

# RELAY® THERAPEUTICS

**Corporate Presentation** 

As of May 2, 2024

1

#### **Disclaimer**



This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, implied and express statements regarding the progress and timing of the clinical development of the programs across our portfolio, including the expected therapeutic benefits of our programs, and potential efficacy and tolerability, and the timing and success of interactions with and approval of regulatory authorities; the timing of clinical data updates across our pipeline, including the timing of a clinical data update for the PI3Ka franchise, the progress of doublet and triplet combinations for RLY-2608, the timing of clinical updates for RLY-2608, and the timing of a clinical data and regulatory update for lirafugratinib; the timing of disclosure of additional pre-clinical programs; the possibility that unconfirmed results from these trials will not be confirmed by additional data as our clinical trials progress; the potential of RLY-2608 to address a major unmet medical need; expected strategic benefits under our collaborations; our ability to successfully establish or maintain collaborations or strategic relationships 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; and the implementation of our business model and strategic plans for our business, current product candidates and any future product candidates. The words "may," "might," "will," "could," "would," "should," "plan," "anticipate," "intend," "believe," "expect," "estimate," "seek," "predict," "future," "project," "potential," "continue," "target" and similar words or expressions, or the negative thereof, are intended to identify forward-looking statements, although not

Any forward-looking statements in this presentation are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this presentation, including, without limitation, risks associated with: the impact of global economic uncertainty, geopolitical instability and conflicts, or public health epidemics or outbreaks of an infectious disease on countries or regions in which we have operations or do business, as well as on the timing and anticipated results of our clinical trials, strategy, future operations and profitability; the delay or pause of any current or planned clinical trials or the development of our drug candidates; the risk that the preliminary results of our preclinical or clinical trials may not be predictive of future or final results in connection with future clinical trials of our product candidates; our ability to successfully demonstrate the safety and efficacy of our drug candidates; the timing and outcome of our planned interactions with regulatory authorities; and obtaining, maintaining and protecting our intellectual property. 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 and 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. No representations or warranties (expressed or implied) are made about the accuracy of any such forward-looking statements.

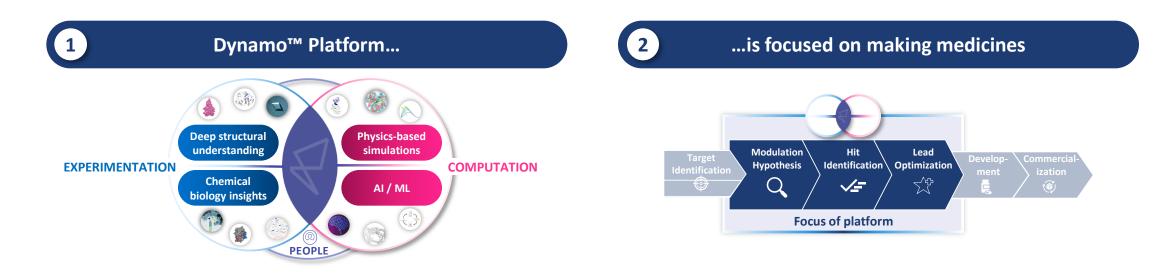
Certain information contained in this presentation relates to or is based on studies, publications, surveys and other data obtained from third-party sources and our own internal estimates and research. While we believe these third-party studies, publications, surveys and other data to be reliable as of the date of this presentation, we have not independently wrified, and make no representation as to the adequacy, fairness, accuracy or completeness of, any information obtained from third-party sources. In addition, no independent source has evaluated the reasonableness or accuracy of our internal estimates or research and no reliance should be made on any information or statements made in this presentation relating to or based on such internal estimates and research.

This presentation contains trademarks, trade names and service marks of other companies, which are the property of their respective owners.









#### ...aims to address selectivity on validated targets



3



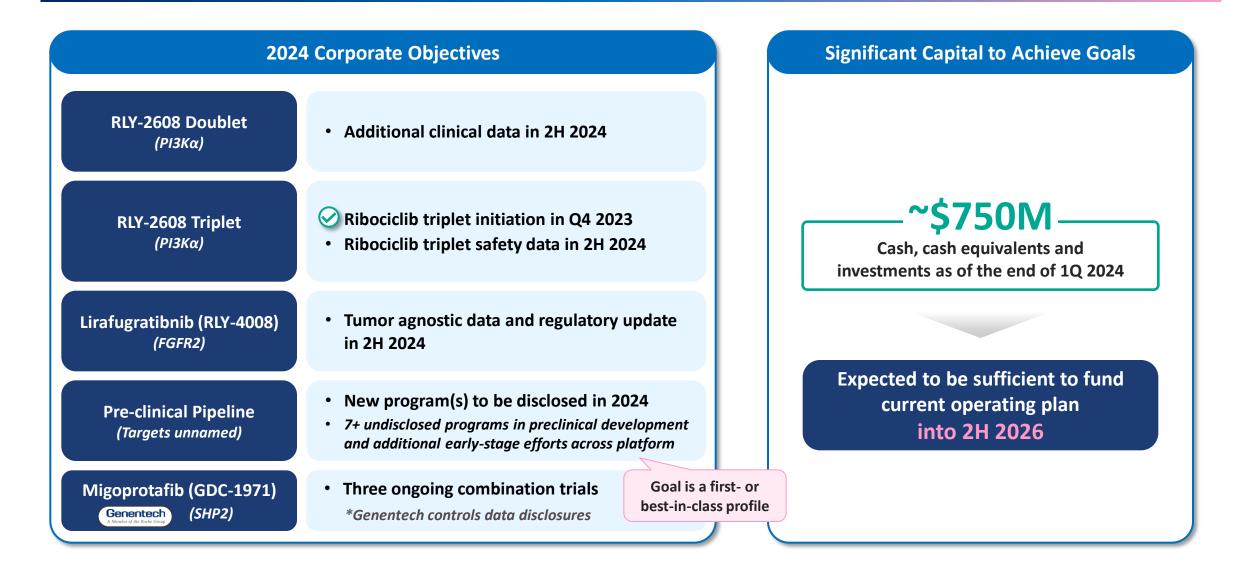
5

Target	Program	Preclinical <b>Early Clinical</b>	ate Clinical Annual US Patient #
	Monotherapy		
	RLY-2608 PI3Kα <sup>PAN</sup> Endocrine Tx (ET) doublet		~10-71K breast cancer
PI3Kα franchise	CDK4/6i + ET triplet		~76-243K all solid tumors
	<b>RLY-5836</b> (PI3Kα <sup>PAN</sup> ) Dose Escalation	Deprioritized	
	ΡΙ3Κα <sup>μ1047R</sup>		~4-27K breast cancer ~15-50K all solid tumors
FGFR2	Lirafugratinib (RLY-4008)		~11-35K <sup>4</sup>
Solid Tumor	2 programs		To be announced
Genetic Disease	2 programs		To be announced
CDK2	RLY-2139	Paused; IND ready	~35K²
ΕRα	RLY-1013 (Degrader)	Paused at DC	~30-205K <sup>3</sup>
SHP2	Migoprotafib (GDC-1971) Genentech A Member of the Racke Group	3 ongoing combo studies	~36-69К⁵

#### 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. ~35K HR+/HER2- breast cancer patients expected to receive CDK 4/6 inhibitors in adjuvant setting, first-line setting, and second-line setting in 2024, per Decision Resources Breast Cancer Market Forecast report dated November 2023; 3. HR+/HER2- US late-line breast cancer patients compared to HR+/HER2- US incident breast cancer patients; 4. 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 and all breast cancer patients with FGFR2 alterations; 5. SHP2 combo only includes KRAS G12C in lung and colorectal, EGFR mutations in lung, and ALK fusions in lung © 2024 Relay Therapeutics



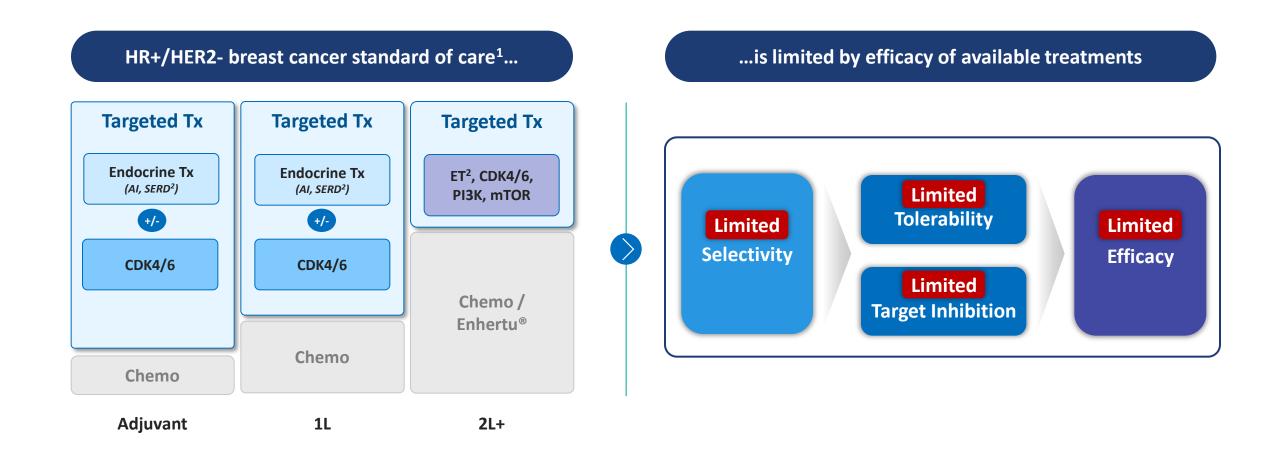


## **Relay Tx – Broad Precision Medicine Pipeline**



Target	Program	Preclinical > Early Clinical > Late Clinical
	Monotherapy	
	RLY-2608 PI3Kα <sup>PAN</sup> Endocrine Tx (ET) doub	blet
PI3Kα franchise	CDK4/6i + ET triplet	
	RLY-5836 (PI3Kα <sup>PAN</sup> ) Dose Escalation	Deprioritized
	ΡΙ3Κα <sup>Η1047R</sup>	
CDK2	RLY-2139	Paused; IND ready
ERα	RLY-1013 (Degrader)	Paused at DC
FGFR2	Lirafugratinib (RLY-4008)	
Solid Tumor	2 programs	
Genetic Disease	2 programs	
SHP2	Migoprotafib (GDC-1971) Genentech	

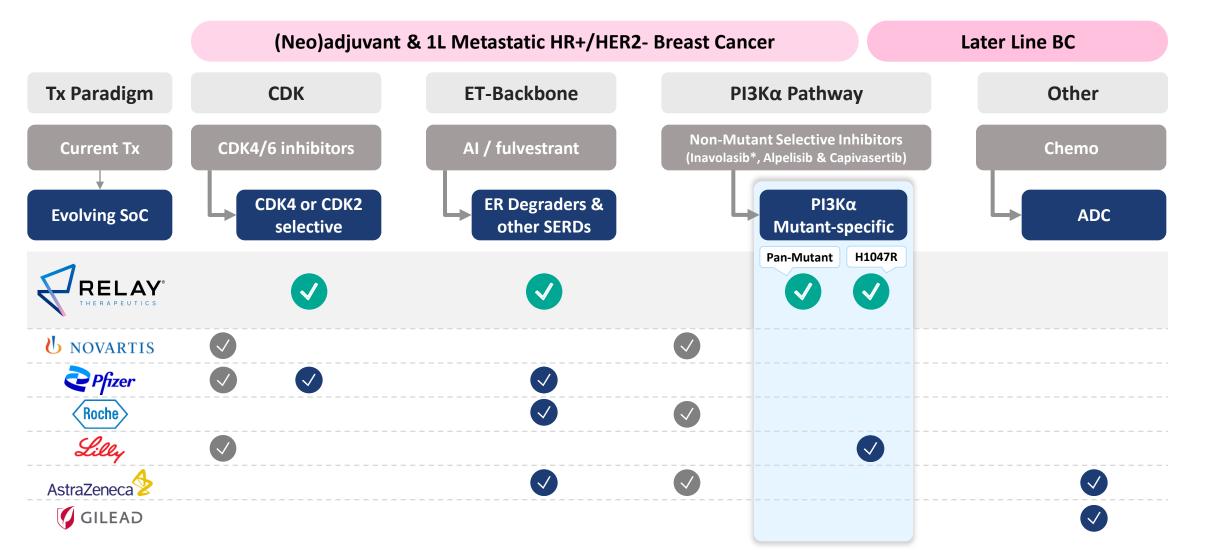




Source: Internal analysis based on third party industry data

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





\* Inavolisib is an investigational therapy in Ph3 studies

Source: Decision Resources Group – Breast Cancer Disease Landscape & Forecast (Nov 2023). 2031 Projection

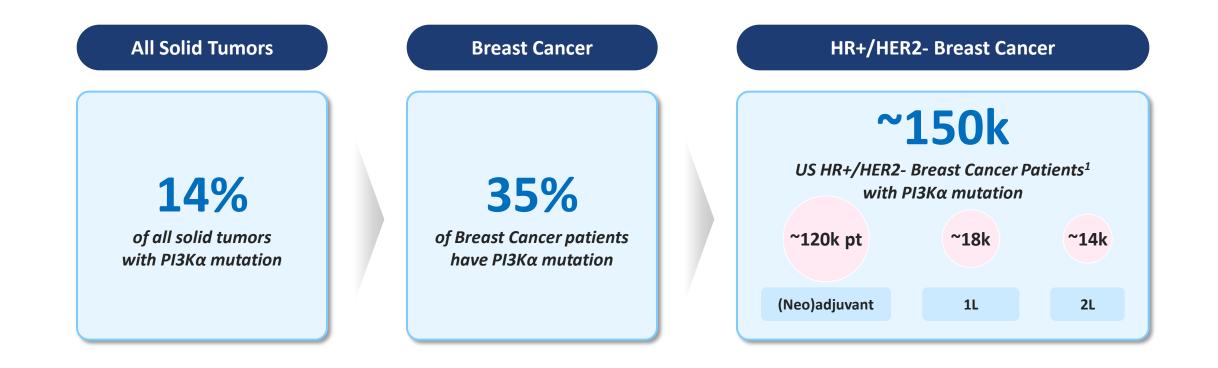
© 2024 Relay Therapeutics

## **Relay Tx – Broad Precision Medicine Pipeline**



Target	Program	Preclinical > Early Clinical > Late Clinical
	Monotherapy	
	RLY-2608 PI3Kα <sup>PAN</sup> Endocrine Tx (ET) doublet	
PI3Kα franchise	CDK4/6i + ET triplet	
	RLY-5836 (PI3Kα <sup>PAN</sup> ) Dose Escalation	Deprioritized
	<b>ΡΙ3Κα<sup>Η1047R</sup></b>	
CDK2	RLY-2139	
ΕRα	RLY-1013 (Degrader)	
FGFR2	Lirafugratinib (RLY-4008)	
Solid Tumor	2 programs	
Genetic Disease	2 programs	
SHP2	Migoprotafib (GDC-1971) Genentech	





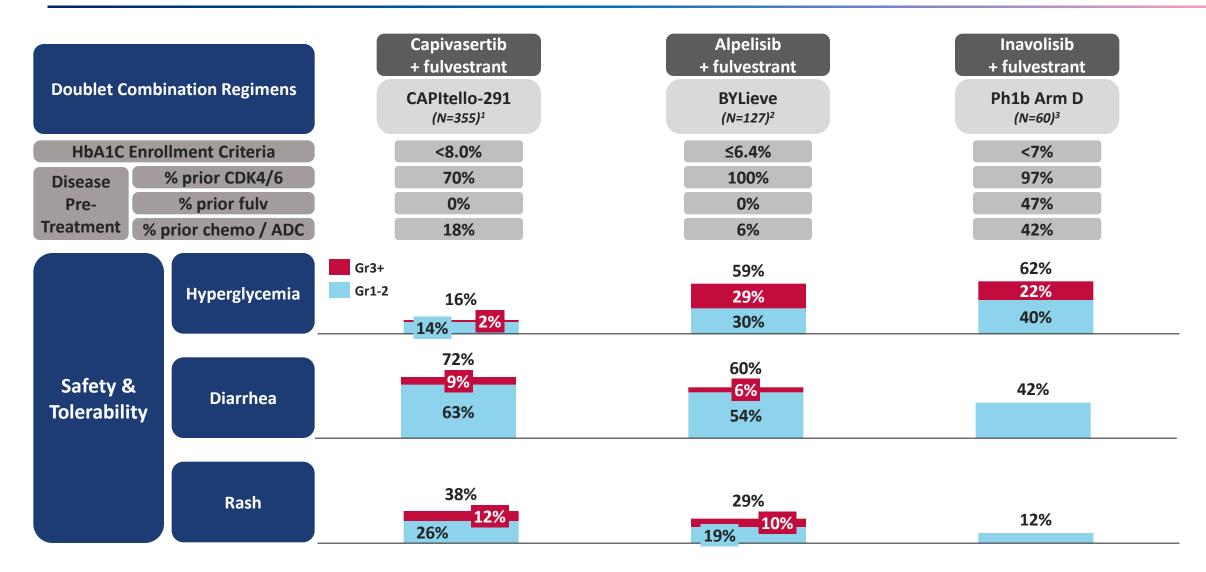
#### **RLY-2608** has the potential to address very large patient population

Sources: 3rd party data; Global Data HER2-/HR+ Breast Cancer Global Patient Forecast, October 2023;

1. Includes prevalent PI3Kα mutated HR+/HER2- patients receiving therapy in Neo/Adjuvant setting (includes incident patients in 2023 receiving endocrine or non-endocrine therapy in Neo/Adjuvant settings [~50k], and patients diagnosed in previous years with local/regional disease receiving sequential endocrine therapy in 2023 [~69k]), and prevalent PI3Kα mutated HR+/HER2- metastatic patients receiving therapy in 1L or 2L setting

#### **RLY-2608 – Safety Profiles of Existing PI3Kα Pathway Compounds**



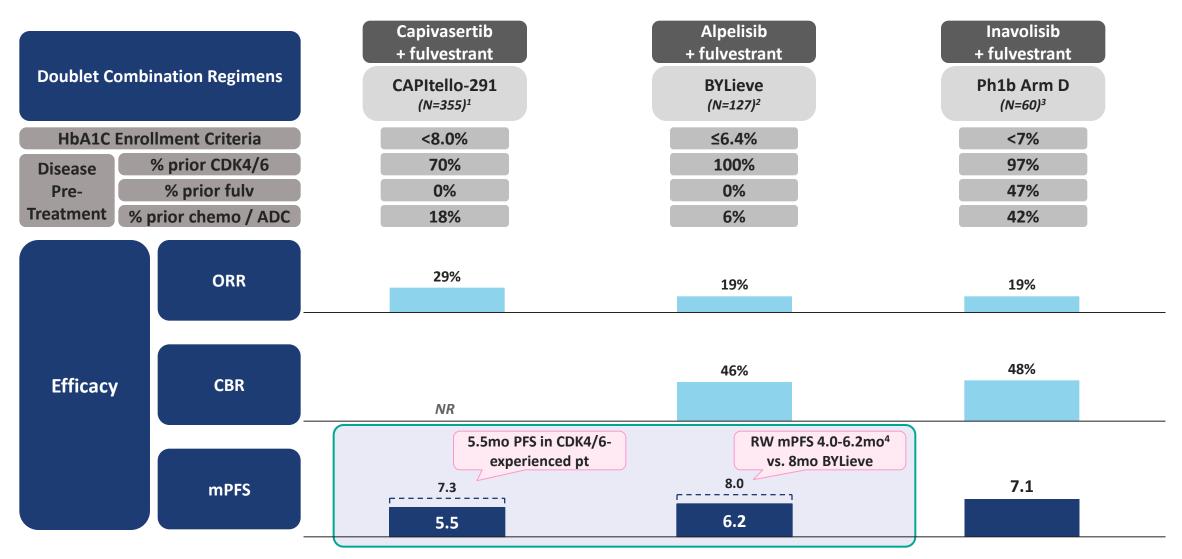


Sources: 1. Turner N Engl J Med 2023; 388:2058-2070; 2. Rugo 2021 Lancet Oncol 22:489; 3. SABCS 2021 #P5-17-05

Note: These data are derived from different clinical trials at different points in time, with differences in trial design and patient populations. As a result, cross-trial comparisons cannot be made, and no head-to-head clinical trials have been conducted. © 2024 Relay Therapeutics

#### **RLY-2608 – Efficacy Profiles of Existing PI3Kα Pathway Compounds**



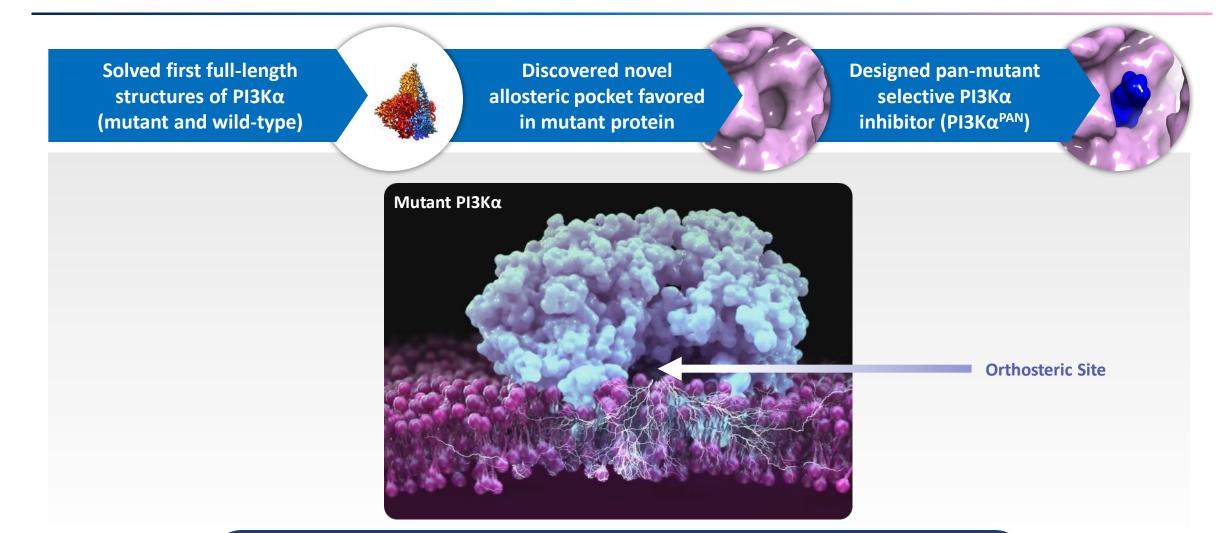


Sources: 1. Turner N Engl J Med 2023; 388:2058-2070; 2. Rugo 2021 Lancet Oncol 22:489; 3. SABCS 2021 #P5-17-05; 4. ASCO 2022 #1055 (Novartis-sponsored real-world evidence study for alpelisib + fulvestrant)

Note: These data are derived from different clinical trials at different points in time, with differences in trial design and patient populations. As a result, cross-trial comparisons cannot be made, and no head-to-head clinical trials have been conducted. © 2024 Relay Therapeutics

#### **PI3K**α – **Proprietary Insights Unlock Novel Approaches**

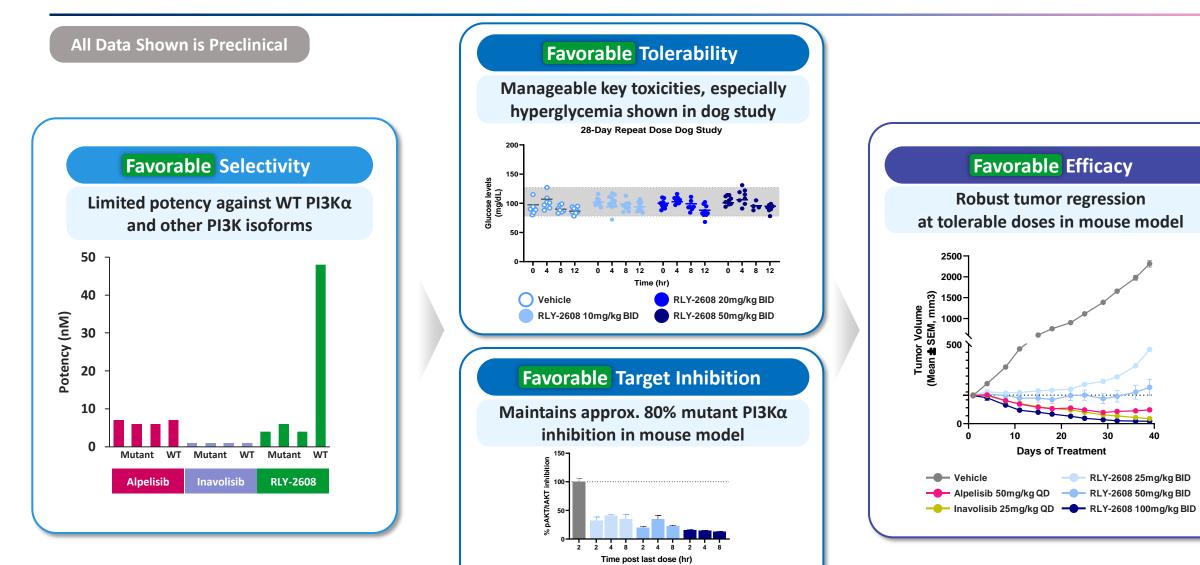




A differentiated understanding of the structure of PI3Kα and its relationship to function equips Relay Tx to design optimal mutant-selective inhibitors of PI3Kα

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





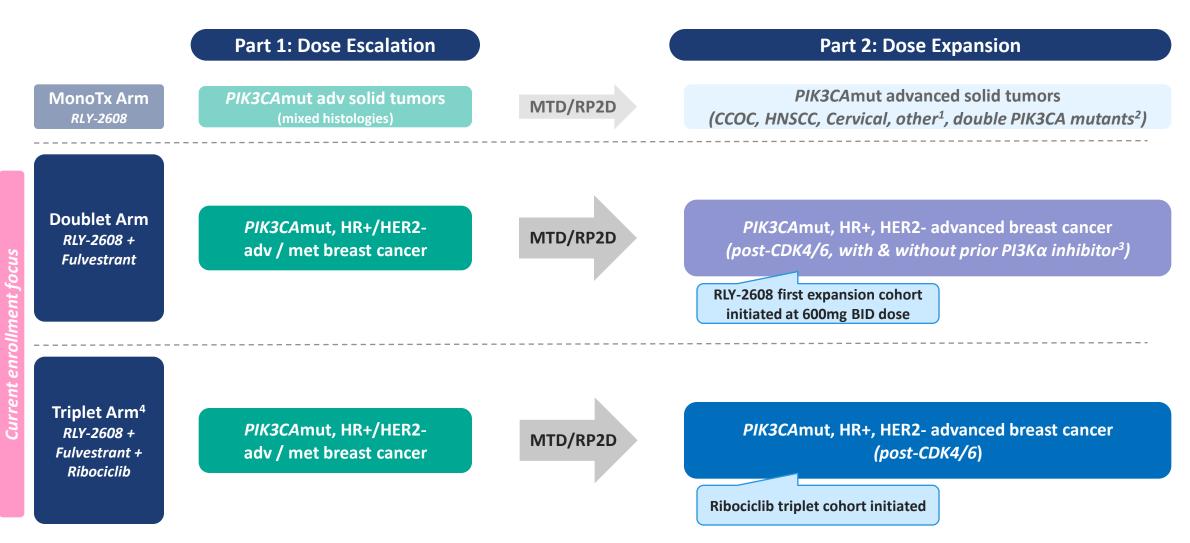
Vehicle

RLY-2608 25mg/kg BID

RLY-2608 50mg/kg QD

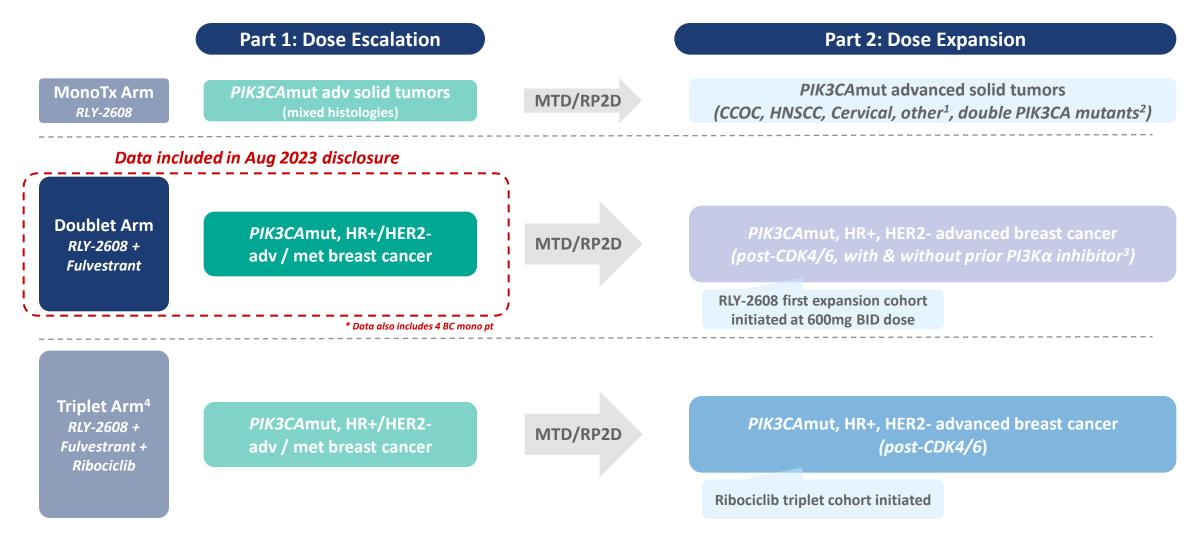
RLY-2608 100mg/kg BID





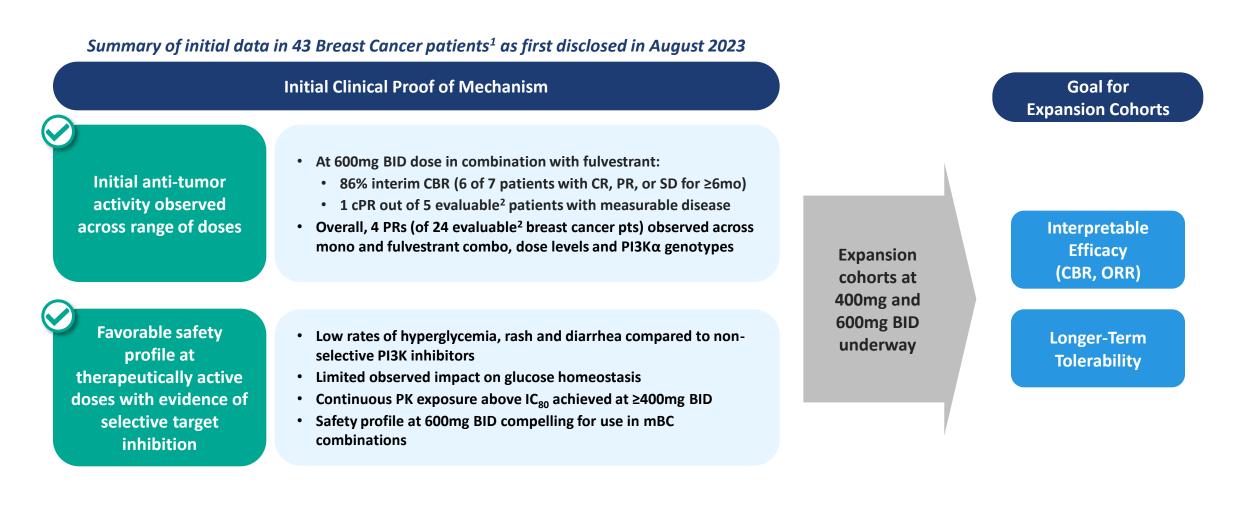
1. Excludes PIK3CAmut clear cell OvCA, HNSCC, Cervical cancer, and colorectal patients; 2. Double mutation defined as one major PIK3CA mutation (E542X, E545X, H1047X) +  $\geq$ 1 additional PIK3CA mutation per local assessment; 3. Patients with previous PI3K $\alpha$  inhibitor include those with intolerance to PI3K $\alpha$  idefined 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; 4. RLY-2608 + fulvestrant + CDK4/6 arm expected to be added in a protocol amendment © 2024 Relay Therapeutics





1. Excludes PIK3CAmut clear cell OvCA, HNSCC, Cervical cancer, and colorectal patients; 2. Double mutation defined as one major PIK3CA mutation (E542X, E545X, H1047X) + ≥1 additional PIK3CA mutation per local assessment; 3. Patients with previous PI3Kα inhibitor include those with intolerance to PI3Kαi 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; 4. RLY-2608 + fulvestrant + CDK4/6 arm expected to be added in a protocol amendment © 2024 Relay Therapeutics

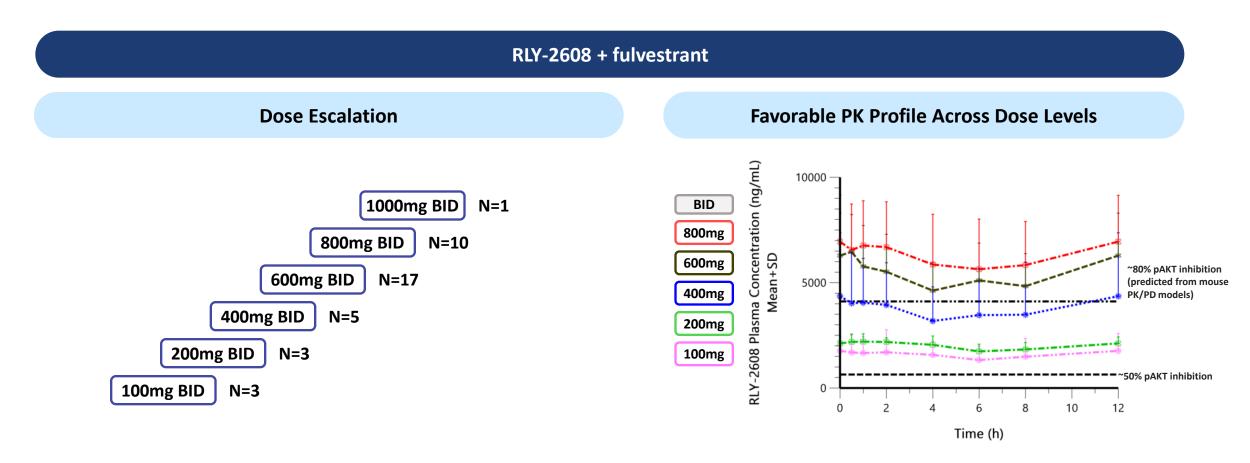




DLTs = dose limiting toxicities; CBR: Clinical Benefit defined as all patients with confirmed complete response or partial response or stable disease  $\geq 24$  weeks; evaluable patients started treatment  $\geq 24$  weeks prior to the data cutoff 1. N=43 Breast Cancer patients: 39 fulvestrant combo (17 at 600 mg BID), 4 monotherapy; 2. Efficacy analysis includes patients with measurable disease who had opportunity for  $\geq 1$  tumor assessment or discontinued treatment with <1 tumor assessment; 3. per CTCAE v5.0 © 2024 Relay Therapeutics

Preliminary data as of 07/24/2023 18





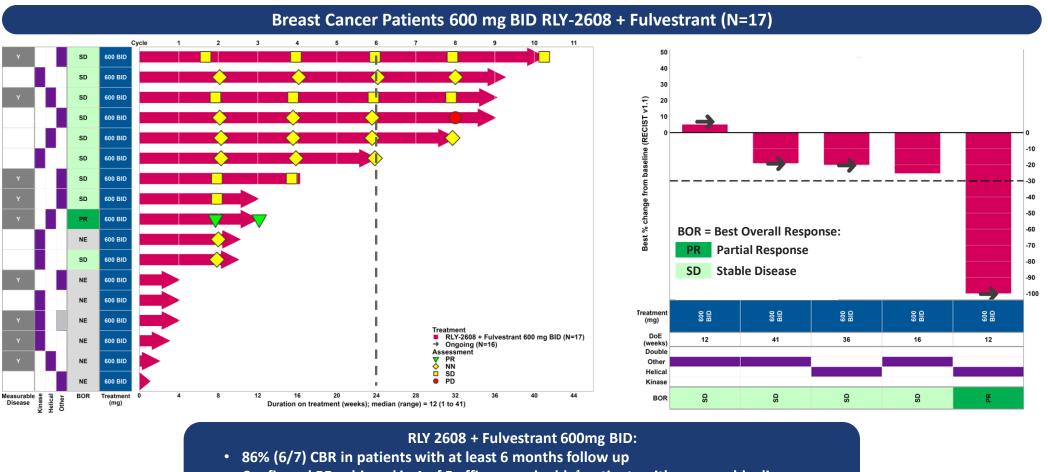
No DLTs and MTD has yet to be defined Dose-dependent increase in exposure and low peak to trough fluctuations across dose levels Continuous coverage at ~IC80+ across dosing interval at 400mg BID combo and above

# RLY-2608 – ReDiscover Trial Breast Cancer Baseline Demographics and Genotype



	RLY-2608 + fulvestrant (N=39)	RLY-2608 + fulvestrant 600 mg BID (N=17)	RLY-2608 Monotherapy (N=4)
Age, median (range), years	59 (40-82)	60 (49-80)	64 (58, 85)
Female, n (%)	39 (100%)	17 (100%)	4 (100%)
Ethnicity, %			
White / Asian / American Indian / Black / Unknown	67% / 3% / 3% / 3% / 23%	59% / 0% / 0% / 0% / 41%	100% / 0% / 0% / 0% / 0%
ECOG, n (%)			
0	21 (54%)	8 (47%)	2 (50%)
1	18 (46%)	9 (53%)	2 (50%)
BMI, kg/m², median (range)	25 (18-41)	23 (19-36)	26 (18, 44)
<30, n (%)	29 (74%)	14 (82%)	3 (75%)
≥30, n (%)	10 (26%)	3 (18%)	1 (25%)
Prior regimens of therapy in metastatic setting, median (range)	1 (1,6)	2 (1,6)	5 (1, 12)
Pending data entry	2 (5%)	1 (6%)	0 (0%)
1	19 (49%)	6 (35%)	1 (25%)
2	10 (26%)	6 (35%)	0 (0%)
3+	8 (21%)	4 (24%)	3 (75%)





- Confirmed PR achieved in 1 of 5 efficacy evaluable<sup>1</sup> patients with measurable disease
- 17 patients treated, 15 remain on treatment\*
- mDoT: 12wk (range: 1-41wk)

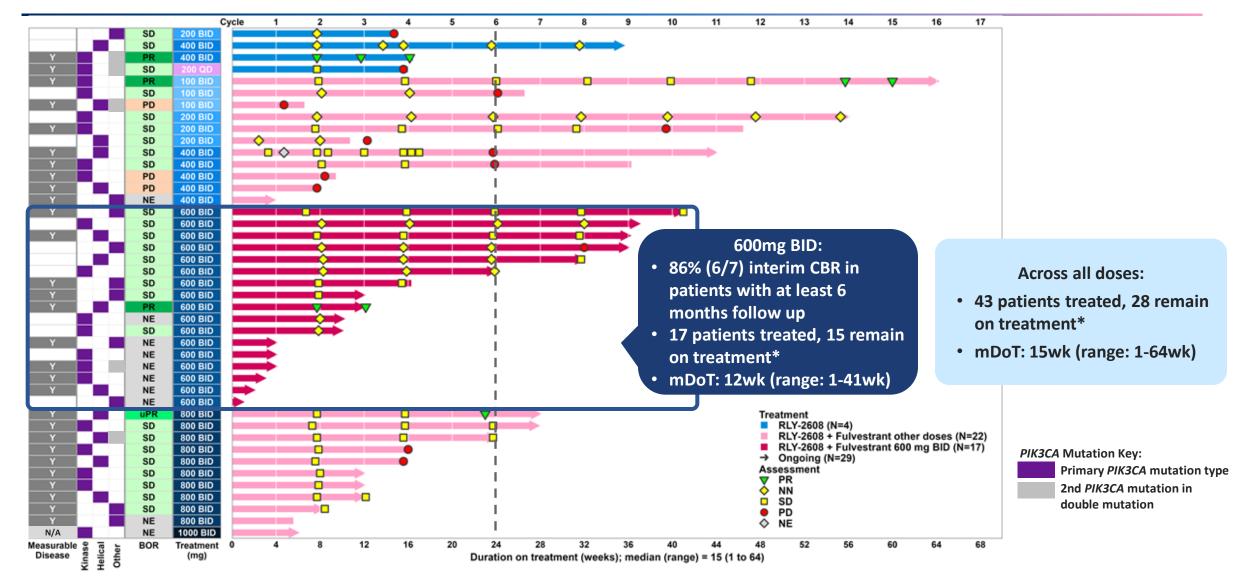
CBR: Clinical Benefit defined as all patients with confirmed complete response or partial response or stable disease  $\geq$ 24 weeks; evaluable patients started treatment  $\geq$ 24 weeks prior to the data cutoff

\* Note: one additional pt at 600mg BID dose remains on treatment after PD assessment; 1. Efficacy analysis includes patients with measurable disease who had opportunity for >1 tumor assessment or discontinued treatment with <1 tumor assessment

© 2024 Relay Therapeutics

#### RLY-2608 – Breast Cancer Disease Control Across Dose Levels

43 Breast Cancer Patients – Measurable and Non-Measurable Disease



CBR: Clinical Benefit defined as all patients with confirmed complete response or stable disease >24 weeks; evaluable patients started treatment >24 weeks prior to the data cutoff; N/A: not available as of data cut off, pending data entry \* Note: one additional pt at 600mg BID dose remains on treatment after PD assessment © 2024 Relay Therapeutics

22 Preliminary data as of 07/24/2023

Preliminary data as of 24 July 2023

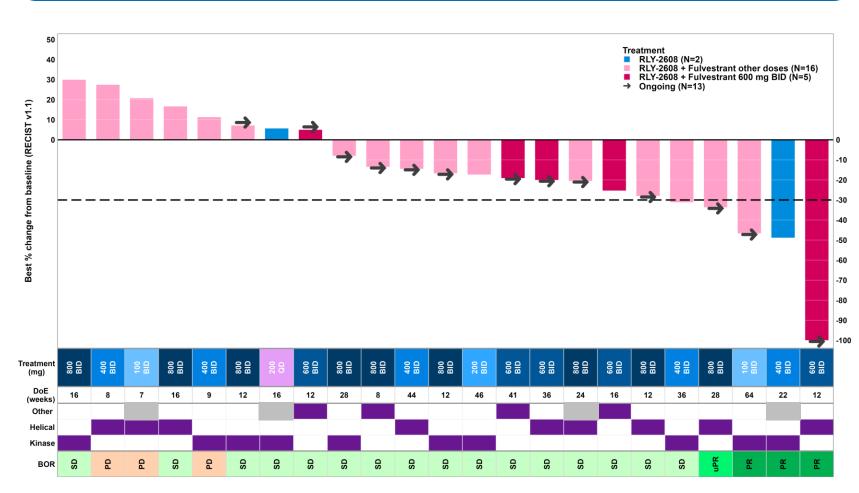
REI

#### **RLY-2608 – Evidence of Anti-Tumor Activity Supports Selective Target Engagement**

Breast Cancer Patients (RECIST Measurable Disease) N=24\*

Preliminary data as of 24 July 2023

24 Breast Cancer Patients\* – Measurable Disease Only



 At 600mg BID combo, 80% of patients (4/5) exhibited radiographic tumor reductions

- 1 pt experienced a partial response and remains on treatment
- Overall, 63% of patients (15/24) exhibited radiographic tumor reductions; 13/24 patients ongoing
- 4 partial responses observed across mono and combo, dose levels and PI3Kα genotypes



- PR Partial Response
- uPR Unconfirmed Partial Response
- SD Stable Disease
- PD Progressive Disease

\* one patient discontinued prior to first scan and is not shown on waterfall plot © 2024 Relay Therapeutics

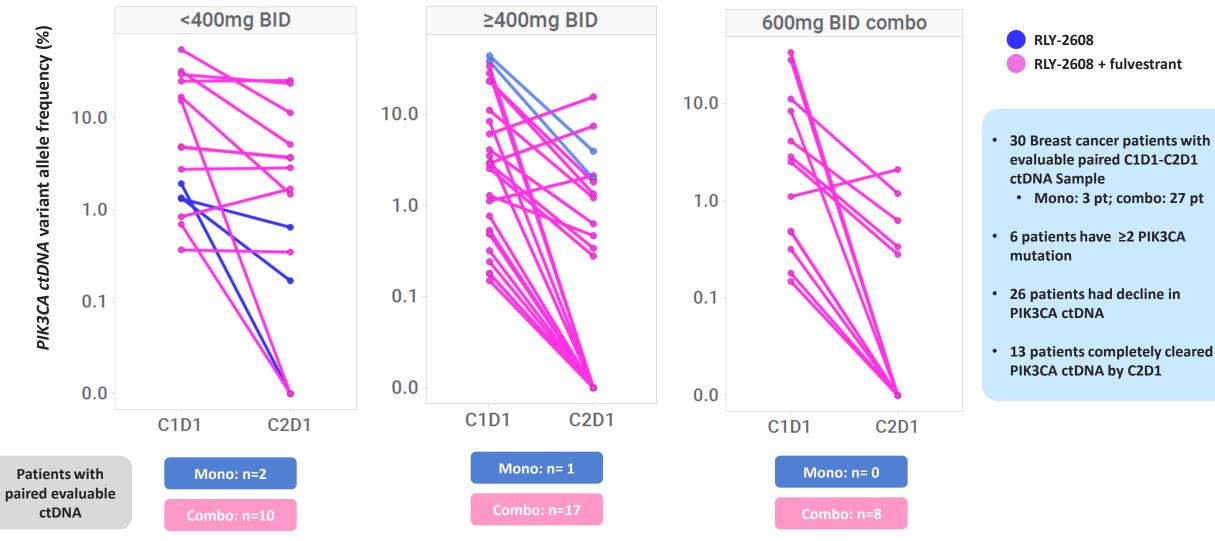


Primary PIK3CA mutation type

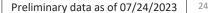
2nd PIK3CA mutation in double mutation

23

#### **RLY-2608 – Mutant PIK3CA Decline Supports Dose Dependent Target Inhibition**



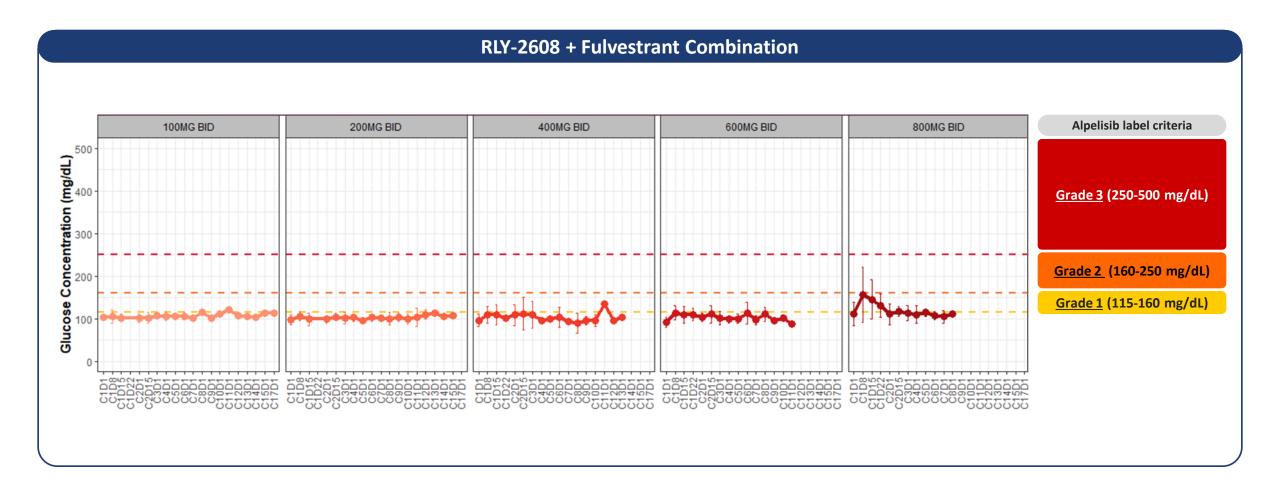
Note: data points at zero are below limits of detection Source: Central lab analysis



Preliminary data as of 24 July 2023

REL

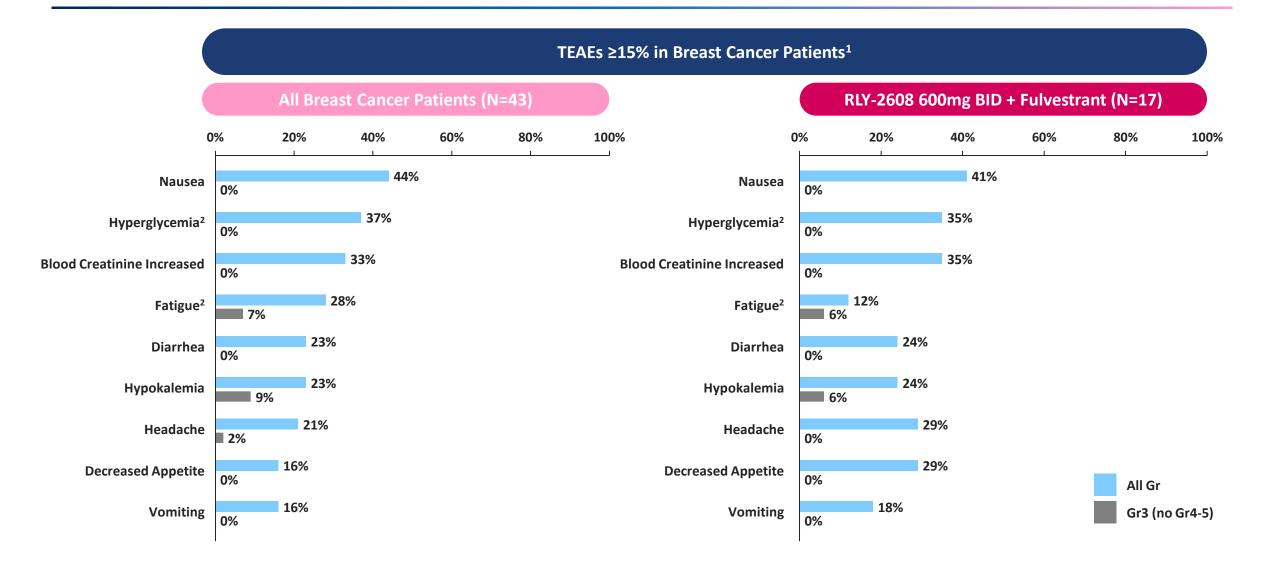




Note: one 1000mg BID combo pt not shown; pt had Gr2 glucose elevation per alpelisib label criteria; Data represent mean per cohort +/- standard deviation Source: Central lab analysis

© 2024 Relay Therapeutics





1. TEAEs that occurred in >=15% of the Breast Cancer Safety Set (N=43) are shown for both populations; 2. Hyperglycemia includes the MedDRA v26.0 Preferred Terms (PT): Hyperglycemia and Blood Glucose Increased, Fatigue includes the PTs: Fatigue and Asthenia.

© 2024 Relay Therapeutics

Preliminary data as of 07/24/2023 26

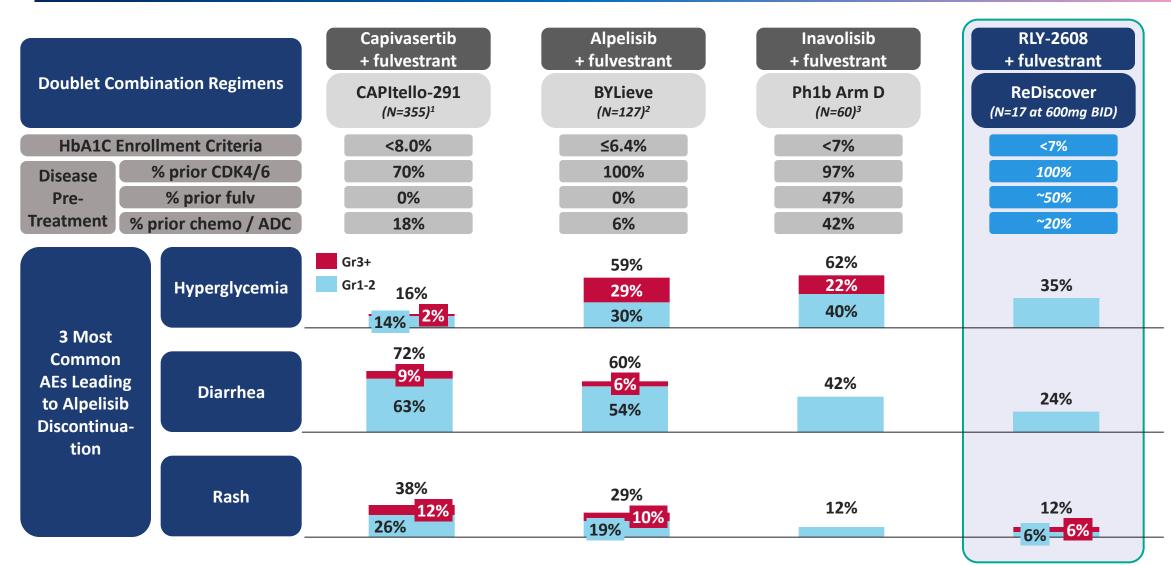
# **RLY-2608** – Safety Profiles of Existing PI3Kα Pathway Compounds



27

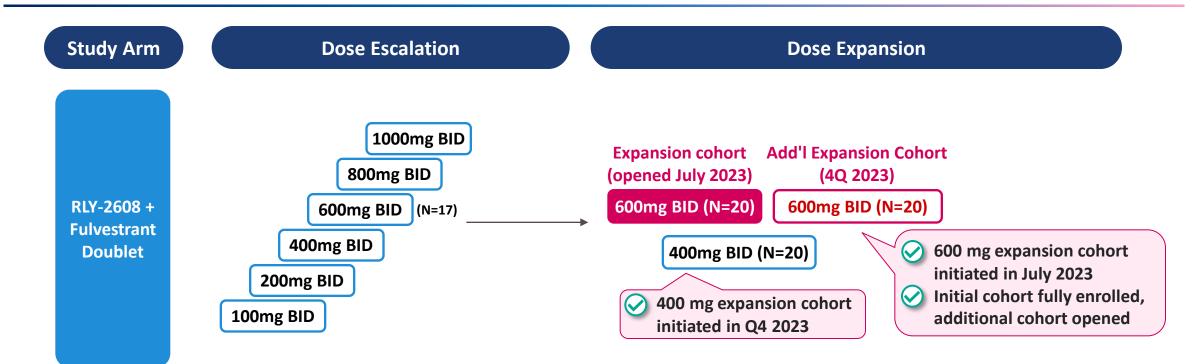
Data below are not from head-to-head studies.

Cross-trial data interpretation should be considered with caution as it is limited by differences in study population and many other factors.



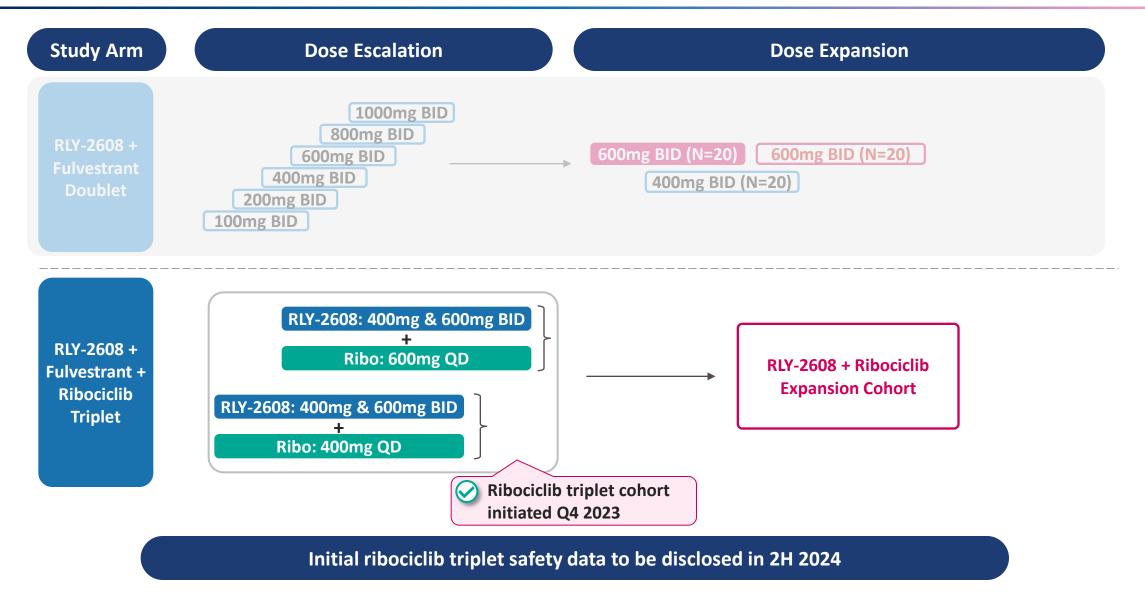
Sources: 1. Turner N Engl J Med 2023; 388:2058-2070; 2. Rugo 2021 Lancet Oncol 22:489; 3. SABCS 2021 #P5-17-05; \* For *PIK3CA*mut HR+/HER2- breast cancer in combination with fulvestrant; Note: These data are derived from different clinical trials at different points in time, with differences in trial design and patient populations. As a result, cross-trial comparisons cannot be made, and no head-to-head clinical trials have been conducted.
© 2024 Relay Therapeutics
Preliminary data as of 07/24/2023



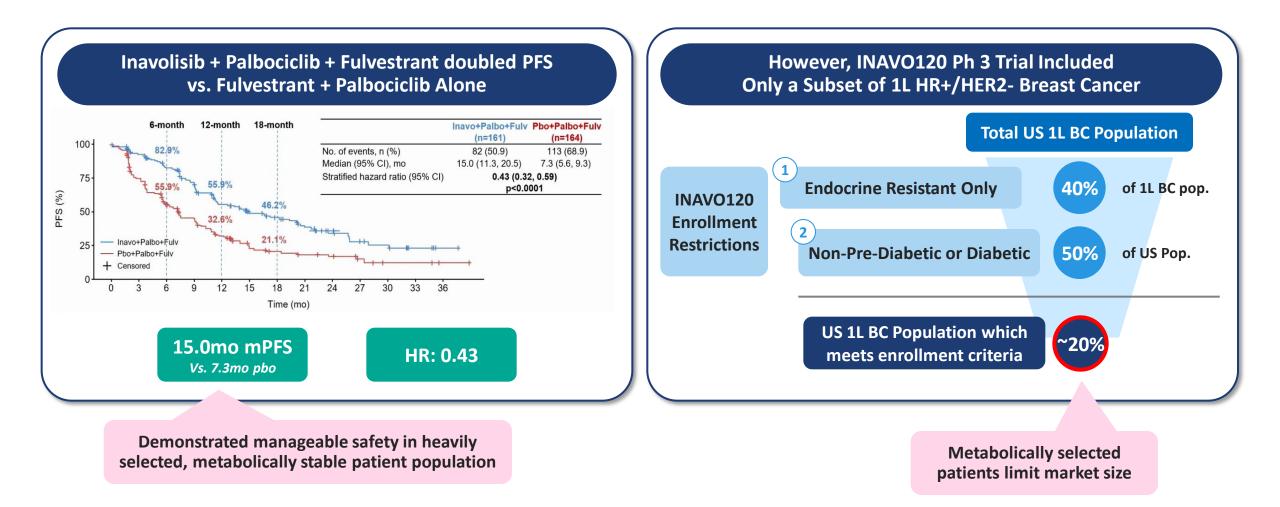


Next RLY-2608 doublet data to be disclosed in 2H 2024 after further data maturation







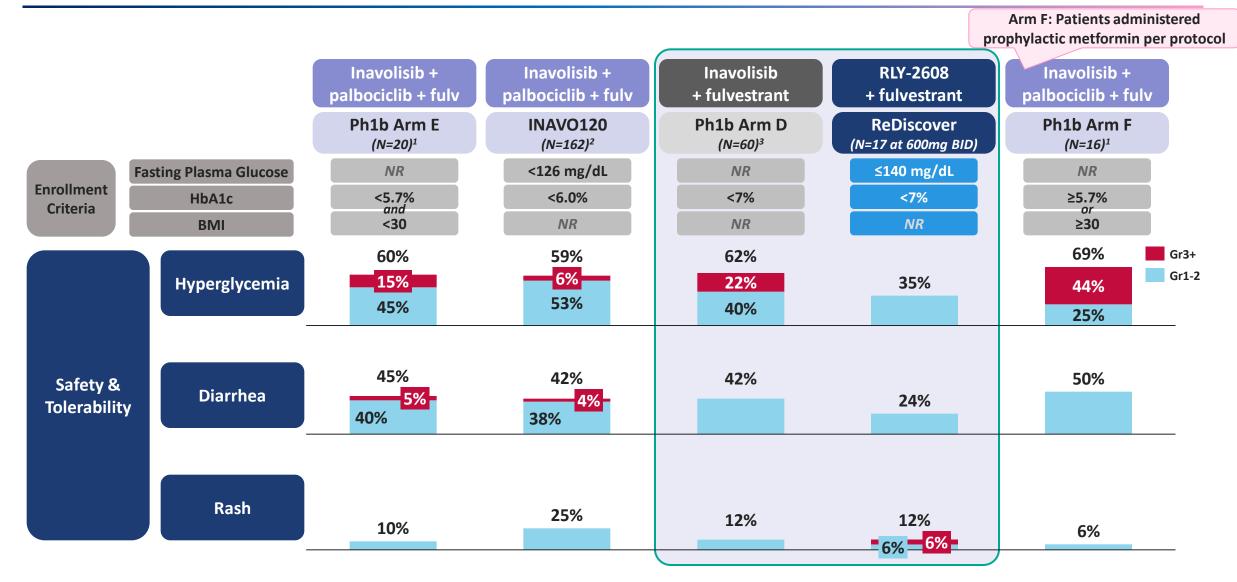


## **RLY-2608 – Safety Profiles of Existing PI3Kα Pathway Compounds**

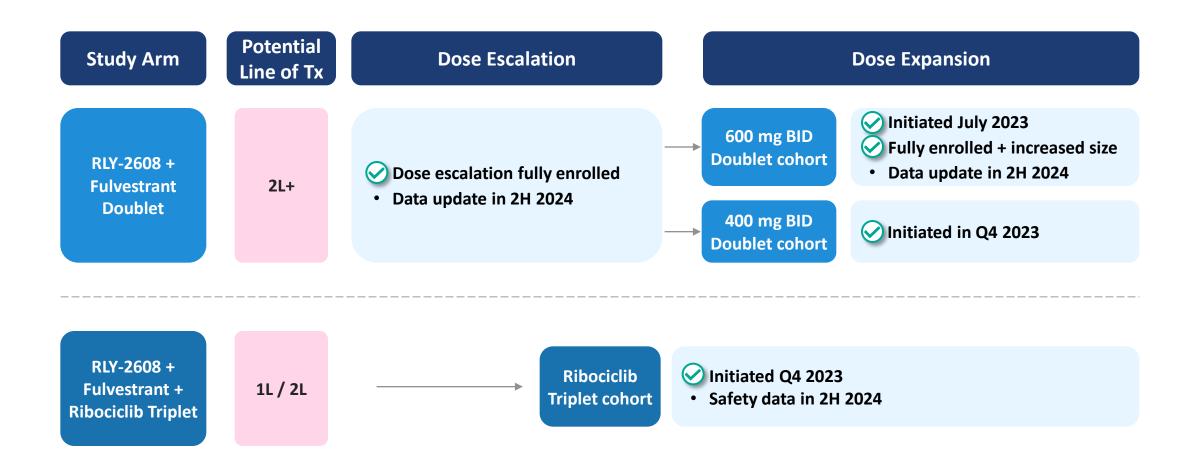
Data below are not from head-to-head studies.

Cross-trial data interpretation should be considered with caution as it is limited by differences in study population and many other factors.









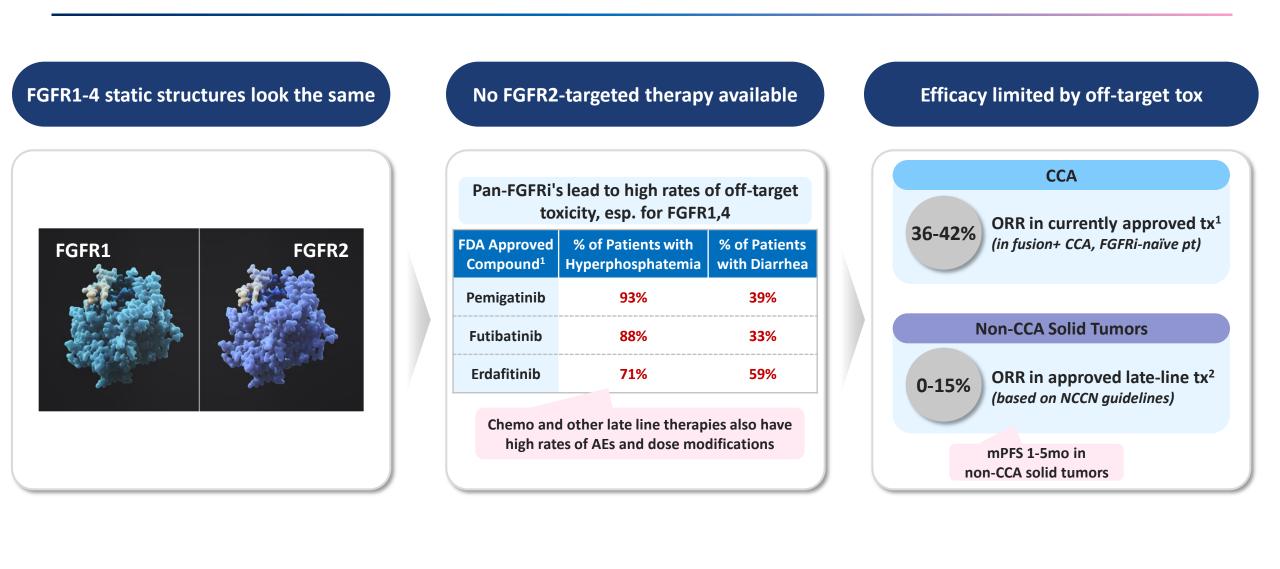
#### Next RLY-2608 data update in 2H 2024

## **Relay Tx – Broad Precision Medicine Pipeline**



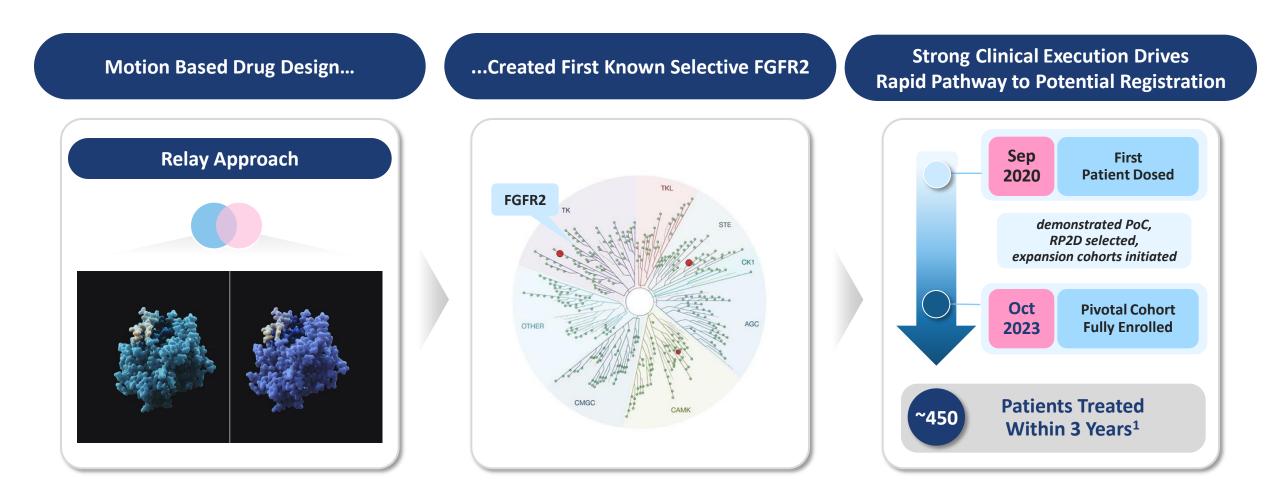
Target	Program Preclinical	Early Clinical Late Clinical
	Monotherapy	
	RLY-2608 PI3Kα <sup>PAN</sup> Endocrine Tx (ET) doublet	
PI3Kα franchise	CDK4/6i + ET triplet	
	<b>RLY-5836</b> (PI3KαPAN)Dose EscalationDeprioritized	
	<b>ΡΙ3Κα<sup>Η1047R</sup></b>	
FGFR2	Lirafugratinib (RLY-4008)	
Solid Tumor	2 programs	
Genetic Disease	2 programs	
CDK2	RLY-2139 Paused; IND rea	
ΕRα	ERa Degrader Paused at DC	
SHP2	Migoprotafib (GDC-1971) Genentech A Menter of the Rock Group	



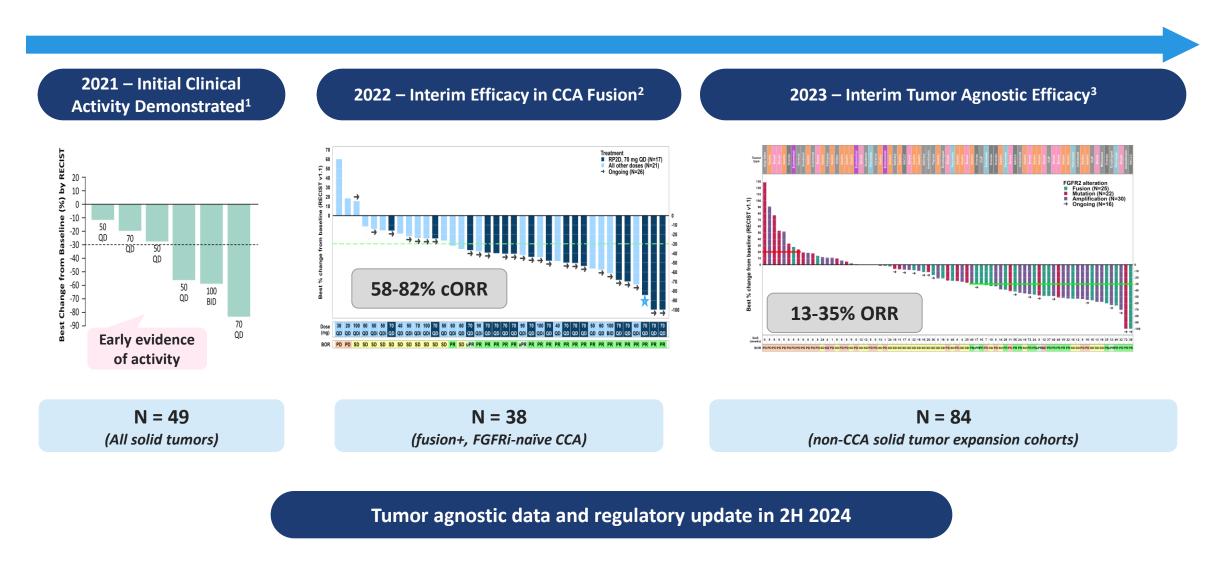


1. Sources: Pemigatinib – prescribing information; futibatinib – prescribing Information; erdafitinib – prescribing information; (note: AEs are reflective of respective label indications); 2. Reflects reported ORRs in key randomized studies evaluating NCCN recommended regimens for recurrent/metastatic patients (second/third line or later) for the following tumor types: HR+ breast cancer, gastric cancer, pancreatic cancer, NSCLC, ovarian cancer, and head and neck







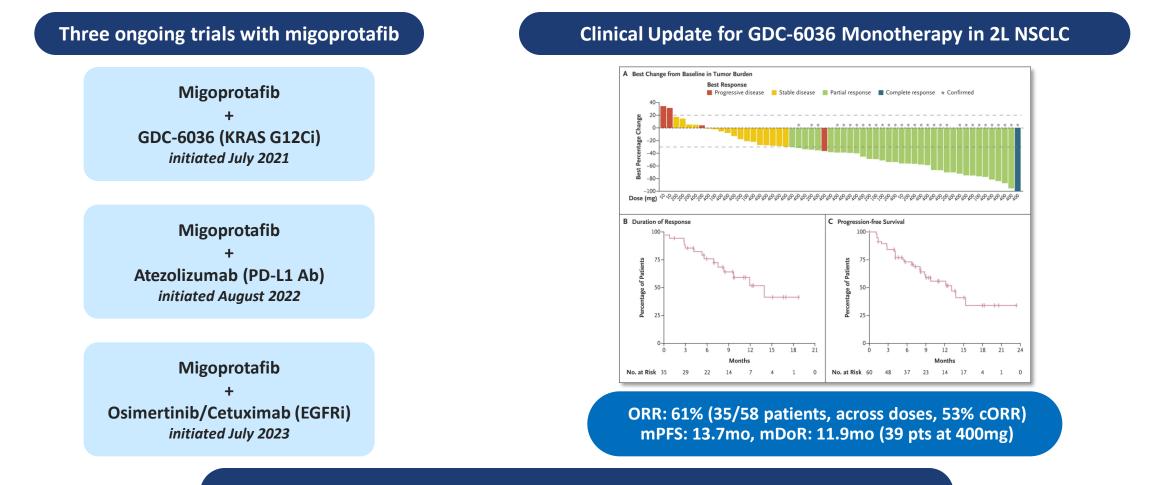


## **Relay Tx – Broad Precision Medicine Pipeline**



Target	Program	Preclinical
	Monotherapy	
	RLY-2608 PI3Kα <sup>PAN</sup> Endocrine Tx (ET) doublet	
PI3Kα franchise	CDK4/6i + ET triplet	
	RLY-5836 (ΡΙ3Κα <sup>PAN</sup> ) Dose Escalation	
	<b>ΡΙ3Κα</b> <sup>Η1047R</sup>	
FGFR2	Lirafugratinib (RLY-4008)	
Solid Tumor	2 programs	
Genetic Disease	2 programs	
CDK2	RLY-2139	
ERα	ERa Degrader	
SHP2	Migoprotafib (GDC-1971) Genentech	3 ongoing combo studies





Collaboration provides meaningful economics to Relay Tx<sup>1</sup>

Source: Sacher 2023 N Engl J Med 389:710

1. As of the date of this presentation: \$120 million in upfront & milestone payments received, and eligible to receive up to \$675M in potential additional total milestones, low-to-mid teen royalties on global net sales plus additional royalties upon approval of GDC-1971 and GDC-6036 in combination

#### © 2024 Relay Therapeutics

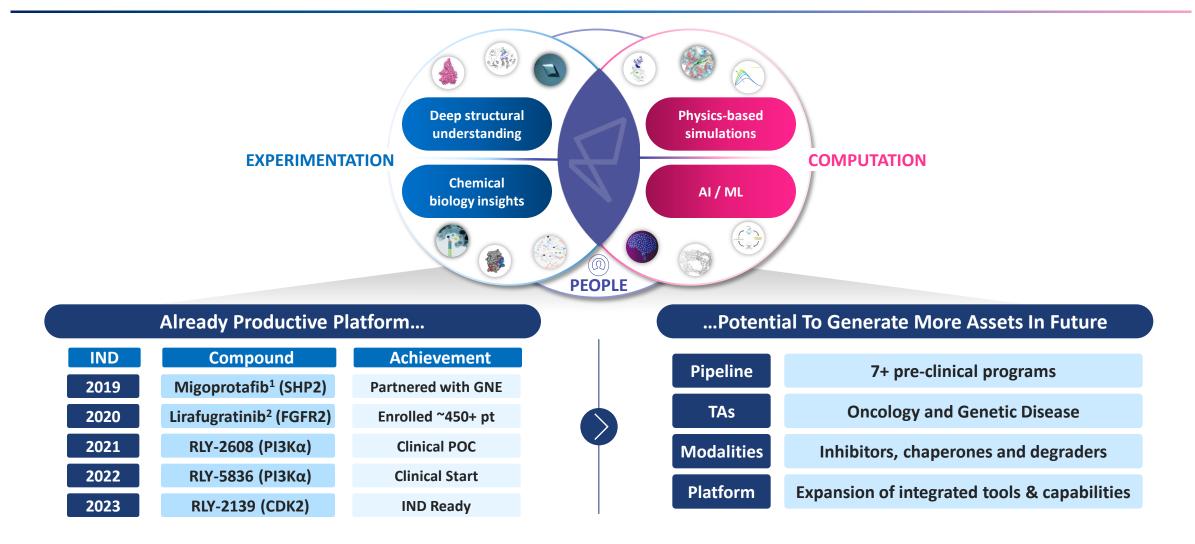
## **Relay Tx – Broad Precision Medicine Pipeline**



Target	Program	Preclinical
	Monotherapy	
	RLY-2608 PI3Kα <sup>PAN</sup> Endocrine Tx (ET) doublet	
PI3Kα franchise	CDK4/6i + ET triplet	
	<b>RLY-5836</b> (ΡΙ3Κα <sup>PAN</sup> ) Dose Escalation	
	<b>ΡΙ3Κα</b> <sup>Η1047R</sup>	
FGFR2	Lirafugratinib (RLY-4008)	
Solid Tumor	2 programs	
Genetic Disease	2 programs	
CDK2	RLY-2139 Paused; IND ready	
ΕRα	ERa Degrader	
SHP2	Migoprotafib (GDC-1971) Genentech	

#### **Relay Tx – Productive and Evolving Platform**







Target	Program	Preclinical > Early Clinical > Late Clinical	Annual US Patient #
Pl3Kα franchise	Monotherapy		
	RLY-2608 PI3Kα <sup>PAN</sup> Endocrine Tx (ET) doublet		~10-71K breast cancer
	CDK4/6i + ET triplet		~76-243K all solid tumors
	RLY-5836 (PI3Kα <sup>PAN</sup> ) Dose Escalation	Deprioritized	
	ΡΙ3Κα <sup>Η1047R</sup>		~4-27K breast cancer ~15-50K all solid tumors
FGFR2	Lirafugratinib (RLY-4008)		~11-35K⁴
Solid Tumor	2 programs		To be announced
Genetic Disease	2 programs		To be announced
CDK2	RLY-2139	Paused; IND ready	~35K²
ERα	RLY-1013 (Degrader)	Paused at DC	~30-205K <sup>3</sup>
SHP2	Migoprotafib (GDC-1971) Genentech A Member of the Rocke Group	3 ongoing combo studies	~36-69К⁵

#### 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. ~35K HR+/HER2- breast cancer patients expected to receive CDK 4/6 inhibitors in adjuvant setting, first-line setting, and second-line setting in 2024, per Decision Resources Breast Cancer Market Forecast report dated November 2023; 3. HR+/HER2- US late-line breast cancer patients compared to HR+/HER2- US incident breast cancer patients; 4. 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 and all breast cancer patients with FGFR2 alterations; 5. SHP2 combo only includes KRAS G12C in lung and colorectal, EGFR mutations in lung, and ALK fusions in lung © 2024 Relay Therapeutics



2024 Corporate Objectives		Significant Capital to Achieve Goals
RLY-2608 Doublet (ΡΙ3Κα)	• Additional clinical data in 2H 2024	
RLY-2608 Triplet (ΡΙ3Κα)	<ul> <li>Ribociclib triplet initiation in Q4 2023</li> <li>Ribociclib triplet safety data in 2H 2024</li> </ul>	Cash, cash equivalents and investments as of the end of 1Q 2024
Lirafugratibnib (RLY-4008) <i>(FGFR2)</i>	<ul> <li>Tumor agnostic data and regulatory update in 2H 2024</li> </ul>	
Pre-clinical Pipeline (Targets unnamed)	<ul> <li>New program(s) to be disclosed in 2024</li> <li>7+ undisclosed programs in preclinical development and additional early-stage efforts across platform</li> </ul>	Expected to be sufficient to fund current operating plan into 2H 2026
Migoprotafib (GDC-1971) Genentech A Menter of the Kacke Carey (SHP2)	• Three ongoing combination trials *Genentech controls data disclosures	



