UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): April 18, 2023

RELAY THERAPEUTICS, INC.

(Exact name of Registrant as Specified in Its Charter)

Delaware	**001-39385**	**47-3923475**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

399 Binney Street **Cambridge, Massachusetts** **(Address of Principal Executive Offices)**	**02139** **(Zip Code)**

Registrant's Telephone Number, Including Area Code: (617) 370-8837

Not Applicable
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common Stock, par value $0.001 per share	RLAY	Nasdaq Global Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

Relay Therapeutics, Inc. (the "Company") intends to host a conference call and live webcast on April 18, 2023 at 1:30 p.m. E.T. to discuss the initial clinical data for RLY-2608, the first known investigational allosteric, pan-mutant and isoform-selective phosphoinostide 3 kinase alpha, also known as PI3Kα, inhibitor that is being presented at the American Association for Cancer Research ("AACR") Annual Meeting 2023. The Company has made available a slide presentation to accompany the call, a copy of which is being furnished as Exhibit 99.1 to this Current Report on Form 8-K.

The information in this Item 7.01, including Exhibit 99.1 attached hereto, is intended to be furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such filing.

Item 8.01 Other Events.

On April 18, 2023, the Company issued a press release announcing the initial clinical data for RLY-2608 that was presented at the AACR Annual Meeting 2023, a copy of which is filed herewith as Exhibit 99.2 to this Current Report on Form 8-K and incorporated herein by reference.

Item 9.01 Exhibits.

99.1	RLY-2608 Initial Clinical Data Presentation at AACR Annual Meeting, dated April 2023, furnished herewith.
99.2	Press release issued by Relay Therapeutics, Inc. on April 18, 2023.
104	Cover Page Interactive Data File (embedded within Inline XBRL document).

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

RELAY THERAPEUTICS, INC.

Date: April 18, 2023

By: /s/ Brian Adams
Brian Adams
Chief Legal Officer

RELAY®
THERAPEUTICS

RLY-2608 Initial Clinical Data Presentation at AACR Annual Meeting

April 2023

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, timing of enrollment completion, and potential efficacy and tolerability; the timing of a clinical data update for RLY-4008, RLY-2608, and RLY-5836, and the clinical initiation of RLY-2139, and the nomination of a development candidate for our ERα degrader program; 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 or RLY-5836 to address a major unmet medical need; expectations regarding our pipeline, operating plan, use of capital, expenses and other financial results; our cash runway projection; the competitive landscape and potential 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 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. 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 all forward-looking statements contain these identifying words.

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, or public health epidemics or outbreaks of an infectious disease, such as COVID-19, 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 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, whether as a result of new information, the occurrence of certain events or otherwise. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. No representations or warranties (expressed or implied) are made about the accuracy of any such forward-looking statements.

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

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

Relay Tx – Patient-Driven

New Breed of Biotech

EXPERIMENTATION — COMPUTATION

Clear Focus

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

~$1B

Cash, cash equivalents and investments as of the end of 4Q 2022

Validated Approach

Clinical

- FGFR2 *RLY-4008*
- PI3Kα^{PAN} *RLY-2608* *RLY-5836*
- SHP2 *GDC-1971*

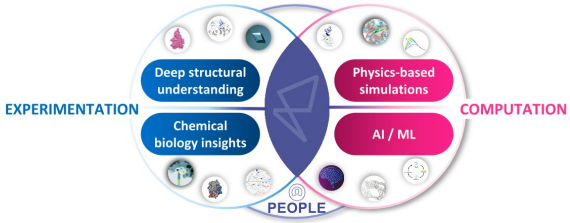
Pre-clinical

- ERα Degrader
- CDK2 *RLY-2139*
- 5+ Add'l programs

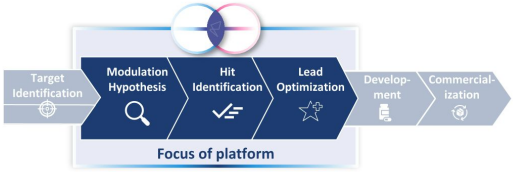
Execution-Focused

Relay Tx – Dynamo™ Platform

1 Dynamo™ Platform…

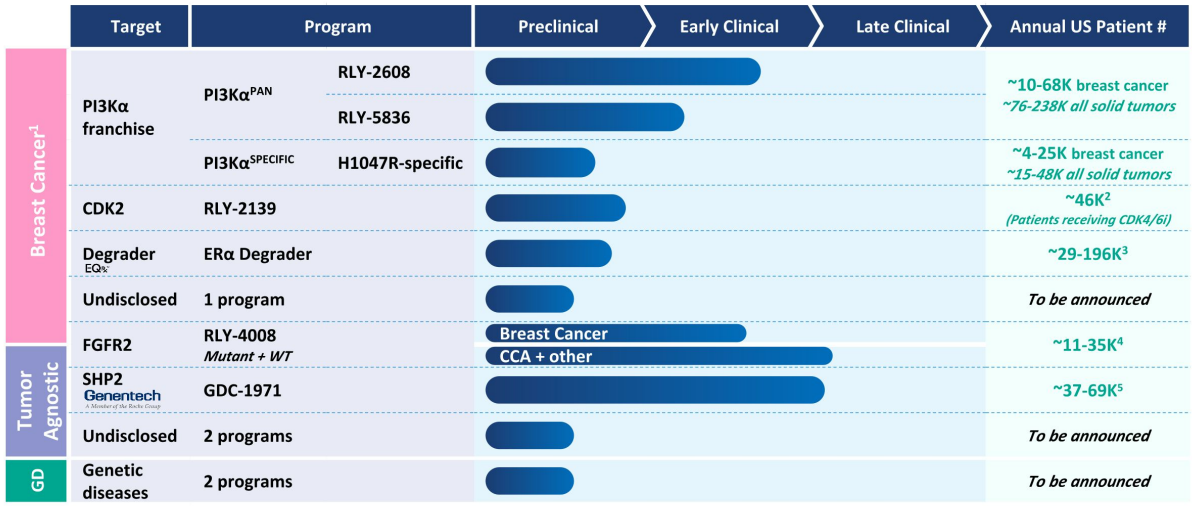


2 …is focused on making medicines



3 …aims to address selectivity on validated targets

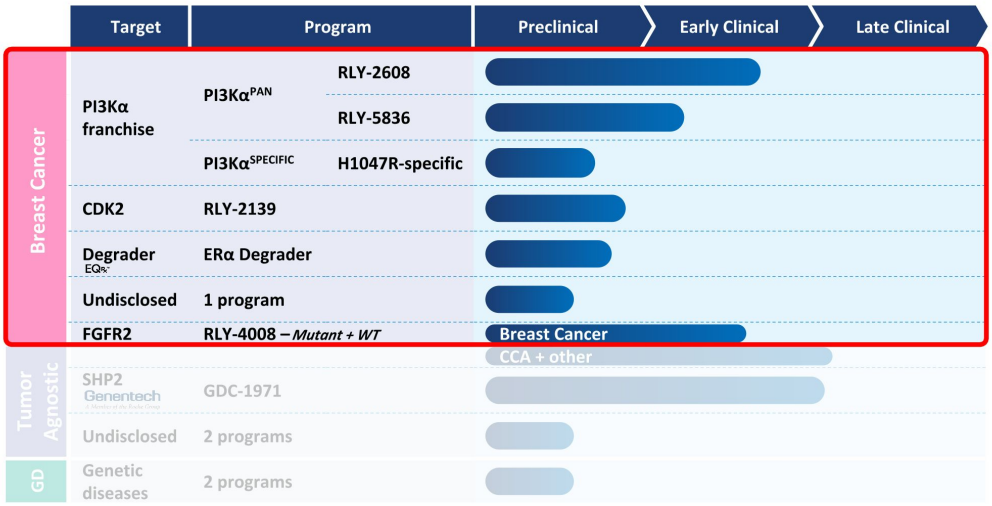
Relay Tx – Extensive Precision Medicine Pipeline



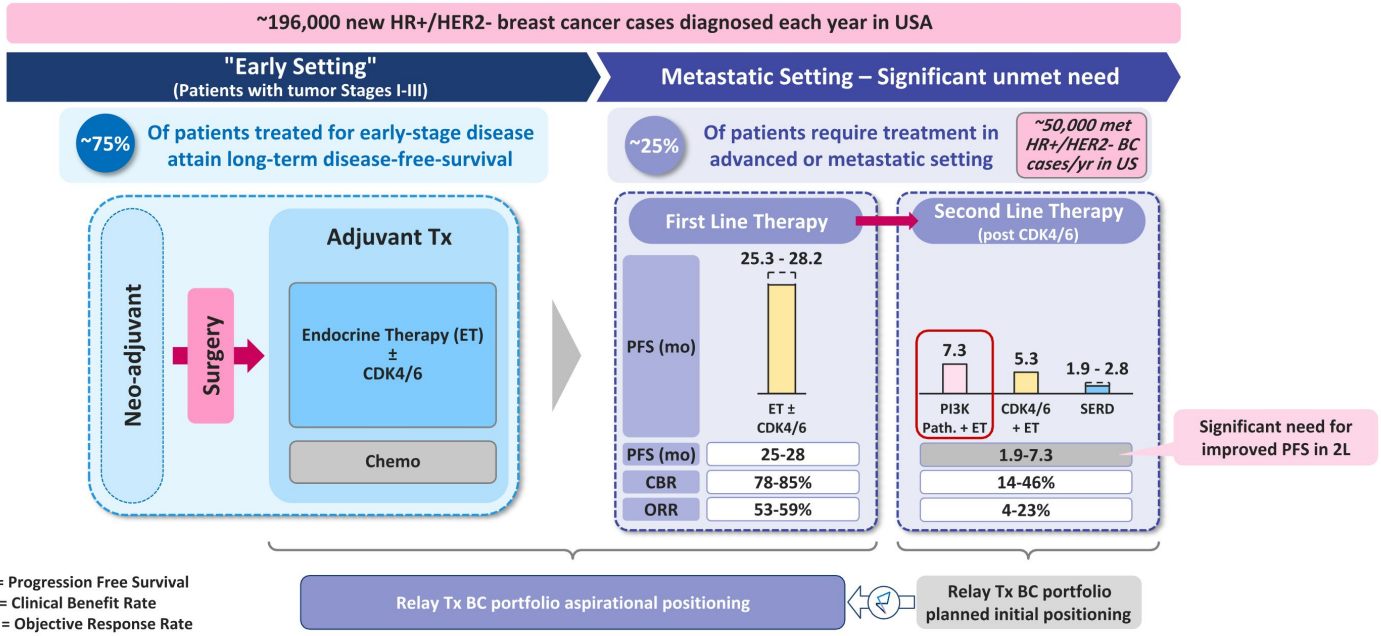
Note: Unless otherwise indicated, patient #'s refer to total annual number of US patients with late-line cancers compared to comprehensive annual incidence that may be amenable to treatment with our programs

1. Unless otherwise indicated, all breast cancer patient numbers refer to HR+/HER2- breast cancer tumors; 2. ~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; 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

Relay Tx – Emerging Breast Cancer Franchise



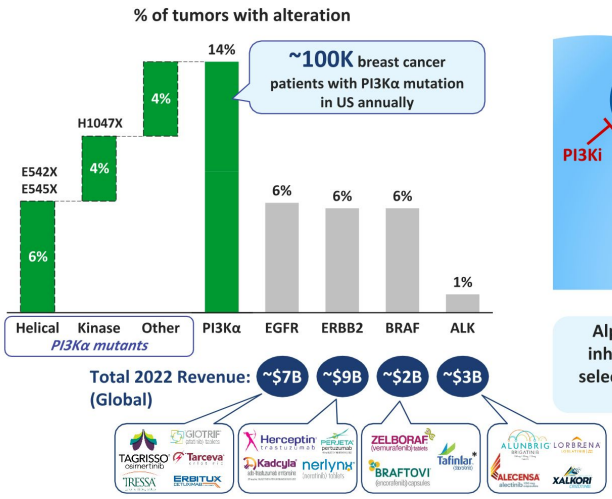
Breast Cancer – Significant Unmet Need



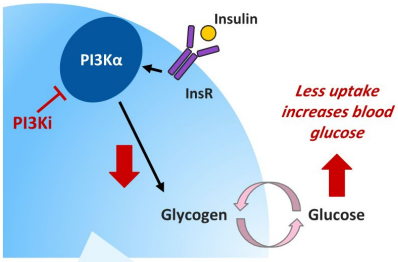
Figures generated based on publicly available data for both approved and investigational products (alpelisib, ribociclib, elacastrant (investigatonal), fulvestrant (investigatonal), palbociclib, ribociclib, abemaciclib, capivasertib (investigational)).
Sources: SEER, Metastatic Breast Cancer Network (MBCN), Johnston 2019 NPJ Breast Cancer 5:5, Goetz 2017 JCO 35:3638, Rugo 2019 Breast Cancer Res Treat 174:719, Ibrance Label, Finn 2016 N Engl J Med 375:1925, Hortobagyi 2018 Ann Oncol 29:1541, Kisqali label, SABCS 2021 #P1-18-03, SABCS 2022 #GS3-04, ASCO 2022 #LBA1004, Bardia 2022 Cancer Research 82, ASCO 2022 LBA3, ASCO 2022 LBA1001, Wander 2021 J NCCN 24:1, ASCO 2022 #1055, Xi J 2019 J NCCN 17:141

PI3Kα – A Validated Target with Significant Unrealized Therapeutic Potential

PI3Kα is the most frequently mutated kinase in solid tumors



PI3Kα regulates glucose homeostasis



Alpelisib, the only FDA-approved PI3Kα inhibitor for solid tumors, is not mutant-selective and disrupts glucose metabolism, causing hyperglycemia

WT PI3Kα and off-isoform toxicity limit the clinical benefit of alpelisib

AEs frequently leading to treatment discontinuation for alpelisib

AE	All Gr (Gr3+)
Hyperglycemia	65% (37%)
Diarrhea	60% (7%)
Rash	36% (10%)

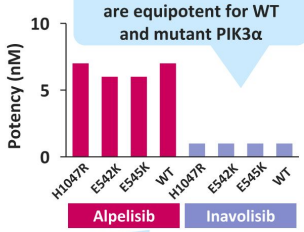
*Tafinlar + Mekinist

Sources: Internal analysis based on third party industry data; Alpelisib data: SOLAR-1 (long-term follow up): Andre 2021 Ann Oncol 32:208

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

Alpelisib: Observed coverage (based on IC_{80}) at median dose intensity 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%
Capivasertib[14-18]	21-62%	16-43%	2-20%	64-82%	22-53%

AKT inhibitor

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%
Capivasertib+fulv[18]	35%	20%	13%

Limited Efficacy

Regimen	ORR	CBR	PFS (mo)
Alpelisib Mono Ph 1a[7]	4%	17%	5.5
Alpelisib + fulv Ph 2[4]	19%	46%	7.3
Inavolisib + fulv Ph 1b[13]	19%	48%	7.1
Capivasertib + fulv Ph 3[18]	29%	*NR**	7.3

Data from RP2D of alpelisib, inavolisib, and capivasertib

* NR = Not Recorded

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

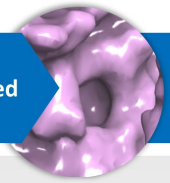
Sources: Alpelisib – 1. SOLAR-1: Andre 2019 N Engl J Med 380:1929, 2. Ph 1b: SABCS 2013 P2-16-14, 3. Ph 1b: SABCS 2014 PD5-5, 4. Ph 2 ByLIEVE: Rugo 2021 Lancet Oncol 22:489, SABCS 2021 #P1-18-03, 5. Ph 1b mono: Annals of Oncol 25 2014 (suppl 4), 6. Ph 2 mono: Savas Cancer Discov 2022 Sep 12:2058, 7. Ph 1a mono: Juric 2018 J Clin Oncol 36:1291 ; Inavolisib – 8. ASCO 2022 #1052 (note: pooled rates across cohorts), 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; Capivasertib – 14. Ph 1 mono: Banerji 2018 Clin Cancer Res 24:2050, ASCO 2015 #2500; 15. Ph 2 mono: SABCS 2019 P1-19-14; 16. Ph 1 combo: Smyth 2020 Clin Cancer Res 26:3947; 17. Ph 2 FAKTION: ASCO 2022 #1005; 18. Ph 3 CAPItello-291: SABCS 2022 #GS3-04

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.

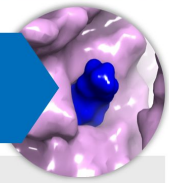
PI3Kα – Proprietary Insights Unlock Novel Approaches

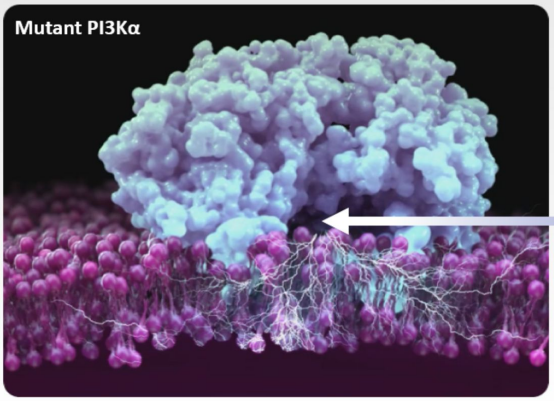
Solved first full-length structures of PI3Kα (mutant and wild-type)

Discovered novel allosteric pocket favored in mutant protein



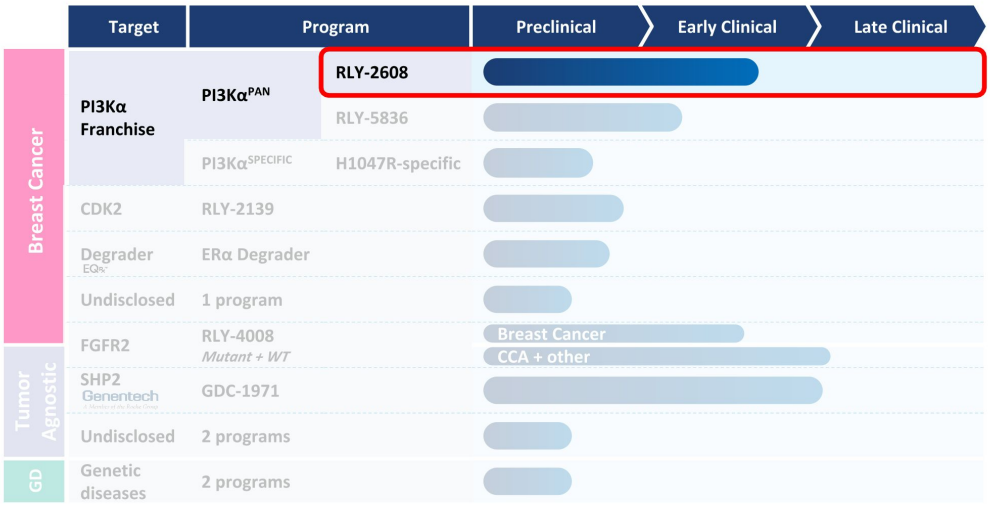
Designed pan-mutant selective PI3Kα inhibitor ($PI3K\alpha^{PAN}$)





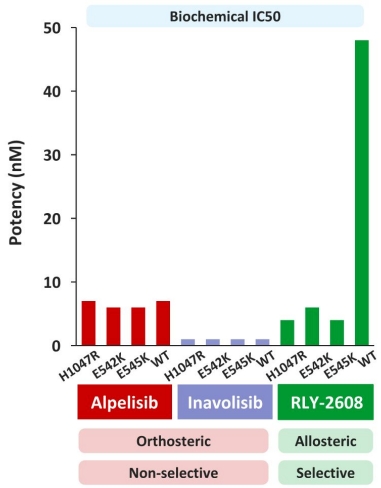
A differentiated understanding of the structure of PI3Kα and its relationship to function equips Relay Tx to design optimal mutant-selective inhibitors of PI3Kα

Relay Tx – Extensive Precision Medicine Pipeline

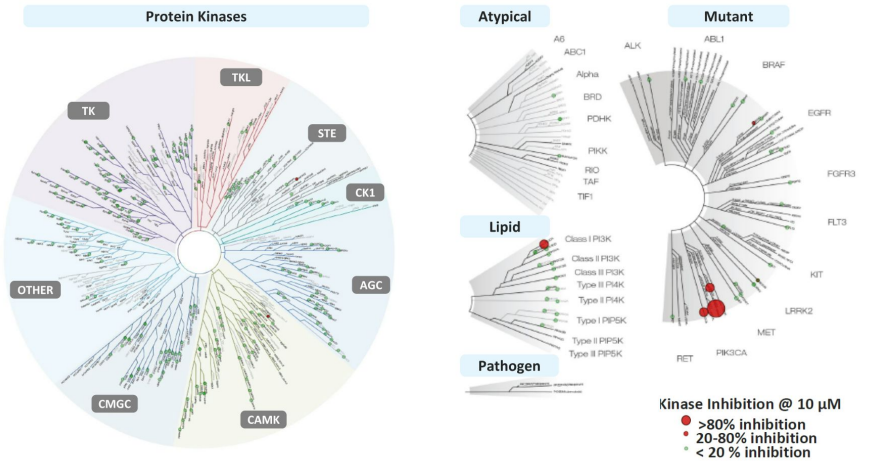


RLY-2608 – Allosteric Mutant Selective PI3Kα Inhibitor

RLY-2608 selectively inhibits mutant PI3Kα



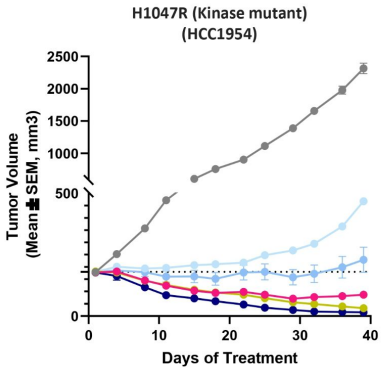
High selectivity over the kinome and within PI3K family

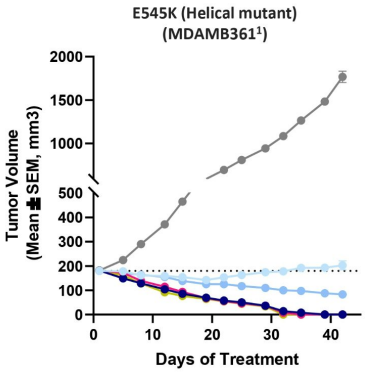


Pazolli M, Discovery and characterization of RLY-2608, the first allosteric, mutant, and isoform-selective inhibitor of PI3Kα. Oral presentation at: AACR-NCI-EORTC Virtual International Conference on Molecular Targets Conference; October 7-10, 2021; Virtual.

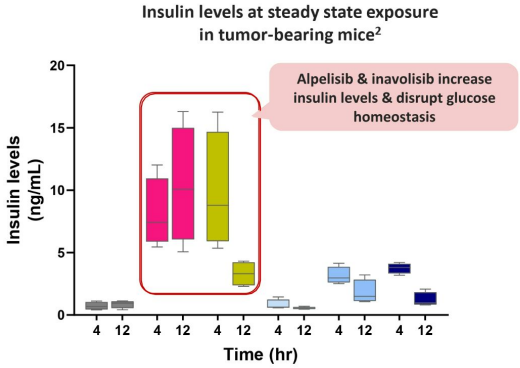
RLY-2608 – Shows Robust Efficacy with Limited Impact on Glucose Homeostasis in Preclinical Models

Tumor regression in PI3Kα mouse breast cancer models





Minimal perturbation of insulin levels



Not clinically achievable doses of alpelisib & inavolisib[3]

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

Higher doses/exposures lead to increased modulation of pAKT across *PIK3CA* mutant models

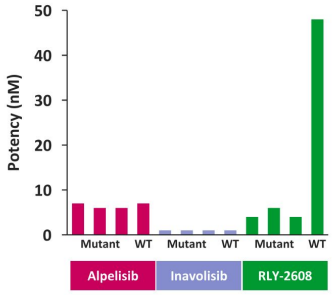
Pazolli M, Discovery and characterization of RLY-2608, the first allosteric, mutant, and isoform-selective inhibitor of PI3Kα. Oral presentation at: AACR-NCI-EORTC Virtual International Conference on Molecular Targets Conference; October 7-10, 2021; Virtual.
1. This model also carries a second mutation at K567R; 2. HSC2 model; 3. Source: J Clin Oncol 2018 Vol. 36 Issue 13 Pages 1291-1299, SABCS 2019 OT1-08-04

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

All Data Shown is Preclinical

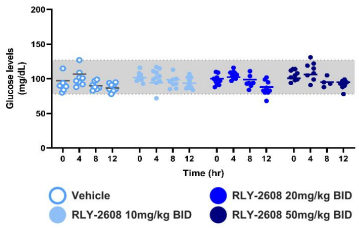
Favorable Selectivity

Limited potency against WT PI3Kα and other PI3K isoforms



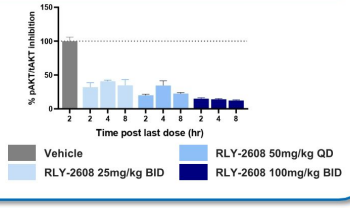
Favorable Tolerability

Manageable key toxicities, especially hyperglycemia shown in dog study



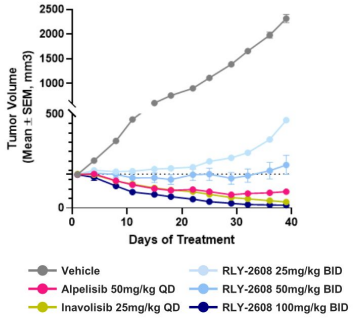
Favorable Target Inhibition

Maintains approx. 80% mutant PI3Kα inhibition in mouse model

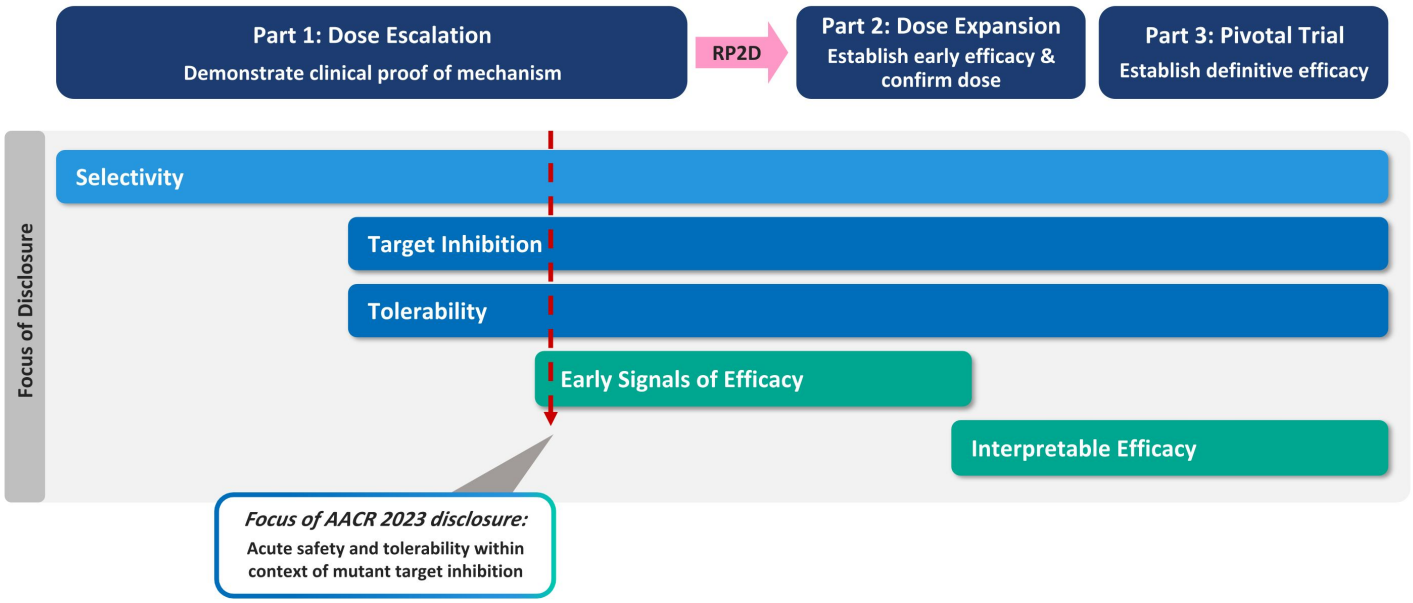


Favorable Efficacy

Robust tumor regression at tolerable doses in mouse model



RLY-2608 – Data Disclosure Goals



RLY-2608 – Summary of AACR 2023 Data Disclosure

RLY-2608 Initial Data Support Selective Targeting of Mutant PI3Kα

Focus of AACR disclosure

Initial Clinical Proof of Mechanism

Selective target inhibition over IC_{80}

- Continuous pAKT inhibition ~80%+ achieved at 400mg BID mono and ≥600mg BID combo with fulvestrant
- Limited observed impact on glucose homeostasis
- No grade 3 hyperglycemia observed[1]

Favorable safety profile at therapeutically active doses

- Low rates of hyperglycemia, rash and diarrhea
- No DLTs and no AEs leading to treatment discontinuation
- 6/7 600mg BID patients remained on treatment for median of ~4 months

Initial anti-tumor activity observed across range of doses

- uPR* observed in a heavily pretreated breast cancer pt (RLY-2608 monoTx)
- 9/16 breast cancer patients[2] exhibit radiographic tumor shrinkage
- Declines in mutant ctDNAs observed
- 19/27 breast cancer pt remained on treatment with mDoE of ~4 months

* Response confirmed after data cut-off

Potential for greater dose intensity

Goal for Expansion Cohorts

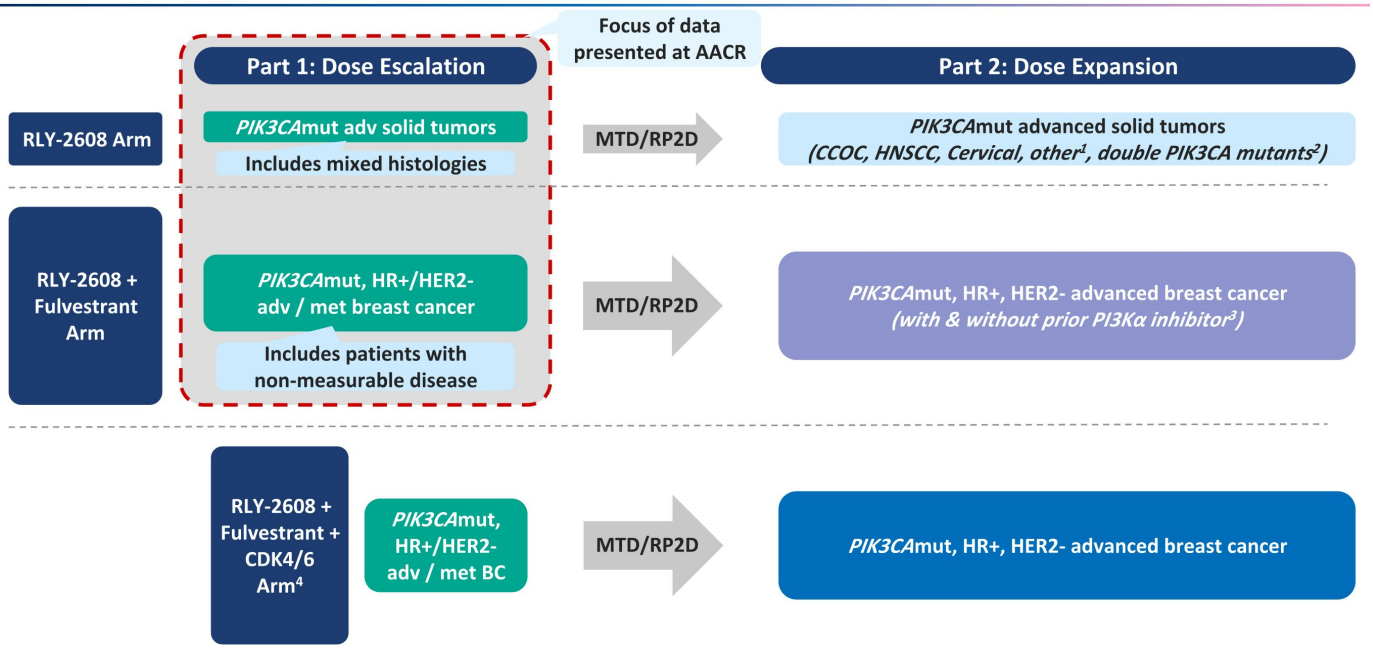
- Interpretable Efficacy (CBR, ORR)
- Longer-Term Tolerability

2H 2023: Expansion initiation

DLTs = dose limiting toxicities; 1. per CTCAE v5.0; 2. with measurable disease per RECIST

Preliminary data as of 03/09/2023

RLY-2608 –Trial Design



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

ReDiscover Trial – Interim Part 1 Results

Part 1: Dose Escalations – Bayesian optimal interval design with cohort enrichment
RLY-2608 daily via continuous oral administration

RLY-2608
***PIK3CA*-mutant advanced solid tumors (N=19)**

Start: Dec 2021

- Ongoing
- 400mg BID N=4
- 300mg BID N=3
- 200mg BID N=3
- 400mg QD N=3
- 100mg BID N=1
- 200mg QD N=3
- 50mg BID N=2

RLY-2608 + fulvestrant
***PIK3CA*-mutant, HR+, HER2– advanced / metastatic breast cancer (N=23)**

Start: April 2022

- Ongoing
- 800mg BID N=6
- 600mg BID N=7
- 400mg BID N=4
- 200mg BID N=3
- 100mg BID N=3

Current enrollment focus

Across both dose escalation cohorts:
- **No dose limiting toxicities (DLTs)**
- **MTD not reached & dose escalation continues**
- **Cohort enrichment ongoing**

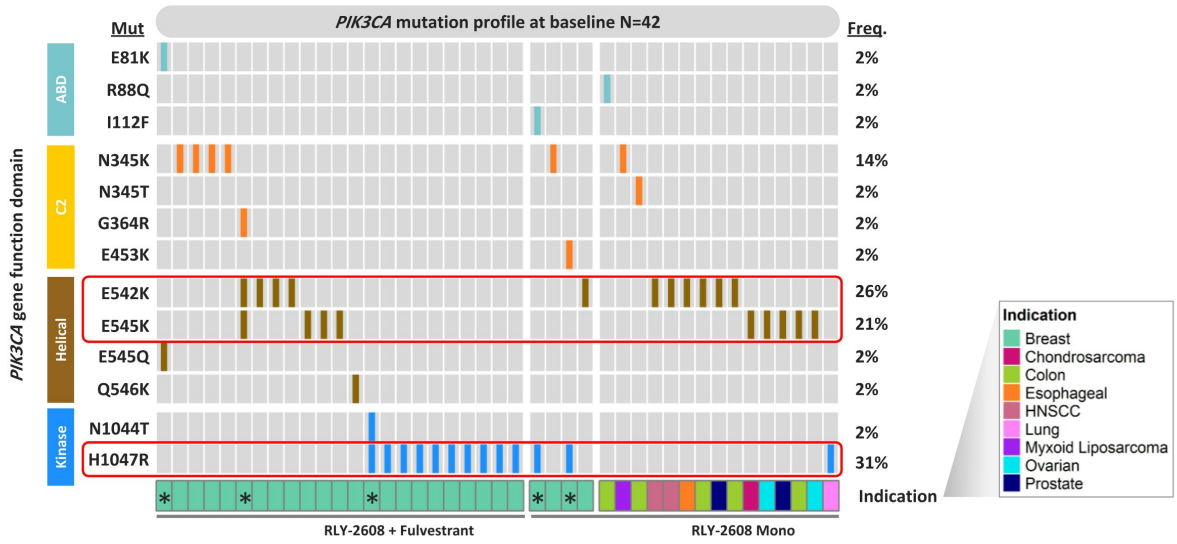
Preliminary data as of 03/09/2023

ReDiscover Trial – Baseline Demographics and Tumor Genotype

	RLY-2608 (N=19)	RLY-2608 + fulvestrant (N=23)	Total (N=42)
Age, median (range), years	63 (42-85)	57 (40-83)	60 (40-85)
Female, n (%)	11 (58%)	23 (100%)	34 (81%)
Ethnicity, %			
White / Asian / American Indian / Black / Unknown	95% / 0% / 0% / 0% / 5%	78% / 4% / 4% / 4% / 9%	86% / 2% / 2% / 2% / 7%
ECOG, n (%)			
0	8 (42%)	13 (57%)	21 (50%)
1	11 (58%)	9 (39%)	20 (48%)
BMI, kg/m^2, median (range)	25 (16-44)	25 (18-38)	25 (16-44)
<30, n (%)	14 (74%)	17 (74%)	31 (74%)
≥30, n (%)	5 (26%)	6 (26%)	11 (26%)
Prior regimens of therapy in metastatic setting, median (range)	3 (0,12)	1 (1, 12)	2 (0,12)
0	1 (5%)	0	1 (2%)
1	4 (21%)	12 (52%)	16 (38%)
2	2 (11%)	3 (13%)	5 (12%)
3+	12 (63%)	8 (35%)	20 (48%)
Type of prior therapy, n (%)			
Endocrine therapy + CDK4/6 inhibitor	NA	23 (100%)	NA
Chemotherapy / ADC	12 (63%)	6 (26%)	18 (43%)
mTOR / AKT inhibitor	0	4 (17%)	4 (10%)

Preliminary data as of 03/09/2023

Broad *PIK3CA* Mutation Landscape Among ReDiscover Patients



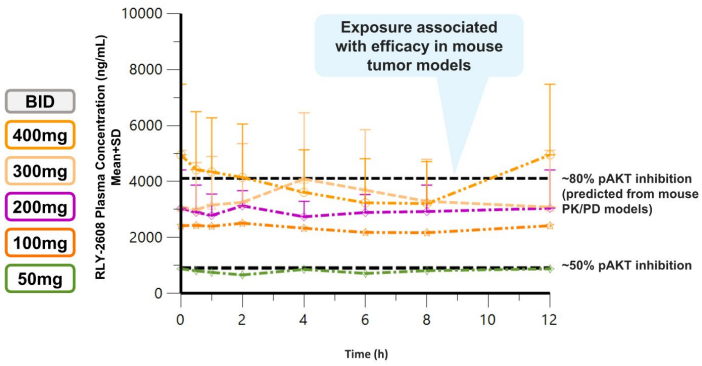
PIK3CA* mutations: 14 Kinase, 22 Helical, 5 double mutations

* Double mutation defined as one major PIK3CA mutation (E542K, E545X or H1047X) and ≥1 additional PIK3CA mutation. Kinase, Helical, and double mutations are not mutually exclusive
Mutation per local assessment

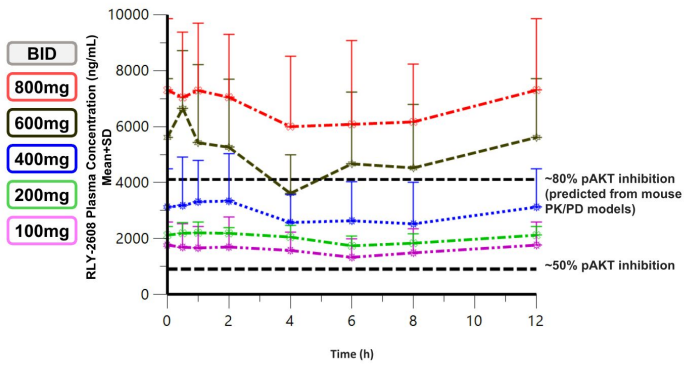
Preliminary data as of 03/09/2023

RLY-2608 – Favorable PK profile

RLY-2608 C1D15



RLY-2608 + fulvestrant C1D15

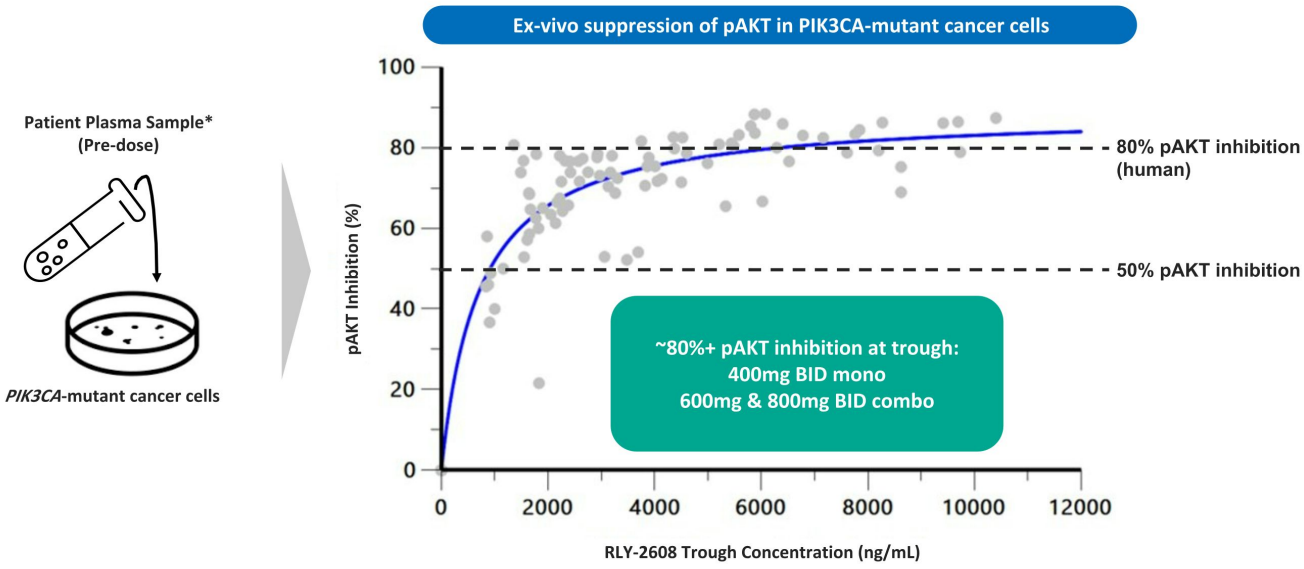


Dose-dependent increase in exposure and low peak to trough fluctuations across dose levels
Continuous exposure over IC80 correlates with efficacy in preclinical models*
Constant coverage at IC80 across dosing interval at 400mg BID mono and 600mg and 800mg BID combo

* Fritsch et al Mol Can Therapeutics 2014 13(5) 1117-1129. Piqray - European Medicines Agency Public Assessment Report 28 May 2020

Preliminary data as of 03/09/2023

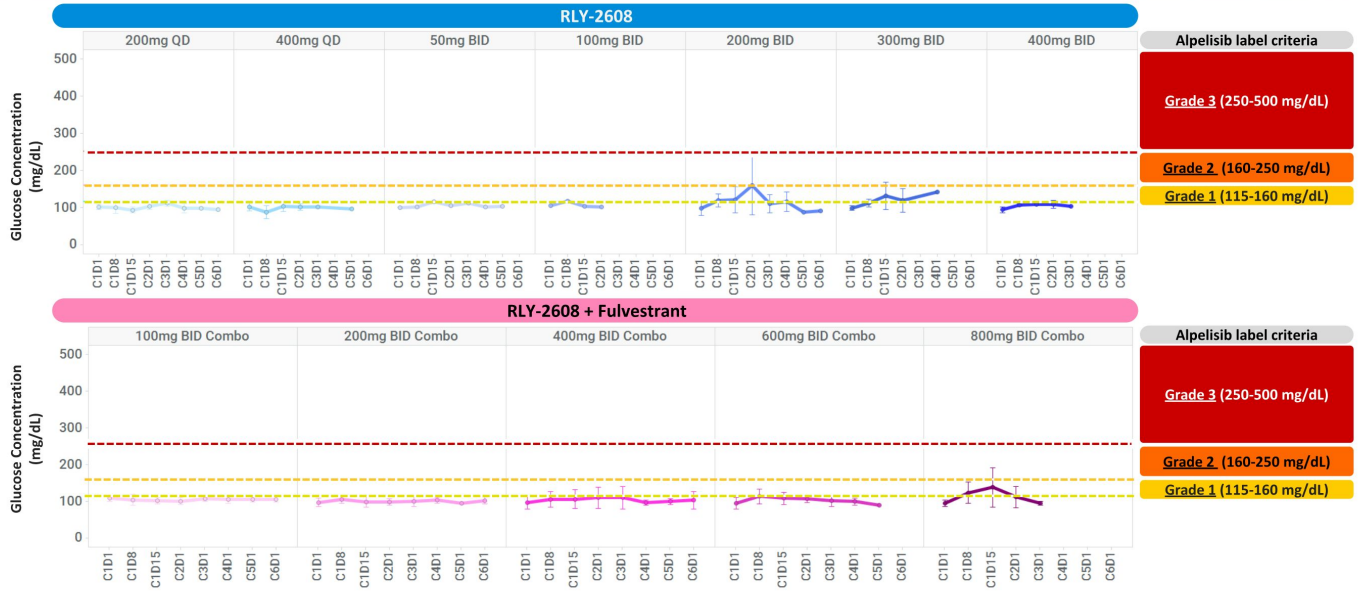
RLY-2608 – Multiple Doses Achieve ~80%+ Target Inhibition at Trough



* Plasma samples taken at C1D1, C1D15, C2D1, C3D1, C4D1, then odd cycles starting at C5D1 until end of treatment

Preliminary data as of 03/09/2023

RLY-2608 – Limited Observed Impact on Glucose Homeostasis Supports Mutant Selective Targeting Across All Doses

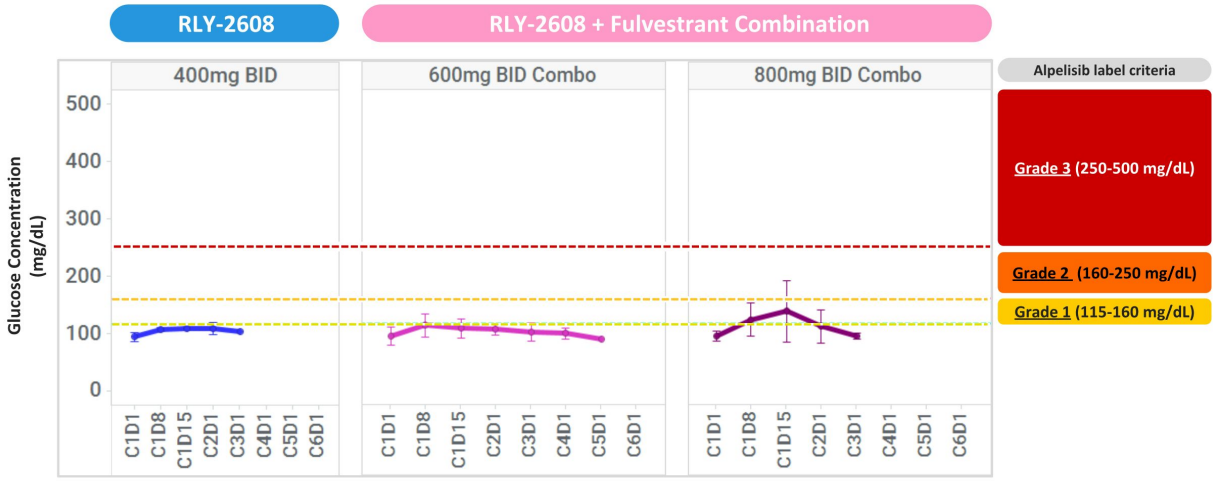


No Grade 3 hyperglycemia per CTCAE v5.0
No dose interruptions or dose reductions due to hyperglycemia

* Data represent mean per cohort +/- standard deviation

Preliminary data as of 03/09/2023

RLY-2608 – Limited Observed Impact on Glucose Homeostasis Supports Mutant Selective Targeting for Doses Above Target Exposure



No Grade 3 hyperglycemia per CTCAE v5.0
No dose interruptions or dose reductions due to hyperglycemia

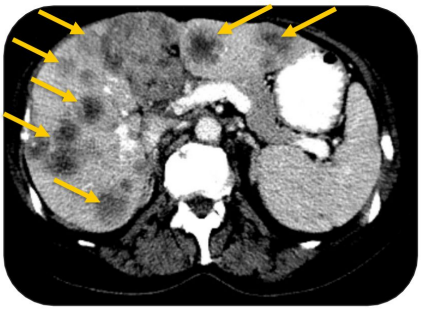
* Data represent mean per cohort +/- standard deviation

Preliminary data as of 03/09/2023

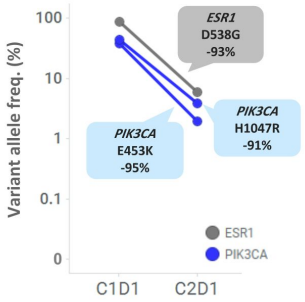
RLY-2608 – Anti-tumor Activity: Partial Response per RECIST*

uPR* with -36% tumor reduction per RECIST
Marked regression of multiple liver metastases
No adverse events reported

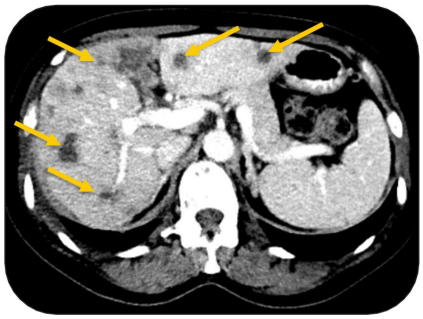
Baseline



ctDNA at 4 weeks



First Assessment (8 weeks)



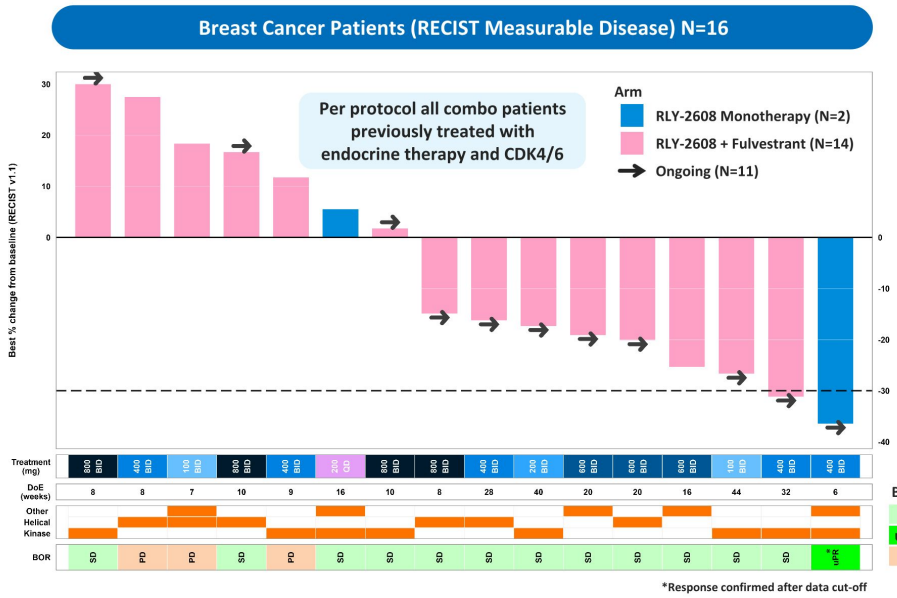
58 y/o female, *PIK3CA* H1047R + E453K mutation, HR+ HER2- (IHC2+FISH-)
12 prior lines of therapy (chemo, endocrine, multiple HER2-directed, including Enhertu)
RLY-2608 400mg BID monotherapy, ongoing at cycle 4

*Response confirmed after data cut-off
Courtesy Varkaris, MGH

Preliminary data as of 03/09/2023

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

16 Breast Cancer Patients – Measurable Disease Only



*Response confirmed after data cut-off

56% of patients (9/16) exhibited radiographic tumor reductions

81% of patients (13/16) with SD/uPR* across genotypes

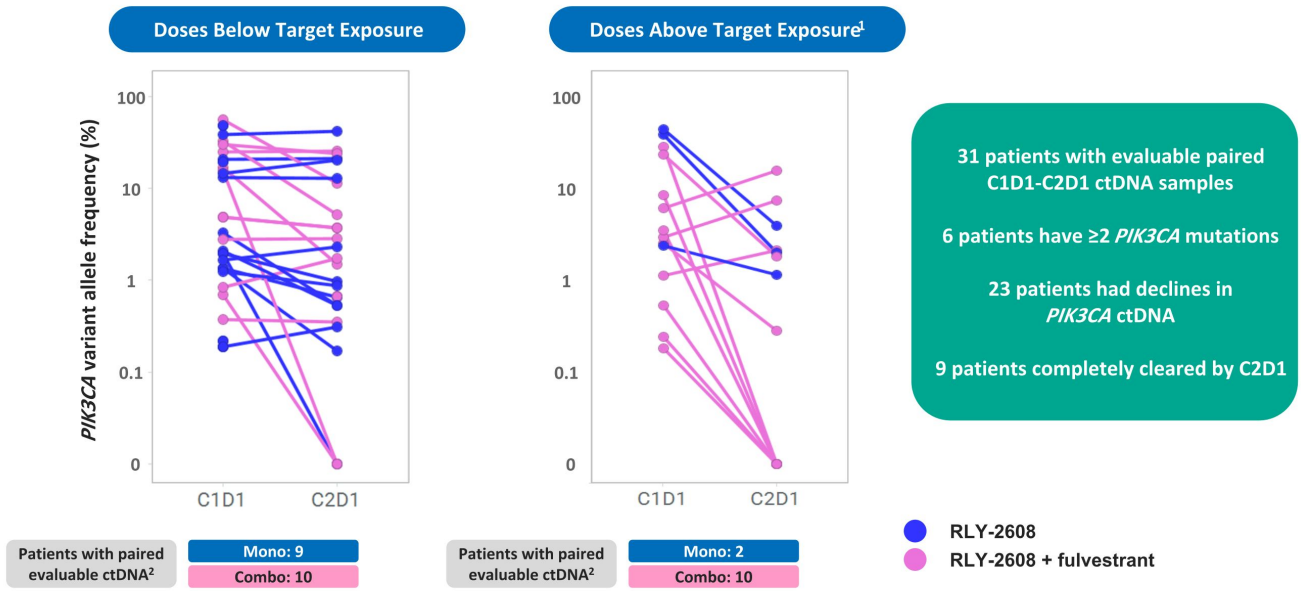
11/16 patients ongoing

BOR = Best Overall Response:

SD	Stable Disease
uPR*	Unconfirmed Partial Response*
PD	Progressive Disease

Preliminary data as of 03/09/2023

RLY-2608 – Decline of Mutant *PIK3CA* ctDNA

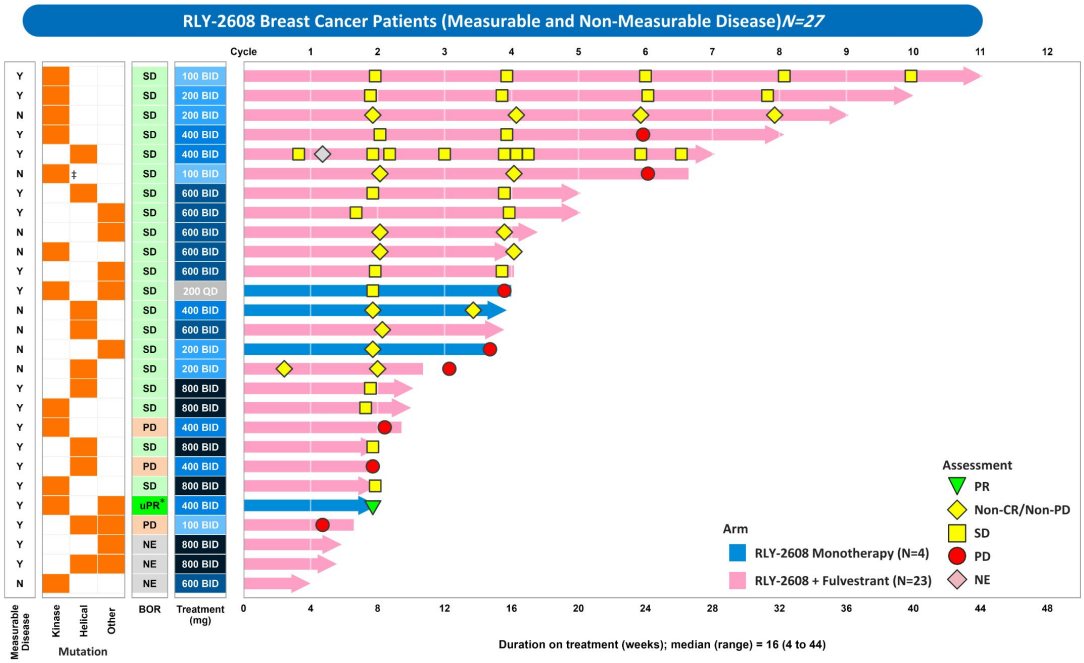


1. Doses above target exposure: 400mg BID mono, 600mg BID combo, 800mg BID combo; 2. 6 patients are represented by more than one *PIK3CA* mutation in the ctDNA graphs shown

Preliminary data as of 03/09/2023

RLY-2608 – Breast Cancer Disease Control Across Dose Levels

27 Breast Cancer Patients – Measurable and Non-Measurable Disease



19/27 patients (70%) ongoing

Duration on treatment:
- **Median: 16 weeks**
- **Range: 4 – 44 weeks**

21/24 RECIST evaluable patients (88%) had non-CR/non-PD, SD or response

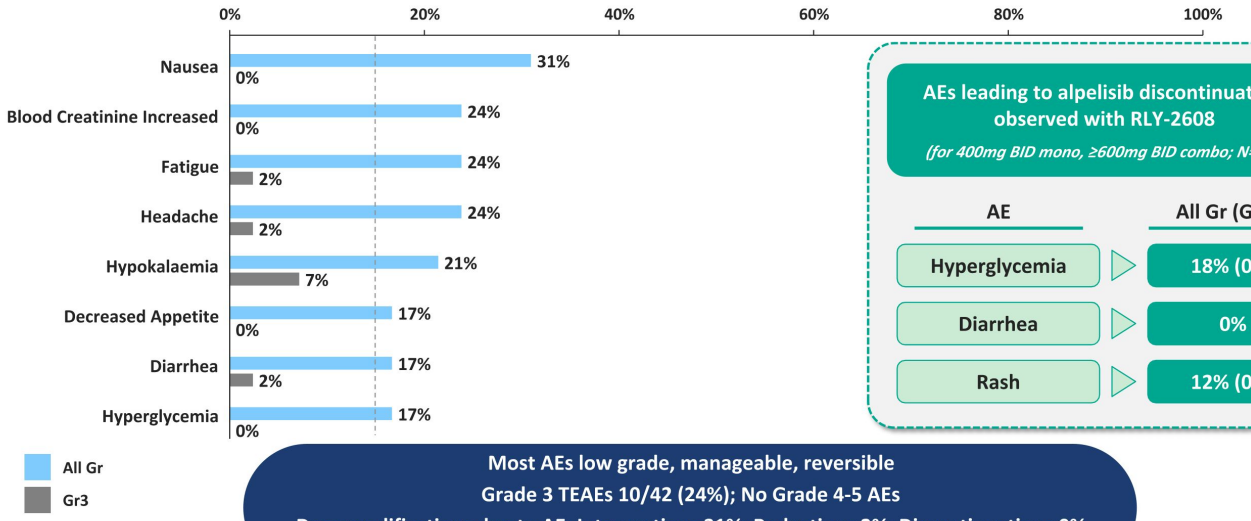
Most patients (7/8) discontinued due to progressive disease
- **No AEs leading to treatment discontinuation**

*Response confirmed after data cut-off; ‡ = double mutation with two mutations in kinase domain

Preliminary data as of 03/09/2023

RLY-2608 – Treatment-Emergent Adverse Events (TEAEs) ≥15%

RLY-2608 TEAEs Across Monotherapy and Combo Arms (N=42)



AEs leading to alpelisib discontinuation observed with RLY-2608

(for 400mg BID mono, ≥600mg BID combo; N=17)

AE	All Gr (Gr3+)
Hyperglycemia	18% (0%)
Diarrhea	0%
Rash	12% (0%)

No Gr3+

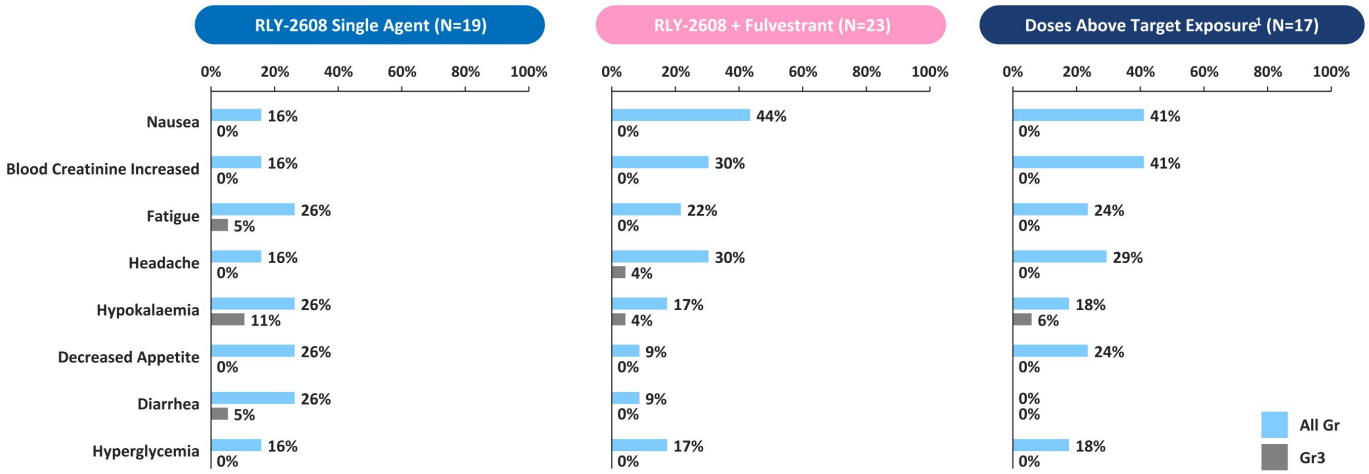
Most AEs low grade, manageable, reversible
Grade 3 TEAEs 10/42 (24%); No Grade 4-5 AEs
Dose modifications due to AE: Interruptions 31%; Reductions 2%; Discontinuations 0%
Median Relative Dose Intensity: 98%[1]

1. Relative dose intensity is calculated as the Actual Dose Intensity/Planned Dose Intensity*100%.
Actual dose intensity is calculated as the cumulative dose (mg)/duration of study treatment exposure (day). Planned dose intensity is the assigned dose (mg)/duration of study treatment exposure (day).

Preliminary data as of 03/09/2023

RLY-2608 – TEAEs Consistent with Mutant-Selective Inhibition

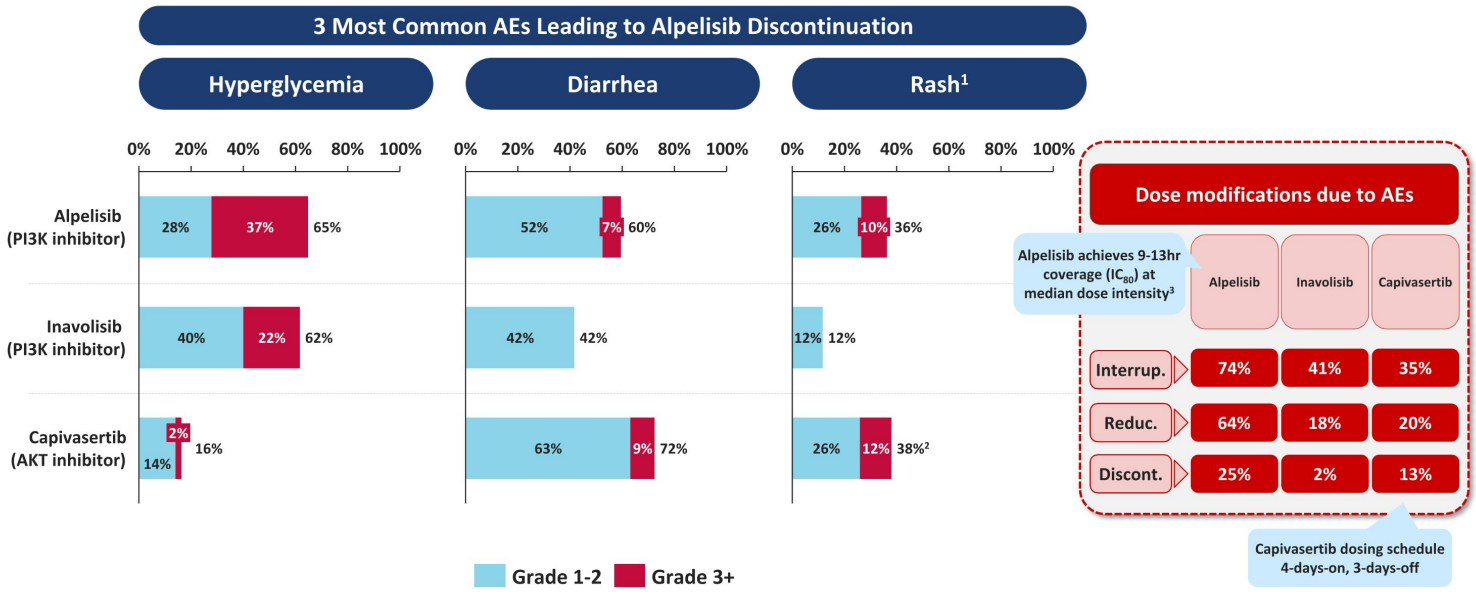
Note: TEAEs ≥15% across all patients



1. Doses above target exposure: 400mg BID mono, 600mg BID combo, 800mg BID combo

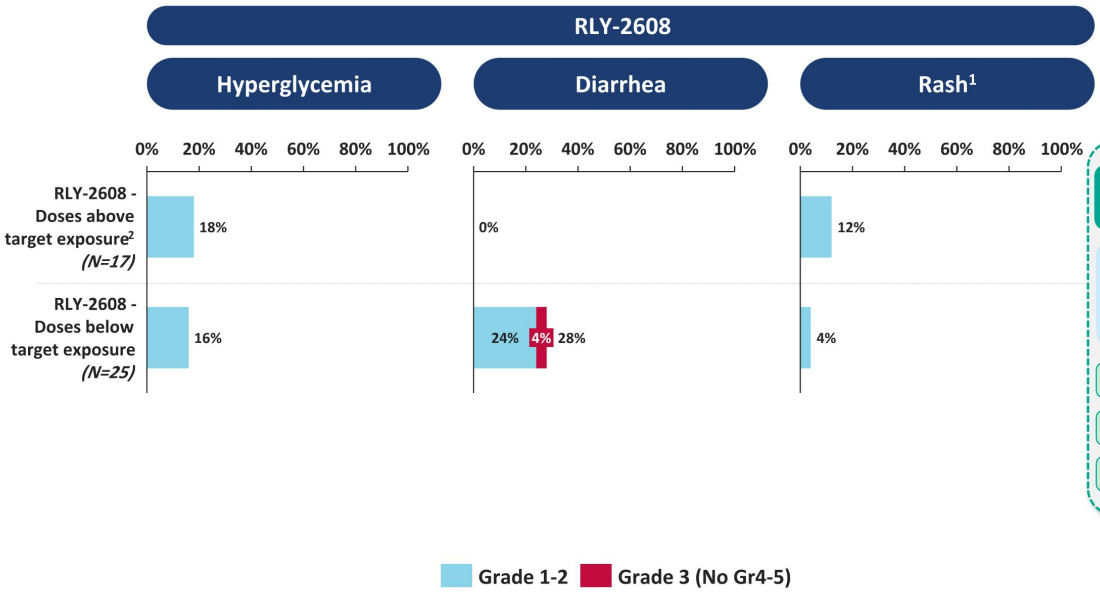
Preliminary data as of 03/09/2023

Tolerability Profile of Non-Selective Inhibitors for Relevant Off-Target Toxicities



1. Grouped term: rash and rash maculo-papular; 2. Capivasertib rash includes events related to rash including: rash, rash macular, maculo papular rash, rash papular and rash pruritic; 3. Alpelisib median dose intensity 83%
Sources: alpelisib: SOLAR-1 (initial publication): Andre 2019 N Engl J Med 380:1929, inavolisib: ASCO 2022 #1052 (note: reported rates are for invavolisib-related AEs pooled across study cohorts including monotherapy and combinations with letrozole, fulvestrant, and palbociclib), capivasertib: CAPItello-291: SABCS 2022 #GS3-04
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.

RLY-2608 – Low Rates of Hyperglycemia, Rash and Diarrhea



Dose modifications due to AEs

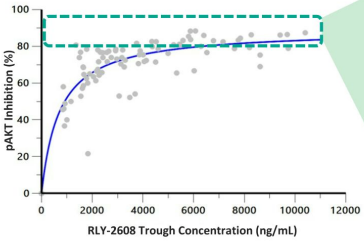
	Low rate of dose mods allowed for median dose intensity ≥98%	Below target exposure (N =25)	Above target exposure[2] (N =17)
Interrup.		24%	41%
Reduc.		4%	0%
Discont.		0%	0%

1. Grouped term: rash and rash maculo-papular; 2. Doses above target exposure: 400mg BID mono, 600mg BID combo, 800mg BID combo

Preliminary data as of 03/09/2023

RLY-2608 – Potential to Achieve Greater Dose Intensity

Achieved ≥80% mutant target inhibition at multiple doses → **Doses at or above target exposure have not led to key AEs** → **Low rate of dose modifications maintained dose intensity** → **Early anti-tumor activity seen across range of doses**



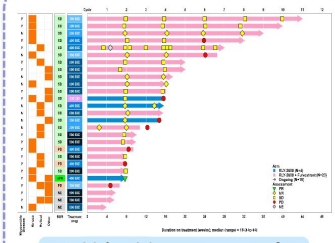
RLY-2608 TEAE for doses above target exposure[1]

AE	All Gr (Gr3)
Hyperglycemia	18% (0%)
Diarrhea	0%
Rash	12% (0%)

RLY-2608 dose modifications due to AEs

Low rate of dose mods allowed for median dose intensity ≥98%

	Below target exposure *(N =25)*	Above target exposure[1] *(N =17)*
Interrup.	24%	41%
Reduc.	4%	0%
Discont.	0%	0%



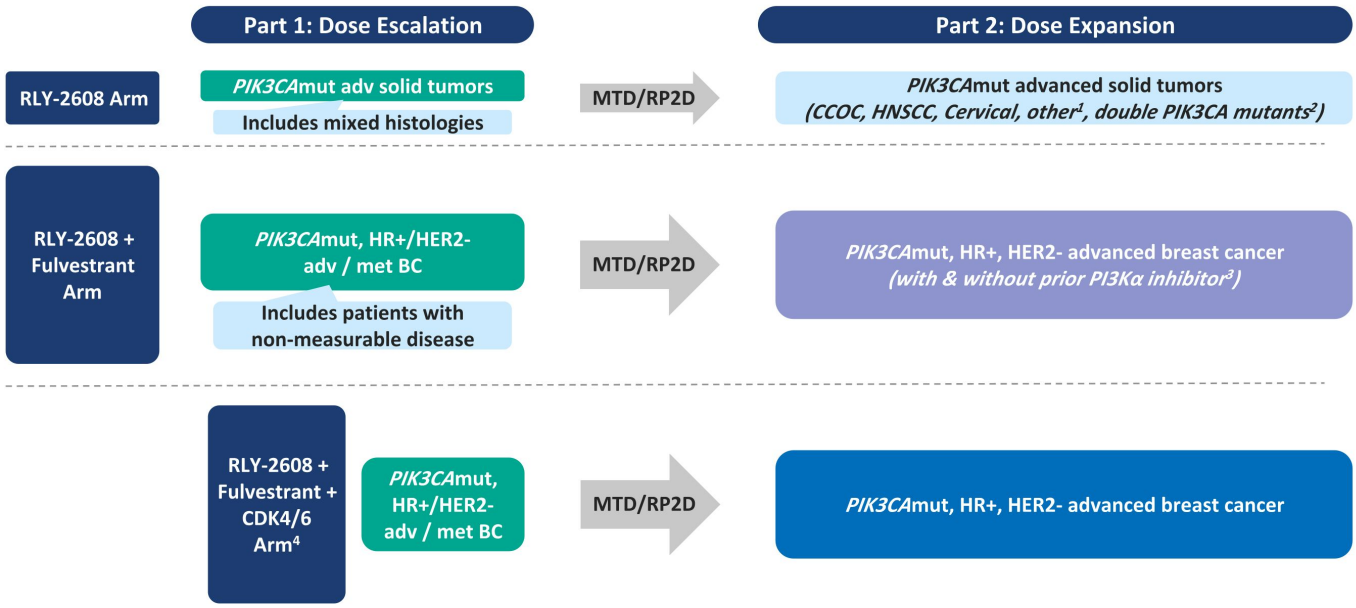
Initial activity across range of PI3Kα mutation types

Greater dose intensity against a validated target in breast cancer suggests potential to achieve greater duration of clinical benefit in patients with any *PIK3CA* mutation

1. Doses above target exposure: 400mg BID mono, 600mg BID combo, 800mg BID combo

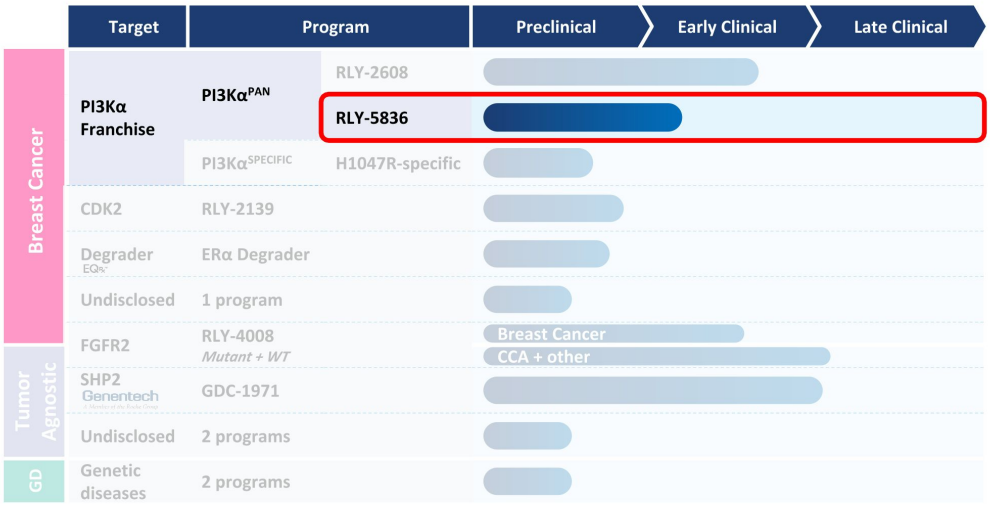
Preliminary data as of 03/09/2023

RLY-2608 –Trial Design

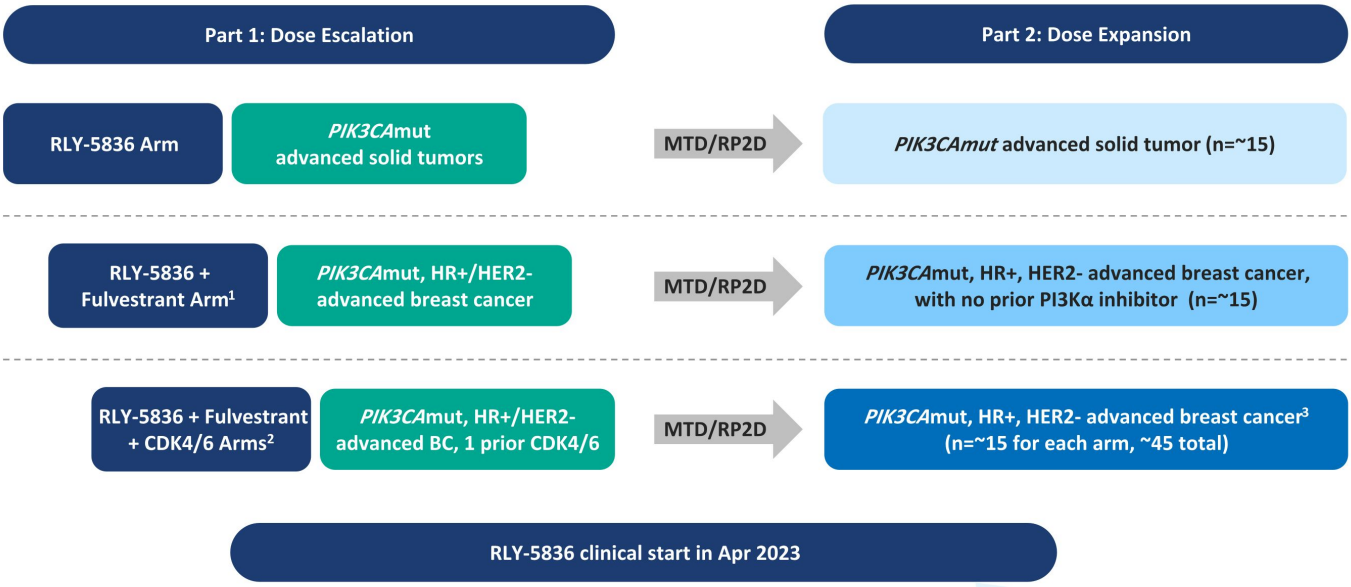


1. Excludes PIK3CAmut clear cell OvCA, HNSCC, Cervical cancer, and colorectal patients; 2. Double mutation defined as one major PIK3CA mutation (E542X, E545X, H1047X) + ≥1 additional PIK3CA mutation per local assessment; 3. Patients with previous PI3Kα inhibitor include those with intolerance to PI3Kαi 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

Relay Tx – Extensive Precision Medicine Pipeline



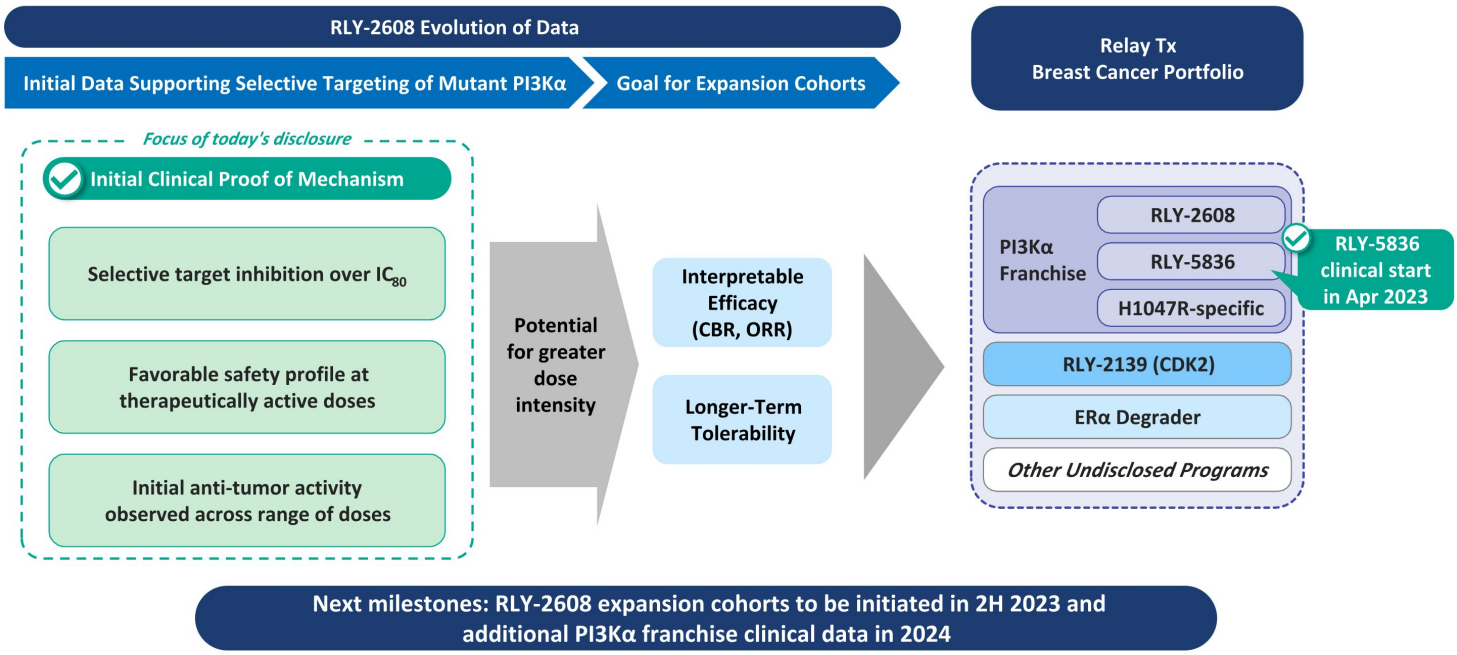
RLY-5836 –Trial Design



- BOIN design with molecular enrichment
- PIK3CA mutation status per local assessment
- RLY-5836 PO BID or QD

1. RLY-5836 + Fulvestrant combination arm may start after one dose level higher of RLY-5836 single agent is cleared and determined tolerable
2. RLY-5836 + CDK4/6i + ET combination arms may start after one dose level higher of RLY-5836 + Fulvestrant combination is cleared and determined tolerable. Three separate CDK4/6 arms, one for each of the following CDK4/6 agents: pablociclib, abemaciclib, ribociclib
3. One or more of the RLY-5836 + CDK4/6i + Fulvestrant arms may open at Sponsor discretion and SRC agreement

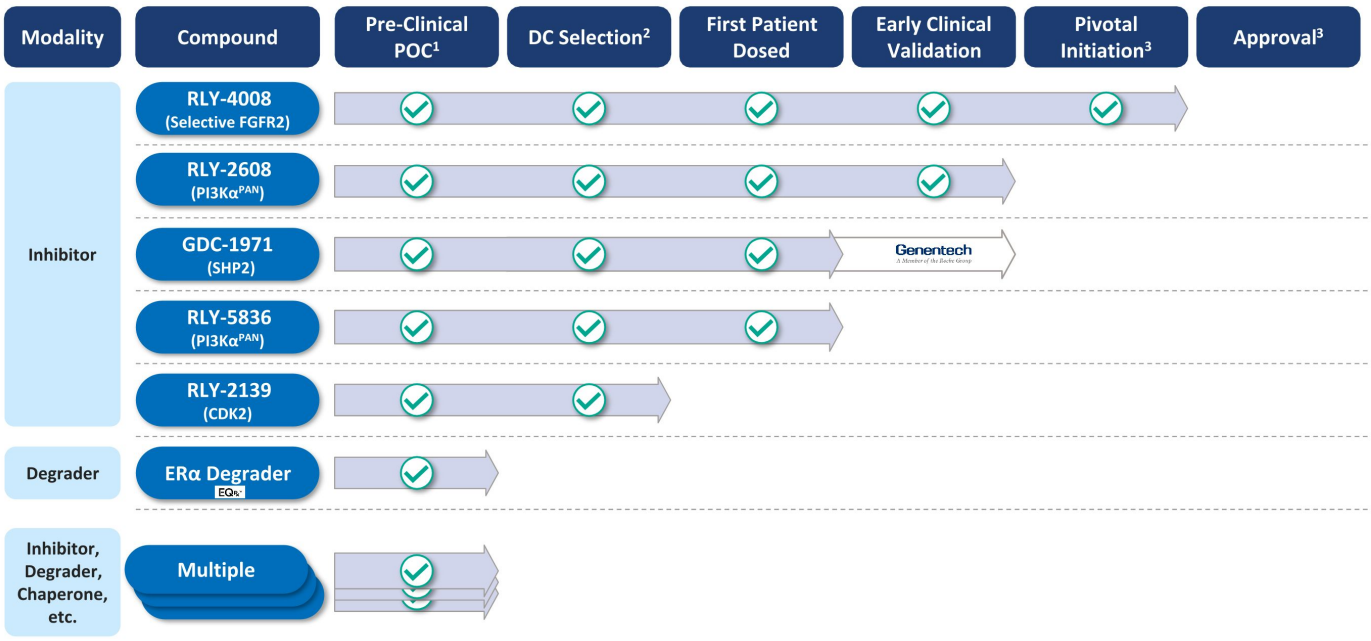
Breast Cancer Franchise Continues to Progress



Next milestones: RLY-2608 expansion cohorts to be initiated in 2H 2023 and additional PI3Kα franchise clinical data in 2024

Preliminary data as of 03/09/2023

Relay Tx – Continued Dynamo™ Platform Validation



1. POC - proof-of-concept. 2. DC - development candidate. 3. Subject to alignment with regulatory authorities

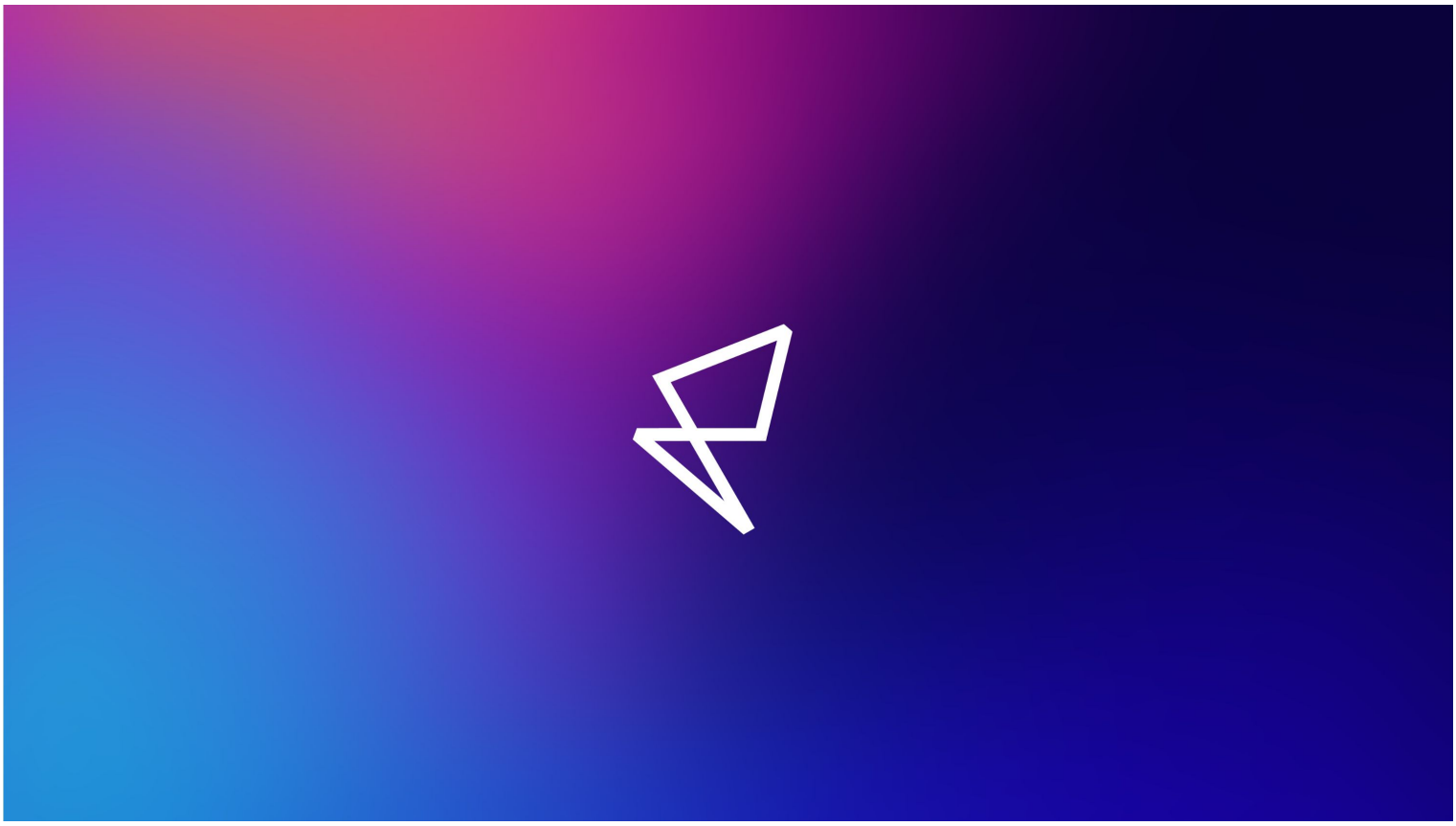
Relay Tx – Capital, Team & Execution Focus to Deliver on Key Milestones

Breast Cancer Franchise			Tumor Agnostic		Undisclosed
 PI3Kα^{PAN}	 RLY-2139 (Selective CDK2)	 ERα Degrader	 RLY-4008 (Selective FGFR2)	 GDC-1971 (SHP2)	 *To be announced*
✓ Initial RLY-2608 data in 1H 2023 ✓ RLY-5836 clinical start in 2Q 2023 RLY-2608 expansion cohorts initiated in 2H 2023 Additional data update in 2024	Clinical start in early 2024	Development candidate nomination in 2023	Full dose escalation data in 1H 2023 Non-CCA expansion cohorts data in 2H 2023 Pivotal cohort full enrollment in 2H 2023	Ongoing combo trials; Genentech controls data disclosures	*5+ undisclosed programs in preclinical development and additional early-stage efforts across platform*

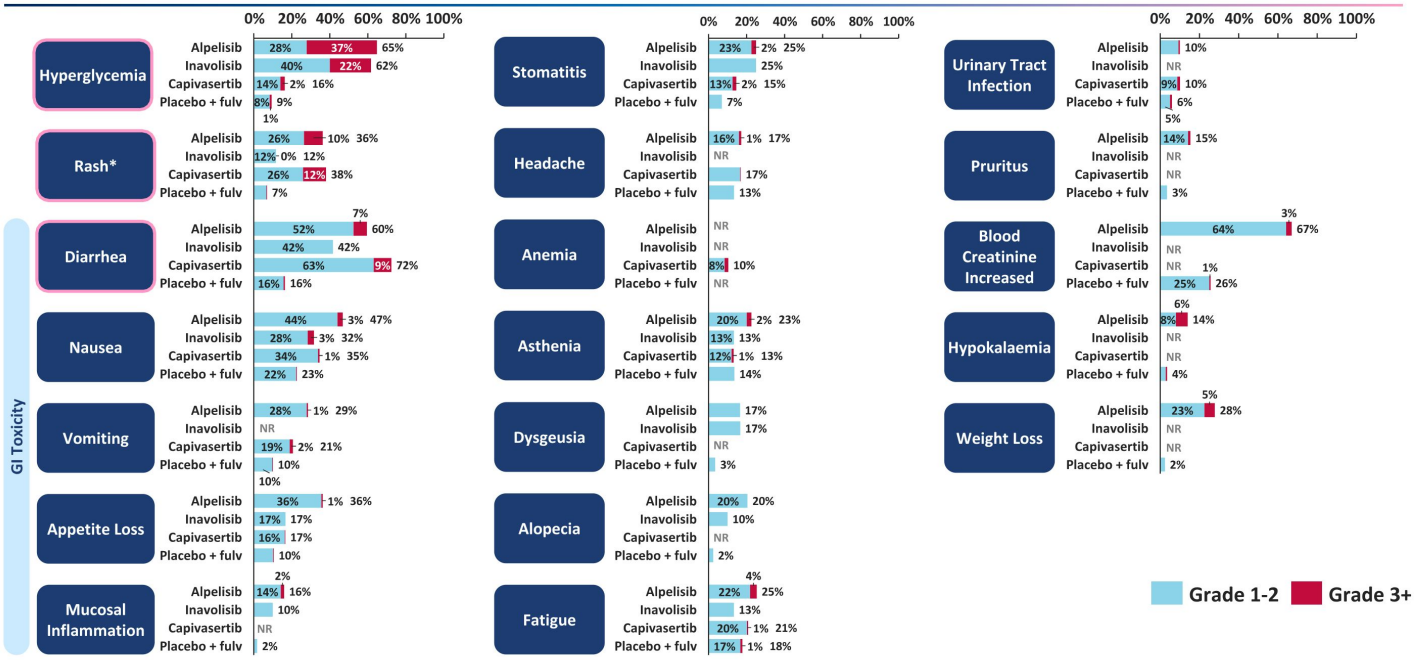
~$1B

Cash, cash equivalents and investments as of the end of 4Q 2022

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

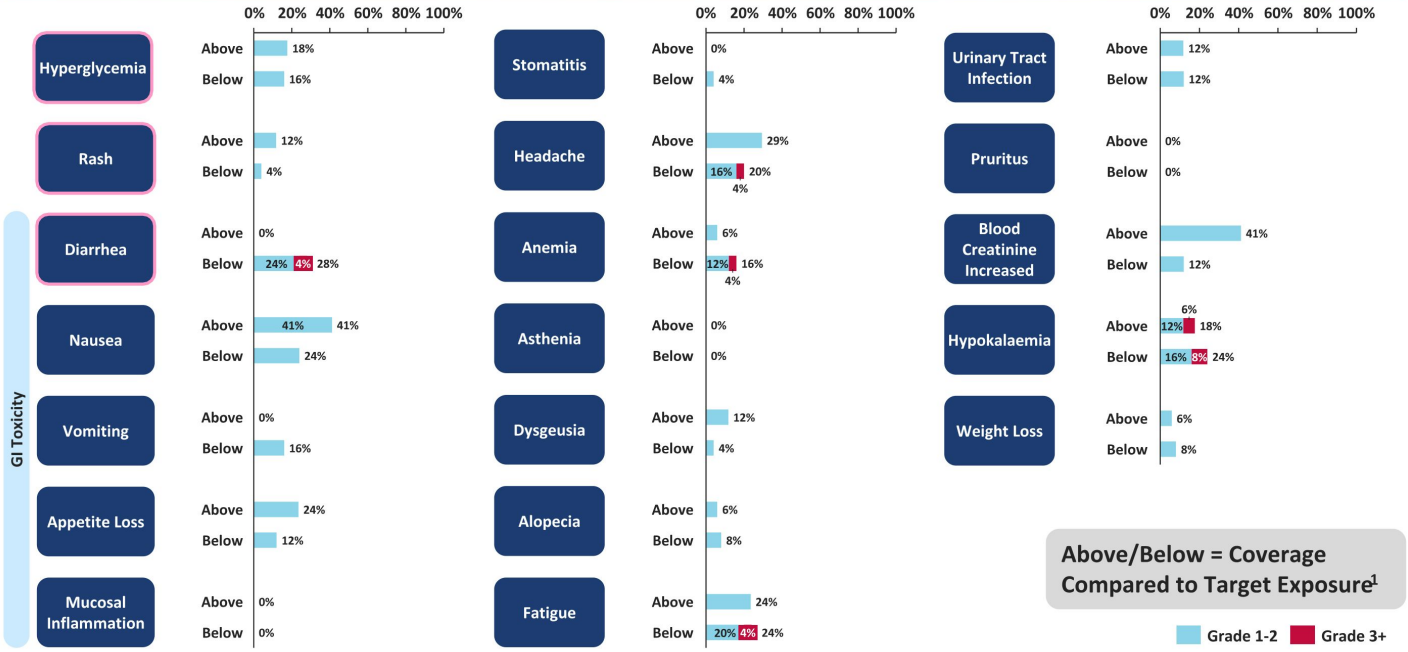


Tolerability Profile of Non-Selective Inhibitors



Sources: 1. SOLAR-1 (long-term follow up): Andre 2021 Ann Oncol 32:208, 2. SOLAR-1 (initial publication): Andre 2019 N Engl J Med 380:1929, 3. Alpelsib FDA Label 4. Inavolisib first-in-human study: SABCS 2021 #P5-17-05, 5. CAPItello-291: SABCS 2022 #GS3-04; Placebo + fulv data from SOLAR-1 placebo + fulvestrant group; *Grouped term: rash and rash maculo-papular; ^Gr 3 AE rate for rash + rash maculo-popular not reported, although 6.2% Gr 3 AEs for rash maculo-papular, so assume at 6% Gr 3 for pooled terms
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.

RLY-2608– Summary of Preliminary AEs



Preliminary data as of 03/09/2023

1. Doses above target exposure: 400mg BID mono, 600mg BID combo, 800mg BID combo; 2. Grouped term: rash and rash maculo-papular

Exhibit 99.2

Relay Therapeutics Announces Initial Clinical Data Demonstrating that RLY-2608 Selectively Targets Multiple PI3Kα Mutations

Multiple doses achieved sustained target exposure of ~80%+ mutant PI3Kα inhibition

No Grade 3 hyperglycemia, rash or diarrhea observed at target exposures

Favorable initial safety profile at target exposures

Confirmed partial response in breast cancer patient with 12 prior lines of therapy

Initial anti-tumor activity in breast cancer patients observed across range of doses

Relay Therapeutics to host a conference call today, April 18, at 1:30 p.m. ET

Orlando, Fla. – April 18, 2023 – Relay Therapeutics, Inc. (Nasdaq: RLAY), a clinical-stage precision medicine company transforming the drug discovery process by combining leading-edge computational and experimental technologies, today announced initial clinical data for RLY-2608, the first known investigational allosteric, pan-mutant and isoform-selective inhibitor of PI3Kα. The data support initial clinical proof of mechanism, demonstrating that RLY-2608 achieved selective target engagement at multiple predicted efficacious doses with a favorable initial safety and tolerability profile. These data are being presented today at the American Association for Cancer Research (AACR) Annual Meeting 2023.

“While early, these data suggest that by selectively inhibiting mutant PI3Kα and avoiding key off-target toxicities that typically limit the use of non-selective PI3Kα pathway inhibitors, RLY-2608 has the potential to transform treatment for patients with a broad range of PI3Kα mutations,” said Don Bergstrom, M.D., Ph.D., President of R&D at Relay Therapeutics. “At doses achieving target exposure, there was no observed Grade 3 hyperglycemia, rash or diarrhea – the three most common adverse events leading to discontinuation of existing investigational and approved treatments, and radiographic tumor reductions were seen across multiple dose levels. We are continuing dose escalation and expect to initiate expansion cohorts in the second half of 2023.”

ReDiscover – RLY-2608 First-in-Human Trial

RLY-2608 is currently being evaluated in an ongoing dose-escalation portion of ReDiscover, a first-in-human trial, which was designed to evaluate the safety, tolerability, pharmacokinetics, pharmacodynamics and preliminary antitumor activity across two separate arms. The monotherapy arm started in December 2021 and enrolled 19 patients with unresectable or metastatic solid tumors with a PI3Kα mutation. This arm included a broad diversity of solid tumors, predominantly tumor types not predicted to be sensitive to single agent PI3Kα inhibition. The RLY-2608 + fulvestrant combination arm started April 2022 and enrolled 23 patients with PI3Kα-mutant, HR+, HER2– locally advanced or metastatic breast cancer. Across both arms of the study, enrolled patients had received a significant level of prior therapy, including all breast cancer patients who had received at least one prior endocrine therapy and CDK4/6 inhibitor. The cut-off date for data reported at AACR was March 9, 2023.

Broad Range of PI3Kα Mutations Represented in Enrolled Patients

Among the 27 patients with breast cancer (4 mono + 23 combo), 12 had kinase mutations, 10 had helical mutations and nine had other mutations.

Sustained Target Exposure of ~80%+ Mutant PI3Kα Inhibition Achieved at Multiple Doses

In the monotherapy arm, patients received seven different doses, ranging from 50mg twice daily (BID) to 400mg BID. In the combination arm, patients received five different BID doses, ranging from 100mg to 800mg BID.

RLY-2608 reached selective target exposure at multiple doses, with target exposure being defined as continuous inhibition of mutant PI3Kα of approximately 80 percent or greater. This was reached at 400mg BID monotherapy and at 600mg BID and 800mg BID combination doses.

Selective PI3Kα Inhibition Demonstrated

RLY-2608 demonstrated mutant selective PI3Kα target engagement at multiple doses. There was limited observed impact on glucose homeostasis overall and no Grade 3 hyperglycemia was observed. Glucose homeostasis is believed to be an important indicator of both RLY-2608's clinical selectivity profile and its potential ability to avoid this key off-target toxicity associated with wild-type inhibition.

Declines of PI3Kα mutations in ctDNA from patient samples support initial clinical validation of RLY-2608's ability to selectively inhibit a wide range PI3Kα mutations in a dose-dependent manner.

Initial Safety Analysis Supports a Meaningfully Differentiated Profile

RLY-2608 has been generally well tolerated in the 42 patients treated as of the cut-off date:

- The overall safety profile consisted of mostly low-grade adverse events (AEs) that were manageable and reversible
- Across all doses, there were no dose-limiting toxicities, no AEs leading to treatment discontinuation and no Grade 4-5 AEs

Among patients receiving doses at target exposures (mono: 400mg BID; combo: 600mg BID & 800mg BID; n=17), AEs were mostly low-grade events that were manageable and reversible:

- No Grade 3 hyperglycemia, diarrhea, or rash, which are the AEs most commonly associated with treatment discontinuation for existing investigational and approved therapies
- No dose reductions or discontinuations due to AEs

The low rate of AE-related dose modifications allowed for median dose intensity of at least 98 percent across all dose levels.

Partial Response Achieved with Monotherapy in Breast Cancer Patient with 12 Prior Lines of Therapy

A patient with metastatic HR+/HER2- breast cancer, with two PI3Kα mutations (H1047R, E453K), who progressed following 12 lines of prior therapy, including chemotherapy (including Enhertu®), endocrine and HER2-directed therapies, received RLY-2608 400mg BID monotherapy. An unconfirmed partial response by Response Evaluation Criteria in Solid Tumors (RECIST) was recorded at 8 weeks. Subsequent

to the data cut-off, this partial response was confirmed, and the patient remains on treatment with no AEs reported as of April 4, 2023.

Initial Anti-Tumor Activity Observed in Breast Cancer Patients Across Range of Doses

Early anti-tumor activity was seen across a range of doses and across helical, kinase and other mutations, demonstrating selective target engagement of mutant PI3Kα.

Among the 16 breast cancer patients with measurable disease:

- Nine experienced radiographic tumor reductions (3 helical, 4 kinase, and 3 other)
- 12 exhibited a best overall response of stable disease and 1 partial response (4 helical, 7 kinase, and 4 other)
- 11 remain on treatment as of the cut-off date

Median duration of treatment for all breast cancer patients was approximately 4 months:

- 70 percent (19/27) remain on treatment as of the cut-off date
- 600mg BID dose: approximately 4-month median follow-up
    - Six of seven 600mg BID patients remain on treatment

To date, a maximum tolerated dose has not been reached and dose exploration is ongoing to determine the recommended dose(s) for the dose expansion cohorts (part 2), which Relay Therapeutics anticipates initiating in the second half of 2023.

RLY-5836 First-in-Human Trial

In April 2023, Relay Therapeutics initiated a first-in-human trial of RLY-5836, the Company's second investigational allosteric, pan-mutant, isoform-selective PI3Kα inhibitor, which is chemically distinct from RLY-2608. The trial design is similar to the first-in-human trial of RLY-2608 and can be found here.

Conference Call Information

Relay Therapeutics will host a conference call and live webcast today, April 18, 2023, at 1:30 p.m. ET. Registration and dial-in for the conference call may be accessed through Relay Therapeutics' website under Events in the News & Events section through the following link: https://ir.relaytx.com/news-events/events-presentations. An archived replay of the webcast will be available following the event.

The data presentation from the AACR Annual Meeting is also available on the Relay Therapeutics website in the "Publications/Presentations" section through the following link: https://relaytx.com/pipeline/.

About RLY-2608 & RLY-5836

RLY-2608 is the lead program of multiple efforts to discover and develop mutant selective inhibitors of PI3Kα. RLY-5836 is Relay Therapeutics' second pan-mutant, isoform-selective PI3Kα inhibitor, which is chemically distinct from RLY-2608. PI3Kα is the most frequently mutated kinase in all cancers, with oncogenic mutations detected in about 14% of patients with solid tumors. RLY-2608 and RLY-5836 have

the potential to address more than 100,000 patients per year in the United States, one of the largest patient populations for a precision oncology medicine.

Traditionally, the development of PI3Kα inhibitors has focused on the active, or orthosteric, site. The therapeutic index of orthosteric inhibitors is limited by the lack of clinically meaningful selectivity for mutant versus wild-type (WT) PI3Kα and off-isoform activity. Toxicity related to inhibition of WT PI3Kα and other PI3K isoforms results in sub-optimal inhibition of mutant PI3Kα with reductions in dose intensity and frequent discontinuation. The Dynamo™ platform enabled the discovery of RLY-2608, the first known allosteric, pan-mutant, and isoform-selective PI3Kα inhibitor and RLY-5836, both designed to overcome these limitations. Relay Therapeutics solved the full-length cryo-EM structure of PI3Kα, performed computational long time-scale molecular dynamic simulations to elucidate conformational differences between WT and mutant PI3Kα, and leveraged these insights to support the design of RLY-2608 and RLY-5836. RLY-2608 and RLY-5836 are currently being evaluated in first-in-human trials designed to treat patients with advanced solid tumors with a PIK3CA (PI3Kα) mutation. For more information on RLY-2608, please visit here, and for more information on RLY-5836, please visit here.

About Relay Therapeutics

Relay Therapeutics is a clinical-stage precision medicine company transforming the drug discovery process by combining leading-edge computational and experimental technologies with the goal of bringing life-changing therapies to patients. As the first of a new breed of biotech created at the intersection of complementary techniques and technologies, Relay Therapeutics aims to push the boundaries of what's possible in drug discovery. Its Dynamo™ platform integrates an array of leading-edge computational and experimental approaches designed to drug protein targets that have previously been intractable or inadequately addressed. Relay Therapeutics' initial focus is on enhancing small molecule therapeutic discovery in targeted oncology and genetic disease indications. For more information, please visit www.relaytx.com or follow us on Twitter.

Cautionary Note Regarding Forward-Looking Statements

This press release 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 potential of RLY-2608 or RLY-5836 to address a major unmet medical need; whether initial clinical results of RLY-2608 or RLY-5836 will be predictive of final results in future clinical trials; potential therapeutic effects and anticipated clinical benefits of RLY-2608 or RLY-5836; Relay Therapeutics' strategy, business plans and focus; the progress and timing of updates on the clinical development of the programs across Relay Therapeutics' portfolio, including RLY-2608; and expected therapeutic benefits of its programs. 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 are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

Any forward-looking statements in this press release 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 press release, including, without limitation, risks associated with: the impact of global economic uncertainty, geopolitical instability, or public health epidemics or outbreaks

of an infectious disease, such as COVID-19, on countries or regions in which Relay Therapeutics has operations or does business, as well as on the timing and anticipated results of its clinical trials, strategy, future operations and profitability; the delay of any current or planned clinical trials or the development of Relay Therapeutics' drug candidates; the risk that the preliminary results of its preclinical or clinical trials, including ReDiscover, may not be predictive of future or final results in connection with future clinical trials of its product candidates; Relay Therapeutics' ability to successfully demonstrate the safety and efficacy of its drug candidates; the timing and outcome of its planned interactions with regulatory authorities; and obtaining, maintaining and protecting its intellectual property. These and other risks and uncertainties are described in greater detail in the section entitled "Risk Factors" in Relay Therapeutics' 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. In addition, any forward-looking statements represent Relay Therapeutics' views only as of today and should not be relied upon as representing its views as of any subsequent date. Relay Therapeutics explicitly disclaims any obligation to update any 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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