RELAY®
THERAPEUTICS

RLY-2608 Initial Clinical Data Presentation at AACR Annual Meeting

April 2023

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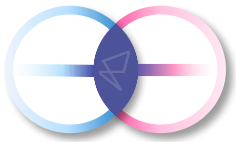
Relay Tx – Patient-Driven

New Breed of Biotech

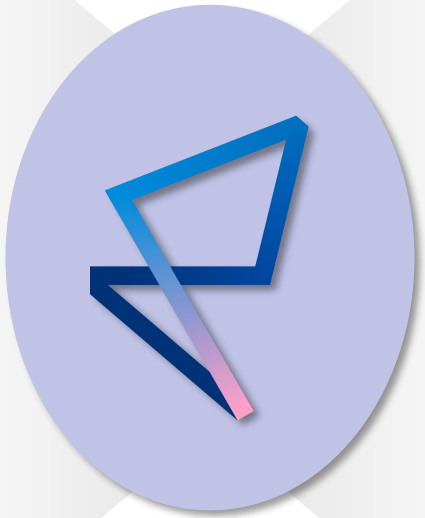
EXPERIMENTATION



COMPUTATION

Clear Focus

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



~$1B

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

Validated Approach

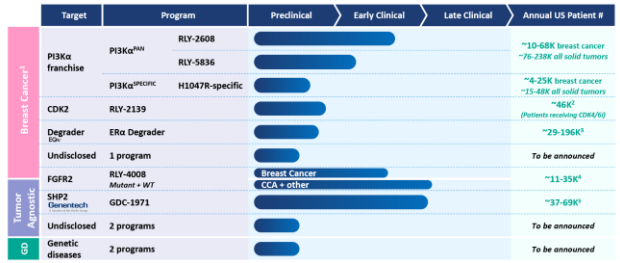
Clinical

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

Pre-clinical

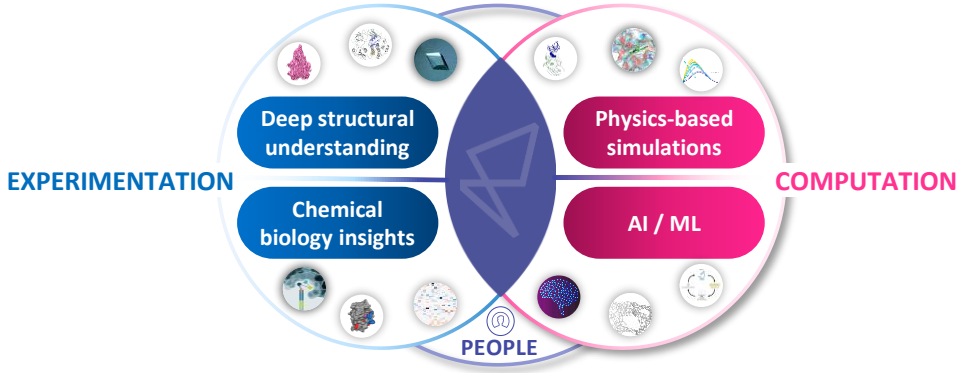
- ERα Degrader
- CDK2 *RLY-2139*
- 5+ Add'l programs

Execution-Focused

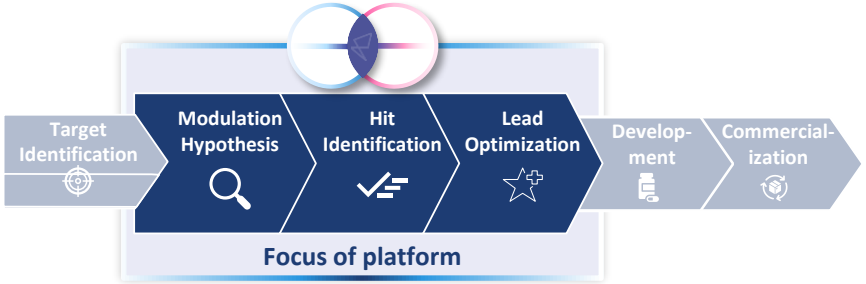


Relay Tx – Dynamo™ Platform

1 Dynamo™ Platform…

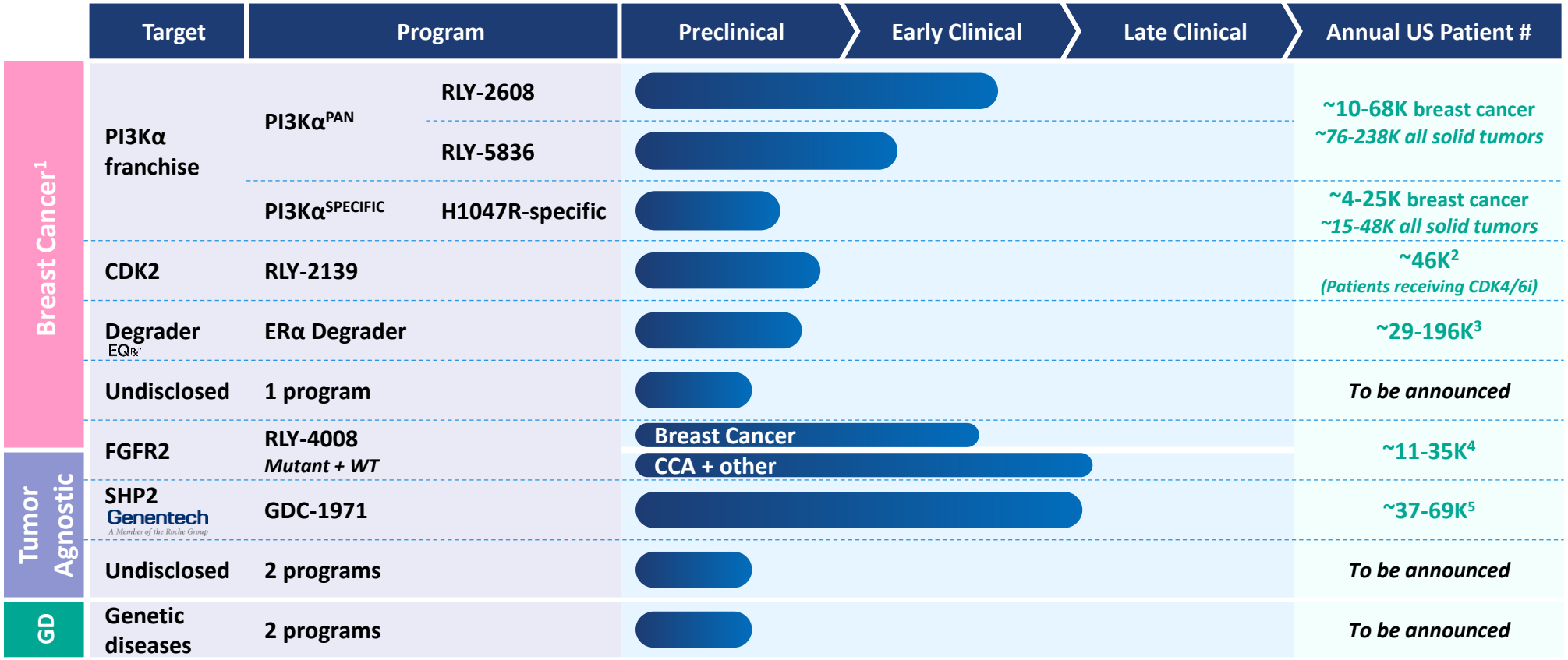


2 …is focused on making medicines



3 …aims to address selectivity on validated targets

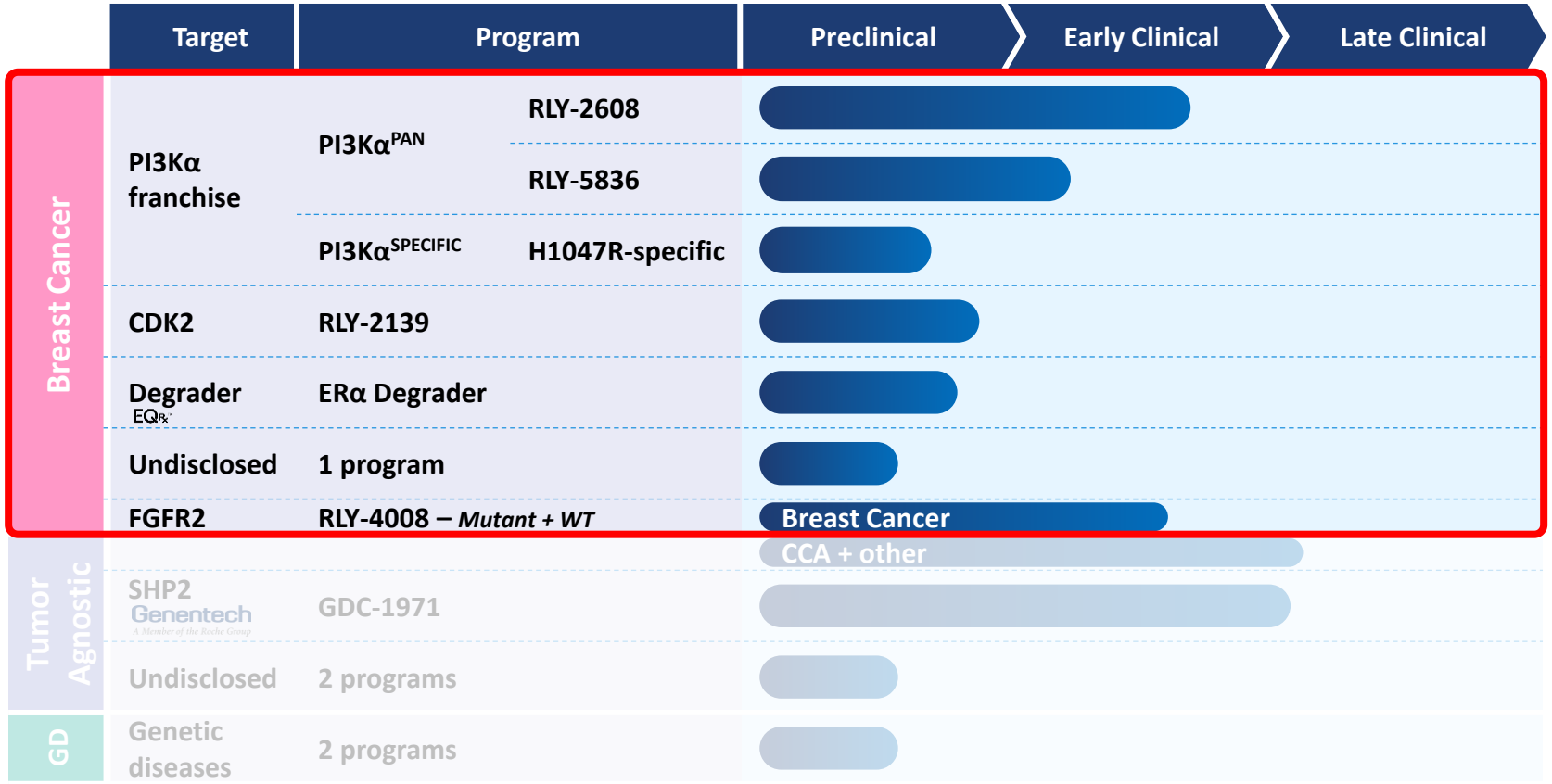
Relay Tx – Extensive Precision Medicine Pipeline



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

~196,000 new HR+/HER2- breast cancer cases diagnosed each year in USA

"Early Setting" (Patients with tumor Stages I-III)

~75% Of patients treated for early-stage disease attain long-term disease-free-survival

Neo-adjuvant

Surgery

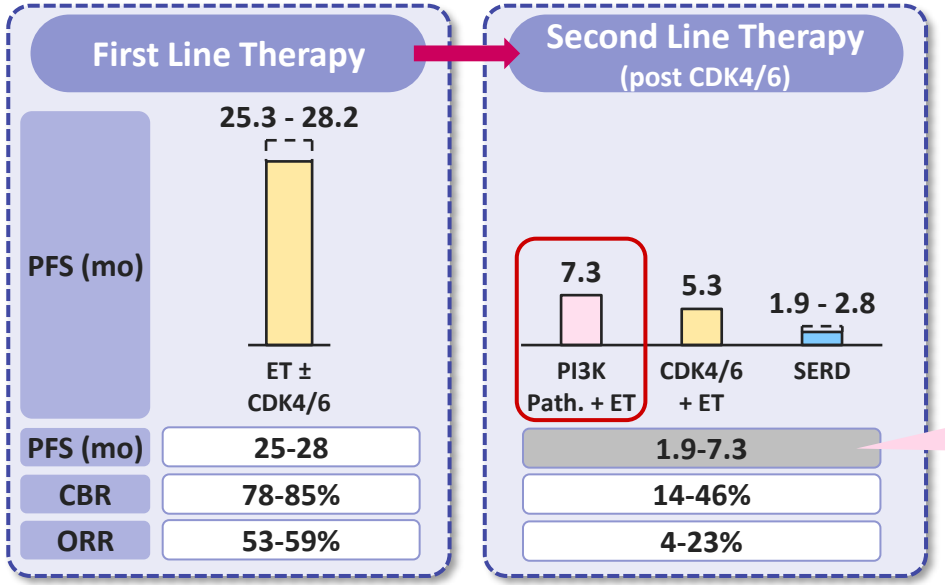
Adjuvant Tx

- Endocrine Therapy (ET) ± CDK4/6
- Chemo

Metastatic Setting – Significant unmet need

~25% Of patients require treatment in advanced or metastatic setting

~50,000 met HR+/HER2- BC cases/yr in US



Significant need for improved PFS in 2L

PFS = Progression Free Survival
CBR = Clinical Benefit Rate
ORR = Objective Response Rate

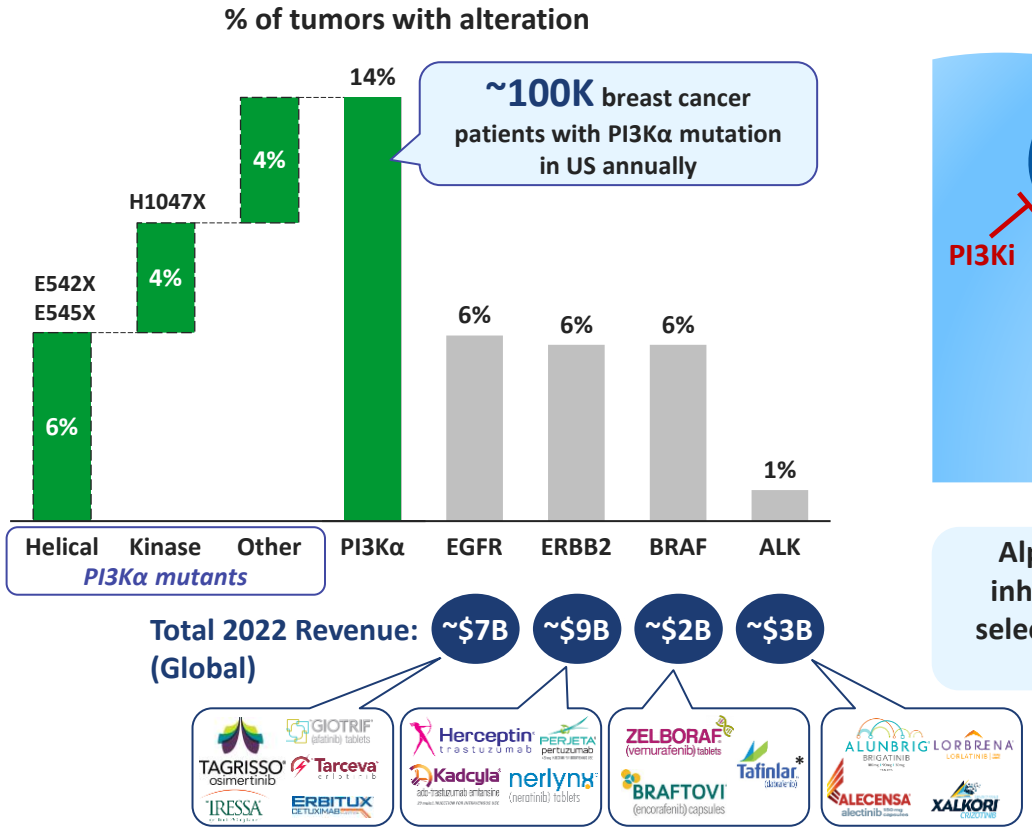
Relay Tx BC portfolio aspirational positioning

Relay Tx BC portfolio planned initial positioning

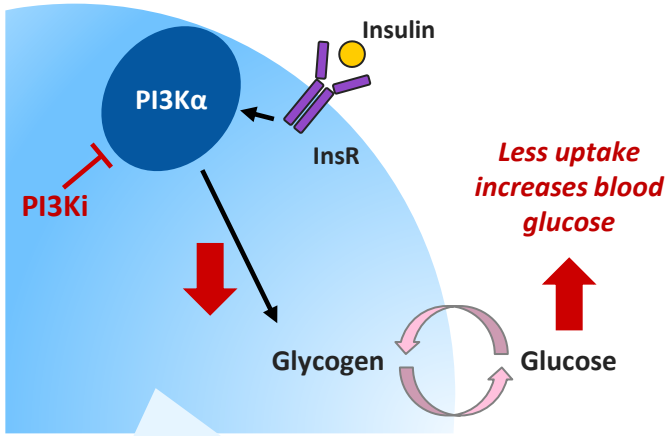
Figures generated based on publicly available data for both approved and investigational products (alpelisib, ribociclib, elacastrant (investigatonal), fulvestrant (investigatonal), palbociclib, ribociclib, abemaciclib, capivasertib (investigational)).
Sources: SEER, Metastatic Breast Cancer Network (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%)

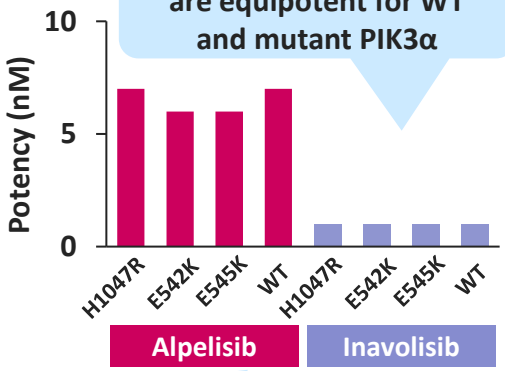
*Tafinlar + Mekinist

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

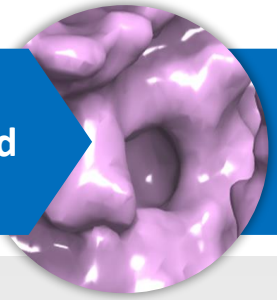
Sources: Alpelisib – 1. SOLAR-1: Andre 2019 N Engl J Med 380:1929, 2. Ph 1b: SABCS 2013 P2-16-14, 3. Ph 1b: SABCS 2014 PD5-5, 4. Ph 2 ByLIEVE: Rugo 2021 Lancet Oncol 22:489, SABCS 2021 #P1-18-03, 5. Ph 1b mono: Annals of Oncol 25 2014 (suppl 4), 6. Ph 2 mono: Savas Cancer Discov 2022 Sep 12:2058, 7. 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.

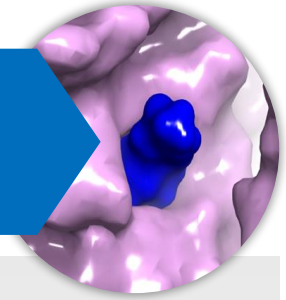
PI3Kα – Proprietary Insights Unlock Novel Approaches

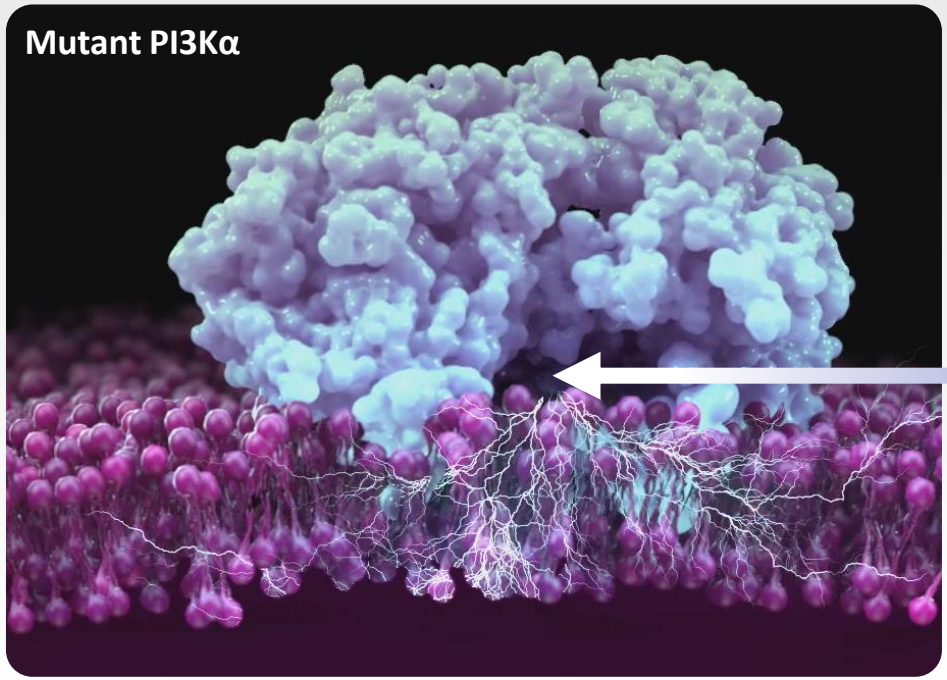
Solved first full-length structures of PI3Kα (mutant and wild-type)

Discovered novel allosteric pocket favored in mutant protein



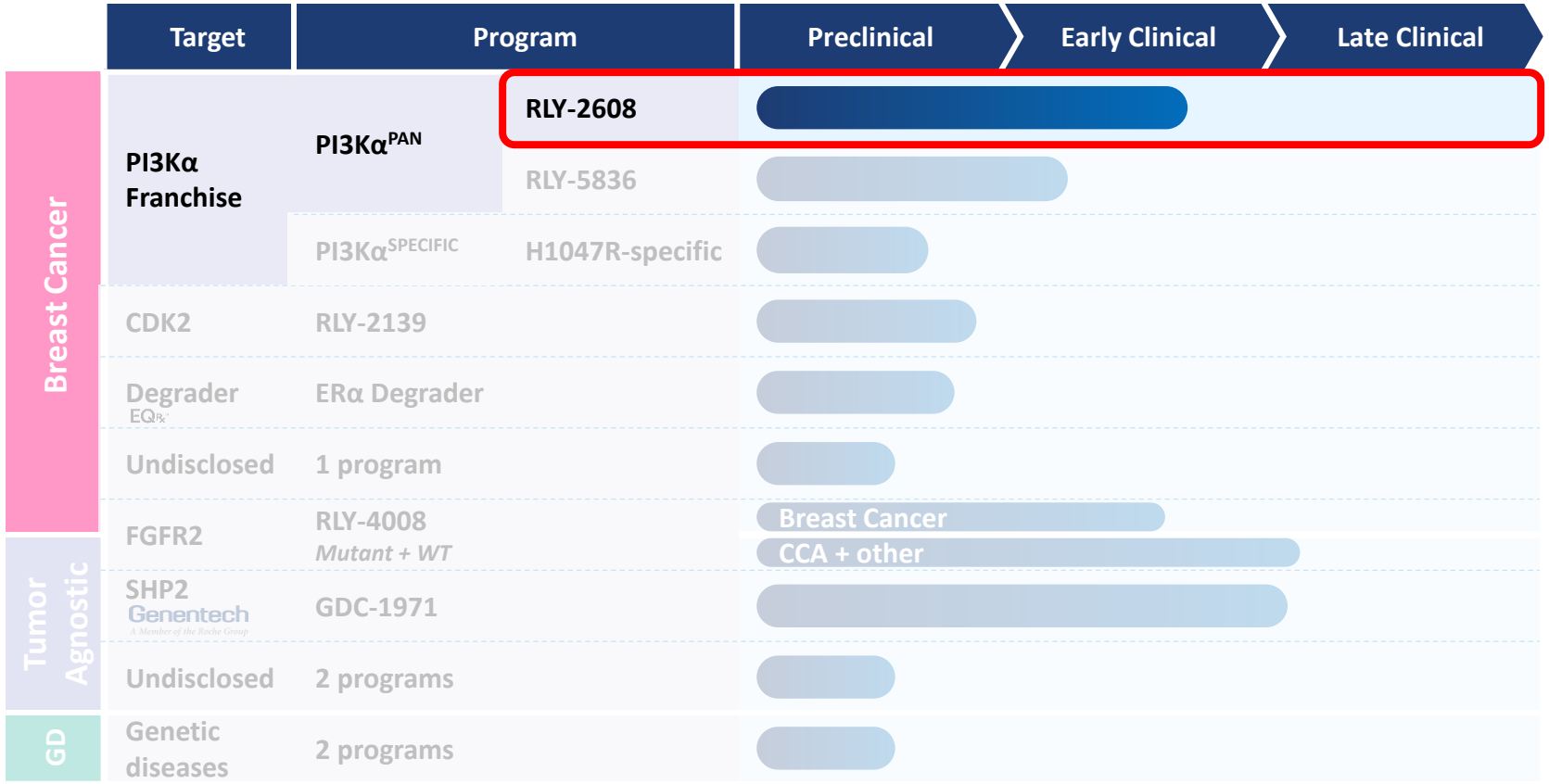
Designed pan-mutant selective PI3Kα inhibitor (PI3Kα^{PAN})





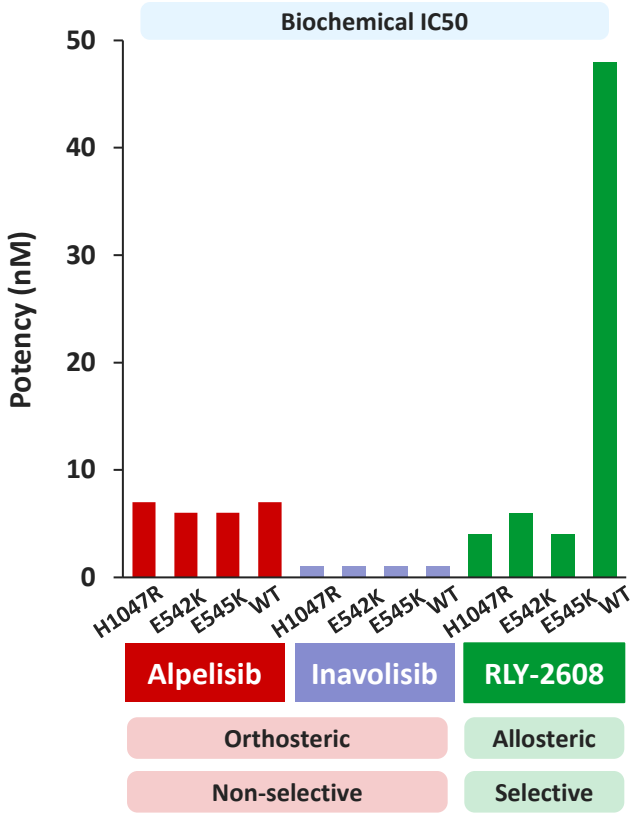
A differentiated understanding of the structure of PI3Kα and its relationship to function equips Relay Tx to design optimal mutant-selective inhibitors of PI3Kα

Relay Tx – Extensive Precision Medicine Pipeline

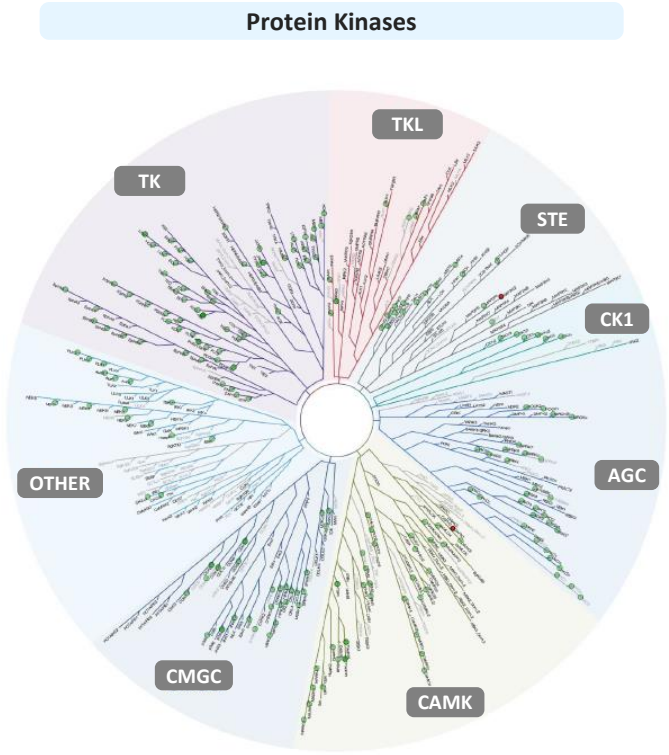


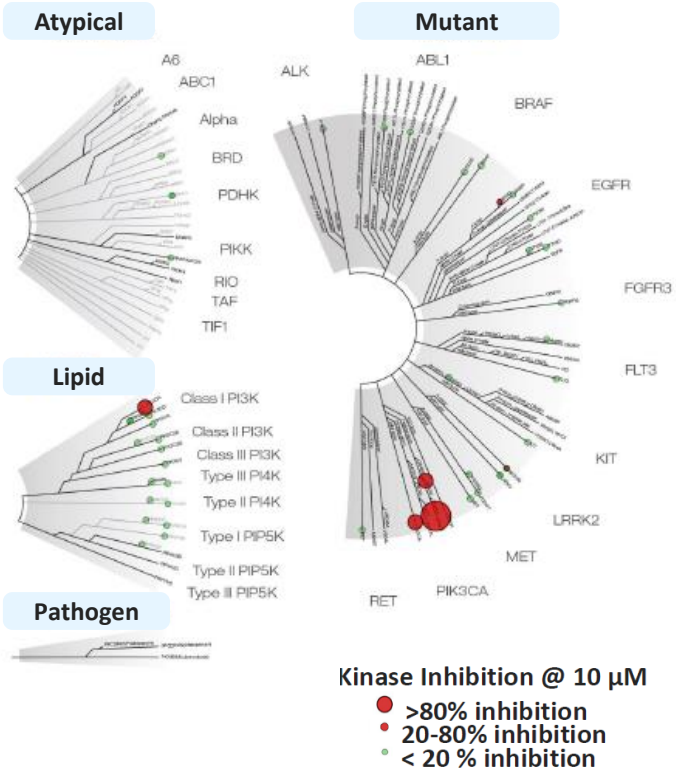
RLY-2608 – Allosteric Mutant Selective PI3Kα Inhibitor

RLY-2608 selectively inhibits mutant PI3Kα



High selectivity over the kinome and within PI3K family



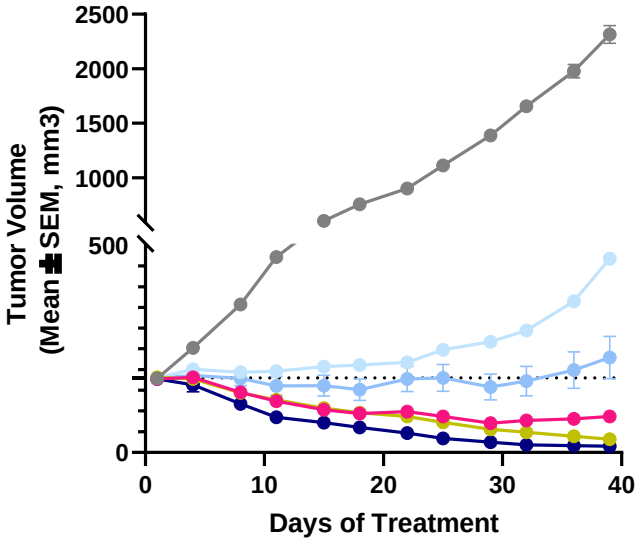


Pazolli M, Discovery and characterization of RLY-2608, the first allosteric, mutant, and isoform-selective inhibitor of PI3Kα. Oral presentation at: AACR-NCI-EORTC Virtual International Conference on Molecular Targets Conference; October 7-10, 2021; Virtual.

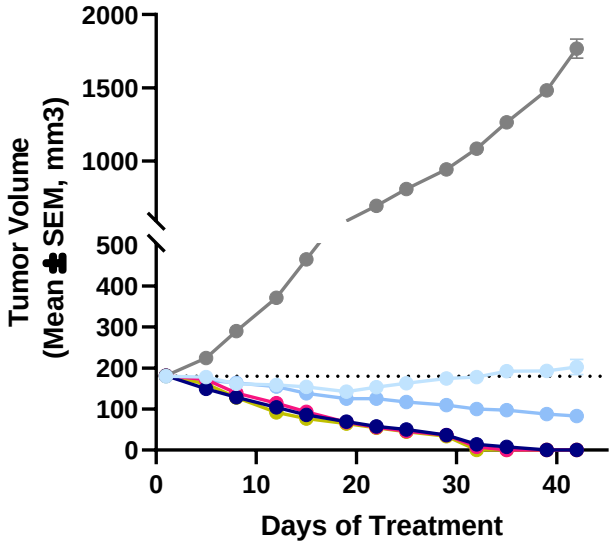
RLY-2608 – Shows Robust Efficacy with Limited Impact on Glucose Homeostasis in Preclinical Models

Tumor regression in PI3Kα mouse breast cancer models

H1047R (Kinase mutant)
(HCC1954)

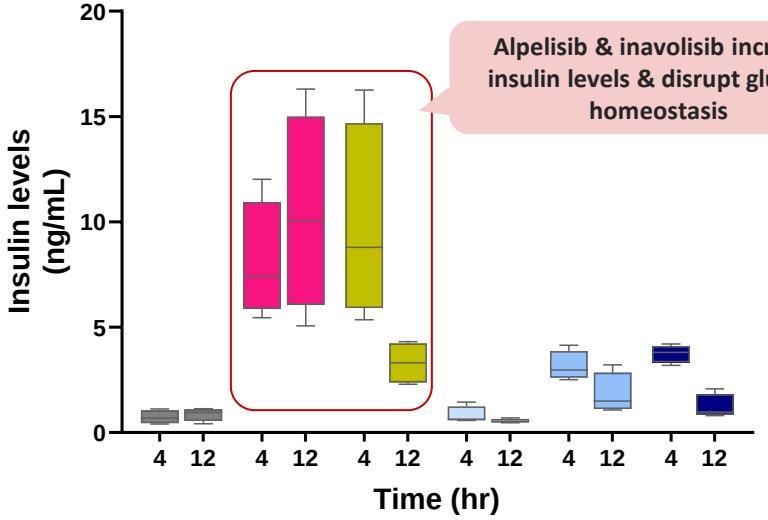


E545K (Helical mutant)
(MDAMB361[1])



Minimal perturbation of insulin levels

Insulin levels at steady state exposure
in tumor-bearing mice[2]



Alpelisib & inavolisib increase insulin levels & disrupt glucose homeostasis

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

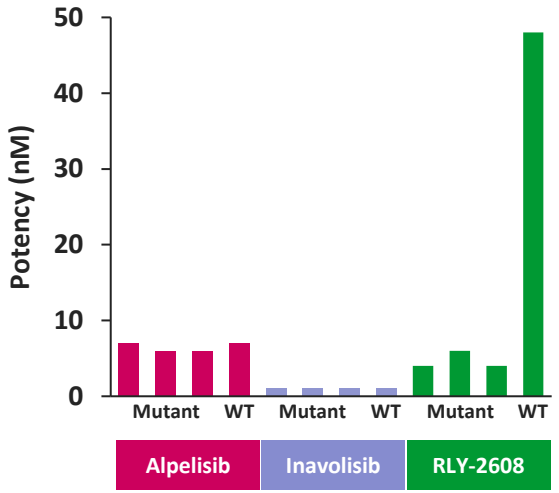
Pazolli M, Discovery and characterization of RLY-2608, the first allosteric, mutant, and isoform-selective inhibitor of PI3Kα. Oral presentation at: AACR-NCI-EORTC Virtual International Conference on Molecular Targets Conference; October 7-10, 2021; Virtual.
1. This model also carries a second mutation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

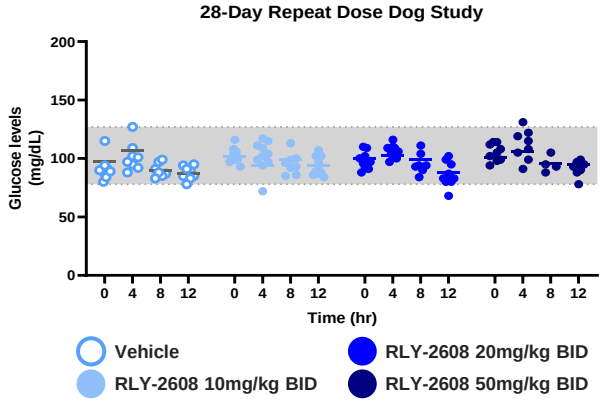
Favorable Selectivity

Limited potency against WT PI3Kα and other PI3K isoforms



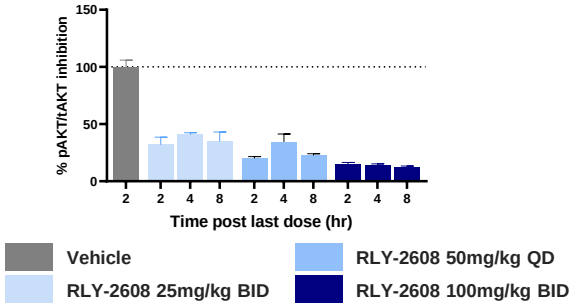
Favorable Tolerability

Manageable key toxicities, especially hyperglycemia shown in dog study



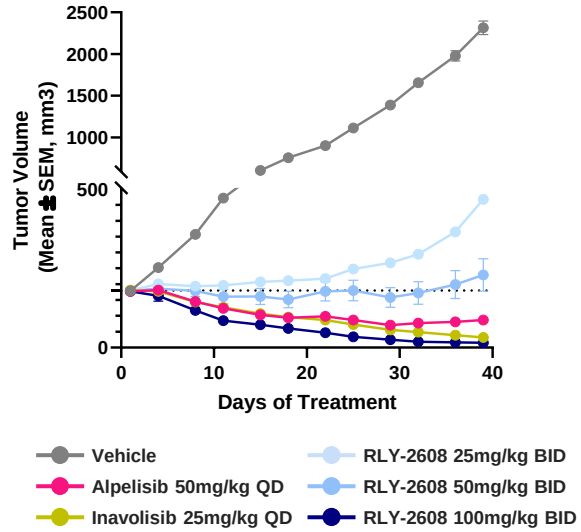
Favorable Target Inhibition

Maintains approx. 80% mutant PI3Kα inhibition in mouse model



Favorable Efficacy

Robust tumor regression at tolerable doses in mouse model



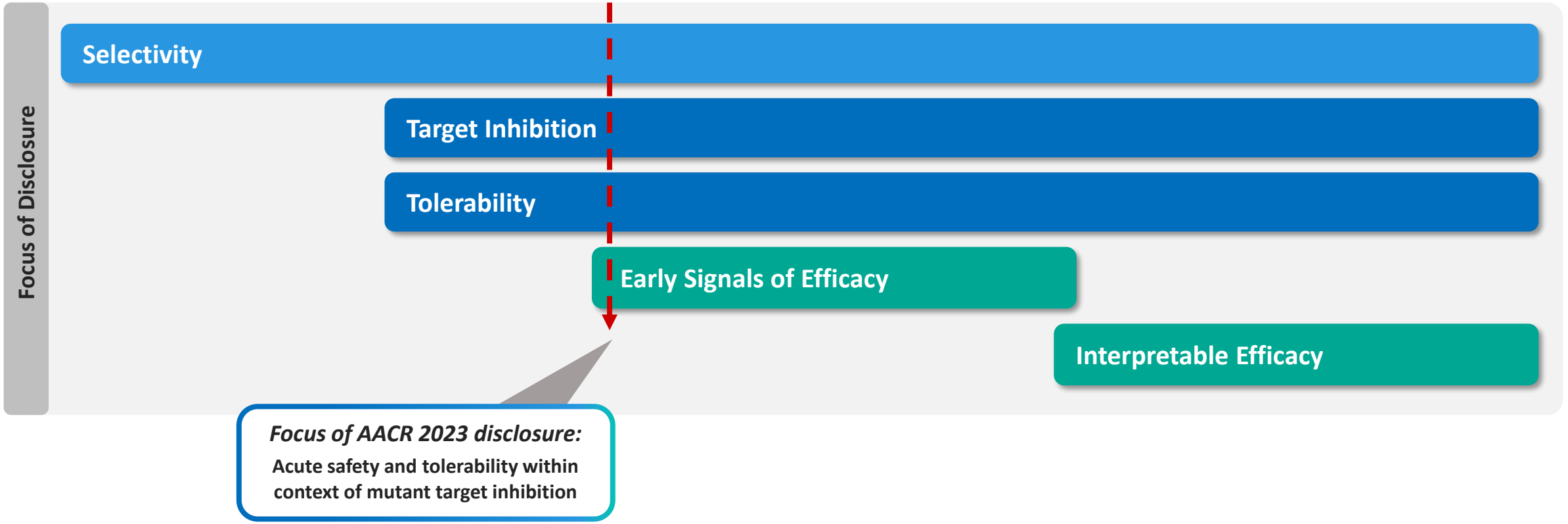
RLY-2608 – Data Disclosure Goals

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



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

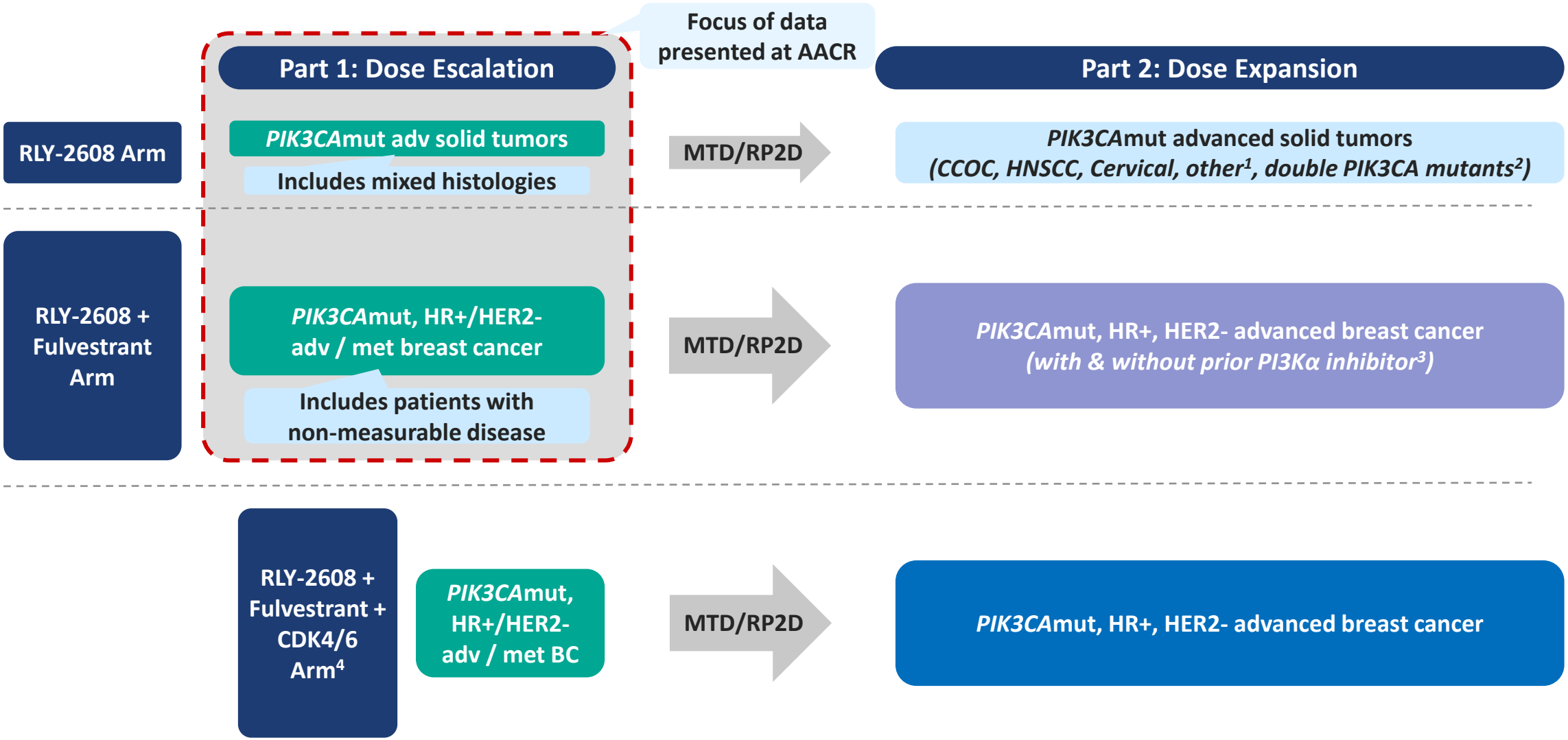
- Interpretable Efficacy (CBR, ORR)
- Longer-Term Tolerability

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

Current enrollment focus

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

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

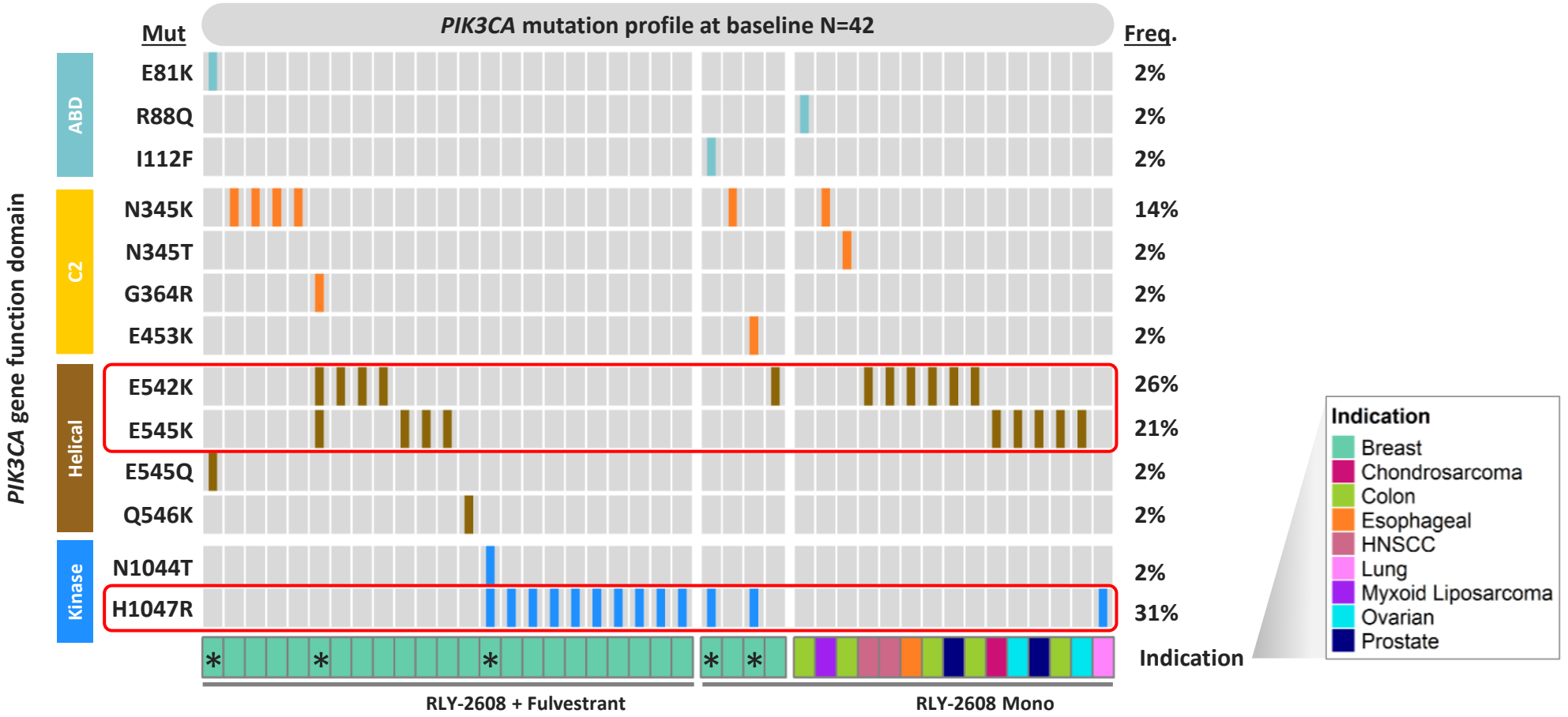
Preliminary data as of 03/09/2023

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



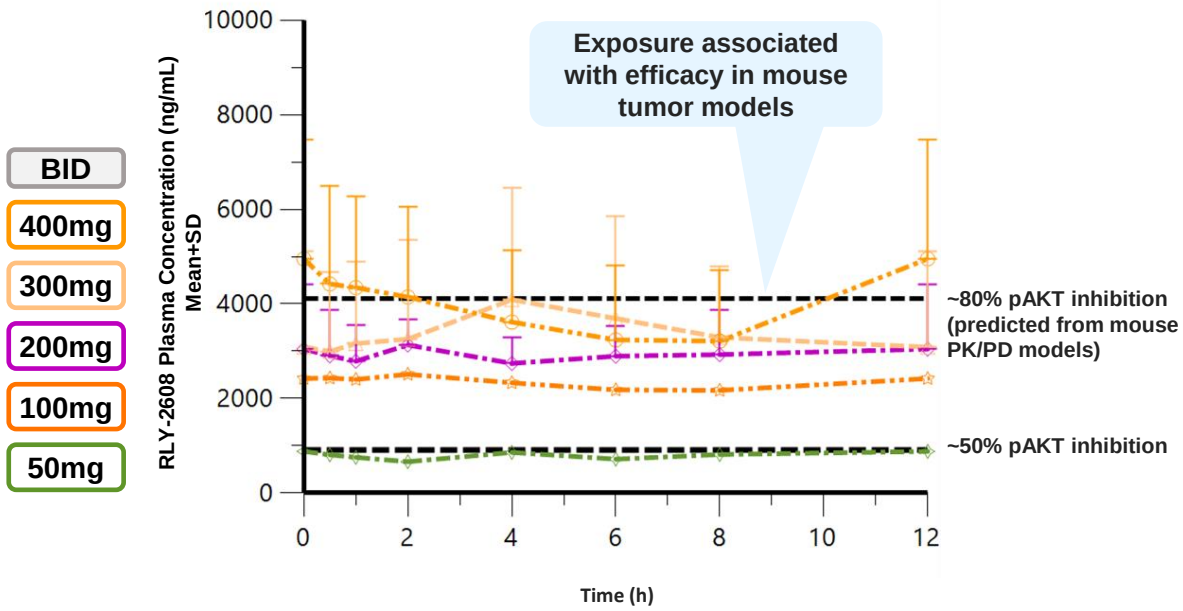
PIK3CA* mutations: 14 Kinase, 22 Helical, 5 double mutations

* 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

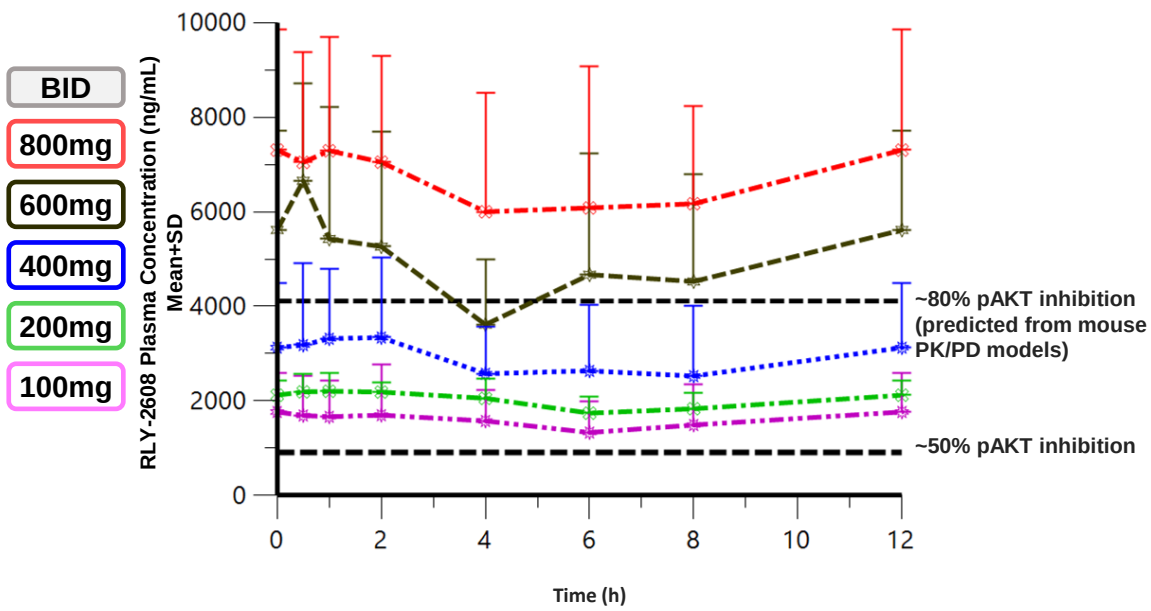
Preliminary data as of 03/09/2023

RLY-2608 – Favorable PK profile

RLY-2608
C1D15



RLY-2608 + fulvestrant
C1D15



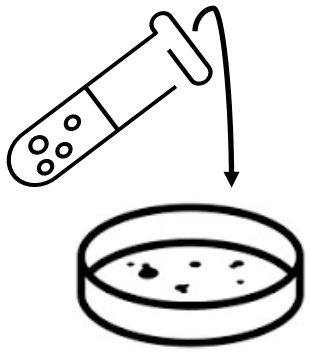
Dose-dependent increase in exposure and low peak to trough fluctuations across dose levels
Continuous exposure over IC80 correlates with efficacy in preclinical models*
Constant coverage at IC80 across dosing interval at 400mg BID mono and 600mg and 800mg BID combo

* 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

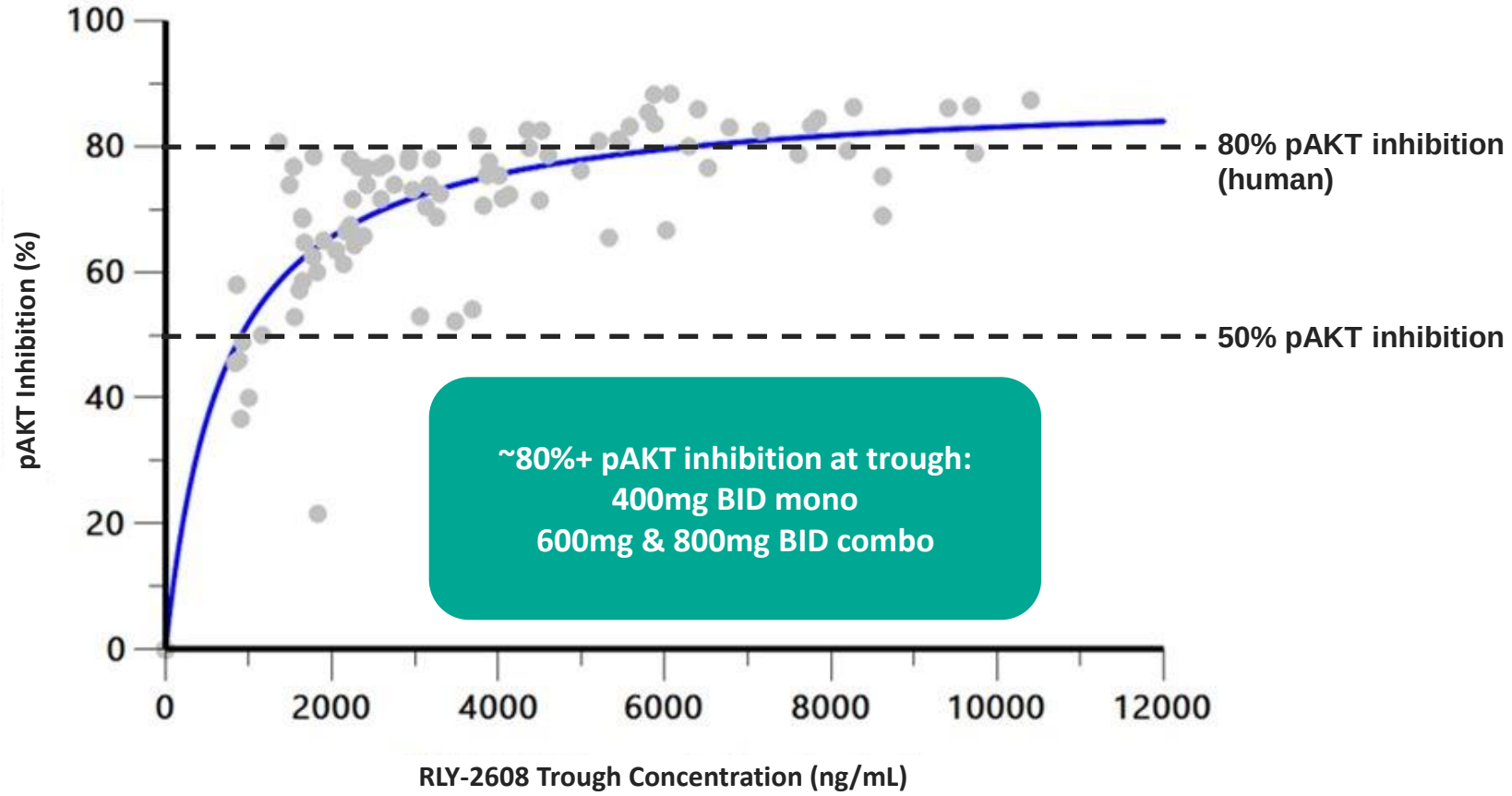
RLY-2608 – Multiple Doses Achieve ~80%+ Target Inhibition at Trough

Patient Plasma Sample*
(Pre-dose)



PIK3CA-mutant cancer cells

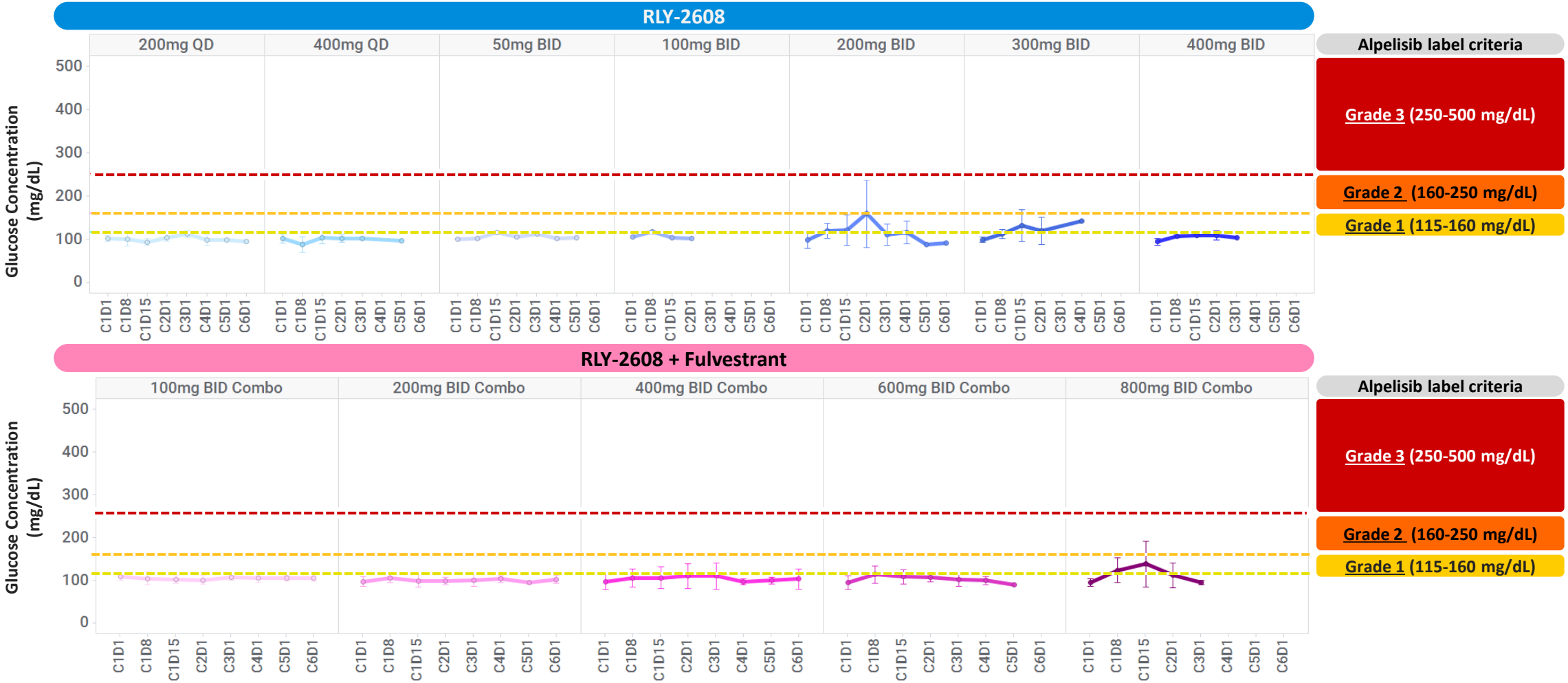
Ex-vivo suppression of pAKT in PIK3CA-mutant cancer cells



* 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

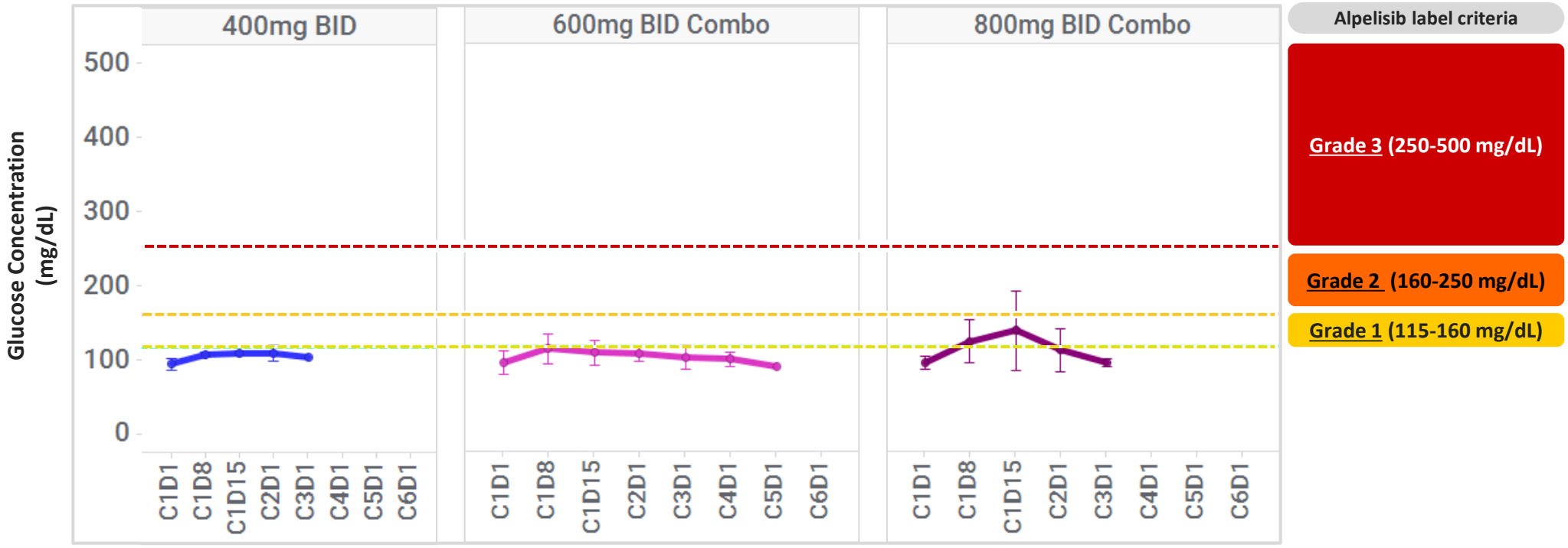
* Data represent mean per cohort +/- standard deviation

Preliminary data as of 03/09/2023

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

RELAY THERAPEUTICS

RLY-2608 | **RLY-2608 + Fulvestrant Combination**



Alpelisib label criteria

- Grade 3 (250-500 mg/dL)
- Grade 2 (160-250 mg/dL)
- Grade 1 (115-160 mg/dL)

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

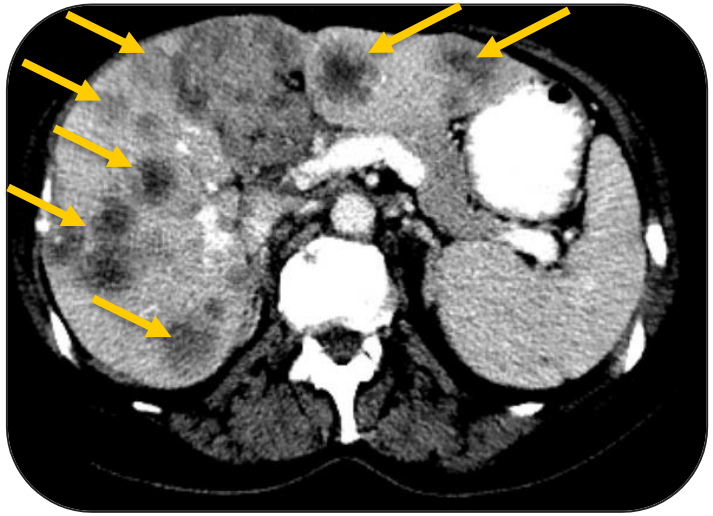
* Data represent mean per cohort +/- standard deviation

Preliminary data as of 03/09/2023

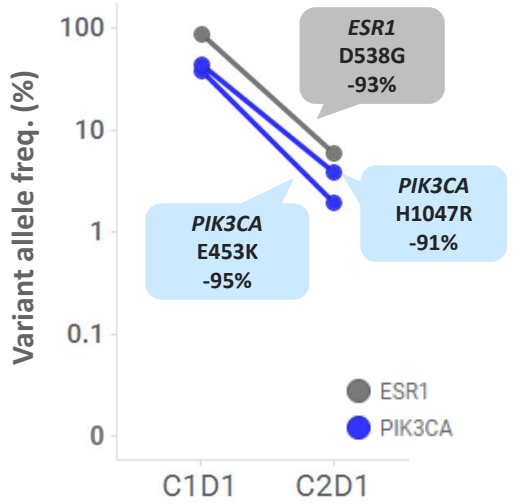
RLY-2608 – Anti-tumor Activity: Partial Response per RECIST*

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

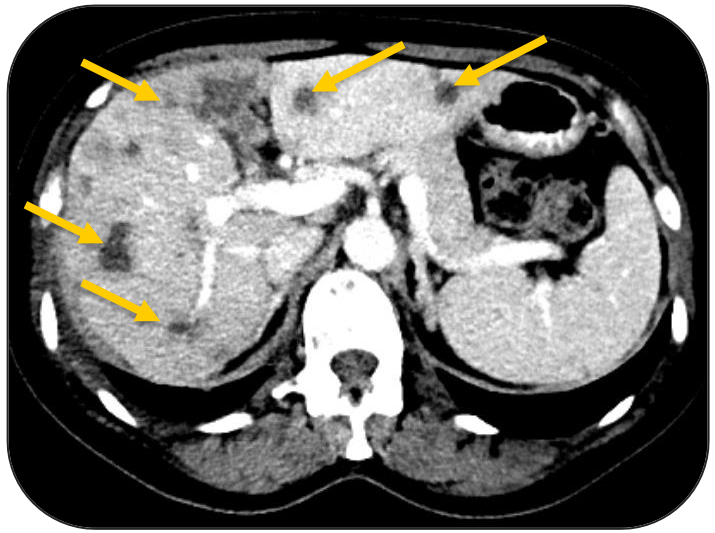
Baseline



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

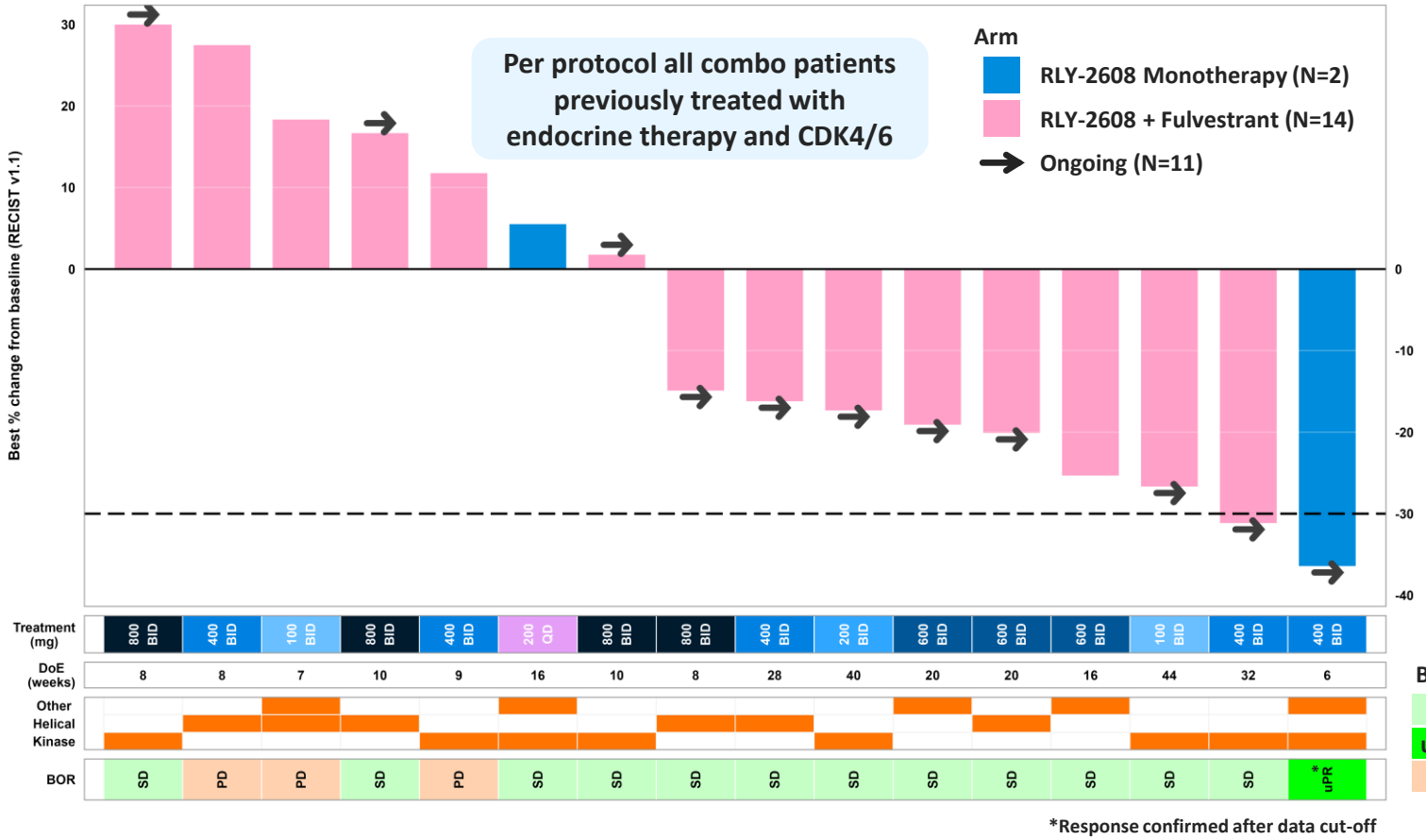
*Response confirmed after data cut-off
Courtesy Varkaris, MGH

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

Breast Cancer Patients (RECIST Measurable Disease) N=16



*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

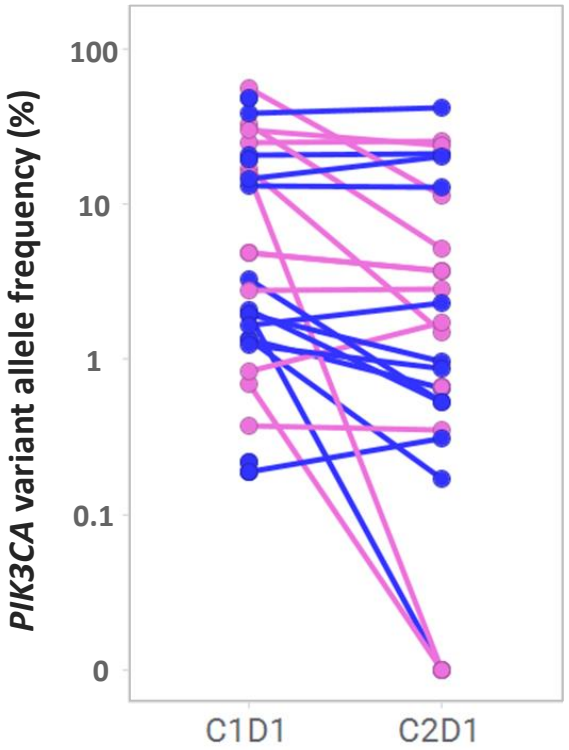
BOR = Best Overall Response:

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

Preliminary data as of 03/09/2023

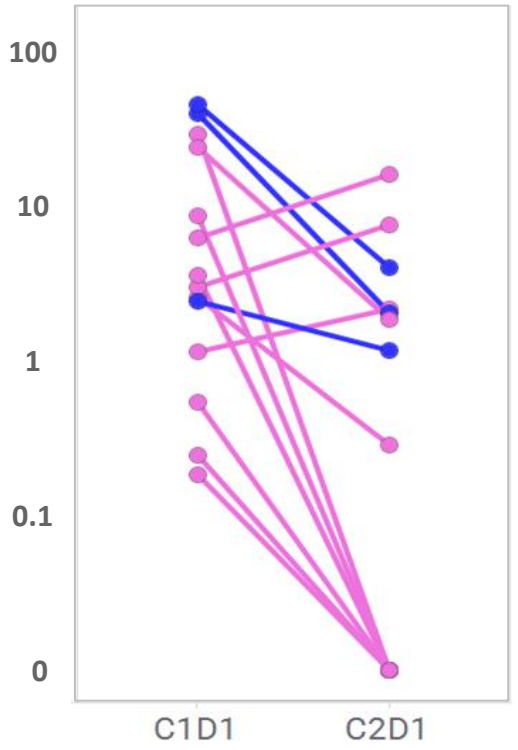
RLY-2608 – Decline of Mutant *PIK3CA* ctDNA

Doses Below Target Exposure



Patients with paired evaluable ctDNA[2]	Mono: 9
	Combo: 10

Doses Above Target Exposure[1]



Patients with paired evaluable ctDNA[2]	Mono: 2
	Combo: 10

31 patients with evaluable paired C1D1-C2D1 ctDNA samples

6 patients have ≥2 *PIK3CA* mutations

23 patients had declines in *PIK3CA* ctDNA

9 patients completely cleared by C2D1

- RLY-2608
- RLY-2608 + fulvestrant

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

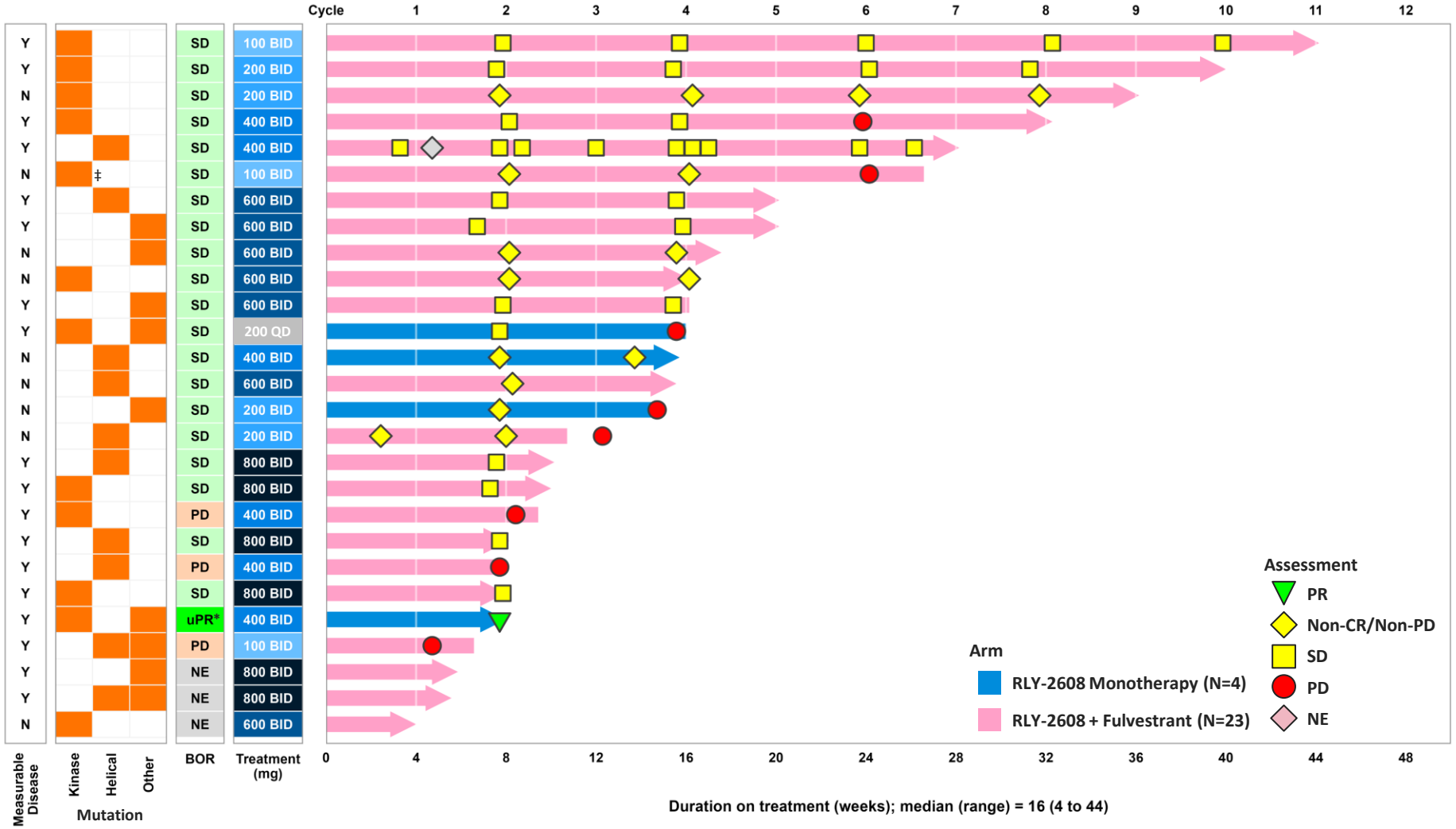
Preliminary data as of 03/09/2023

RLY-2608 – Breast Cancer Disease Control Across Dose Levels

27 Breast Cancer Patients – Measurable and Non-Measurable Disease

RELAY THERAPEUTICS

RLY-2608 Breast Cancer Patients (Measurable and Non-Measurable Disease) *N=27*



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

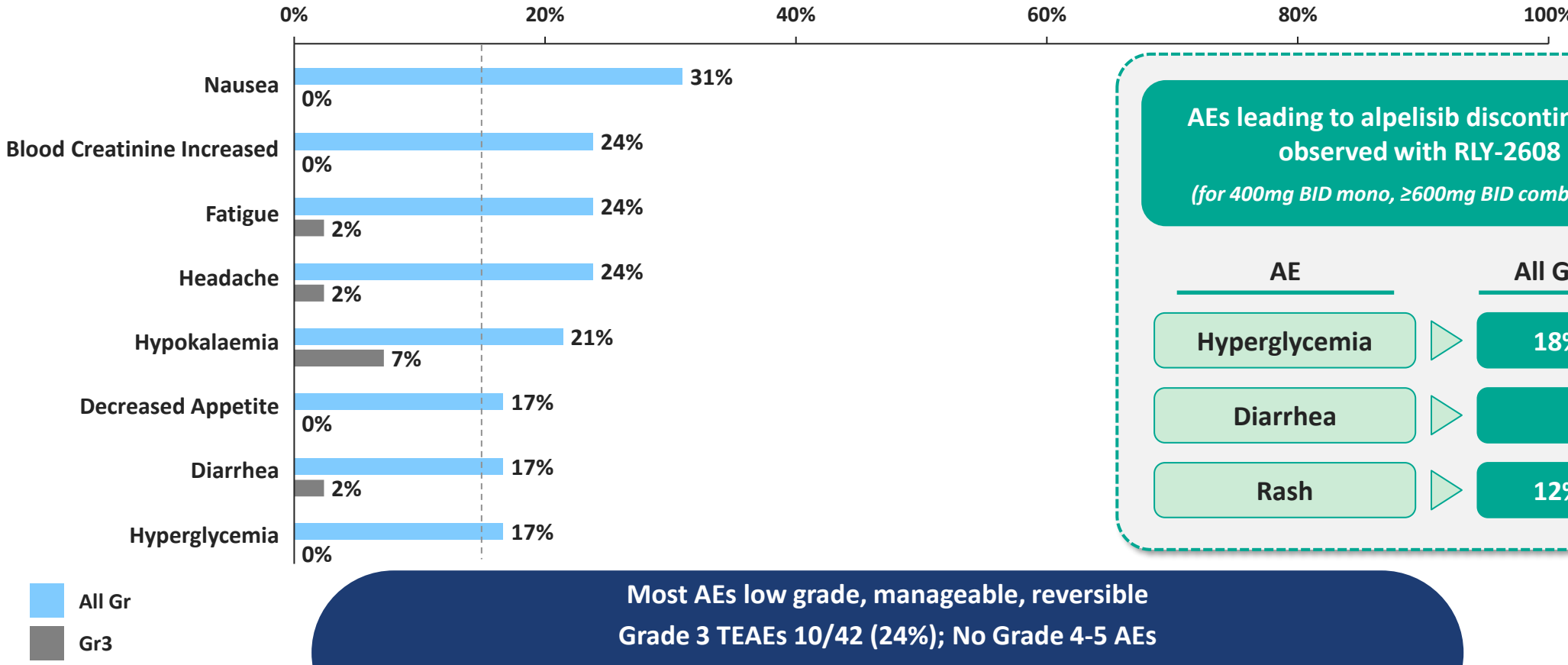
Most patients (7/8) discontinued due to progressive disease
- **No AEs leading to treatment discontinuation**

*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)

No Gr3+

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

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%

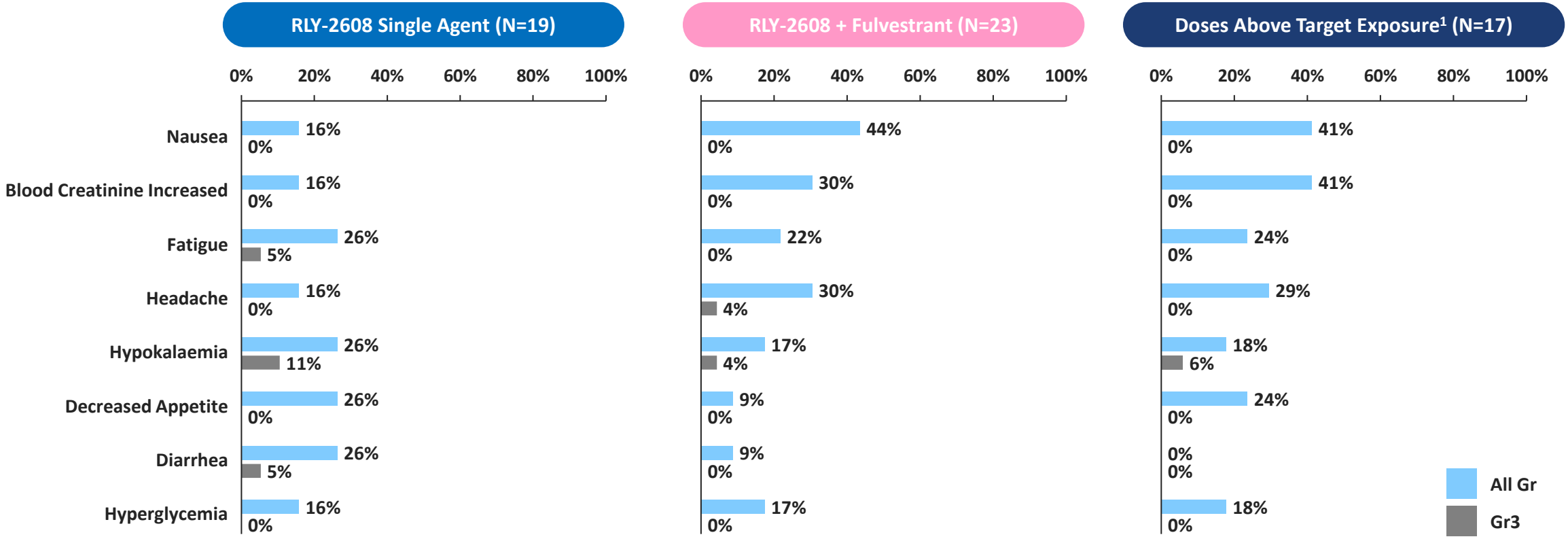
Median Relative Dose Intensity: 98%[1]

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

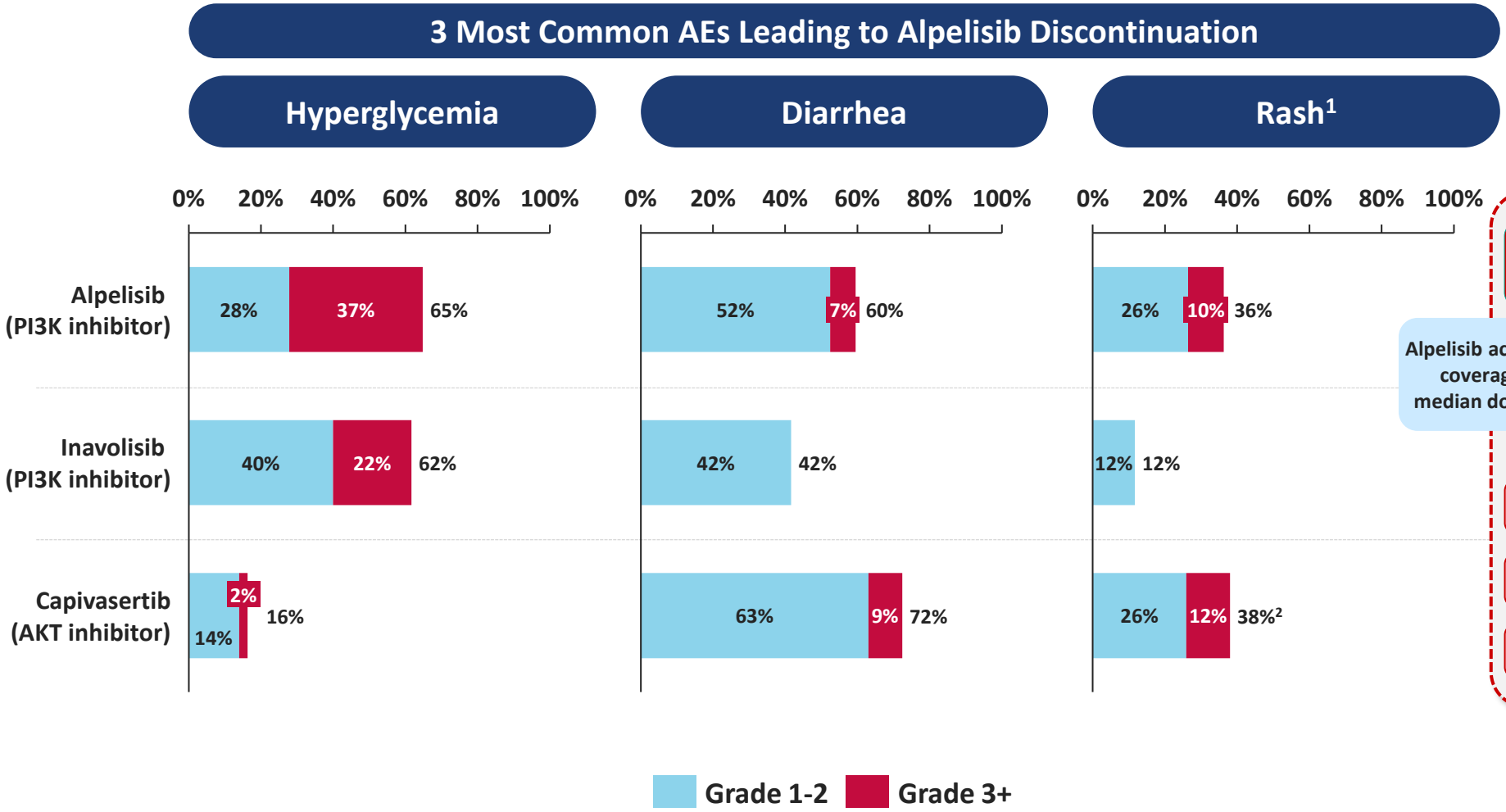
Note: TEAEs ≥15% across all patients

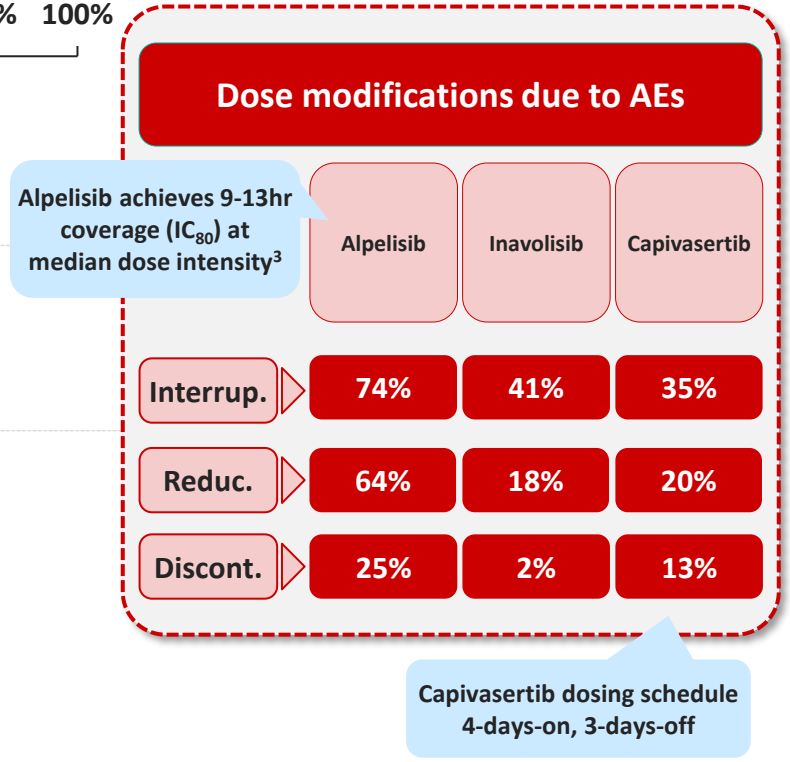


1. Doses above target exposure: 400mg BID mono, 600mg BID combo, 800mg BID combo

Preliminary data as of 03/09/2023

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



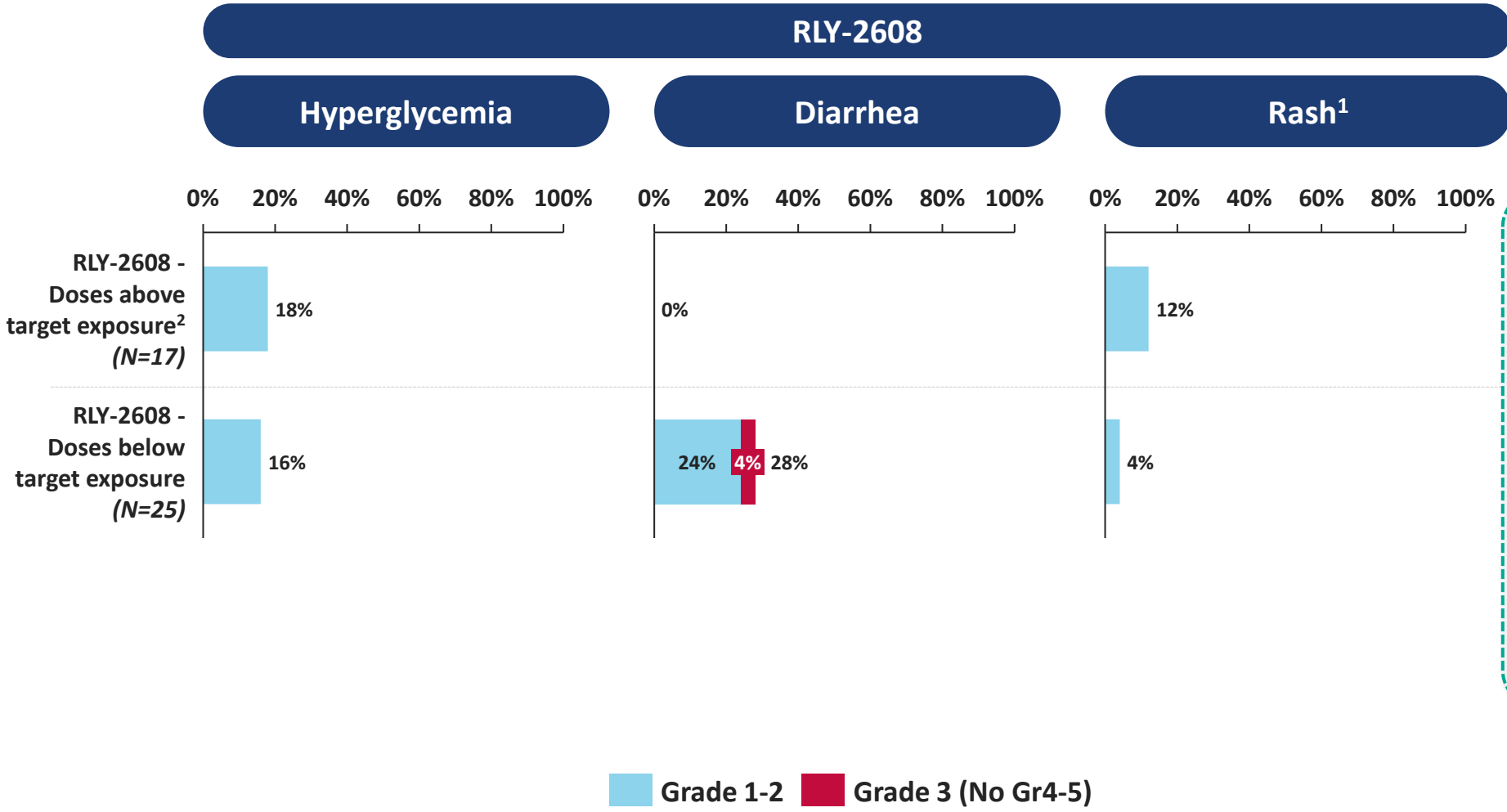


1. Grouped term: rash and rash maculo-papular; 2. Capivasertib rash includes events related to rash including: rash, rash macular, maculopapular rash, rash papular and rash pruritic; 3. Alpelisib median dose intensity 83%

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

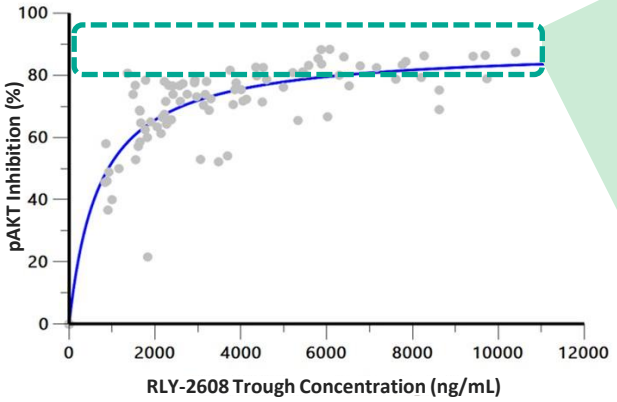
RLY-2608 – Potential to Achieve Greater Dose Intensity

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

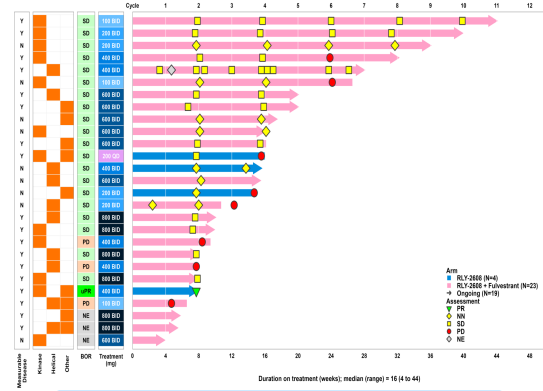


RLY-2608 TEAE for doses above target exposure[1]

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%



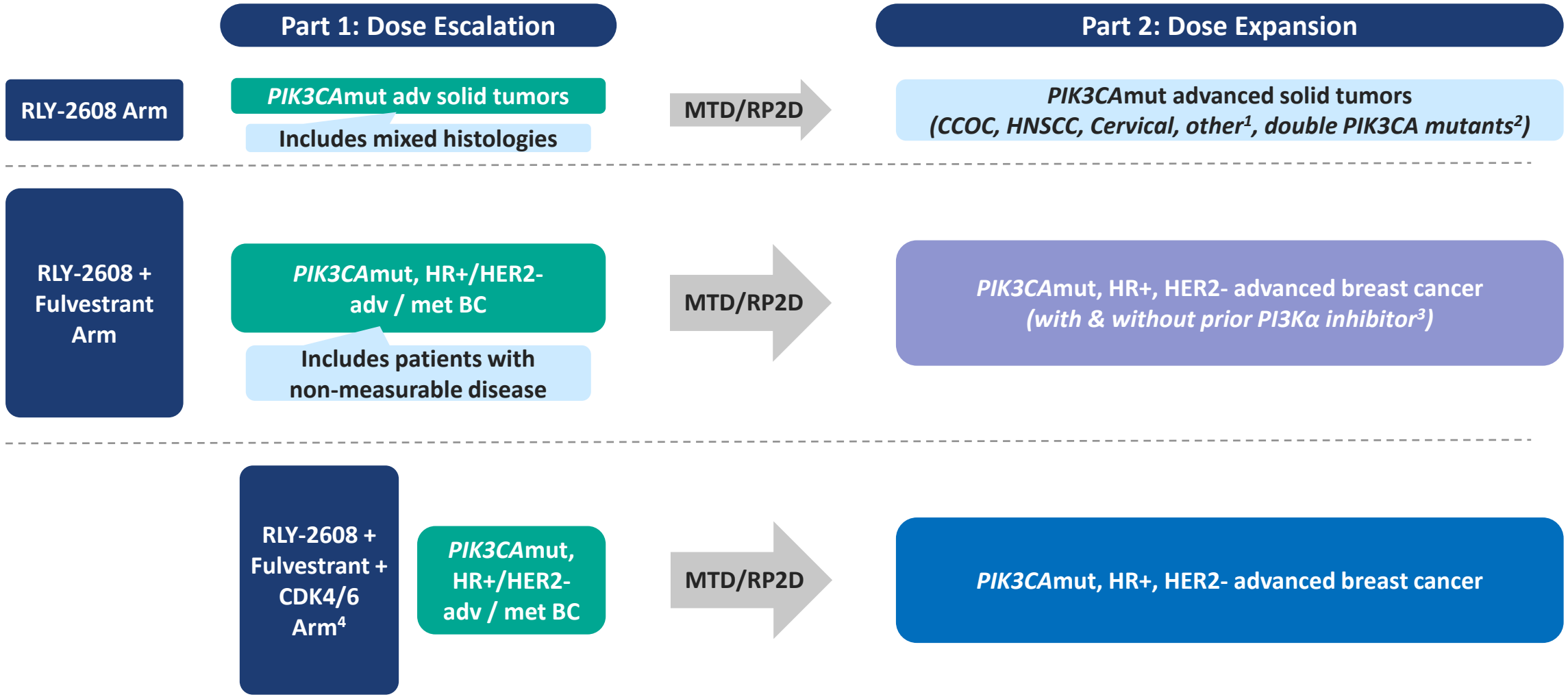
Initial activity across range of PI3Kα mutation types

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

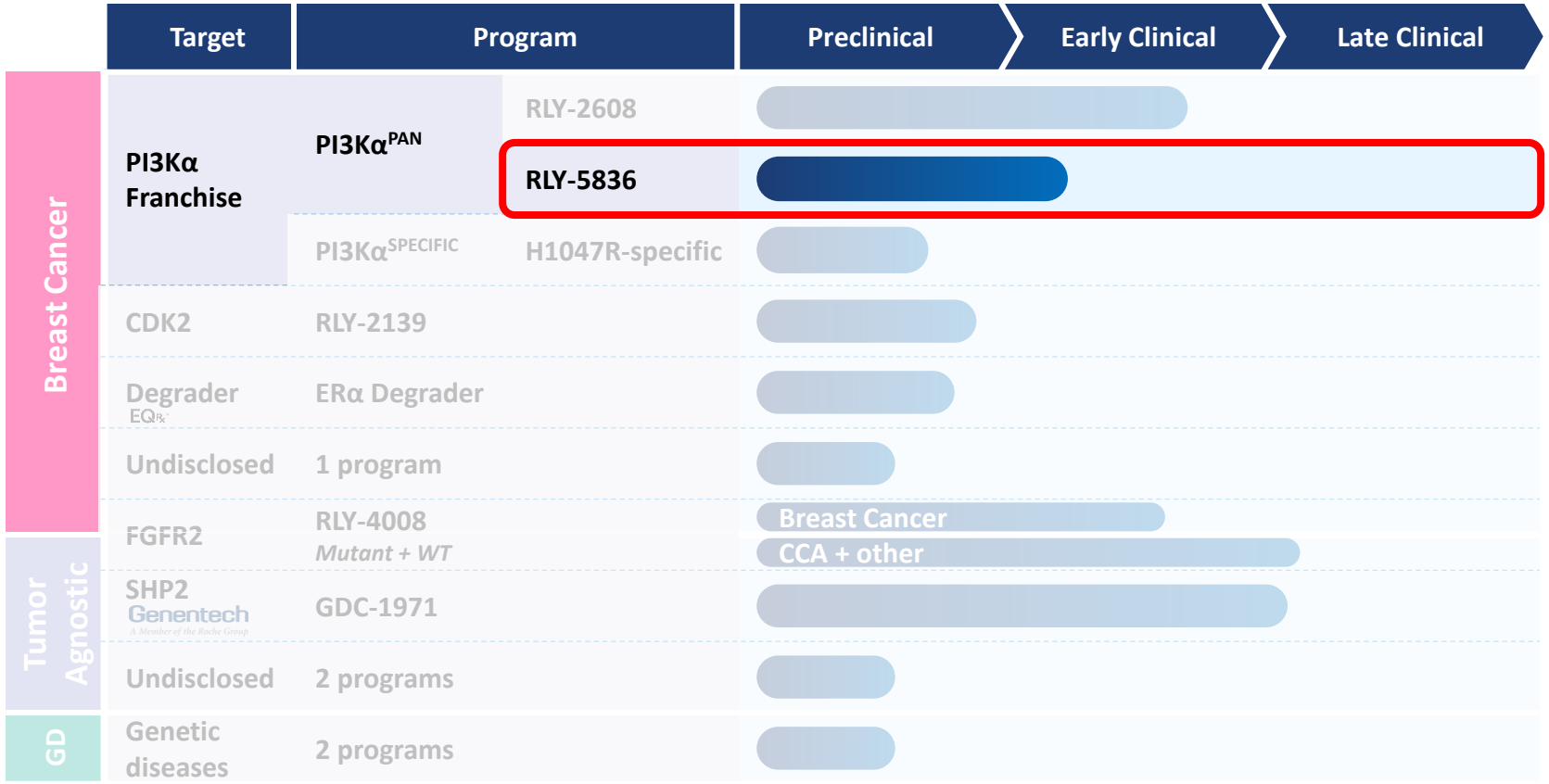
Preliminary data as of 03/09/2023

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

Part 1: Dose Escalation			Part 2: Dose Expansion
RLY-5836 Arm	*PIK3CA*mut advanced solid tumors	MTD/RP2D	*PIK3CAmut* advanced solid tumor (n=~15)
RLY-5836 + Fulvestrant Arm[1]	*PIK3CA*mut, HR+/HER2- advanced breast cancer	MTD/RP2D	*PIK3CA*mut, HR+, HER2- advanced breast cancer, with no prior PI3Kα inhibitor (n=~15)
RLY-5836 + Fulvestrant + CDK4/6 Arms[2]	*PIK3CA*mut, HR+/HER2- advanced BC, 1 prior CDK4/6	MTD/RP2D	*PIK3CA*mut, HR+, HER2- advanced breast cancer[3] (n=~15 for each arm, ~45 total)

RLY-5836 clinical start in Apr 2023

- **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

RLY-2608 Evolution of Data

Initial Data Supporting Selective Targeting of Mutant PI3Kα → **Goal for Expansion Cohorts**

Focus of today's disclosure

Initial Clinical Proof of Mechanism

- Selective target inhibition over IC_{80}
- Favorable safety profile at therapeutically active doses
- Initial anti-tumor activity observed across range of doses

Potential for greater dose intensity

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

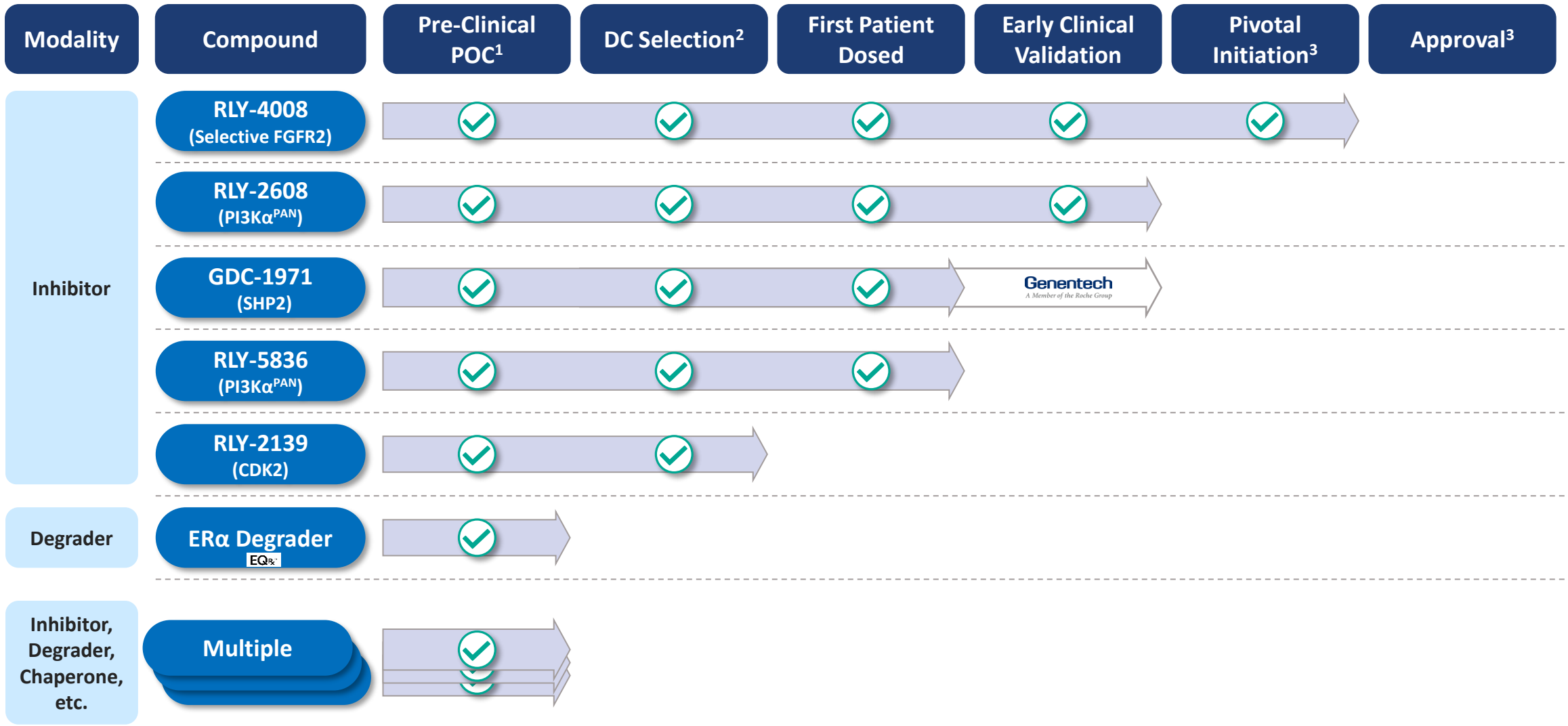
Relay Tx Breast Cancer Portfolio

- PI3Kα Franchise
  - RLY-2608
  - RLY-5836
  - H1047R-specific
- RLY-5836 clinical start in Apr 2023
- RLY-2139 (CDK2)
- ERα Degrader
- *Other Undisclosed Programs*

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



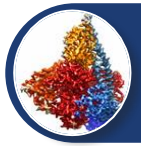
1. POC - proof-of-concept. 2. DC - development candidate. 3. Subject to alignment with regulatory authorities

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

RELAY THERAPEUTICS

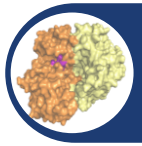
Breast Cancer Franchise

PI3Kα^{PAN}



- 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

RLY-2139 (Selective CDK2)



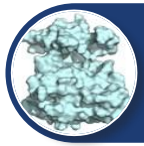
- Clinical start in early 2024

ERα Degrader

- Development candidate nomination in 2023

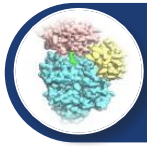
Tumor Agnostic

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

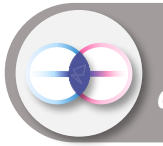
GDC-1971 (SHP2)



- Ongoing combo trials; Genentech controls data disclosures

Undisclosed

To be announced

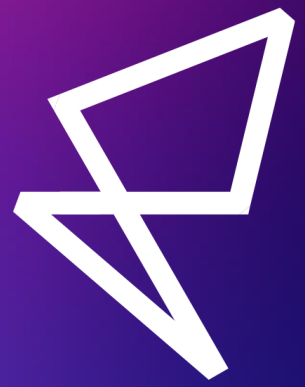


- *5+ undisclosed programs in preclinical development and additional early-stage efforts across platform*

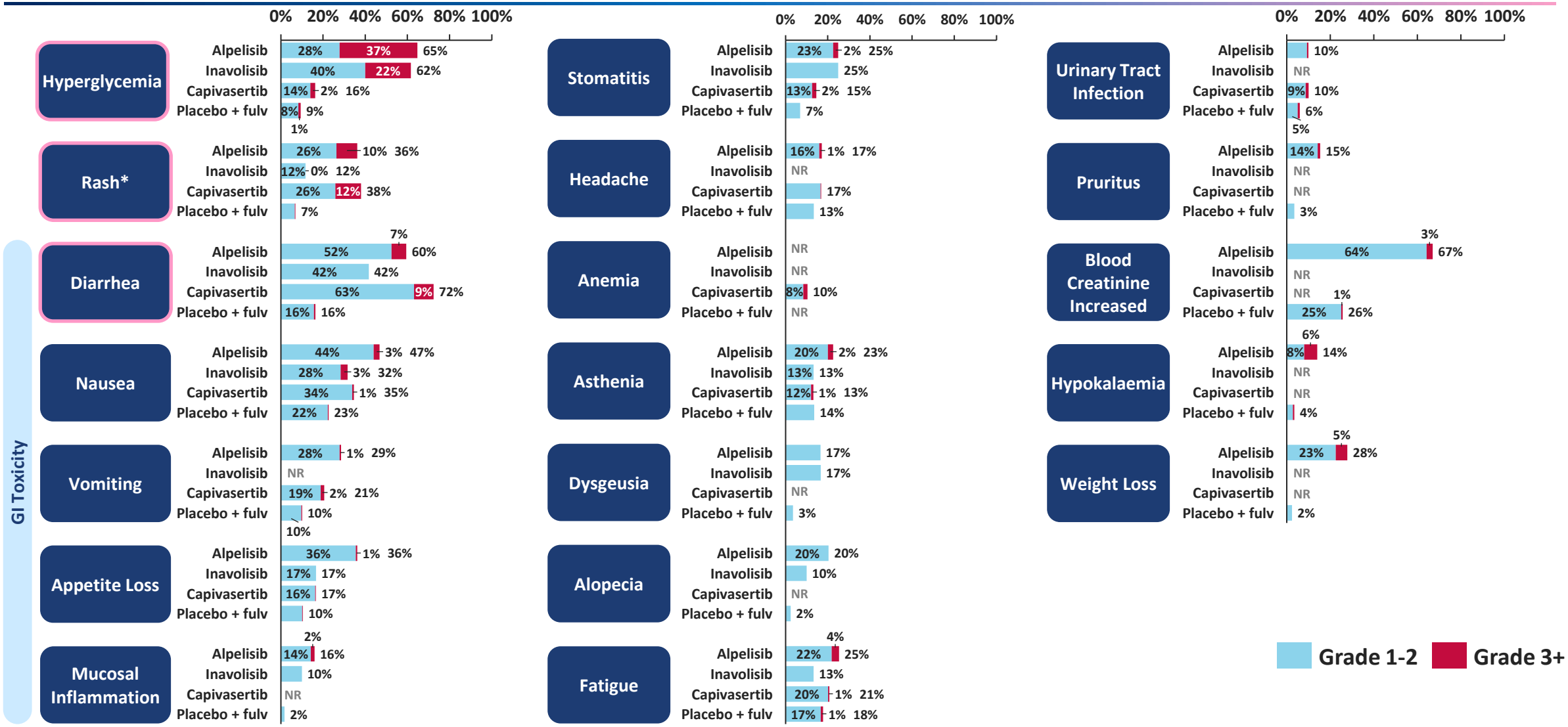
~$1B

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

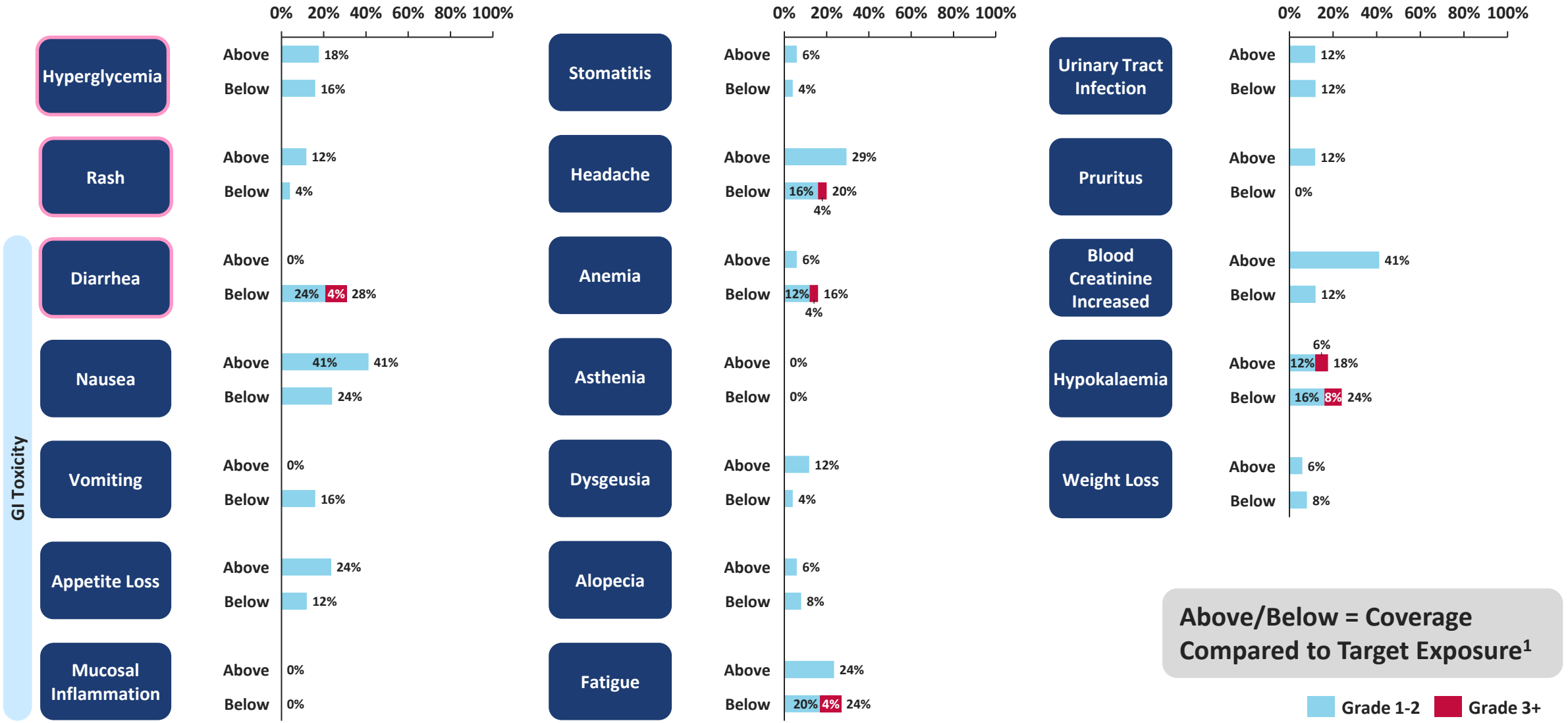


Tolerability Profile of Non-Selective Inhibitors



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