



# RELAY<sup>®</sup>

THERAPEUTICS

**RLY-2608 Data**

**September 9, 2024**

*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 Relay Therapeutics' strategy, business plans and focus; the progress and timing of the clinical development of the programs across Relay Therapeutics' portfolio; the expected therapeutic benefits and potential efficacy and tolerability of RLY-2608, both as a monotherapy and in combination with other agents, and its other programs, including lirafugratinib as well as the clinical data for RLY-2608; the interactions with and approval of regulatory authorities and any related approvals; the potential market opportunity for RLY-2608; and the expected strategic benefits under Relay Therapeutics' clinical trial collaboration with Pfizer; the cash runway projection and the expectations regarding Relay Therapeutics' use of capital and expenses. 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 and conflicts, or public health epidemics or outbreaks of an infectious disease on countries or regions in which we have operations or do business, as well as on the timing and anticipated results of our clinical trials, strategy, future operations and profitability; the delay or pause of any current or planned clinical trials or the development of our drug candidates; the risk that the preliminary or interim 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 and that interim and early clinical data may change as more patient data become available and are subject to audit and verification procedures; 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*

**1**

**ReDiscover Trial Update – RLY-2608 + Fulvestrant Doublet Data**

**2**

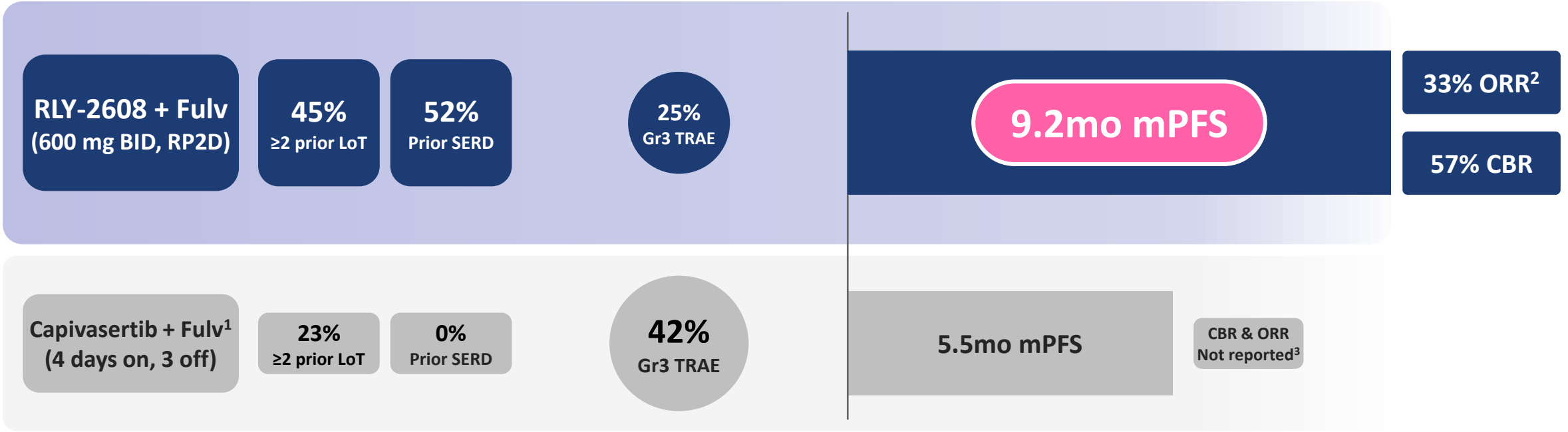
**RLY-2608 – Next steps**

**RLY-2608 abstract submitted to San Antonio Breast Cancer Symposium**

# RLY-2608 – Interim Clinical Data Show Clinically Meaningful PFS



**More Heavily Pre-Treated Patients**      **Favorable Tolerability**      **Favorable Efficacy**  
*PIK3CAmut, HR+/HER2- Advanced / Metastatic Breast Cancer (post CDK4/6)*



**Interim RLY-2608 safety and efficacy data supportive of pivotal trial in 2L Breast Cancer against capivasertib**

1. CAPitello-291: Turner N Engl J Med 2023; 388:2058-2070; 2. ORR includes 2 ongoing unconfirmed partial response as of the data cut-off. After the data cut-off, one uPR patient has confirmed and the other uPR patient remains on treatment; Additionally, one stable disease patient has converted to an unconfirmed partial response, remains on treatment and is not included in the ORR; 3. In CAPitello-291, CBR and ORR not reported for CDK4/6-experienced patient population; ORR = objective response rate, mPFS = median progression free survival, LoT = line of therapy (metastatic setting), SoC = Standard of Care, TRAE = treatment related adverse effects, RP2D = recommended Phase 2 dose, CBR = clinical benefit rate, SERD = selective estrogen receptor degrader; Note: data shown are not from head-to-head studies, and no head-to-head studies have been conducted.

# PI3K $\alpha$ Mutations Represent a Large Commercial Opportunity

## PI3K $\alpha$ mutations represent a large commercial opportunity

Breast Cancer

~150k pts  
(prevalence<sup>1</sup>)

Vascular Malformations

~170k pts  
(prevalence<sup>2</sup>)

Non-Breast Cancer Solid Tumors

~160k pts  
(incidence<sup>3</sup>)

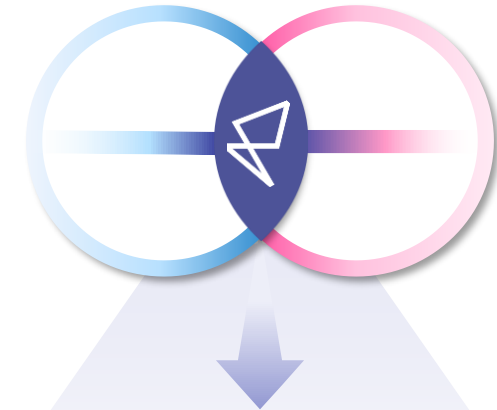
## Non-selective PI3K $\alpha$ targeting has significant limitations

— Challenging Tolerability

— Limited Efficacy

— Limited Combinability

## Relay Tx's Dynamo<sup>®</sup> Platform created mutant selective molecule



RLY-2608

# RLY-2608 – Interim Clinical Data Show Clinically Meaningful PFS



More Heavily  
Pre-Treated Patients

Favorable  
Tolerability

Favorable Efficacy  
*PIK3CA*mut, HR+/HER2- Advanced / Metastatic Breast Cancer (post CDK4/6)

RLY-2608 + Fulv  
(600 mg BID, RP2D)

45%  
≥2 prior LoT

52%  
Prior SERD

25%  
Gr3 TRAE

9.2mo mPFS

33% ORR<sup>2</sup>

57% CBR

Capivasertib + Fulv<sup>1</sup>  
(4 days on, 3 off)

23%  
≥2 prior LoT

0%  
Prior SERD

42%  
Gr3 TRAE

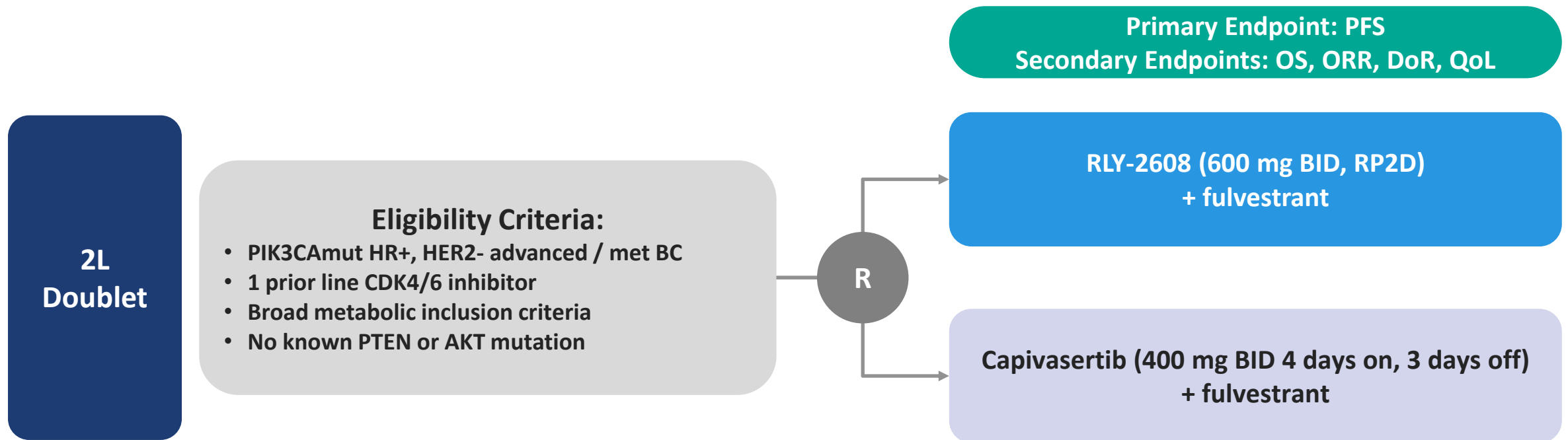
5.5mo mPFS

CBR & ORR  
Not reported<sup>3</sup>

Interim RLY-2608 safety and efficacy data supportive of pivotal trial in 2L Breast Cancer against capivasertib

1. CAPitello-291: Turner N Engl J Med 2023; 388:2058-2070; 2. ORR includes 2 ongoing unconfirmed partial response as of the data cut-off. After the data cut-off, one uPR patient has confirmed and the other uPR patient remains on treatment; Additionally, one stable disease patient has converted to an unconfirmed partial response, remains on treatment and is not included in the ORR; 3. In CAPitello-291, CBR and ORR not reported for CDK4/6-experienced patient population; ORR = objective response rate, mPFS = median progression free survival, LoT = line of therapy (metastatic setting), SoC = Standard of Care, TRAE = treatment related adverse effects, RP2D = recommended Phase 2 dose, CBR = clinical benefit rate, SERD = selective estrogen receptor degrader; Note: data shown are not from head-to-head studies, and no head-to-head studies have been conducted.

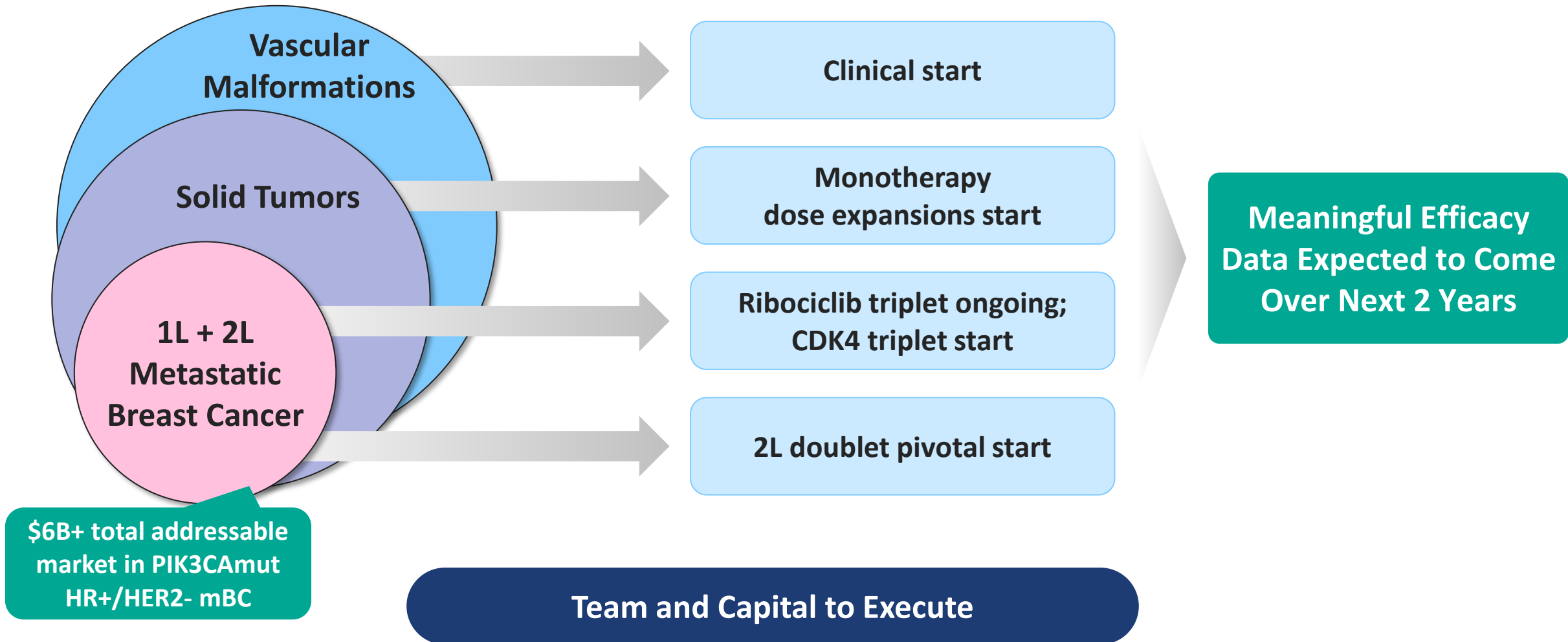
# RLY-2608 – Initial Pivotal Trial Planned for 2L Doublet in 2025\*



**2L doublet pivotal start expected in 2025**

\*Subject to discussions with regulators; eligibility criteria, endpoints, RP2D, and other aspects of trial design have not yet been finalized; OS = overall survival, DoR = duration of response, QoL = quality of life, met BC = metastatic Breast Cancer; 2L = 2<sup>nd</sup> line

# PI3K $\alpha$ Franchise - Opportunity for Multiple Value-Creating Datasets Over Next 2 Yrs





# Relay Tx – Broad Precision Medicine Pipeline



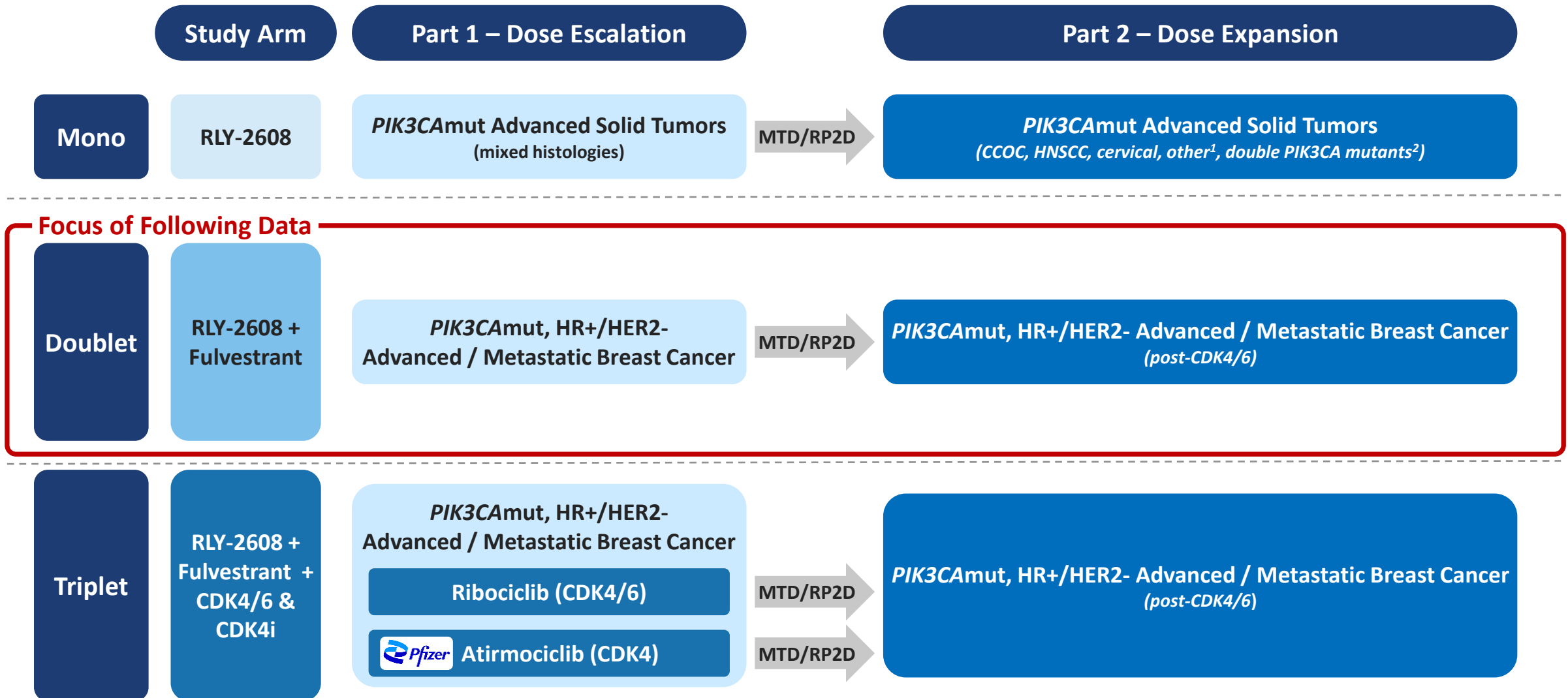
	Target	Program	Preclinical	Early Clinical	Late Clinical	
BREAST CANCER	PI3K $\alpha$	Endocrine Tx (ET) doublet	[Progress bar]			
		RLY-2608 (PI3K $\alpha$ <sup>PAN</sup> )	Ribociclib + ET triplet	[Progress bar]		
			CDK4i + ET triplet	[Progress bar]		
			Other Novel Combinations	[Progress bar]		
	CDK2	RLY-2139	Paused; IND ready			
ER $\alpha$	RLY-1013 (Degradar)	Advance to IND-ready				
GENETIC DISEASE	Fabry Disease	$\alpha$ Gal Chaperone	[Progress bar]			
	Vascular Malformations	RLY-2608 (PI3K $\alpha$ <sup>PAN</sup> )	[Progress bar]			
		Other PI3K $\alpha$ <sup>PAN</sup>	[Progress bar]			
SOLID TUMORS	NRAS	NRAS-selective Inhibitor	[Progress bar]			
	PI3K $\alpha$	RLY-2608 Monotherapy	[Progress bar]			
	FGFR2	Lirafugratinib (RLY-4008)	Seeking global commercialization partner			


**DYNAMO® PLATFORM** | 5+ unnamed research programs

**~\$688M cash as of end 2Q 2024**  
**Expected to fund current operating plan into 2H 2026**

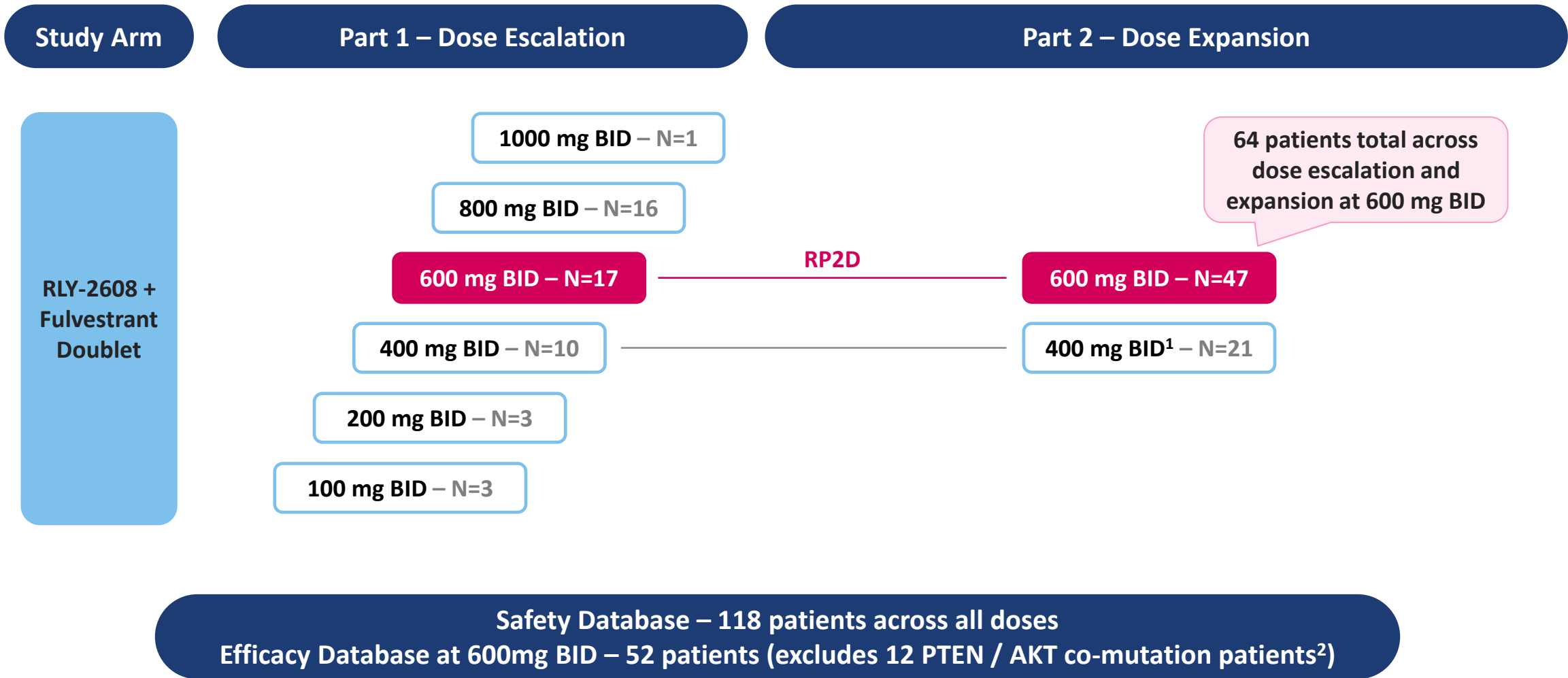
Note: IND = Investigational New Drug Application (FDA)  
© 2024 Relay Therapeutics

# RLY-2608 – ReDiscover Trial Overview



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; CCOC = clear cell ovarian cancer  
© 2024 Relay Therapeutics

# RLY-2608 – ReDiscover Trial Enrollment



1. 400mg cohort is not yet mature for efficacy analysis. Full Phase I results, including 400mg cohort, will be disclosed at a later date; 2. As defined by central ctDNA

# RLY-2608 – ReDiscover Trial Baseline Demographics



	RLY-2608 + Fulvestrant	
	All Patients (N=118)	600 mg BID (RP2D, N=64)
Age, Median (Range), Years	59.0 (34, 85)	59.0 (34, 80)
ECOG, 0 / 1, n (%)	69 (58.5) / 49 (41.5)	38 (59.4) / 26 (40.6)
<b>Local PIK3CA Baseline Results</b>		
Kinase Mutation, n (%)	56 (47.5)	31 (48.4)
Non-Kinase Mutations, n (%)	62 (52.5)	33 (51.6)
BMI $\geq$ 30 and/or HbA1c $\geq$ 5.7%, n (%)	44 (37.3)	22 (34.4)
Measurable Disease, n (%)	83 (70.3)	42 (65.6)
Patients with Visceral Metastases, n (%) <sup>1</sup>	75 (63.6)	38 (59.4)
<b>Prior Lines of Therapy in Advanced Setting</b>		
1, n (%)	59 (50.0)	35 (54.7)
2+, n (%)	59 (50.0)	29 (45.3)
<b>Prior Therapies in Advanced Setting</b>		
CDK4/6, n (%) <sup>2</sup>	118 (100.0)	64 (100.0)
Fulvestrant or Novel SERD, n (%)	66 (55.9)	33 (51.6)
Chemo / ADC, n (%)	30 (25.4)	16 (25.0)
ESR1 Mutation (Central Read) <sup>3</sup> , n (%)	40 (36.0)	18 (29.5)

1. Visceral metastatic sites include lung, liver, brain, pleural, peritoneal involvement; 2. Two patients received prior CDK4/6 in the adjuvant setting which is allowed per protocol; 3. Percentage was based on pts with evaluable ctDNA data at baseline;

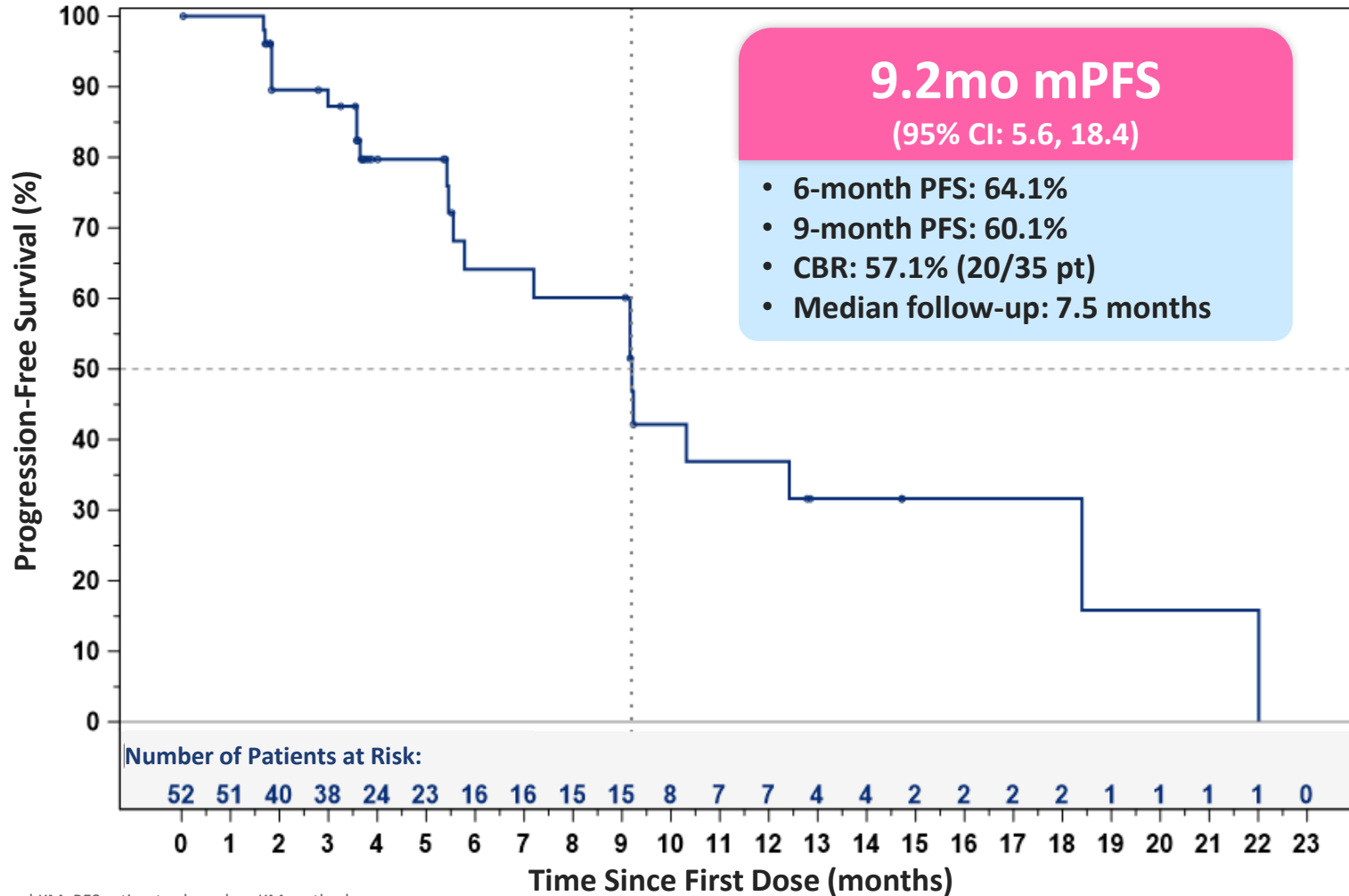
ECOG = Eastern Cooperative Oncology Group performance status

© 2024 Relay Therapeutics

# RLY-2608 – Efficacy: Median PFS 9.2 Months



## RLY-2608 600 mg BID (RP2D) + Fulvestrant Excluding PTEN / AKT Co-Mutations (N=52)

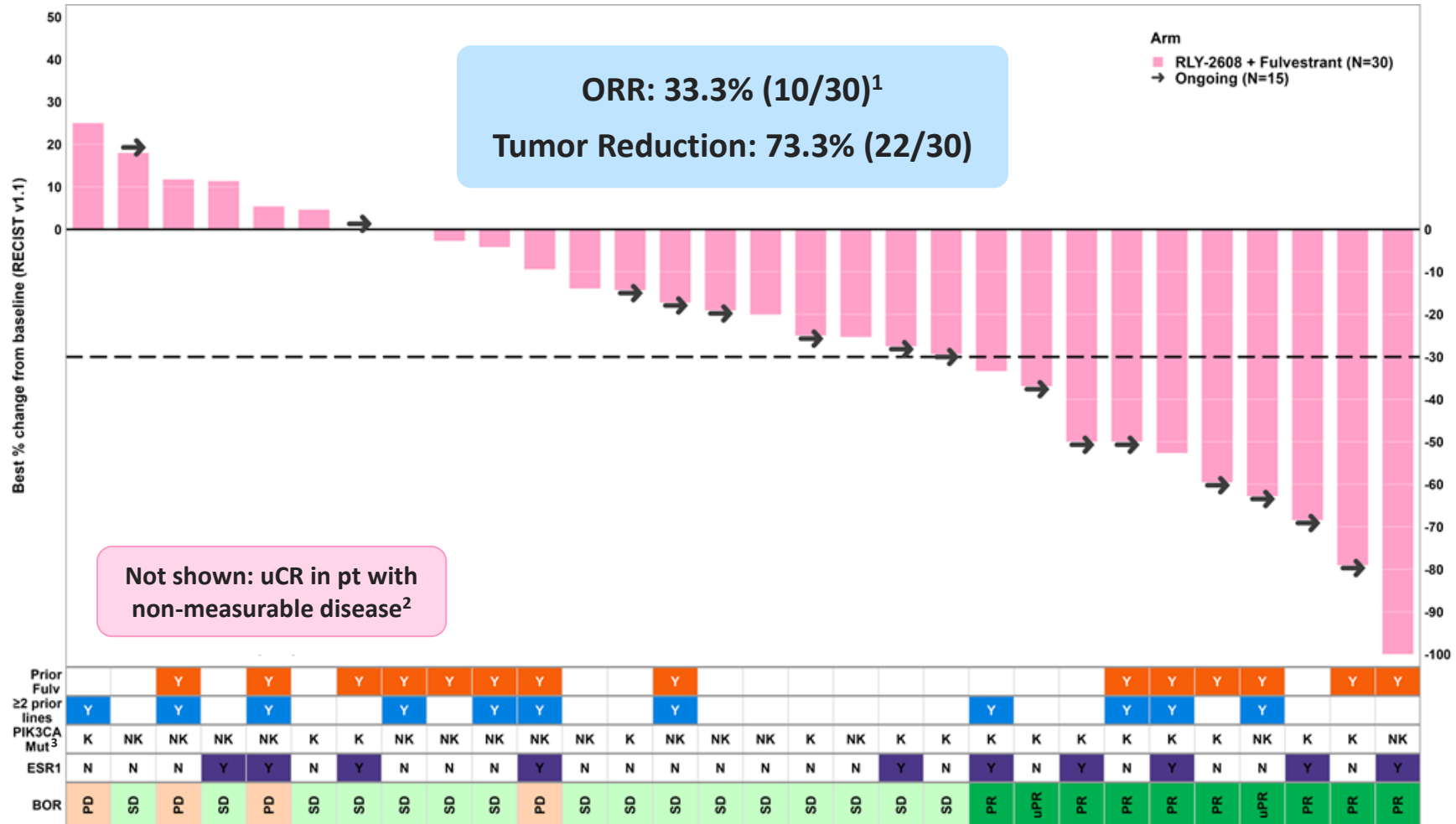


Note: Follow-up estimated based on reversed KM. PFS estimates based on KM methods.  
© 2024 Relay Therapeutics

# RLY-2608 – Efficacy: ORR 33%

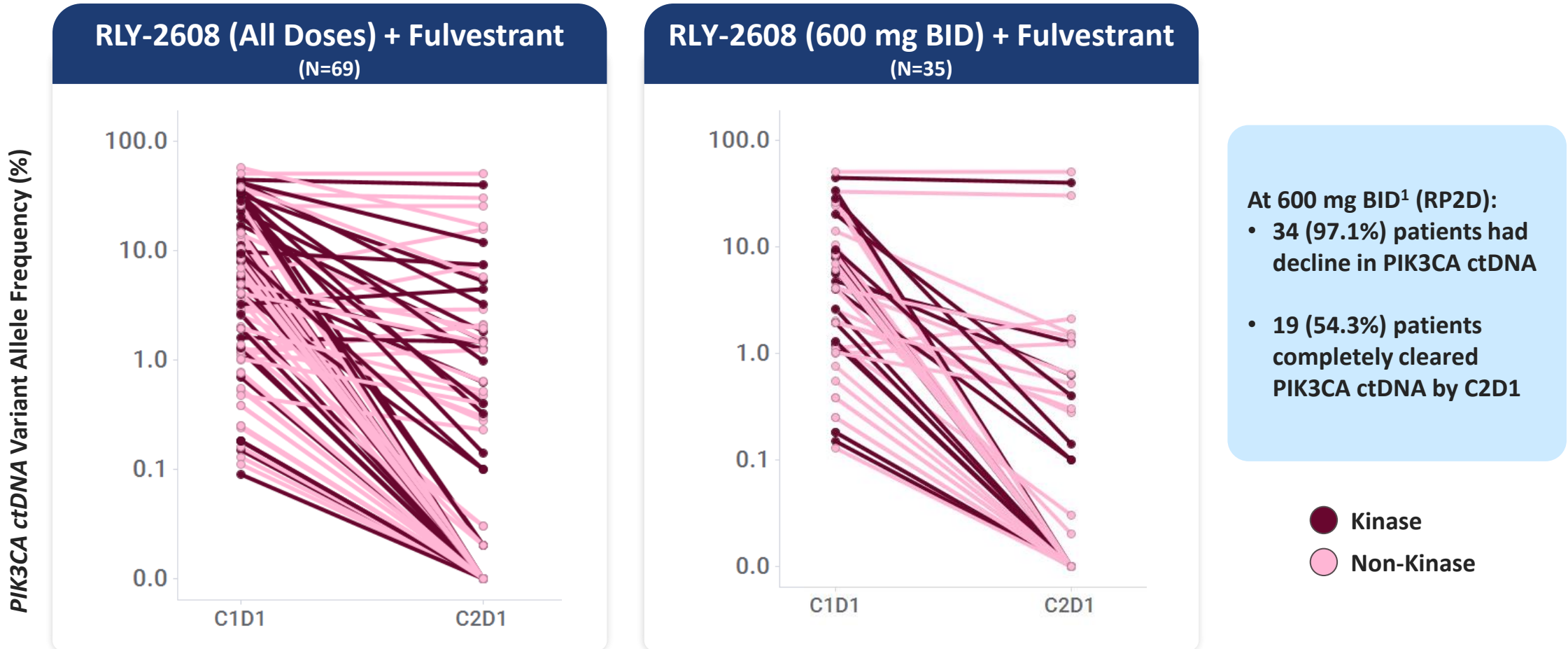


## RLY-2608 600 mg BID (RP2D) + Fulvestrant Excluding PTEN / AKT Co-Mutations – Measurable Disease (N=30)



1. ORR includes 2 ongoing unconfirmed partial response as of the data cut-off. After the data cut-off, one uPR patient has confirmed and the other uPR patient remains on treatment; Additionally, one stable disease patient has converted to an unconfirmed partial response, remains on treatment and is not included in the ORR; 2. Patient confirmed post data cut off and is not included in the ORR; 3. PIK3CA mutation: “K” = Kinase domain mutation, “NK” = Non-Kinase domain mutation; uCR = unconfirmed complete response

# RLY-2608 – Efficacy: ctDNA Clearance



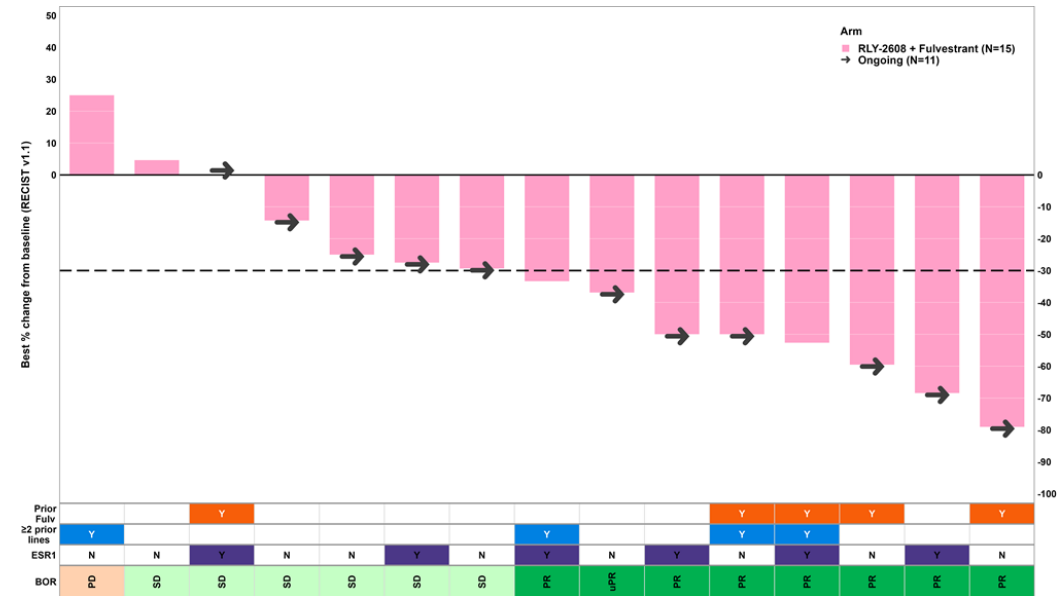
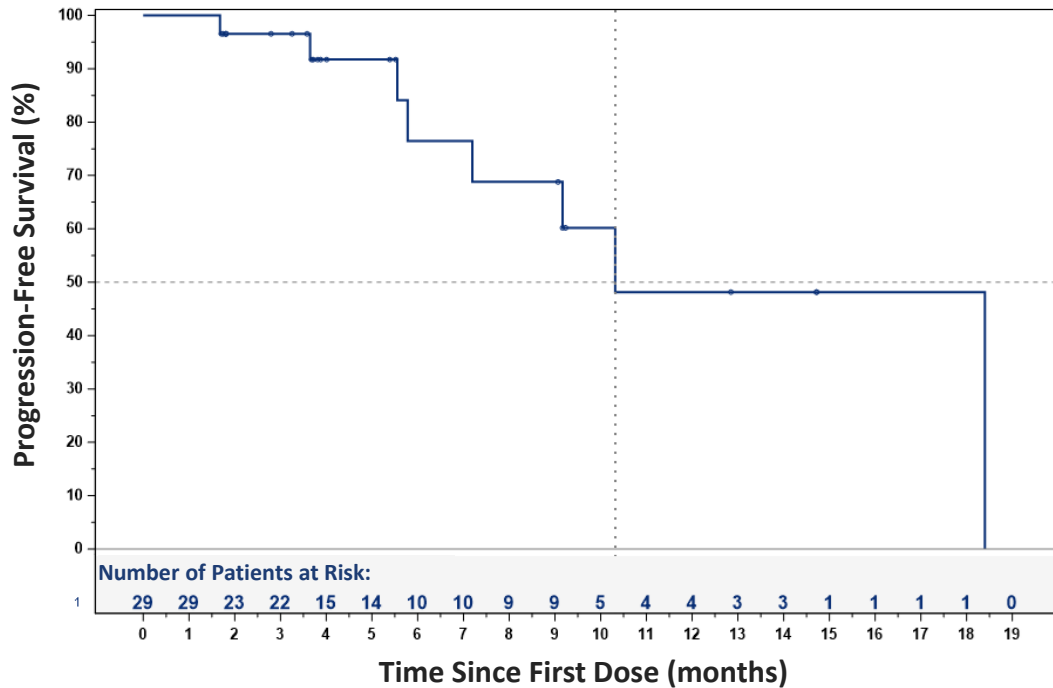
1. N=35 patients without PTEN/AKT co-alterations who have detectable PIK3CA at baseline and a paired C1D1-C2D1 ctDNA result are presented  
© 2024 Relay Therapeutics

# RLY-2608 – Efficacy: Kinase Mutations mPFS 10.3 Months, ORR 53%



## RLY-2608 600 mg BID (RP2D) + Fulvestrant PIK3CA Kinase mutations, excluding PTEN / AKT co-mutations (N=29)

## RLY-2608 600 mg BID (RP2D) + Fulvestrant PIK3CA Kinase mutations, excluding PTEN / AKT co-mutations (N=15)



**10.3mo mPFS**  
(95% CI: 5.8, NR)

**53.3% ORR**  
(8/15 pt)<sup>1</sup>

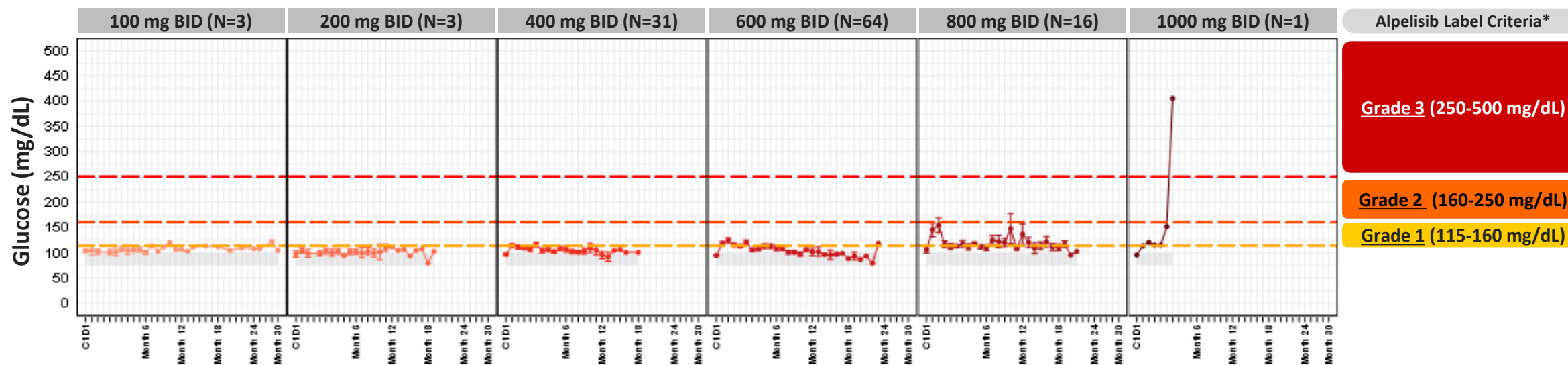
1. ORR includes 1 ongoing unconfirmed partial response as of the data cut-off. After the data cut-off, this 1 uPR patient has confirmed and remains on treatment; Additionally, one stable disease patient has converted to an unconfirmed partial response, remains on treatment and is not included in the ORR



# RLY-2608 – Tolerability: Limited Observed Impact on Glucose Homeostasis



## RLY-2608 + Fulvestrant



Note: \*Based on CTCAE version 4 criteria; Data represent mean per cohort +/- standard deviation; Source: Central lab analysis

# RLY-2608 – Tolerability: TRAEs



		All Patients (N=118)		600mg BID (RP2D, N=64)	
		All Gr	Gr3	All Gr	Gr3
<b>Any TRAE</b>		<b>91.5%</b>	<b>20.3%</b>	<b>93.8%</b>	<b>25.0%</b>
<b>TRAEs ≥15% of 600 mg BID</b>	<b>Hyperglycemia<sup>1</sup></b>	<b>42.4%</b>	<b>1.7%</b>	<b>46.9%</b>	<b>1.6%</b>
	<b>Nausea</b>	<b>39.8%</b>	<b>0.8%</b>	<b>48.4%</b>	<b>1.6%</b>
	<b>Creatinine Increased<sup>2</sup></b>	<b>33.9%</b>	<b>0%</b>	<b>32.8%</b>	<b>0%</b>
	<b>Fatigue<sup>1</sup></b>	<b>38.1%</b>	<b>7.6%</b>	<b>32.8%</b>	<b>7.8%</b>
	<b>Diarrhea</b>	<b>29.7%</b>	<b>1.7%</b>	<b>34.4%</b>	<b>3.1%</b>
	<b>Decreased Appetite</b>	<b>16.1%</b>	<b>0%</b>	<b>18.8%</b>	<b>0%</b>
	<b>Hypokalemia<sup>1</sup></b>	<b>15.3%</b>	<b>1.7%</b>	<b>17.2%</b>	<b>1.6%</b>
<b>Other select TRAEs</b>	<b>Rash<sup>1</sup></b>	<b>11.9%</b>	<b>0.8%</b>	<b>10.9%</b>	<b>1.6%</b>
	<b>Stomatitis</b>	<b>3.4%</b>	<b>0.8%</b>	<b>4.7%</b>	<b>0%</b>

30% Gr1 hyperglycemia (no intervention required)

**No Gr4-5 TRAEs**

1: Hyperglycemia includes the MedDRA v26.0 Preferred Terms (PTs): Hyperglycemia, Blood Glucose Increased, Glucose Tolerance Impaired; Fatigue includes the PTs: Fatigue and Asthenia; Hypokalemia includes the PTs: Hypokalemia and blood potassium decreased; Rash includes the PTs: Rash, Rash Macular, Rash Maculo-Papular; 2. No acute kidney injury reported

# RLY-2608 – Tolerability: Dose Intensity and Modifications



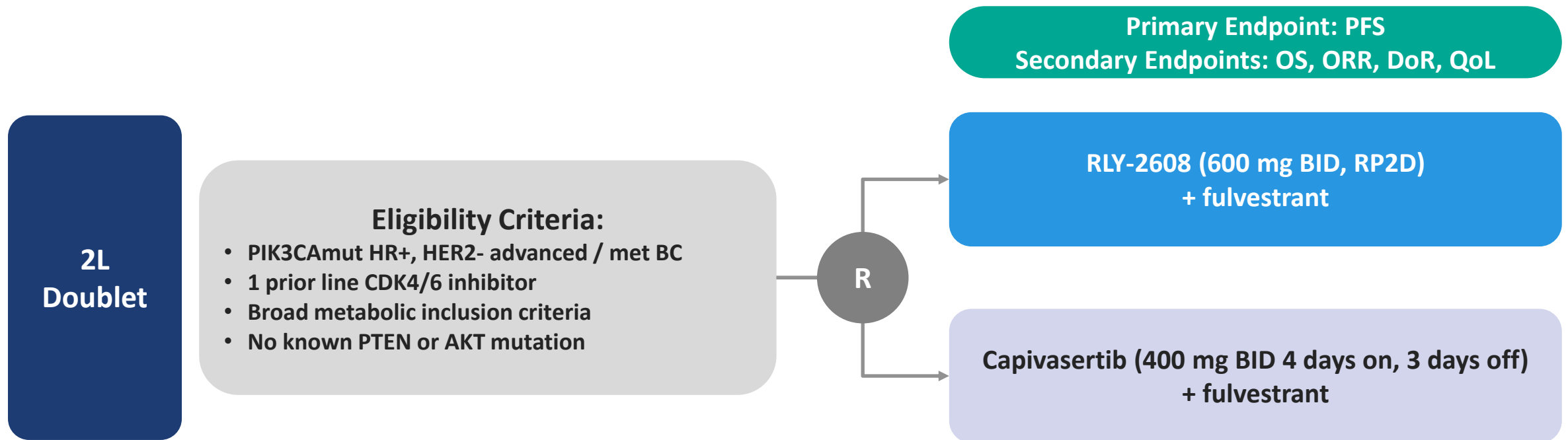
		All Patients (N=118)	600mg BID (RP2D, N=64)
<b>Dose Intensity</b>	Relative Dose Intensity (%), Median	97.54	95.16
<b>Dose Modifications Due to TRAE</b>	Dose Reduction, n (%)	36 (30.5)	23 (35.9)
	Dose Interruption, n (%)	49 (41.5)	27 (42.2)
	Dose Discontinuation, n (%)	7 (5.9)	2 (3.1)
<b>TRAEs Leading to Dose Reduction</b>	Fatigue*	11 (9.3)	5 (7.8)
	Blood Creatinine Increased	8 (6.8)	3 (4.7)
	Diarrhea	6 (5.1)	3 (4.7)

Grade 1 pruritis;  
Grade 1 nausea and  
loss of appetite

**Maintained 95% dose intensity with very low TRAE discontinuations at 600mg BID**

Note: \* Fatigue includes the Preferred Terms: Fatigue and Asthenia; TRAEs leading to Dose Reduction in more than 2 patients within 600 mg BID are presented.

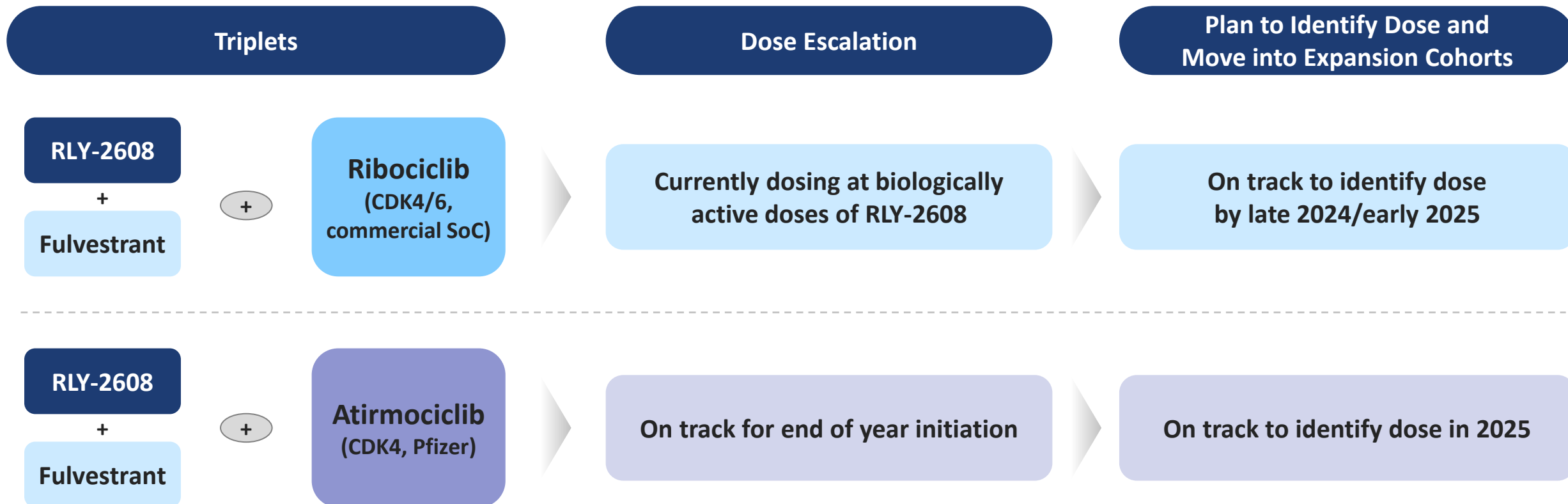
# RLY-2608 – Initial Pivotal Trial Planned for 2L Doublet in 2025\*



**2L doublet pivotal start expected in 2025**

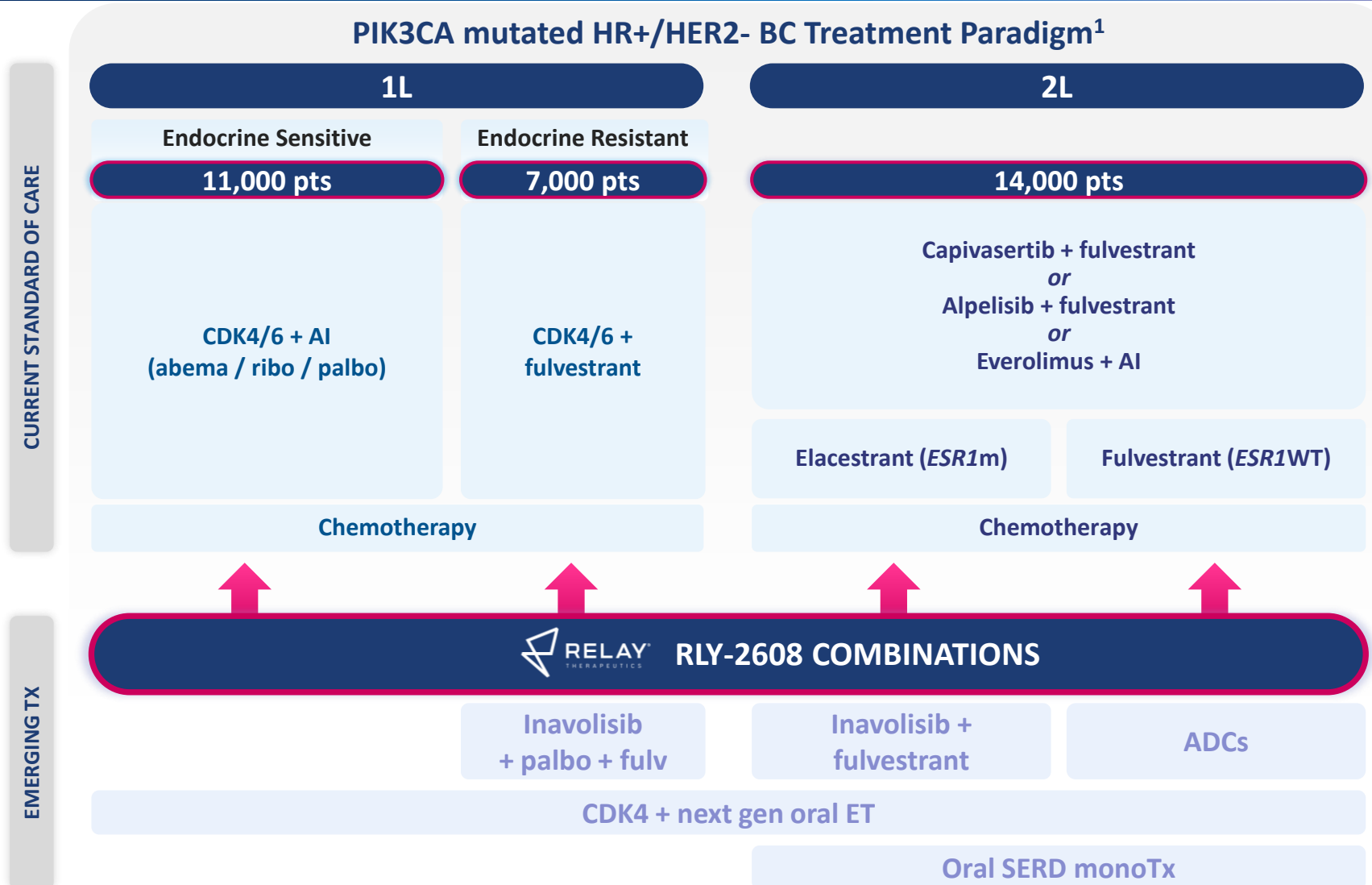
\*Subject to discussions with regulators; eligibility criteria, endpoints, RP2D, and other aspects of trial design have not yet been finalized; OS = overall survival, DoR = duration of response, QoL = quality of life, met BC = metastatic Breast Cancer; 2L = 2<sup>nd</sup> line

# RLY-2608 – On Track to Realize 1L Potential with Triplet Combinations



**Phase 1 Aim for Triplets: Demonstrate safety, tolerability and preliminary efficacy with both current generation CDK4/6 and next-gen CDK4 to enable pivotal development potential in both**

# Breast Cancer – Large Market in Current and Emerging Standards of Care



**\$6B+**  
 Current PI3Kα Pathway  
 Total Addressable Market<sup>2</sup>  
 (Metastatic HR+/HER2-  
 Breast Cancer)

1. Prevalent US patient population with a PIK3CA mutation in each line of therapy (Global Data HR+/HER2- Breast Cancer Global Forecast, November 2023; 3rd party source for alteration rate); 2. Relay Tx PIK3CA internal market forecast (patient-based – US, EU5, Japan). Forecast includes estimates for genetic testing, class share, market access, compliance, duration of therapy and assumes current PIK3CA therapy net price (primary sources: SEER; GloboCan; Global Data; Evaluate Pharma; DRG Market Forecast; PIK3CAi PIs)  
 © 2024 Relay Therapeutics

# PI3K $\alpha$ Inhibitors – Tolerability Profiles

Data below are not from head-to-head studies. Cross-trial data interpretation should be considered with caution as it is limited by differences in study population, design and many other factors.

## Doublet Combination Regimens

**Inavolisib + fulvestrant**  
*not approved*

**Alpelisib + fulvestrant**  
*approved 2019*

**Capivasertib + fulvestrant**  
*approved 2023*

**RLY-2608 + fulvestrant**  
*(600mg BID, RP2D)*

**Data Benchmark**

	Ph1b Arm D <sup>1</sup> (n=60)	BYLieve <sup>2</sup> (n=127)	FDA Label <sup>3</sup> (n=355)	ReDiscover (n=64)
--	-----------------------------------	---------------------------------	-----------------------------------	----------------------

**All Grade 3+ TRAEs**



**Grade 3+ Hyperglycemia**



**Dose Discontinuation due TRAEs**



Discontinuous dosing:  
4 days on, 3 days off

34% of pt BMI  $\geq$ 30  
and/or HbA1c  $\geq$ 5.7%

# PI3Kα Inhibitors – Tolerability Profiles

Data below are not from head-to-head studies. Cross-trial data interpretation should be considered with caution as it is limited by differences in study population, design and many other factors.

## Doublet Combination Regimens

**Inavolisib + fulvestrant**  
*not approved*

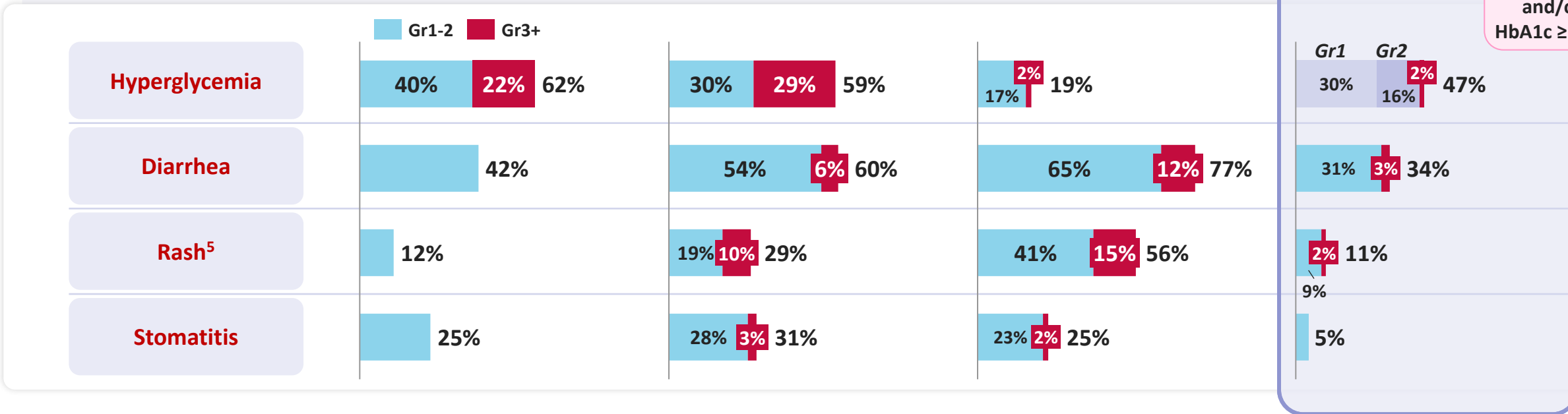
**Alpelisib + fulvestrant**  
*approved 2019*

**Capivasertib + fulvestrant**  
*approved 2023*

**RLY-2608 + fulvestrant**  
*(600mg BID, RP2D)*

Data Benchmark	Ph1b Arm D <sup>1</sup> (n=60)	BYLieve <sup>2</sup> (n=127)	FDA Label <sup>3</sup> (n=355)	ReDiscover (n=64)
----------------	-----------------------------------	---------------------------------	-----------------------------------	----------------------

HbA1c Enrollment Criteria	<7%	≤6.4%	<8% <sup>4</sup>	<7% <i>34% of pt BMI ≥30 and/or HbA1c ≥5.7%</i>
---------------------------	-----	-------	------------------	--



1. SABCS 2021 #P5-17-05; 2. Rugo 2021 Lancet Oncol 22:489; 3. FDA Prescribing Information Document; 4. per CAPItello-291 enrollment criteria; 5. Rash for capivasertib references Cutaneous Adverse Reactions grouped term includes a number of preferred terms listed in FDA prescribing information  
Note: These data are derived from different clinical trials at different points in time, with differences in molecule composition, trial design and patient populations. As a result, cross-trial comparisons cannot be made, and no head-to-head clinical trials have been conducted.



# PI3K $\alpha$ Inhibitors – Efficacy Profiles



Data below are not from head-to-head studies. Cross-trial data interpretation should be considered with caution as it is limited by differences in study population, design and many other factors.

## Doublet Combination Regimens

**Inavolisib + fulvestrant**

*not approved*

**Alpelisib + fulvestrant**

*approved 2019*

**Capivasertib + fulvestrant**

*approved 2023*

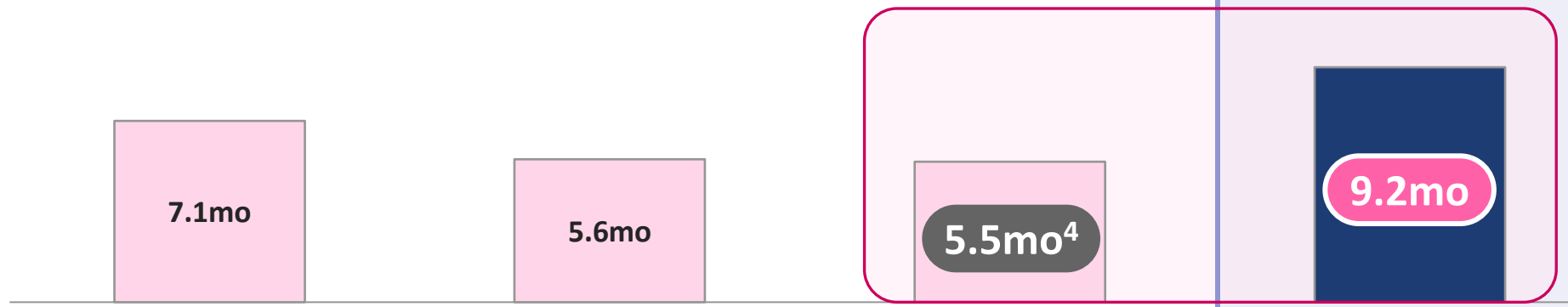
**RLY-2608 + fulvestrant**

*(600mg BID, RP2D)*

### Data Benchmark

	Ph1b Arm D <sup>1</sup> (N=60)	BYLieve Cohort C <sup>2</sup> (N=126)	CAPitello-291 <sup>3,6</sup> (N=355)	ReDiscover (N=52)
% pt with $\geq 2$ prior LoT	57%	63%	23%	44%
% prior SERD <sup>5</sup>	47%	33%	0%	52%

**mPFS**



**CBR**

48%

37%

56%

57%

**ORR**

19%

24%

Capi ORR & CBR include 30% of pts who are CDK4/6-naïve

26%<sup>6</sup>

33%<sup>7</sup>

1. SABCS 2021 #P5-17-05 (n=60); 2. SABCS 2021 #PD-13-05; 3. Turner N Engl J Med 2023; 388:2058-2070 (n=355); 4. 5.5mo mPFS reported in CDK4/6-experienced patient sub-population of CAPitello-291; 5. Prior SERD includes fulvestrant and next-generation SERDs; 6. ORR as reported in FDA Label (from CAPitello-291); 7. ORR includes 2 ongoing unconfirmed partial response as of the data cut-off. After the data cut-off, one uPR patient has confirmed and the other uPR patient remains on treatment; Additionally, one stable disease patient has converted to an unconfirmed partial response, remains on treatment and is not included in the ORR; Note: These data are derived from different clinical trials at different points in time, with differences in molecule composition, trial design and patient populations. As a result, cross-trial comparisons cannot be made, and no head-to-head clinical trials have been conducted.

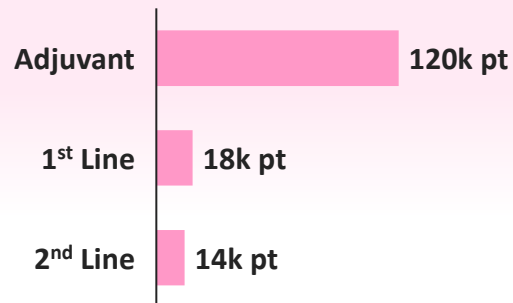
# Relay Tx's PI3K $\alpha$ Franchise – Large Opportunities Across 3 Pillars



## PIK3CA mutant HR+/HER2- Breast Cancer

**~150k Patients**  
(US prevalence)<sup>1</sup>

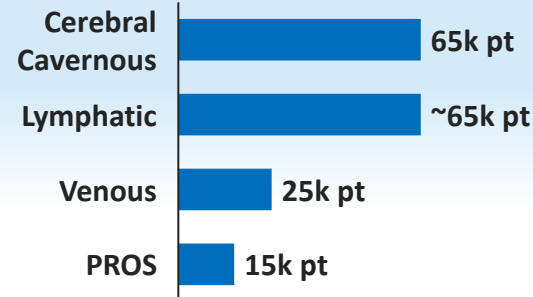
RLY-2608



## PIK3CA mutant Vascular Malformations

**~170k Patients**  
(US prevalence)<sup>2</sup>

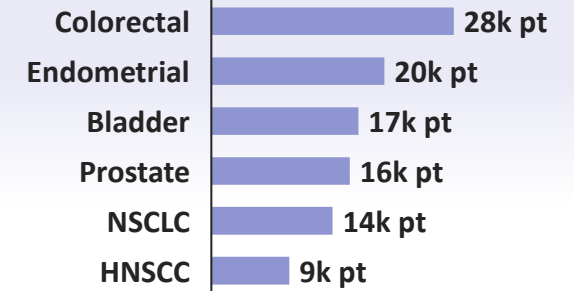
Potential for initial POC with RLY-2608,  
then distinct molecule for pivotal



## PIK3CA mutant Other Solid Tumors

**~160k Patients**  
(US incidence)<sup>3</sup>

RLY-2608



### Anticipated Next Steps

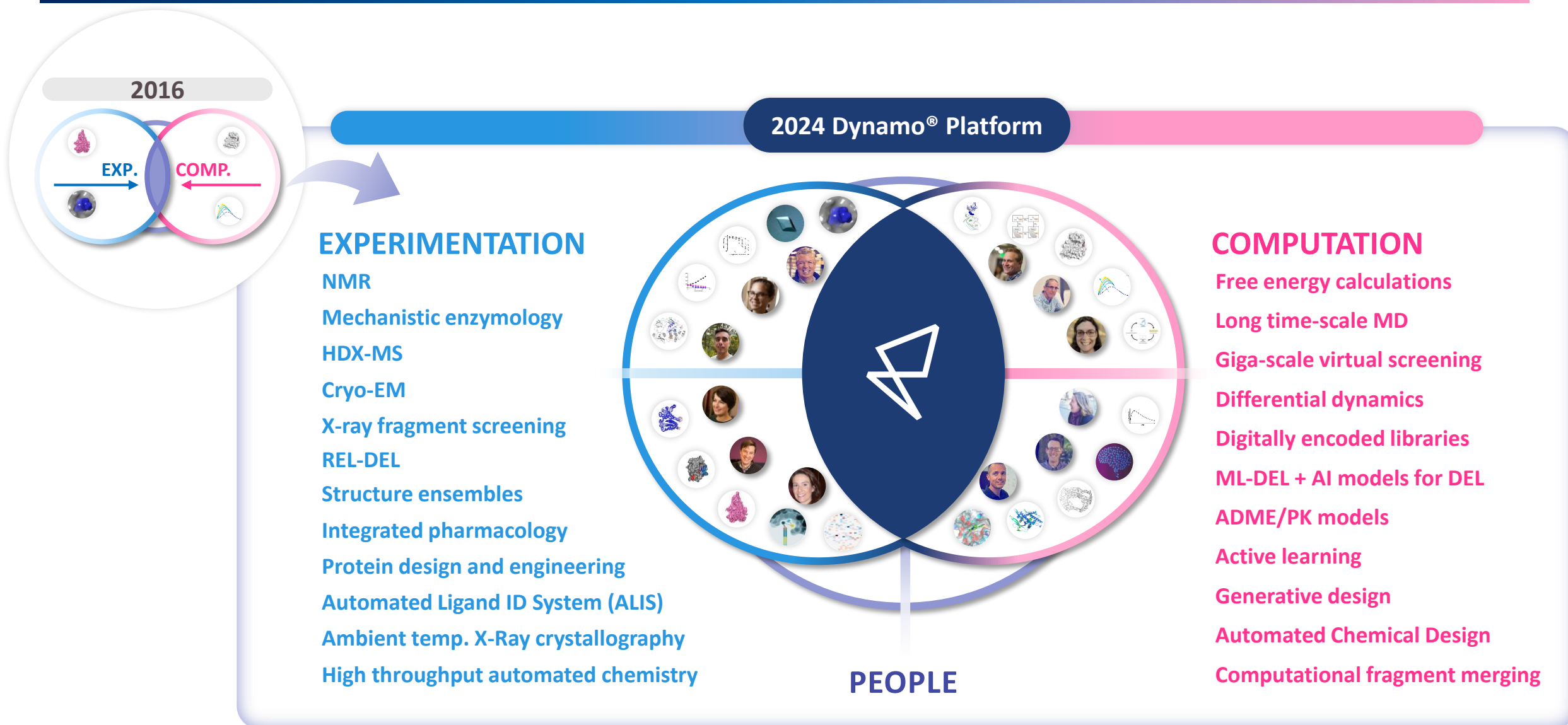
CDK4/6 triplet data – 2024  
CDK4 triplet clinical start – 2024  
CDK4/6 triplet expansion start – 1H25  
2L doublet pivotal start – 2025

Clinical start – Q1 2025

Open monotherapy  
dose expansion – YE 2024

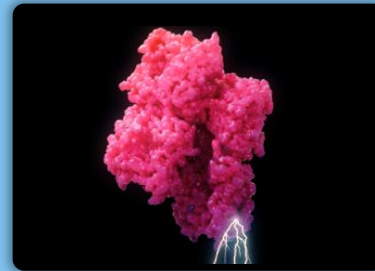
1. Prevalent US patient population with a PIK3CA mutation in each line of therapy (Global Data HR+/HER2- Breast Cancer Global Forecast, November 2023; 3rd party source for alteration rate); 2. Prevalent US patient population of vascular malformation patients with a PIK3CA mutation (multiple sources); 3. Incident US patient population solid tumors annually with a PIK3CA mutation (SEER; 3rd party source for alteration rate, May 2024); POC = proof of concept; PROS = PIK3CA Related Overgrowth Spectrum, NSCLC = non-small cell lung cancer, HNSCC = hand and neck squamous cell carcinoma  
© 2024 Relay Therapeutics ReDiscover preliminary data as of 08/12/2024 26

# Relay Tx's Dynamo<sup>®</sup> – Productive Computationally Enabled Platform



## GENETIC DISEASE

### Fabry Disease



## SOLID TUMORS

### NRAS-Driven Solid tumors



Program Updates

1<sup>st</sup> non-inhibitory  
αGal chaperone

1<sup>st</sup> NRAS-selective  
inhibitor

Large US Opportunity

~8,000 pts<sup>1</sup>  
*(chronic treatment)*

\$2B  
current  
market<sup>3</sup>

~28,000 pts<sup>2</sup>

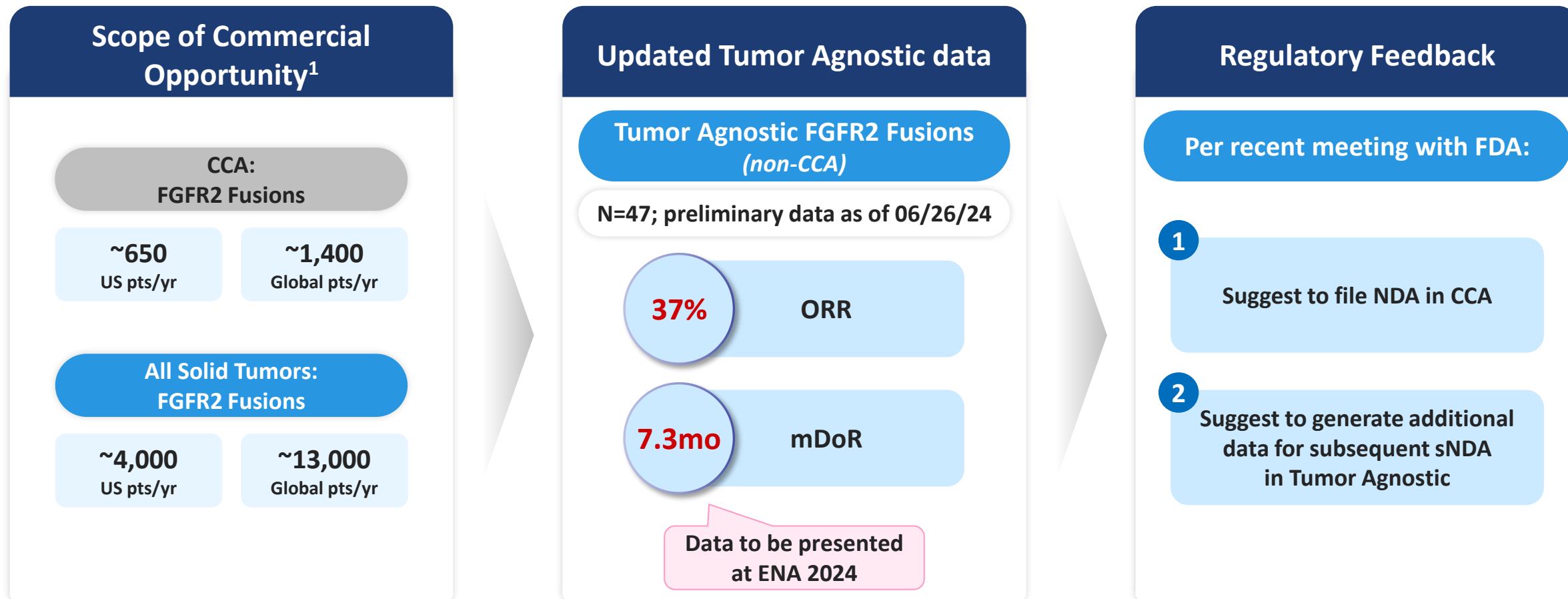
Anticipated Milestones

Clinical start in 2H 2025

Clinical start in 2H 2025

1. Prevalence of Fabry patients (National Fabry Disease Foundation, Jan 2024); 2. Newly diagnosed (incident) solid tumors with an NRAS mutation, excluding melanoma stages 0-II (SEER, 3rd party source for alteration rate, Jan 2024); 3. Fabry disease forecasted 2024 market size per EvaluatePharma, includes Galafold® and ERTs (May 2024)  
© 2024 Relay Therapeutics

# Lirafugratinib (RLY-4008) – Updated Data and Next Steps



**Next Step: Seek global commercialization partner for lirafugratinib**

1. Based on annual number of patient deaths due to expected later-line use. Global figure includes U.S., EU5, Japan.; Sources: SEER 2023, Global Cancer Observatory 2022

# Relay Tx – Broad Precision Medicine Pipeline



	Target	Program	Preclinical	Early Clinical	Late Clinical	
BREAST CANCER	PI3K $\alpha$	Endocrine Tx (ET) doublet	[Progress bar]			
		RLY-2608 (PI3K $\alpha$ <sup>PAN</sup> )	Ribociclib + ET triplet	[Progress bar]		
		CDK4i + ET triplet	[Progress bar]			
		Other Novel Combinations	[Progress bar]			
	CDK2	RLY-2139	Paused; IND ready			
ER $\alpha$	RLY-1013 (Degradar)	Advance to IND-ready				
GENETIC DISEASE	Fabry Disease	$\alpha$ Gal Chaperone	[Progress bar]			
	Vascular Malformations	RLY-2608 (PI3K $\alpha$ <sup>PAN</sup> )	[Progress bar]			
		Other PI3K $\alpha$ <sup>PAN</sup>	[Progress bar]			
SOLID TUMORS	NRAS	NRAS-selective Inhibitor	[Progress bar]			
	PI3K $\alpha$	RLY-2608 Monotherapy	[Progress bar]			
	FGFR2	Lirafugratinib (RLY-4008)	Seeking global commercialization partner			

**DYNAMO® PLATFORM** | 5+ unnamed research programs

# Relay Tx – Anticipated Milestones 2024-25



## BREAST CANCER PORTFOLIO MILESTONES

PI3K $\alpha$   
*RLY-2608*

Doublet 2L pivotal trial start – 2025

Ribociclib triplet data – 2024

Ribociclib triplet expansion start – 1H25

CDK4i triplet clinical start – 2024

## GENETIC DISEASE PORTFOLIO MILESTONES

Vascular Malformations  
*RLY-2608*

Clinical start – 1Q 2025

Fabry Disease  
*Pre-clinical*

Clinical start – 2H 2025

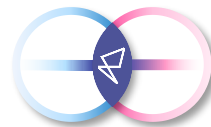
## SOLID TUMORS PORTFOLIO MILESTONES

PI3K $\alpha$   
*RLY-2608*

Open monotherapy dose expansion – YE24

NRAS  
*Pre-clinical*

Clinical start – 2H 2025

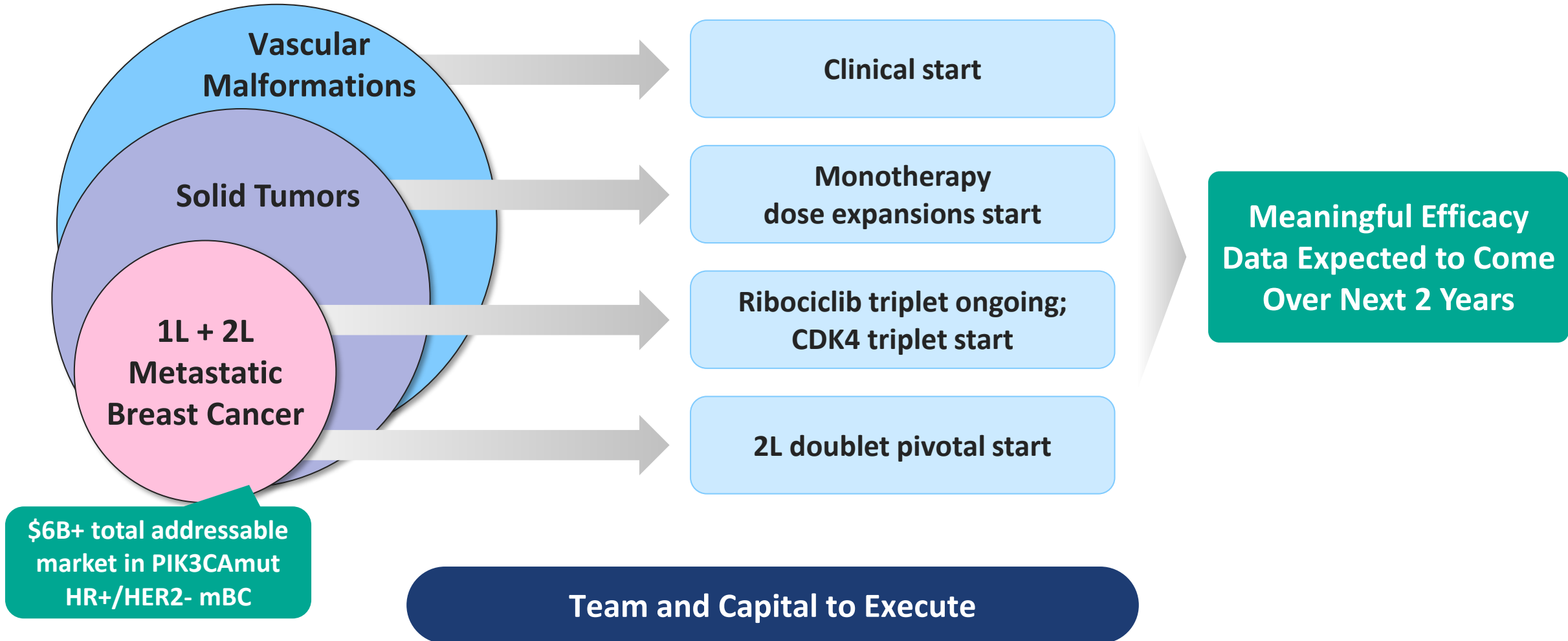


DYNAMO<sup>®</sup> PLATFORM

5+ unnamed research programs

~\$688M cash as of end 2Q 2024  
Expected to fund current operating plan into 2H 2026

# PI3K $\alpha$ Franchise - Opportunity for Multiple Value-Creating Datasets Over Next 2 Yrs



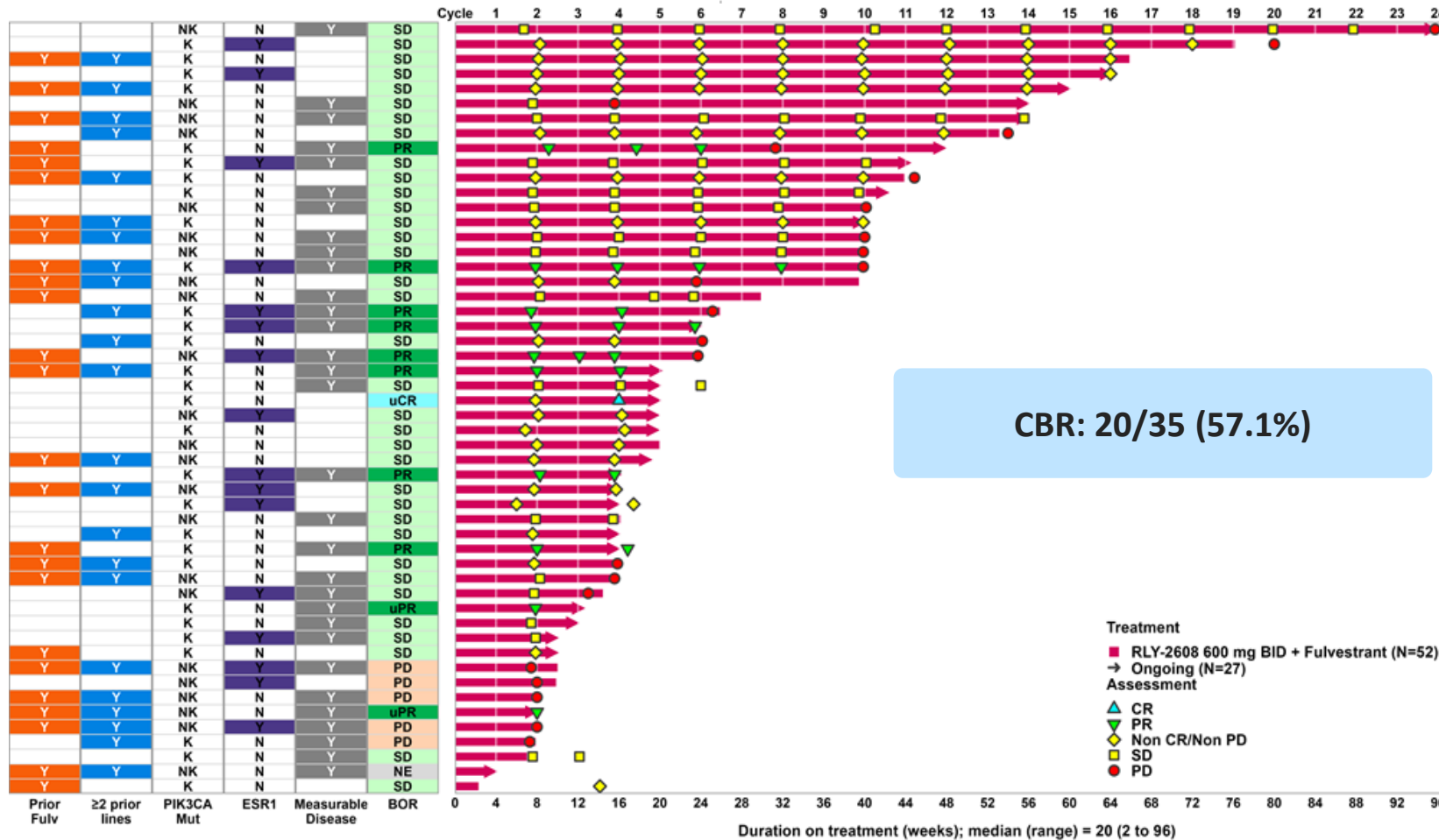




# RLY-2608 – Efficacy: 57.1% CBR



## RLY-2608 600 mg BID (RP2D) + Fulvestrant Excluding PTEN / AKT Co-Mutations (N=52)



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