



RELAY[®]
THERAPEUTICS

J.P. Morgan Conference Presentation
January 2025

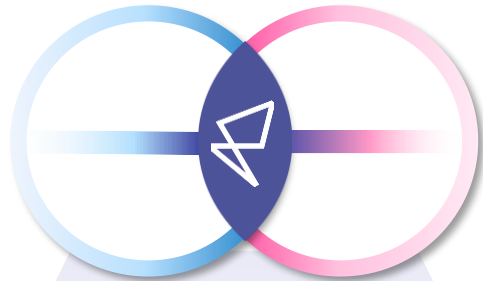
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Productive Platform & Strong Balance Sheet



8 DCs & 4 INDs



2 clinical POC datasets



~\$840M cash
as of end 3Q 2024

Anticipated 2025 Corporate Milestones

Breast Cancer
RLY-2608

- Pivotal trial start – 2025
- Full Ph1-2 data – 2025

Vascular Malformations
RLY-2608

Clinical start – 1Q 2025

NRAS
Pre-clinical

Clinical start – 2H 2025

Fabry Disease
Pre-clinical

Clinical start – 2H 2025

Progress 4 unnamed research programs

RLY-2608 Unlocks Large Breast Cancer Market



Significant Breast Cancer Commercial Opportunity

\$6B+

Current PI3K α Pathway Total Addressable Market¹
(Metastatic HR+/HER2- Breast Cancer)

Robust RLY-2608 Clinical Data

RLY-2608 (600mg BID) + fulvestrant²
Interim data as of 04 Nov 2024

2L+

9.2mo mPFS

2L only

11.4mo mPFS

5.5mo mPFS for capivasertib + fulv
in pt with prior CDK4/6³

Relay Tx's Extensive Global Clinical Experience



13 countries worldwide

~100 clinical sites

800+ patients dosed across trials

Capital to Execute

~\$840M cash
as of end 3Q 2024

RLY-2608 Breast Cancer Combinations

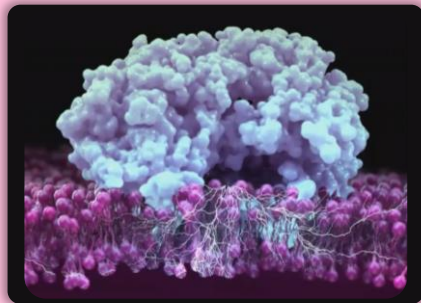
Fulvestrant doublet Expected pivotal start

CDKi + fulv triplets ongoing

Other novel combos

BREAST CANCER

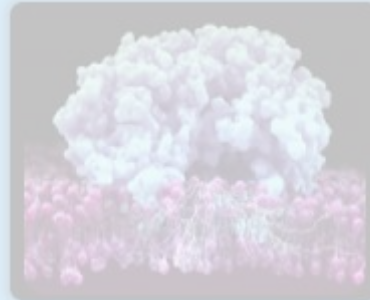
PI3K α -Driven
Breast Cancer



1st mutant-selective
PI3K α inhibitor

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GENETIC DISEASE

Fabry Disease



1st non-inhibitory
 α Gal chaperone

PI3K α Mutations Represent a Large Commercial Opportunity

PI3K α mutations represent a large commercial opportunity

Breast Cancer

~140k pts
(prevalence¹)

Vascular Malformations

~170k pts
(prevalence²)

Non-Breast Cancer Solid Tumors

~90k pts
(incidence³)

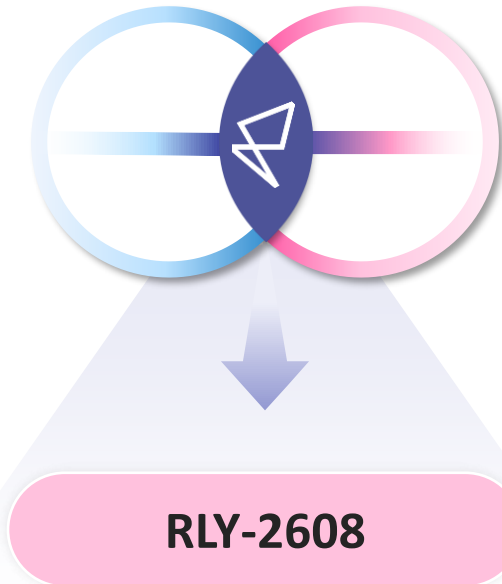
Non-selective PI3K α targeting has significant limitations

— Challenging Tolerability

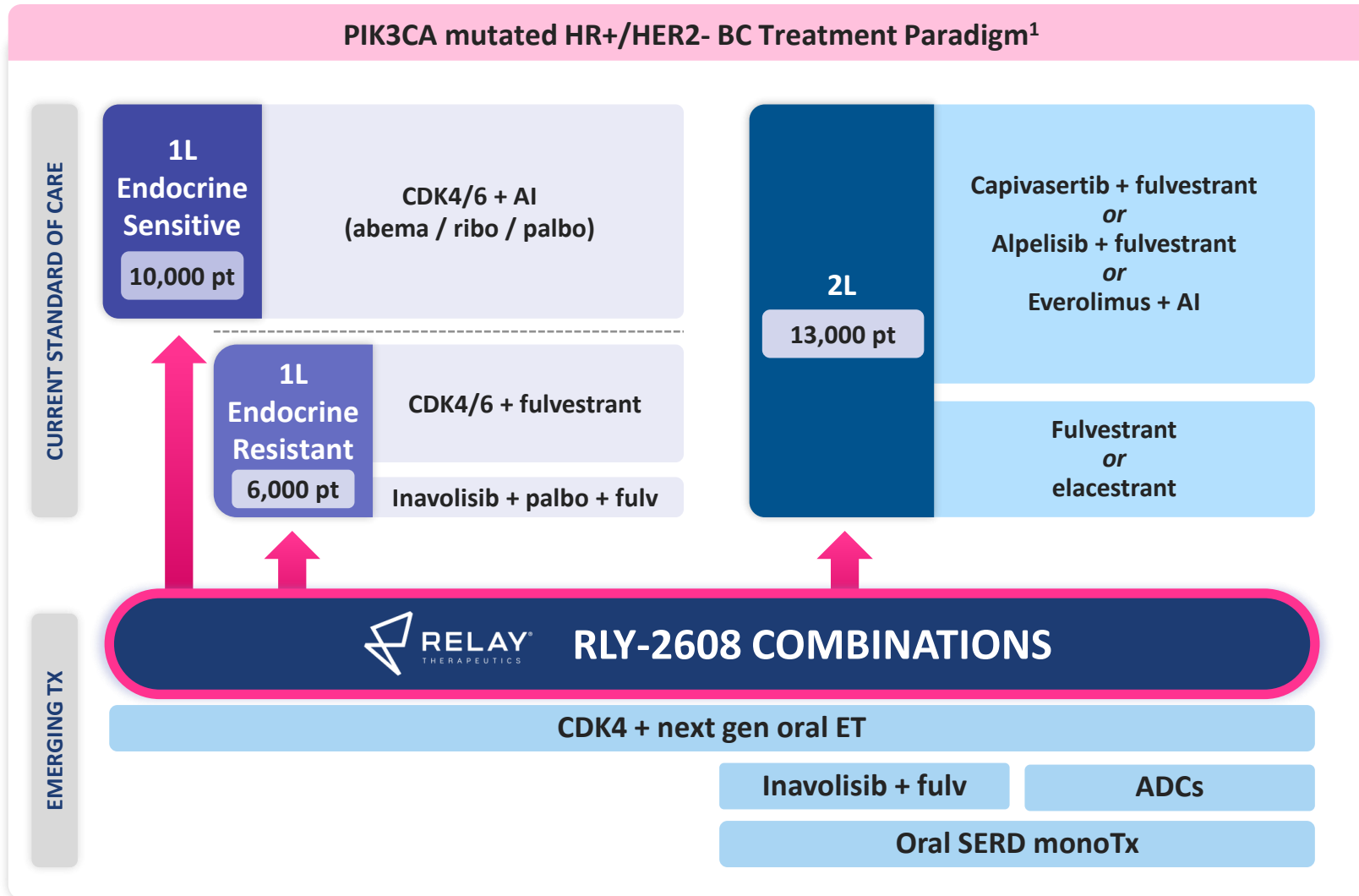
— Limited Efficacy

— Limited Combinability

Relay Tx's Dynamo[®] Platform created mutant selective molecule



Breast Cancer – Large Market for Mutant-Selective PI3K α Targeted Therapies



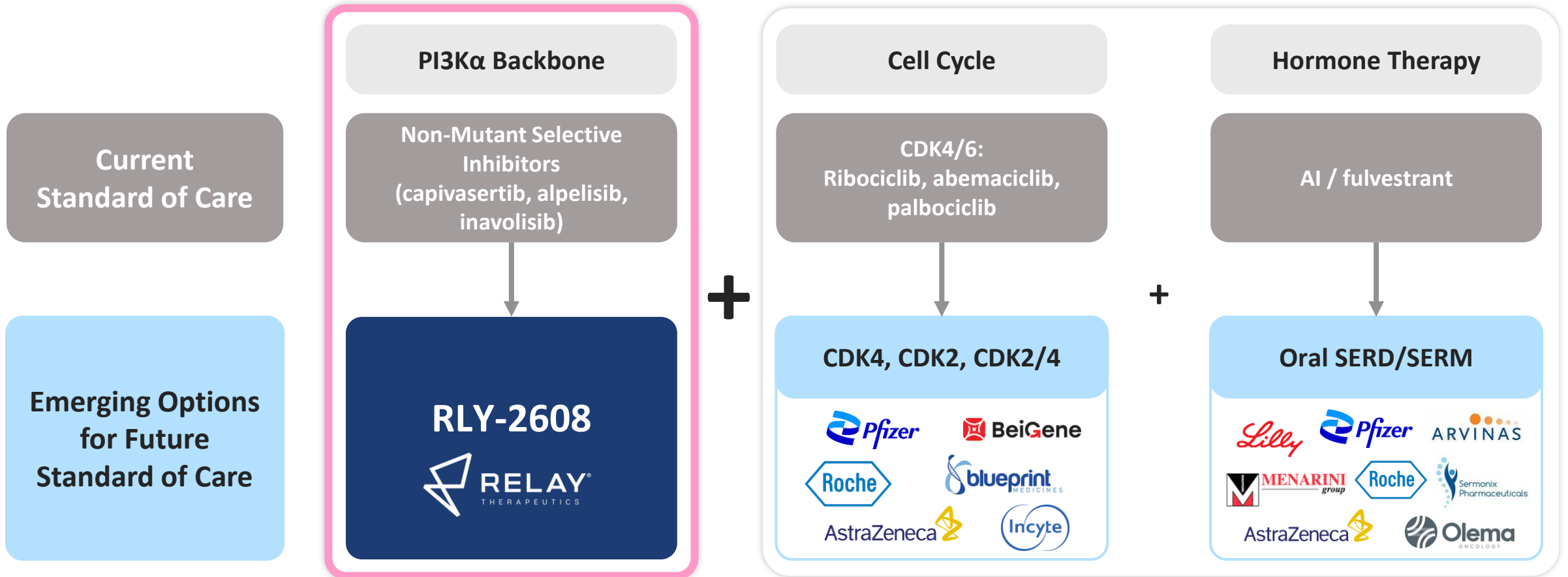
\$6B+
**Current PI3K α Pathway
 Total Addressable Market²**
*(Metastatic HR+/HER2-
 Breast Cancer)*

1. Prevalent US patient population with a PIK3CA mutation in each line of therapy, excluding PTEN co-mutations (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)
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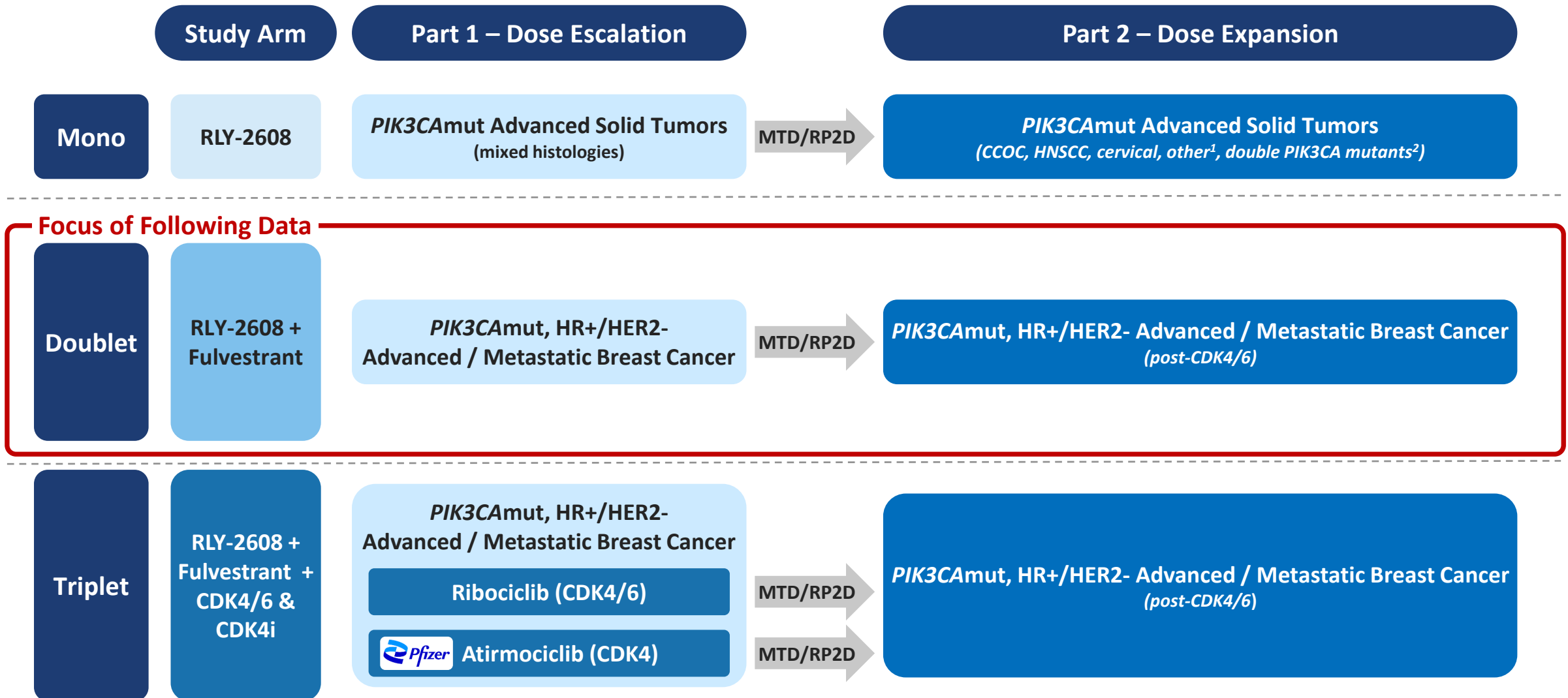
RLY-2608 – Mutant-Selective PI3K α Additive to Many Potential Combinations



PIK3CAmut HR+/HER2- Breast Cancer Treatment Paradigm



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
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PI3K α Inhibitors – Efficacy Profiles



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 D¹
(N=60)

BYLieve Cohort C²
(N=126)

CAPitello-291^{3,6}
(N=355)

ReDiscover
(N=52)

% pt with ≥ 2 prior LoT

57%

63%

23%

39%

% prior SERD⁵

47%

33%

0%

52%

mPFS

7.1mo

5.6mo

5.5mo⁴

9.2mo

CBR

48%

37%

56%

67%

ORR

19%

24%

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

26%⁶

39%

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. FDA Prescribing Information.

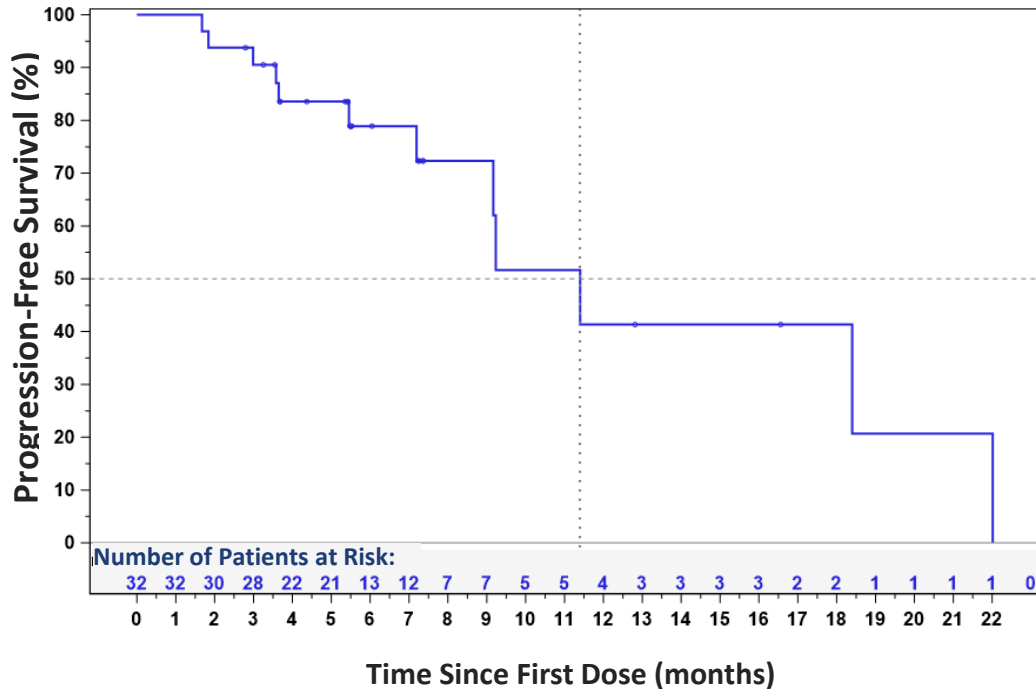
Note: These data are derived from different clinical trials at different points in time, with differences in molecule composition, trial design and patient populations. As a result, cross-trial comparisons cannot be made, and no head-to-head clinical trials have been conducted.

RLY-2608 – Efficacy: 11.4 Month Median PFS in 2L & Kinase Patients



RLY-2608 600 mg BID (RP2D) + Fulvestrant Post-CDK4/6 Patients, excluding PTEN / AKT Co-Mutations

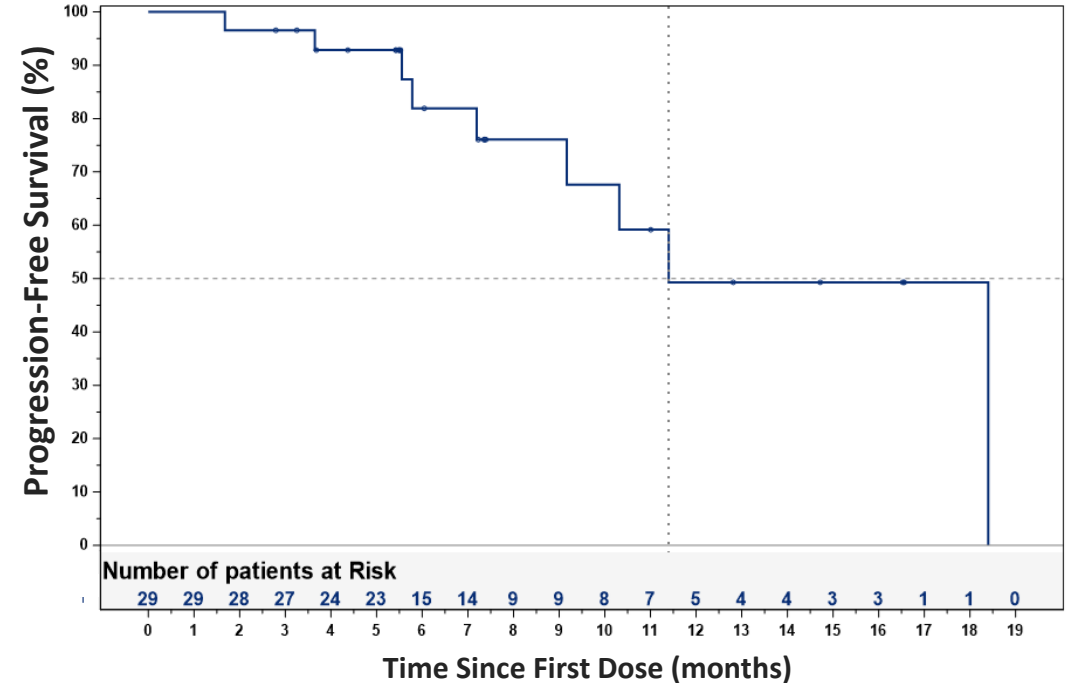
2L Patients (N=32)



11.4mo mPFS
(95% CI: 7.2, NR)

40% ORR
(8/20 pt)

Kinase Mutations (N=29)



11.4mo mPFS
(95% CI: 9.2, NR)

67% ORR
(10/15 pt)

Note: Follow-up estimated based on reversed KM. PFS estimates based on KM methods.
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PI3K α Inhibitors – Tolerability Profiles



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 ¹ (n=60)	BYLieve ² (n=127)	FDA Label ³ (n=355)	ReDiscover (n=64)
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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%

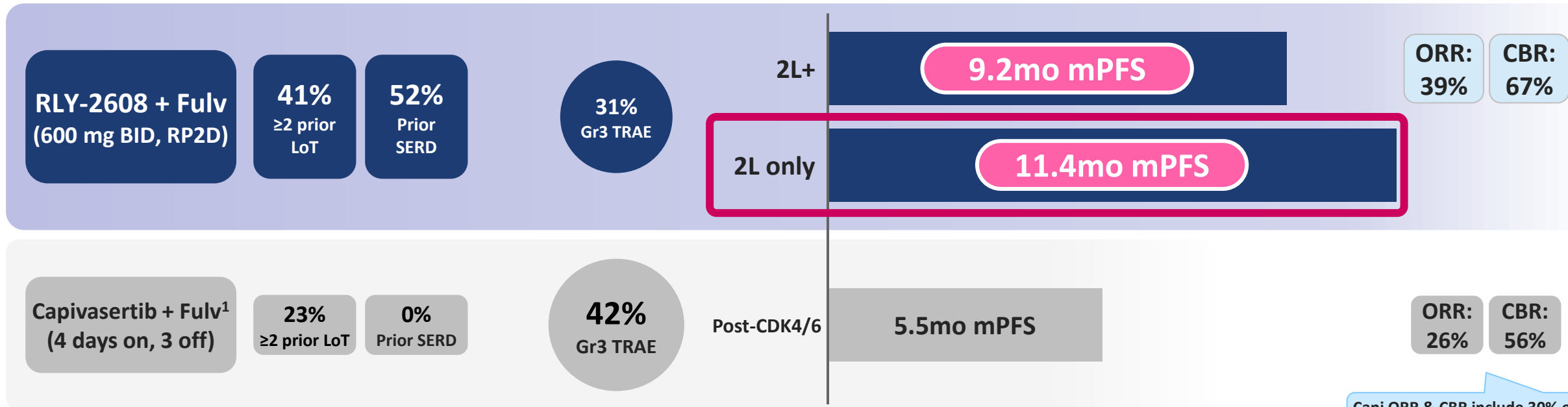
1. SABCS 2021 #P5-17-05; 2. Rugo 2021 Lancet Oncol 22:489; 3. FDA Prescribing Information; 4. CAPItello-291: Turner N Engl J Med 2023; 388:2058-2070.

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.

RLY-2608 – Interim Clinical Data Continue to Show Clinically Meaningful PFS



More Heavily Pre-Treated Pt **Favorable Tolerability** **Favorable Efficacy**
*PIK3CA*mut, HR+/HER2- Advanced / Metastatic Breast Cancer (post CDK4/6)

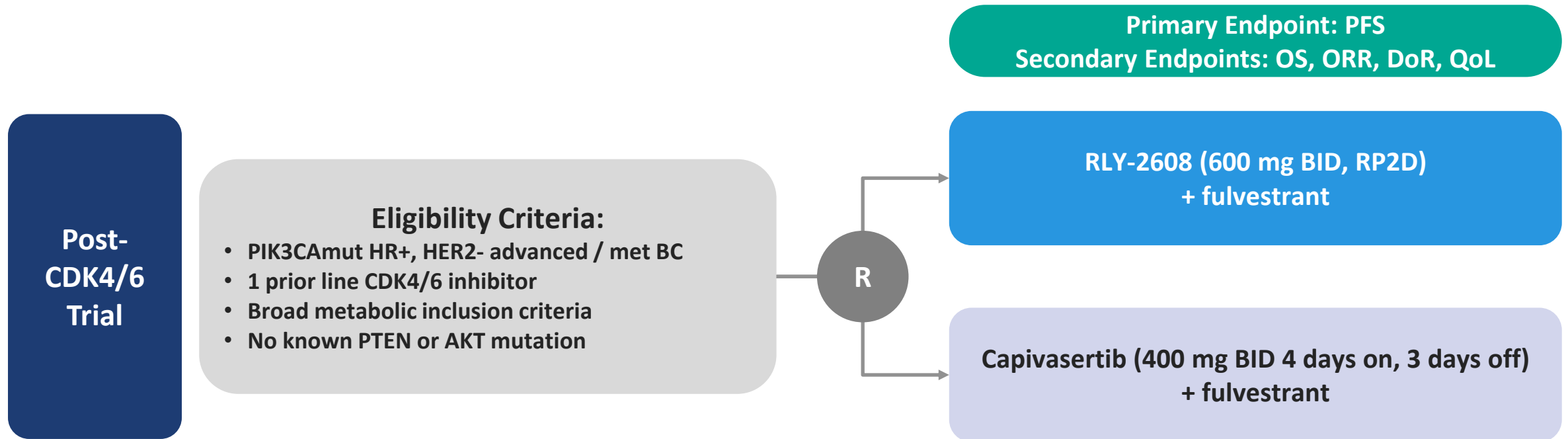


Capi ORR & CBR include 30% of pts who are CDK4/6 naïve

Interim RLY-2608 data supportive of pivotal trial in post-CDK4/6 Breast Cancer against capivasertib

1. CAPitello-291: Turner N Engl J Med 2023; 388:2058-2070; 2. 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 Post-CDK4/6 Patients in 2025*



Post-CDK4/6 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 = 2nd line

Large Unmet Need in Metastatic Breast Cancer



PIK3CAmut, HR+/HER2- mBC¹

Median PFS of Current Standard of Care

Potential Market Opportunity⁹

1L Endocrine Sensitive
10,000 patients

Ribociclib + AI²

25 months

Also abemaciclib or palbociclib

1L Endocrine Resistant
6,000 patients

Ribociclib + fulv³

16-20 months

Inavolisib + palbo + fulv⁴

15 months

2L
13,000 patients

Capivasertib + fulv⁵

5.5mo

Alpelisib + fulv⁶

5.6-8mo

CDK4/6 + fulv⁷

~5-6mo

SERD monox⁸

~2-4mo

Current Market Oppty

~\$4B

Future Market Oppty

~\$6-7B

RLY-2608 Potential to Drive Meaningful Improvement

~\$2B

~\$3-4B

~\$2B

~\$3-4B

Notes: 1. Prevalent US patient population with a PIK3CA mutation in each line of therapy, excluding PTEN co-mutations (Global Data HR+/HER2- Breast Cancer Global Forecast, November 2023; 3rd party source for alteration rate); 2. All-comers and PIK3CAmut sub-group, MONALEESA-2; 3. All-comers and PIK3CAmut sub-group, MONALEESA-3; 4. INAVO120: SABCS 2023 GS03-13; 5. Turner N Engl J Med 2023; 388:2058-2070 (n=355); 6. Rugo 2021 Lancet Oncol 22:489, SABCS 2021 #P1-18-03; 7. MAINTAIN: Kalinsky 2023 J Clin Oncol 41:4004, postMONARCH: Kalinsky 2024 ASCO; 8. Elacestrant Prescribing Information; 9. Informed by qualitative and quantitative primary market research performed in Q2 2024
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RLY-2608 – On Track to Realize 1L Potential with Triplet Combinations

Triplets

RLY-2608
+
Fulvestrant

+

Ribociclib
(CDK4/6,
commercial SoC)



Dose Escalation

Currently dosing at biologically active doses of RLY-2608

RLY-2608
+
Fulvestrant

+

Atirmociclib
(CDK4, Pfizer)



Atirmociclib triplet has initiated

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

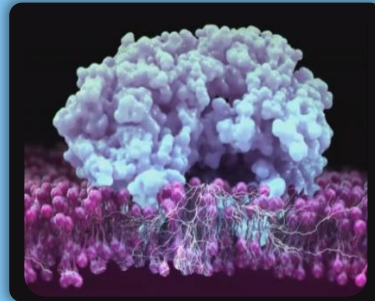
PI3K α -Driven
Breast Cancer



1st mutant-selective
PI3K α inhibitor

GENETIC DISEASE

PI3K α -Driven
Vascular Malformations



1st mutant-selective
PI3K α inhibitor

SOLID TUMORS

NRAS-Driven
Solid tumors



1st NRAS-selective
inhibitor

GENETIC DISEASE

Fabry Disease



1st non-inhibitory
 α Gal chaperone

Vascular Malformations – Over 170,000 US Patients

Vascular Malformation Types

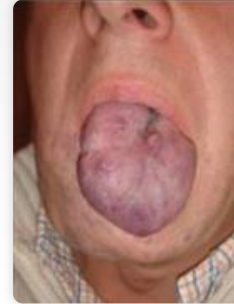
PIK3CA-Related Overgrowth Spectrum (PROS)



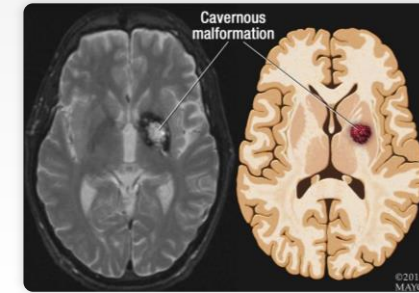
Lymphatic Malformation (LM)



Venous Malformation (VM)



Cerebral Cavernous Malformation (CCM)



US Patients

~5-15k

~80k

~100k

~120k

% PIK3CAmut

100%
~5-15k pt

80%
~65k pt

~20-25%
~20-25k pt

40-55%
~50-65k pt

Approved Therapies

Vioice® (alpelisib)

No approved systemic therapy

Total US pt across types

>300k pt

~170k pt
PIK3CAmut

Referral Pathway

Symptom presentation

PCP, Dermatologist, Surgeon, ENT, etc.



Diagnosis

Geneticist, "Vascular Anomalist"



Treatment

Surgeon, Int. Radiologist, Dermatologist, Heme-Onc

Treatment & Ongoing Management

Frequency of use

Watch and wait; Compression Therapy

Temporary; 50-75% of diagnosed pts receive local or systemic Tx

Local treatment: sclerotherapy, surgery

Invasive, recurrence is common (~25-40% recurrence rate)

Systemic therapy: Alpelisib, sirolimus

Incomplete responses, side effects & toxicities limit widespread use

Current unmet need for selective, systemic therapy for Vascular Malformations

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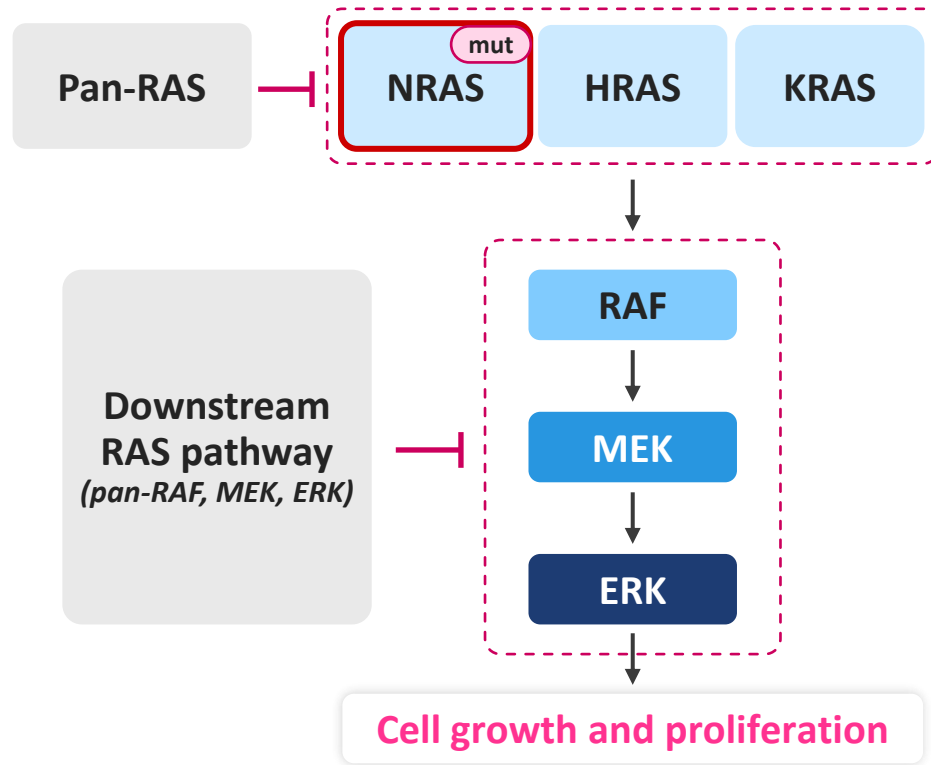
Fabry Disease



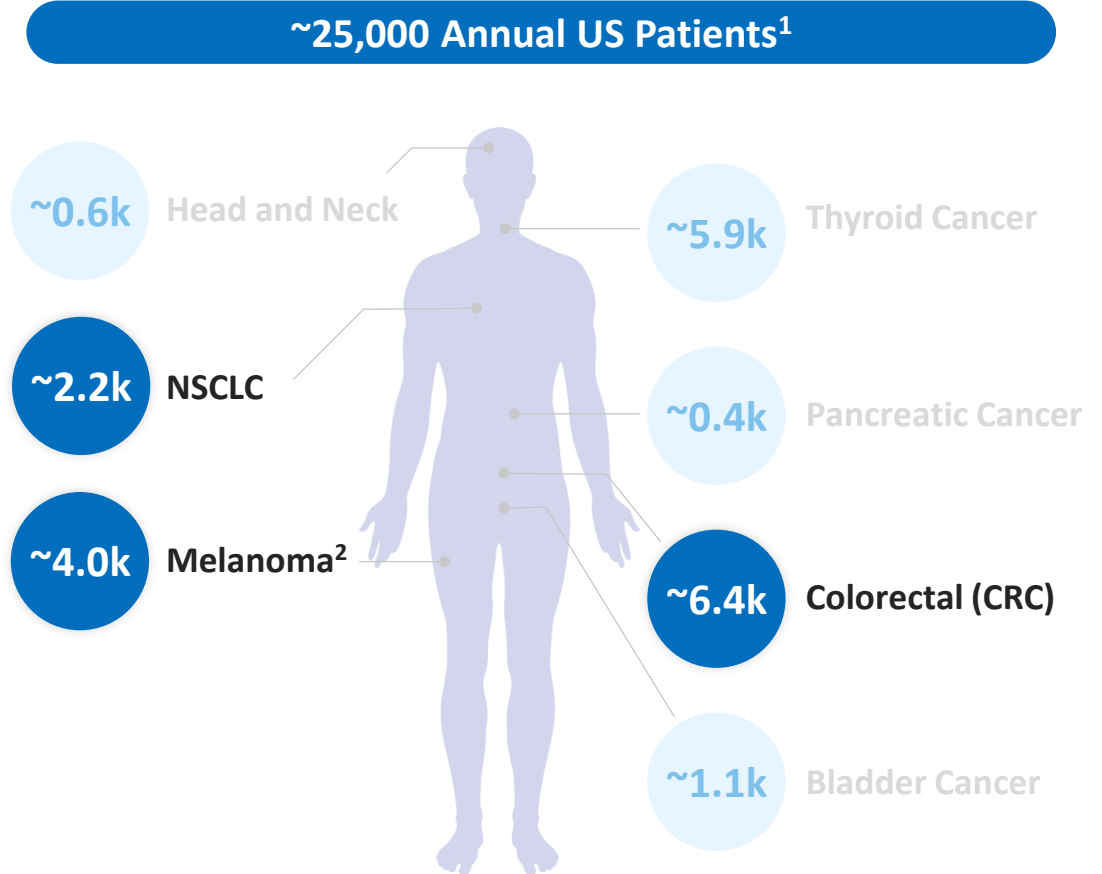
1st non-inhibitory
 α Gal chaperone

NRAS – Large Validated Market With Significant Unmet Need

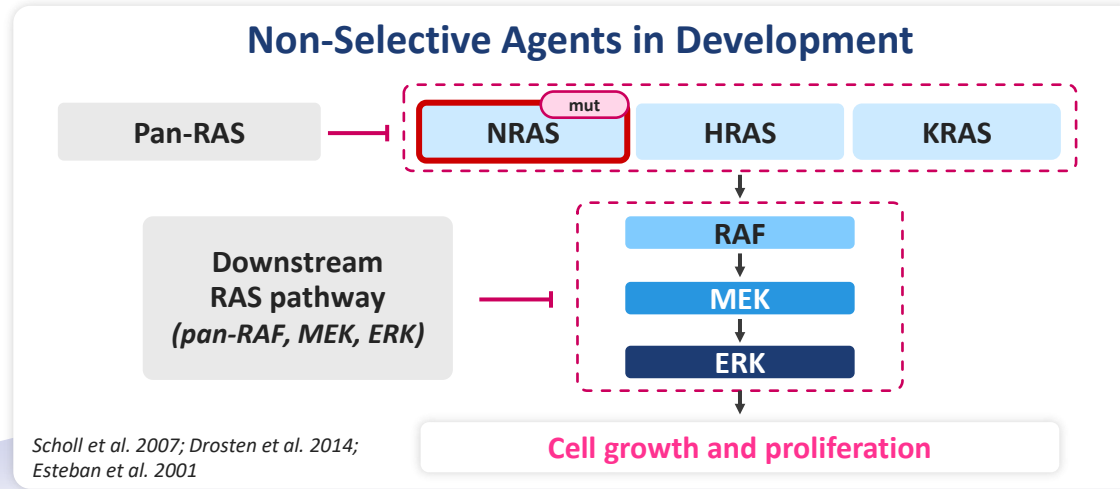
NRAS mutations are a key driver of solid tumors, though no NRAS-selective agent exists



NRAS mutations observed in broad range of tumor types



Limited Therapeutic Window of Current Agents – Pan-RAF/RAS & MEK Inhibitors



Limited Tolerability

	Rash	Liver Toxicity
MEK + RAFi	25 – 80%	Inc. ALT: <10 – 22% Inc. AST: <10 – 20%
Pan-RAS (PDAC)	91%	Inc. ALT: 7% Inc. AST: 5%

KRAS KO is embryonic lethal in mice, whereas NRAS KO is tolerated

Limited Target Inhibition

	Dose Modifications
MEK + RAFi	62 – 100%
Pan-RAS (PDAC)	42%

Limited Efficacy

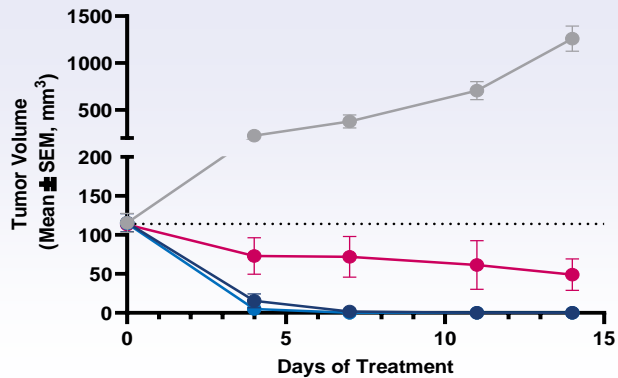
Regimen (2L NRASmut melanoma)	ORR	PFS (mo)
Naporafenib (RAFi) + trametinib (MEKi)	13 – 47%	4.2 – 5.5
Exarafenib (RAFi) + binimetinib (MEKi)	33%	--

Belvarafenib (RAFi) + cobimetinib (MEKi) had shown 39% ORR (n=13), but belvarafenib development discontinued

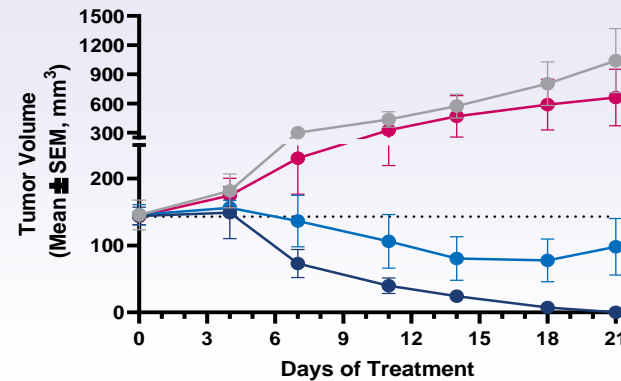
Sources: ESMO 2024 #613MO (exarafenib + binimetinib - efficacy evaluable n=33 and 35% of total n=52 received prior MAPKi), ASCO 2021 #3007 (Belvarafenib + cobimetinib, n=32 all, 13 for efficacy), de Braud 2023 J Clin Oncol 41:2651 (naporafenib + trametinib, n=30 expansion arm), ASCO 2023 #9510 (tunlametinib, n=95), ESMO 2023 652O (RMC-6236, n=111 pts at ≥80mg); Scholl et al. 2007; Drosten et al. 2014; Esteban et al. 2001; Revolution Medicines Corporate Presentation 12/02/2024.

Deep Regressions in PDXs Across Histologies & NRAS Genotypes

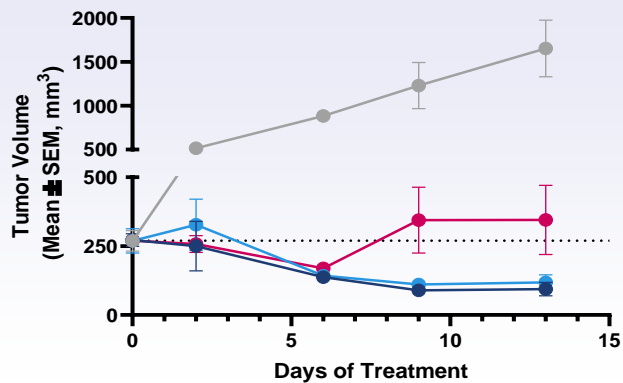
ME12175 Melanoma (NRAS^{Q61R/R})



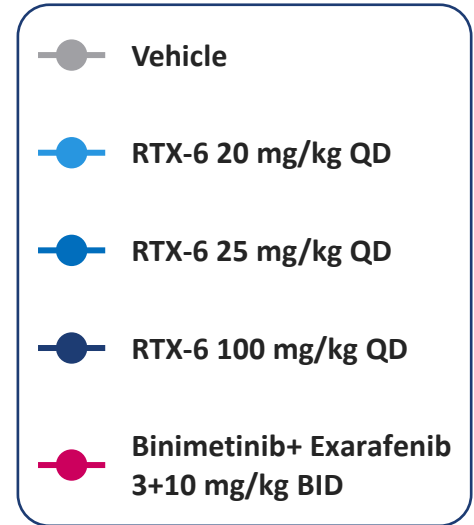
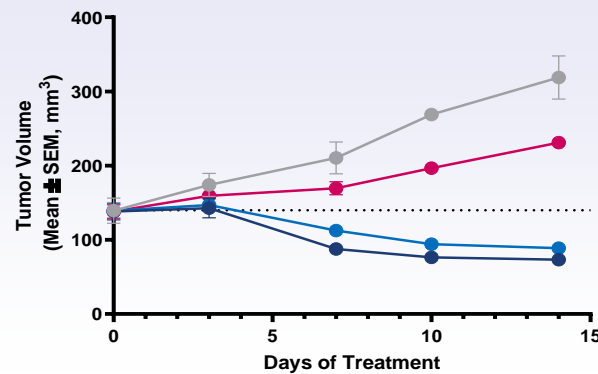
ME11972 Melanoma (NRAS^{Q61K/WT})



CTG-1282 Endometrial (NRAS^{Q61K/WT})



ME11978 Melanoma (NRAS^{Q61K/WT})



Relay Tx compounds well tolerated in exploratory animal toxicology studies at exposures >10X above the predicted efficacious exposure level

BREAST CANCER

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Breast Cancer



1st mutant-selective
PI3K α inhibitor

GENETIC DISEASE

PI3K α -Driven
Vascular Malformations



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SOLID TUMORS

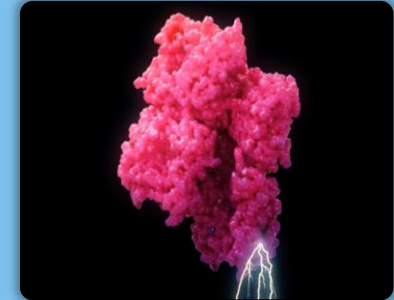
NRAS-Driven
Solid tumors



1st NRAS-selective
inhibitor

GENETIC DISEASE

Fabry Disease



1st non-inhibitory
 α Gal chaperone

Fabry Disease – Large Validated Market With Significant Unmet Need

Fabry disease is a lysosomal storage disorder affecting ~8,000 patients in US

Over 1,000 different *GLA* gene mutations

Reduces α Gal protein levels

Leads to accumulation of toxic Gb3 substrate

Broad clinical manifestations;
Life threatening cardiac & renal dysfunction



Current therapies have established a market but have key limitations

Current Therapies

Enzyme Replacement Therapy (ERT, intravenous)

~\$1.6B peak sales¹

Inhibitory Chaperone Therapy (migalastat)

40% of pts → ~\$780M peak sales²

Limitations of Inhibitory Chaperone

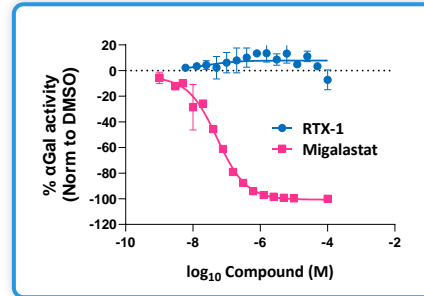
1 Limited α Gal activation

2 Limited mutational coverage

3 Not combined with ERT

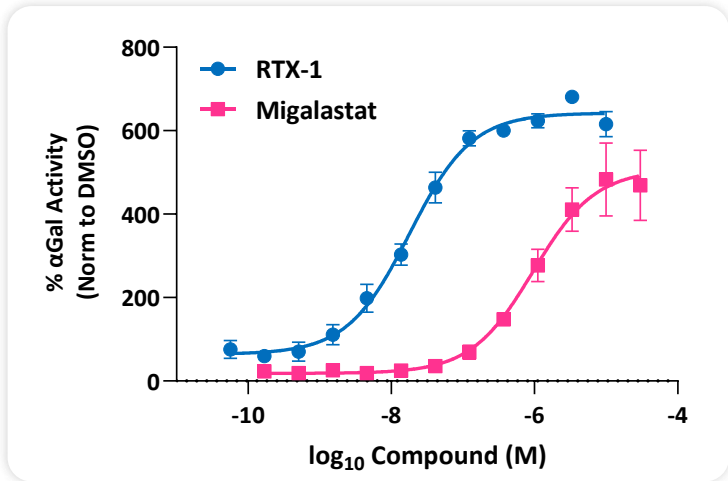
Need for a non-inhibitory α Gal chaperone

Fabry Disease – Potential Benefits of Non-Inhibitory Chaperone Approach

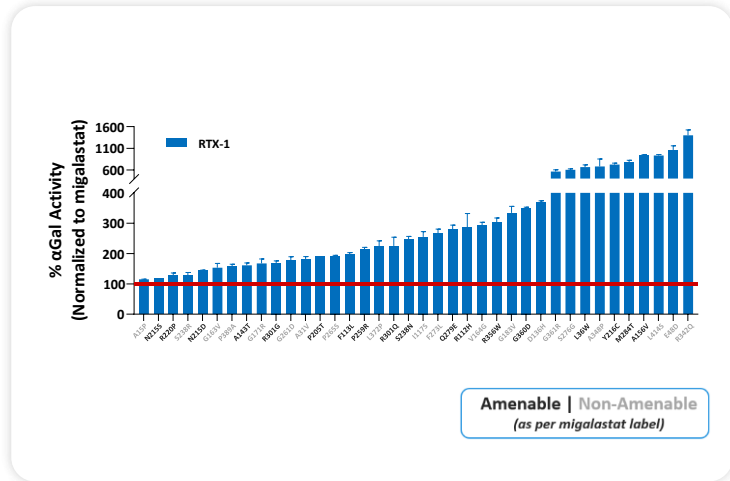


Relay Tx Solution:
Non-Inhibitory Chaperone to Stabilize Protein and Increase Activity

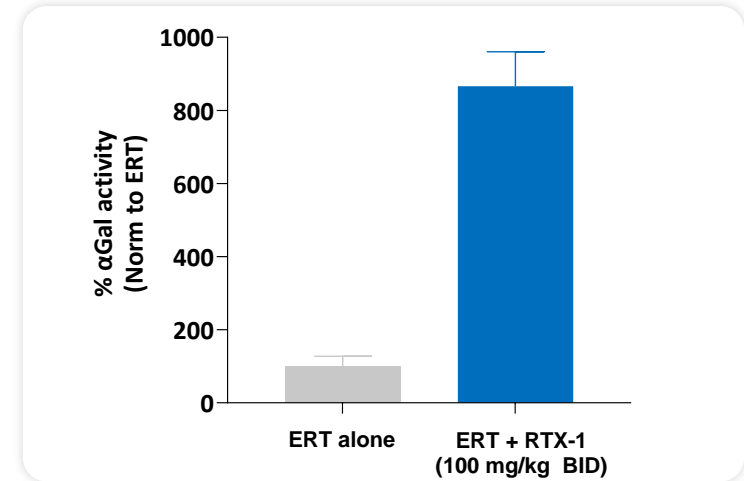
1 Superior αGal activation¹

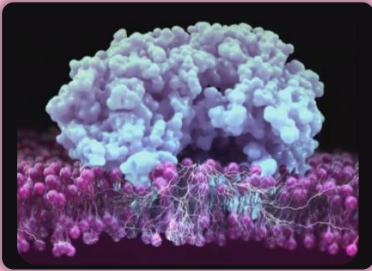
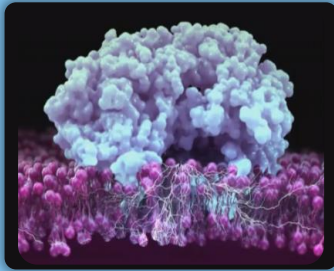

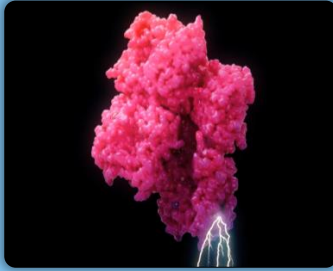


2 Broad mutational coverage²



3 Combinable with ERT³



	BREAST CANCER	GENETIC DISEASE	SOLID TUMORS	GENETIC DISEASE
	<p>PI3Kα-Driven Breast Cancer</p> 	<p>PI3Kα-Driven Vascular Malformations</p> 	<p>NRAS-Driven Solid tumors</p> 	<p>Fabry Disease</p> 
Program	1st mutant-selective PI3Kα inhibitor	1st mutant-selective PI3Kα inhibitor	1st NRAS-selective inhibitor	1st non-inhibitory αGal chaperone
Large US opportunity	~140,000 pts¹	~170,000 pts² <i>(chronic treatment)</i>	~28,000 pts⁴	~8,000 pts³ <i>(chronic treatment)</i>
Anticipated Milestone	<ul style="list-style-type: none"> Pivotal trial start – 2025 Full Ph1-2 data – 2025 	Clinical start – 1Q 2025	Clinical start – 2H 2025	Clinical start – 2H 2025
Progress 4 unnamed research programs				

1. Prevalent US patient population with a PIK3CA mutation (excluding PTEN co-mutations) in adjuvant, first line metastatic and second line metastatic settings (Global Data HR+/HER2- Breast Cancer Global Forecast, November 2023; 3rd party source for alteration rate); 2. Prevalence of vascular malformations with a PIK3CA mutation (Gallagher et al 2022 and several other sources); 3. Prevalence of Fabry patients (National Fabry Disease Foundation, Jan 2024); 4. Newly diagnosed (incident) solid tumors with an NRAS mutation, excluding melanoma stages 0-II (SEER, 3rd party source for alteration rate, Jan 2024); 5. Fabry disease forecasted 2024 market size per EvaluatePharma, includes Galafold® and ERTs (May 2024)

RLY-2608 Unlocks Large Breast Cancer Market



Significant Breast Cancer Commercial Opportunity

\$6B+

Current PI3Kα Pathway Total Addressable Market¹
(Metastatic HR+/HER2- Breast Cancer)

Robust RLY-2608 Clinical Data

RLY-2608 (600mg BID) + fulvestrant²
Interim data as of 04 Nov 2024

2L+

9.2mo mPFS

2L only

11.4mo mPFS

5.5mo mPFS for capivasertib + fulv in pt with prior CDK4/6³

Relay Tx's Extensive Global Clinical Experience



13 countries worldwide

~100 clinical sites

800+ patients dosed across trials

Capital to Execute

~\$840M cash as of end 3Q 2024

RLY-2608 Breast Cancer Combinations

Fulvestrant doublet **Expected pivotal start** →

CDKi + fulv triplets **ongoing** →

Other novel combos →

