relay Tx[1]

Source: World Lung 2022 #OA03.04

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

Relay Tx – Extensive Precision Medicine Pipeline

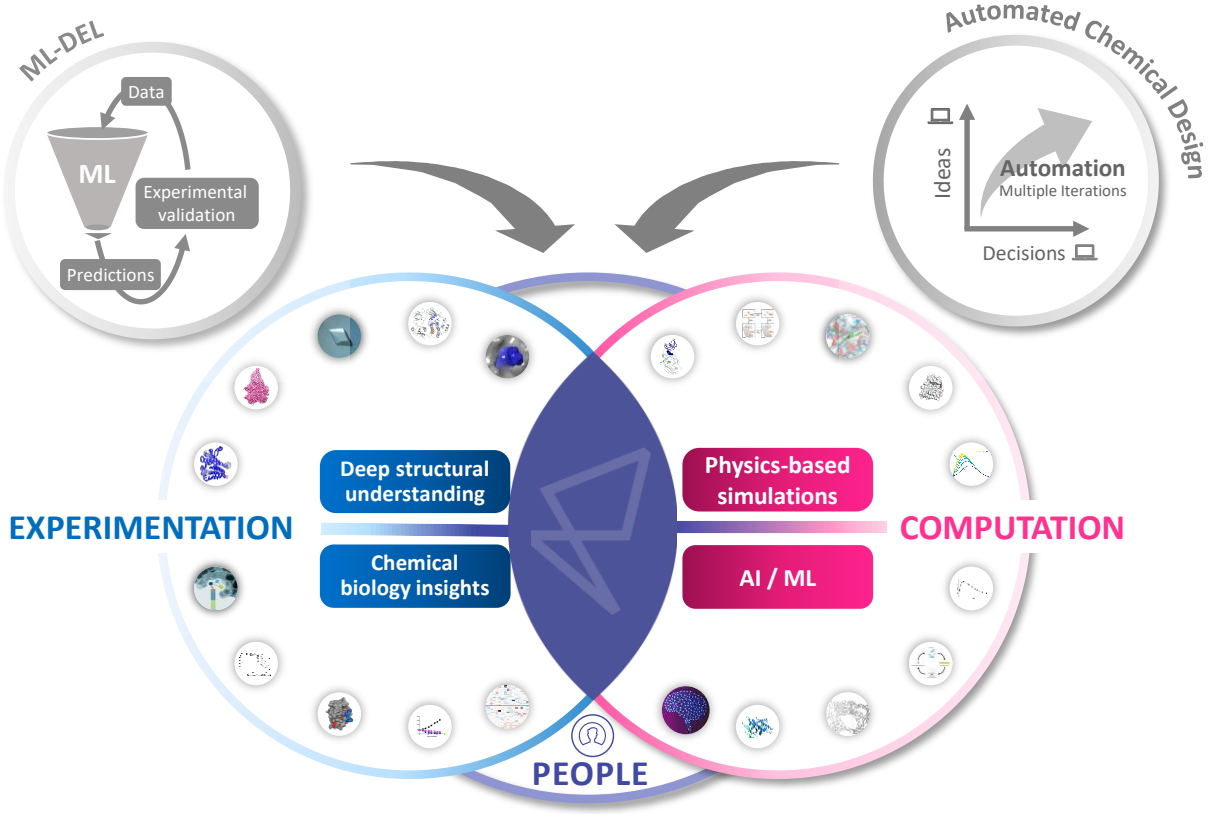


Relay Tx – The Dynamo™ Platform

Platform capabilities and expertise continue to expand

Growing Platform
E.g., ML-DEL

Growing Automation
E.g., Automated Chemical Design (ACD)

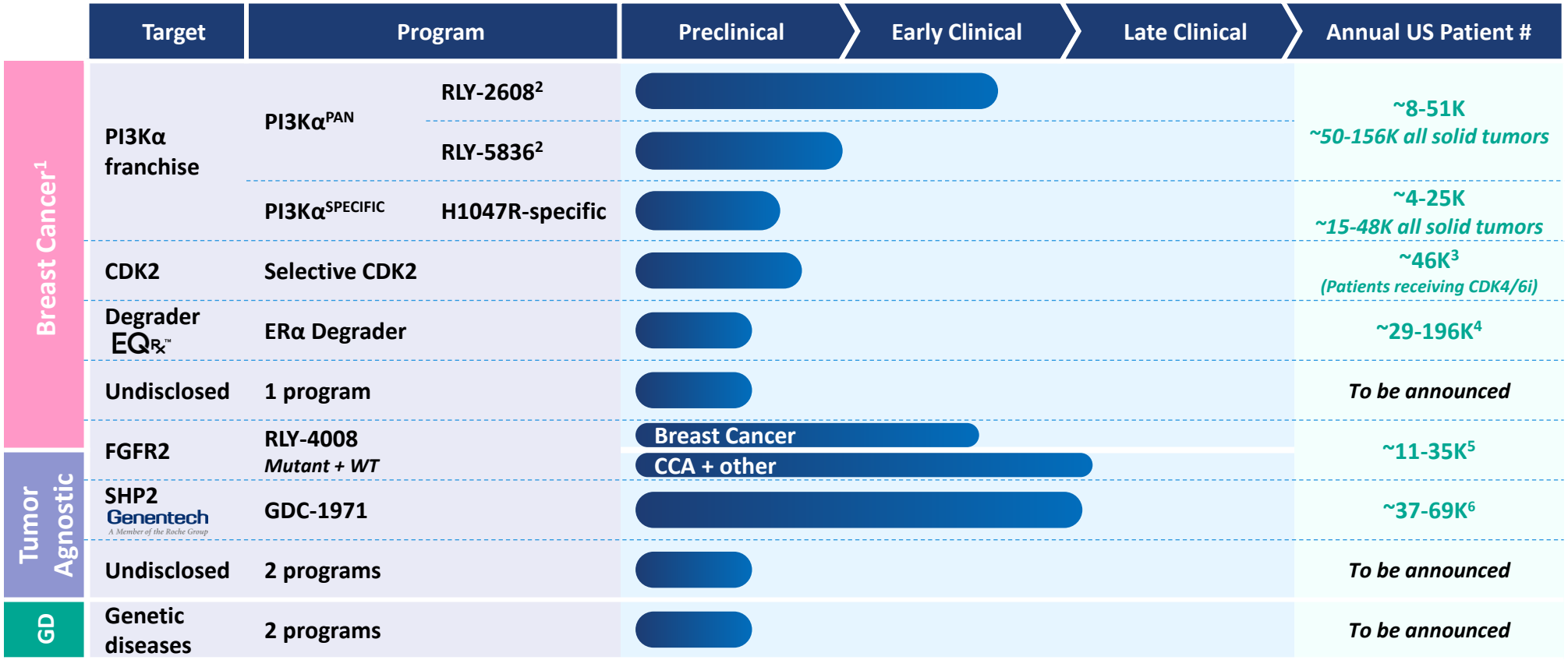


Enabling deep and diversified early pipeline

5+ Undisclosed Programs

- Inhibitors
- Degraders
- Chaperones
- New Modalities

Relay Tx – Extensive Precision Medicine Pipeline



Note: Unless otherwise indicated, patient #'s refer to total annual number of US patients with late-line cancers compared to comprehensive annual incidence that may be amenable to treatment with our programs
1. Unless otherwise indicated, all breast cancer patient numbers refer to HR+/HER2- breast cancer tumors 2. RLY-2608 covers H1047X, E542X, E545X hot spots, and breast cancer patient range assumes HR+/HER2- population 3. ~46k HR+/HER2- breast cancer patients expected to receive CDK 4/6 inhibitors in adjuvant setting, first-line setting, and second-line setting in 2023, per Decision Resources Breast Cancer Market Forecast, report dated June 2022 4. HR+/HER2- US late-line breast cancer patients compared to HR+/HER2- US incident breast cancer patients 5. FGFR2 altered late-line solid tumors compared to comprehensive annual FGFR2 altered incident solid tumors including additional FGFR gene fusions and rearrangements resulting from truncation of the protein at exon 18 6. SHP2 combo only includes KRAS G12C in lung and CRC, EGFR mutations in lung, and ALK fusions in lung

Relay Tx – Capital, Team & Execution Focus to Deliver

Breast Cancer Franchise

PI3Kα^{PAN}

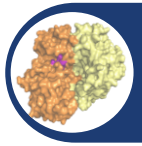
RLY-2608

Initial data in 1H 2023

RLY-5836

Clinical start in 2Q 2023

Selective CDK2



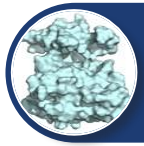
Clinical start in early 2024

ERα Degrader

Development candidate nomination in 2023

Tumor Agnostic

RLY-4008 (Selective FGFR2)

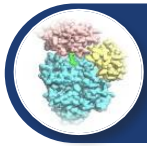


Full dose escalation data in 1H 2023

Non-CCA expansion cohorts data in 2H 2023

Pivotal cohort full enrollment in 2H 2023

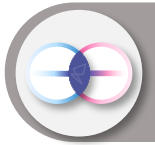
GDC-1971 (SHP2)



Ongoing combo trials; Genentech controls data disclosures

Undisclosed

To be announced

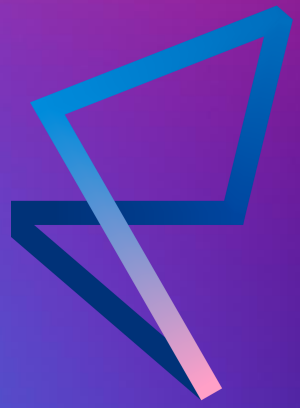


5+ undisclosed programs in preclinical development and additional early-stage efforts across platform

$1.1B

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

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



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