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EXPANDING TREATMENT OPTIONS

**Unlocking the Potential of  
Treating Cancers That Involve the  
PI3K/mTOR Pathway**

*Corporate Presentation*

March 2024

# Forward-Looking Statements

This presentation contains “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995 relating to our business, operations, and financial condition, including but not limited to current beliefs, expectations and assumptions regarding the future of our business, future plans and strategies, our development plans, our preclinical and clinical results and expected timing thereof, our plans to develop and commercialize gedatolisib, our first internally developed drug candidate, our plans to research, discover and develop additional product candidates, our planned milestones and timing of achieving such milestones, the focus and design of our clinical development program, our expectations regarding the timeline of patient enrollment, and receiving results and data, from clinical trials, including our existing Phase 3 VIKTORIA-1 clinical trial and Phase 1b/2 study and clinical trial for gedatolisib, any potential benefits resulting from Breakthrough Therapy designation for gedatolisib, and other expectations with respect to Celcuity's lead product candidate, gedatolisib, our expectations as to the use of proceeds from our recent financing activities and the adequacy of cash to fund operations, and our beliefs related to the perceived advantages of our CELsignia tests compared to traditional molecular or other diagnostic tests and its CELsignia platform. Words such as, but not limited to, “look forward to,” “believe,” “expect,” “anticipate,” “estimate,” “intend,” “plan,” “would,” “should,” and “could,” and similar expressions or words, identify forward-looking statements.

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# Unlocking the Potential of Treating Cancers That Involve the PI3K/AKT/mTOR Pathway

One of the most important oncogenic pathways

**PI3K/AKT/mTOR (PAM) regulates key metabolic functions**

- Plays a key role promoting tumor cell proliferation
- Cross-regulates other oncogenic pathways
- Affects immune response by regulating tumor microenvironment

Most highly altered of all signaling pathways<sup>1</sup>

**Proportion of alterations correlates to pathway's role as a cancer driver**

<b>PAM</b>	<b>38%</b>
RAS	15%
HER2	8%
EGFR	5%

Largest untapped drug development opportunity in solid tumors

**Breast and prostate cancers involve PAM pathway**

- **>500,000** addressable patient population in US, 5EU, and Japan
- Nominal penetration of PAM drugs in these markets

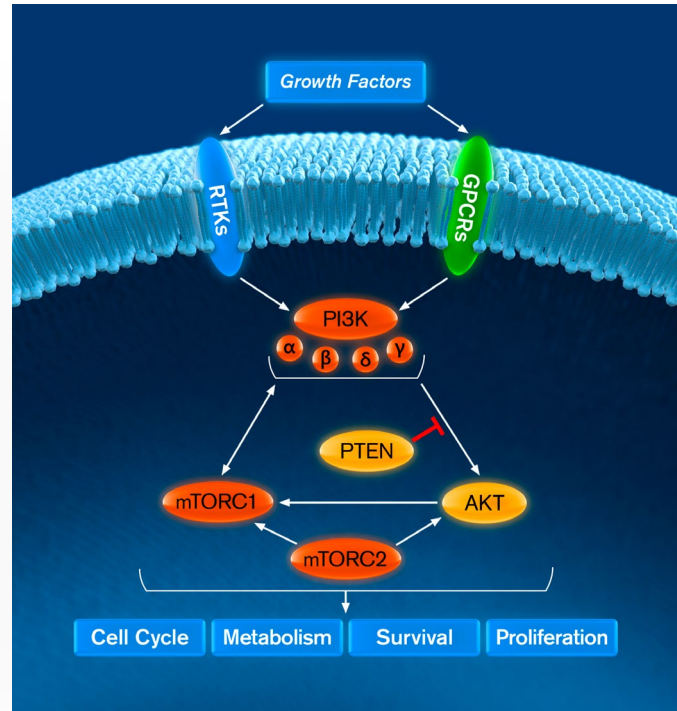
# Difficult to Safely and Efficaciously Inhibit PI3K/mTOR

Maximum efficacy requires inhibition of all Class I PI3K isoforms and mTORC1 and mTORC2

## Multiple pathway components must be targeted

Feedforward and feedback loops between PI3K isoforms, AKT, and mTOR cross-activates uninhibited sub-units

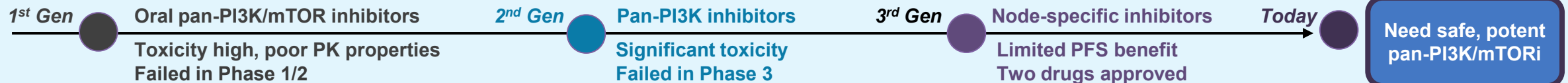
Induces compensatory resistance that reduces efficacy



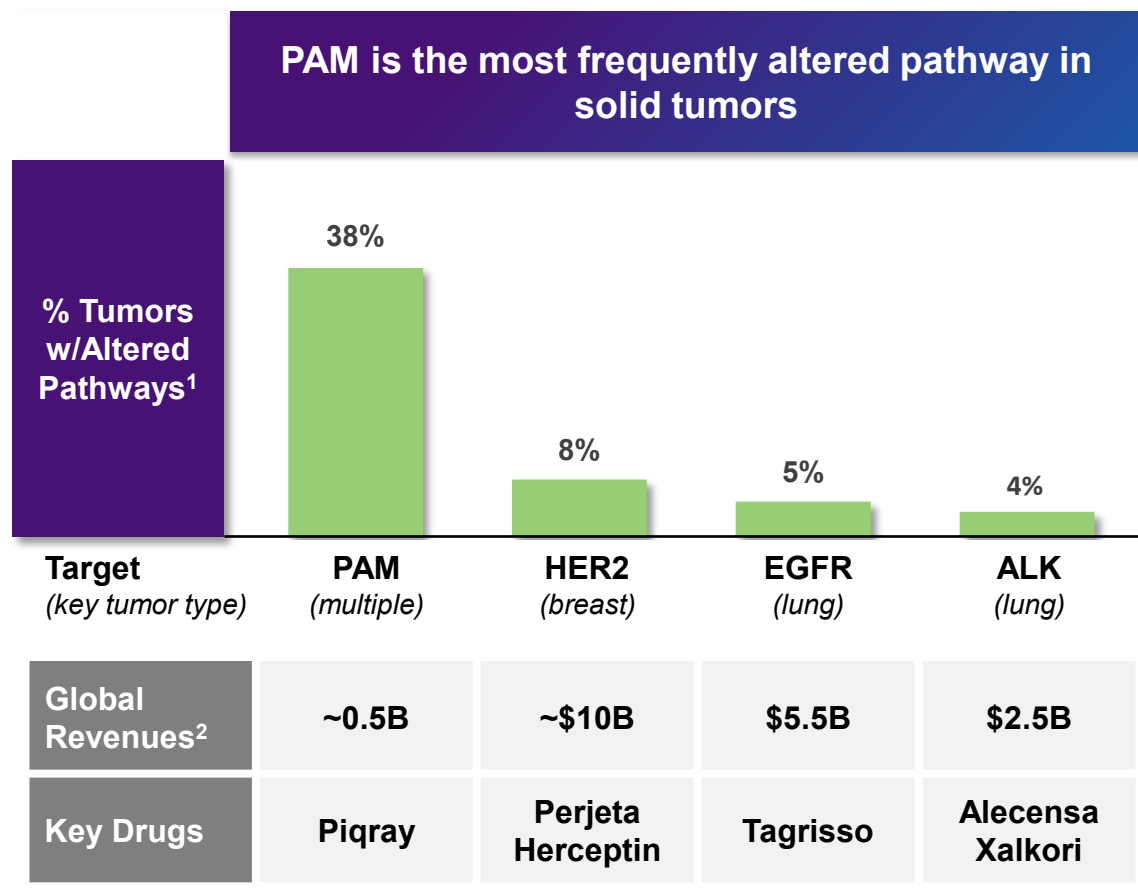
## Therapeutic window for oral PI3K/mTOR inhibitors is narrow

Difficult to optimize pathway inhibition without inducing undue toxicity

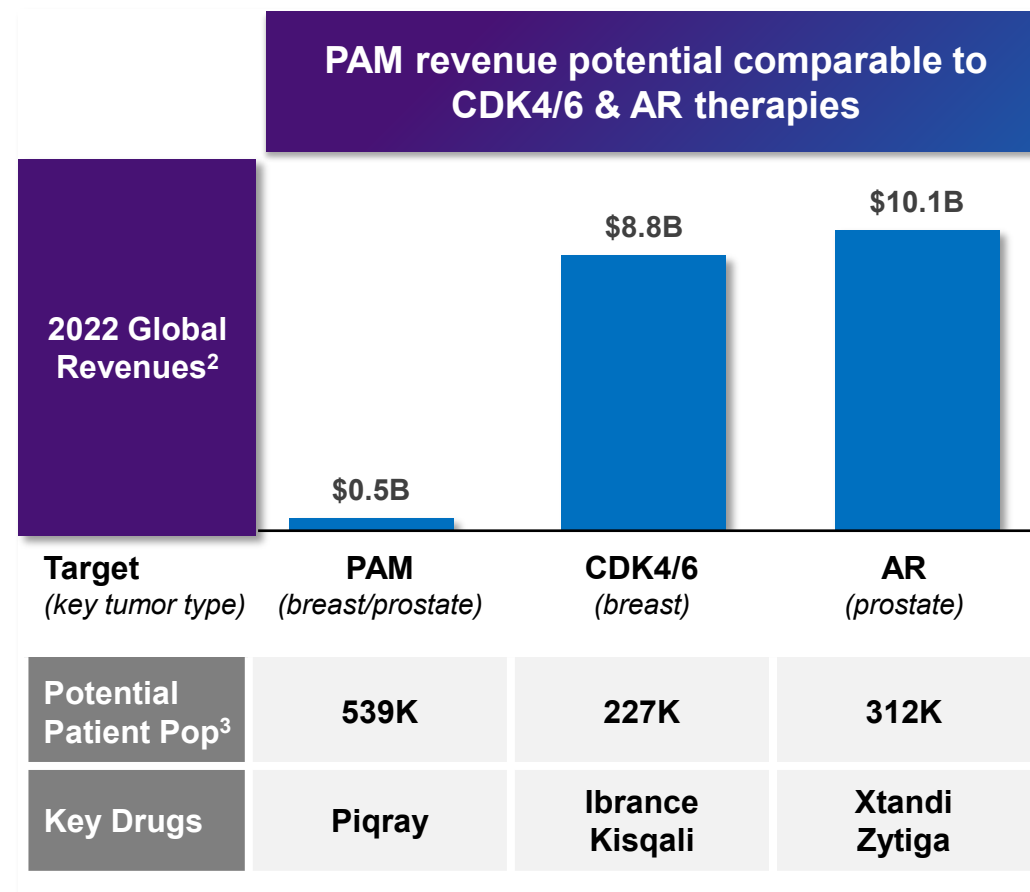
Orally administered pan-PI3K or pan-PI3K/mTOR inhibitors induced unacceptable toxicity



# The PAM Pathway is the Most Underdeveloped Target in Solid Tumors



Drug revenues from PAM inhibitors are a small fraction of other targeted therapy classes



PAM potential patient population is not tumor specific like CDK4/6 or AR inhibitors



# Gedatolisib is a Potential First-in-Class PI3K/mTOR Inhibitor

Breakthrough Therapy Designation granted for 2L HR+/HER2- advanced breast cancer indication

## Highly Differentiated Mechanism

- Inhibits all PI3K/mTOR nodes at **low or sub-nanomolar** concentrations
- **More potent & cytotoxic** than other PAM inhibitors being developed for breast or prostate cancer

## Compelling Efficacy

- Gedatolisib + ET + CDK4/6 in HR+/HER2- ABC patients
- **79% ORR, 48.6 months mPFS** in 1L patients<sup>1</sup>
- **63% ORR, 12.9 months mPFS** in 2L patients<sup>2</sup>

## Well-Tolerated

- Nominal Grade 3, no Gr 4 TEAE's as a single agent
- **Only 4% treatment discontinuation** due to AE with Phase 3 dosing in combination with palbociclib and fulvestrant<sup>2</sup>

## Addressing Large Patient Populations

- **Breast Cancer:** Enrolling Phase 3 trial for 2L patients with HR+/HER2- ABC
- **Prostate Cancer:** Phase 1b/2 trial for 2L patients with mCRPC in Q1 '24
- **211,000 1L/2L patients** in US, 5EU, Japan<sup>3</sup>

# Gedatolisib Has a Highly Differentiated Mechanism of Action and Potency

Results in superior cytotoxicity vs. single node PAM inhibitors

## Cell-Free Biochemical Dose Response Analysis

$IC_{50}$  (nM)<sup>1</sup>

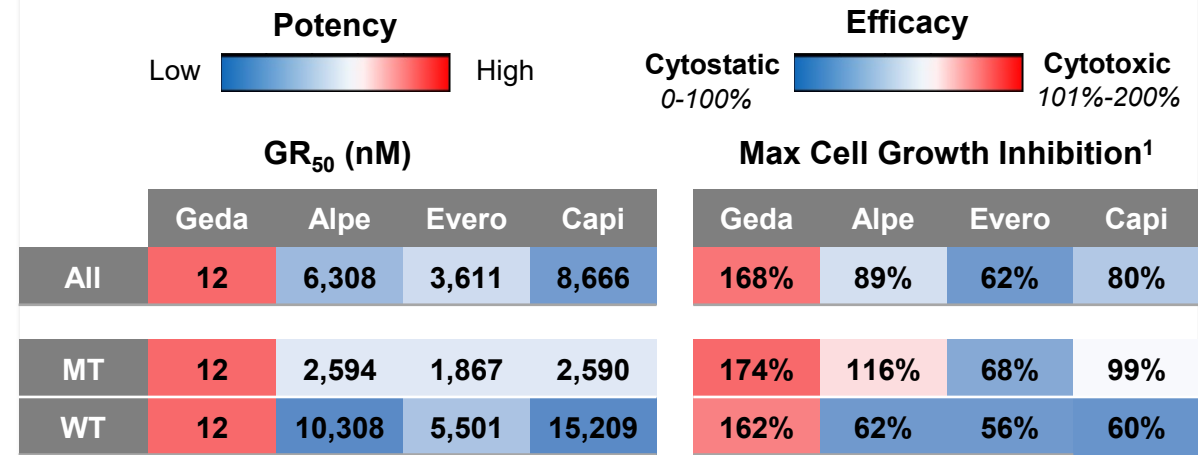
Node	Gedatolisib <sup>2</sup>	Alpelisib <sup>3</sup>	Everolimus <sup>4</sup>	Capivasertib <sup>5</sup>
PI3K-α	0.6	~4.0	-	-
PI3K-β	6.0	1,156	-	-
PI3K-γ	5.4	250	-	-
PI3K-δ	6.0	290	-	-
mTORC1	1.6	-	~2.0	-
mTORC2	1.6	-	-	-
AKT	- <sup>6</sup>	-	-	3.0

### Gedatolisib is potent against all Class I PI3K isoforms & mTORC1/2

- Limits cross-activation that occurs with node-specific drugs
- Gedatolisib is more potent against each node than other PAM inhibitors
  - 70-100x more potent than capivasertib against targets downstream of AKT<sup>6</sup>
- Comprehensive pathway blockade can induce anti-tumor activity independent of PIK3CA status

## Live Cell Proliferation Rate Dose Response Analysis<sup>7</sup>

Average values for 14 PIK3CA MT and 14 PIK3CA WT breast cancer cell lines

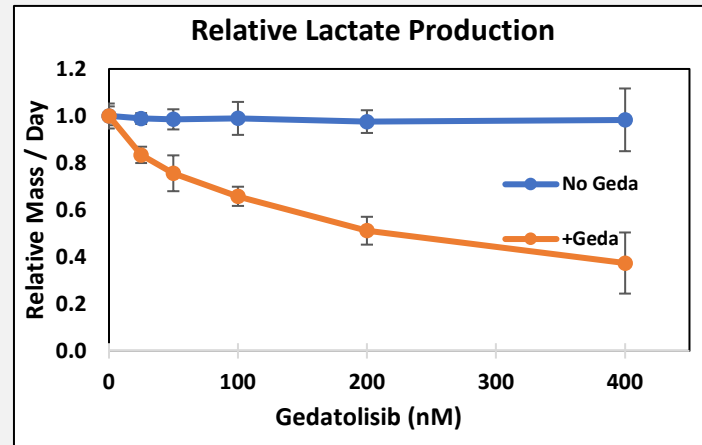
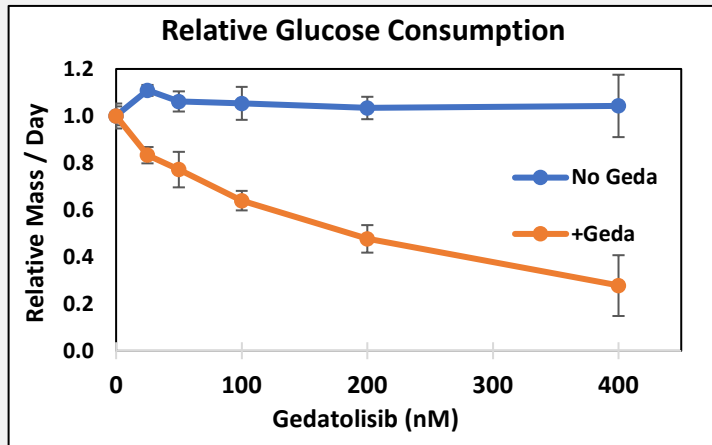
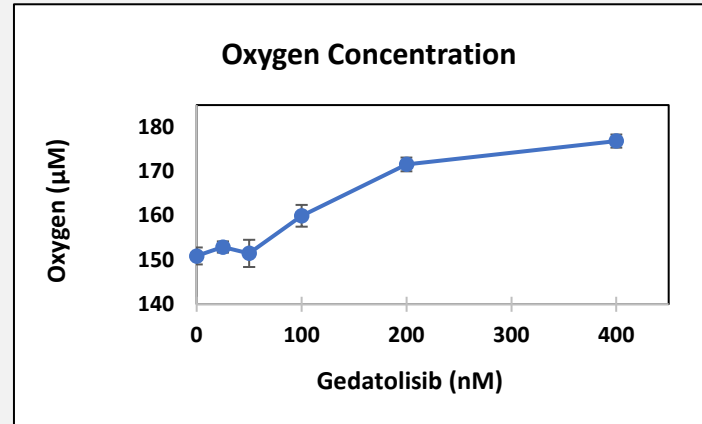
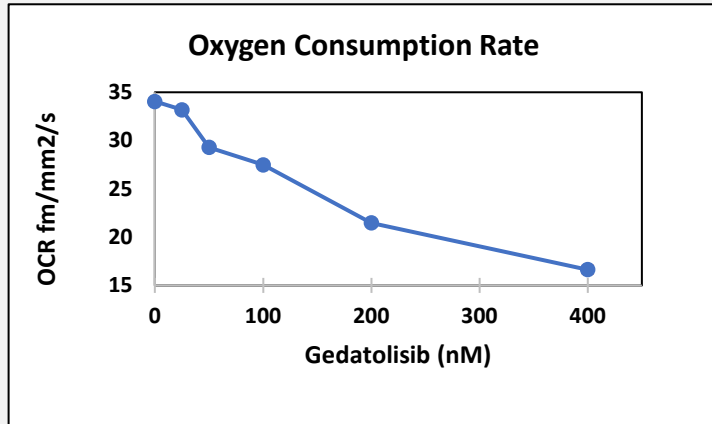


### Gedatolisib is highly potent and cytotoxic in vitro

- Significantly more potent and cytotoxic than other PAM inhibitors in vitro
  - > 300X higher potency
  - 1.5x – 2.8x higher cytotoxicity
- Only PAM inhibitor with similar activity in PIK3CA MT and WT

# Gedatolisib Favorably Impacts Tumor Microenvironment

PAM inhibition decreases O<sub>2</sub> and glucose consumption and lactate production



A TME with low O<sub>2</sub>, low glucose, and high lactate is correlated with immuno-suppression, low anti-tumor activity<sup>1, 2,3,4</sup>

Gedatolisib's dose-dependent reduction of O<sub>2</sub> consumption leads to an increase in O<sub>2</sub> available

Gedatolisib's dose-dependent reduction in glucose consumption leads to decreased lactate production

Data demonstrates Gedatolisib improves TME factors that enable anti-tumor immune function



# Gedatolisib Increases Immune Cell Tumor Infiltration and Activation

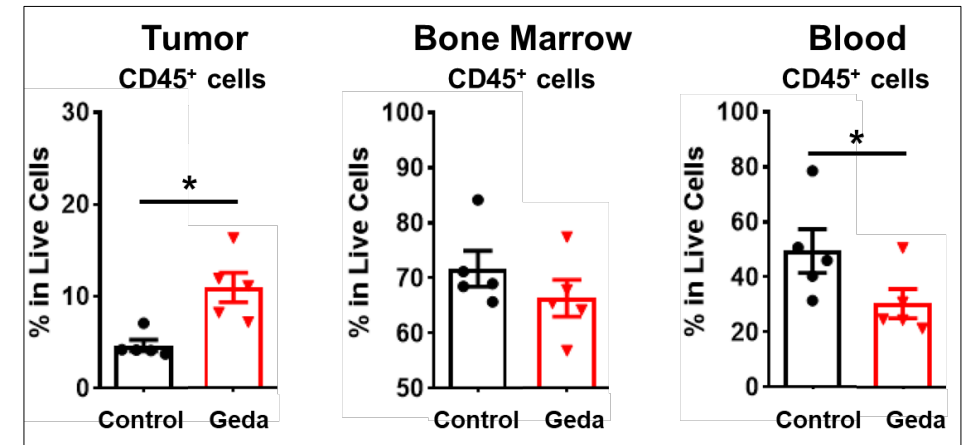
Profiled CD45+ immune cell populations in tumor, bone marrow, peripheral blood

Proportions of CD45+ anti-tumor immune cell subsets in tumor

	Day 10			Day 17		
	Control	Geda	P-Value	Control	Geda	P-Value
% CD45+	4.7	10.9	0.03	-	-	-
% DC (in CD45+)	9.0	15.4	0.0002	2.9	4.0	NA
% CD4+ (in CD45+)	8.6	19.6	0.0002	7.4	19.2	0.014
% CD8+ (in CD45+)	1.7	4.8	NA	13.6	24.5	0.02

## Desired immune cell types infiltrated into the tumor

- Gedatolisib increased CD45+ cells in tumors 2.3 fold vs control
- Gedatolisib induced durable infiltration of key anti-tumor immune cell types - DC, CD4+, CD8+



**Tumor infiltration likely resulted from recruitment of leukocytes from blood circulation into the TME**

## Immune cells that infiltrated are activated

- Gedatolisib induced a 1.5-2 fold increase of activated CD8+ cytotoxic T cells (CD69+) and activated NK cells (CD69+) in tumors at day 10 and day 17

# Gedatolisib PK Properties and IV Administration Optimize Safety Profile

Lower toxicity vs. approved PI3K inhibitors

	Gedatolisib <sup>1</sup>	Alpelisib <sup>2,3</sup>	Copanlisib <sup>3</sup>	Duvelisib <sup>3</sup>	Idelalisib <sup>3</sup>
Target(s)	Pan-PI3K mTOR	PI3K-α	Pan-PI3K	PI3K-δ	PI3K-δ
Administration	IV	Oral	IV	Oral	Oral
Dosing (mmol/month)	0.88	19.03	0.37	3.22	20.22
Volume of distribution (L)	39	114	871	29	23
Hyperglycemia (G 3/4)	1%	26%	41%	-	-
Treatment related SAE's	2%	10%	26%	65-73%	50-77%
Treatment related (TR) Discontinuations	0%	13%	16%	35%	17-53%

## Gedatolisib vs. PI3K-α and pan-PI3K drugs (single-agents)

- >95% lower rate of Grade 3/4 hyperglycemia
  - Due to gedatolisib's lower liver exposure
  - Alpelisib dosage 22x > gedatolisib
  - Copanlisib 50x > retention liver vs plasma
- >80% lower rate of TR discontinuations
- 3x-20x more balanced distribution

## Gedatolisib vs. PI3K-δ drugs (single-agents)

- 73%-97% lower dosage (molar/month)
- No direct GI exposure
- Minimal GI, liver, and infection-related AE's

# Gedatolisib Single Agent Safety Profile

Phase 1 Trial: gedatolisib at maximum tolerated dose (MTD) - 154 mg weekly (IV)<sup>1</sup>

- **Limited incidence of Grade 3 adverse events**
- The most frequent AE, stomatitis, is manageable with prophylactic steroidal mouth rinse
  - Stomatitis was not treated prophylactically in this study
  - **Prophylactic treatment may reduce G2 incidence by 90%; G3 by 100%<sup>2</sup>**
  - Phase 3 study will prescribe prophylaxis
- **Low incidence of Grade 3 hyperglycemia (1%)**
- **No treatment related neutropenia**
- No Grade 4 or 5 adverse events

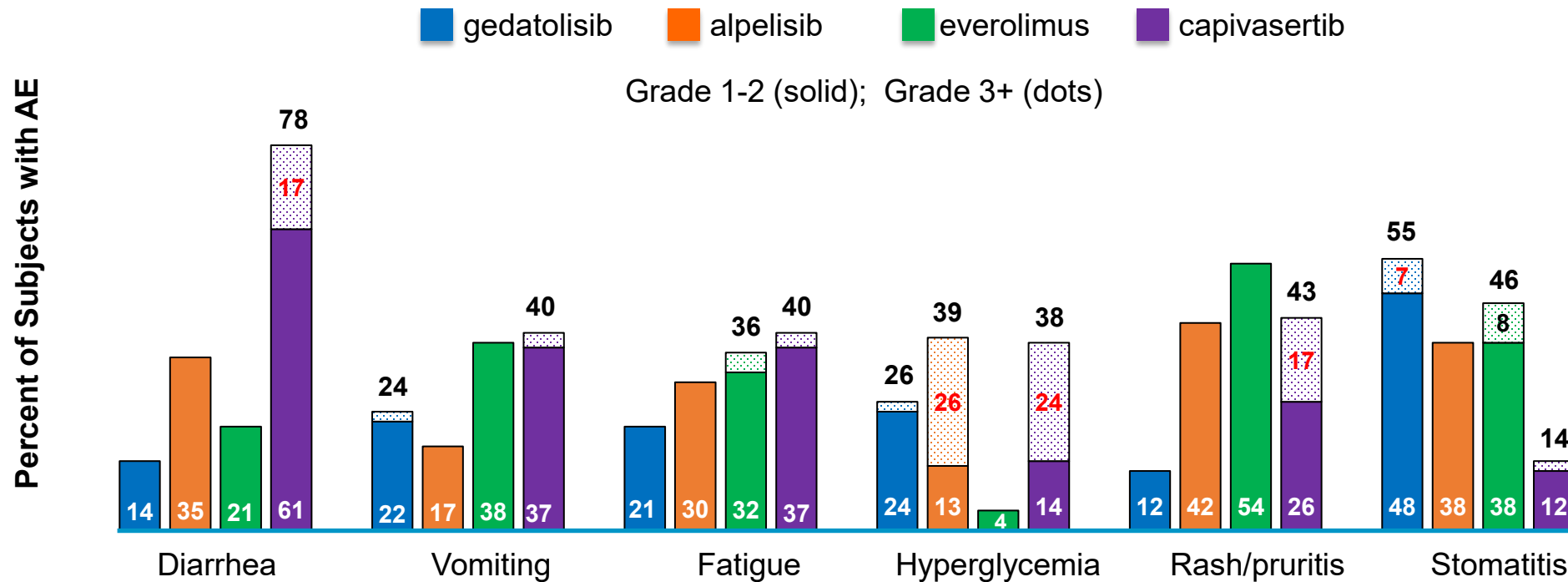
## MTD Arm (n=42)

### Related TEAE's > 20%

	Grade 1	Grade 2	Grade 3/4
Adverse Event	%	%	%
Stomatitis	45	2	7
Nausea	36	2	2
Hyperglycemia	17	7	1
Vomiting	19	2	2
Asthenia	7	12	2
Fatigue	19	2	-
Appetite decrease	14	7	-

# Safety Data for Single-Agent Gedatolisib vs. Single Node PAM Inhibitors

Fewer patients reported AE when treated with gedatolisib as single agent compared to other PAMi



# Clinical Development Programs

## 2<sup>nd</sup> Line HR+/HER2- Advanced Breast Cancer

Pivotal Phase 3 clinical trial for gedatolisib with fulvestrant +/- palbociclib is enrolling

- Enrolling patients with **HR+/HER2- advanced breast cancer** who progressed on CDK4/6 therapy<sup>1</sup>
- All-comer design (*PIK3CA*+/-) includes separate primary endpoints for mutated and non-mutated *PIK3CA* patients
- Breakthrough Therapy Designation for this indication was granted by the FDA in July 2022

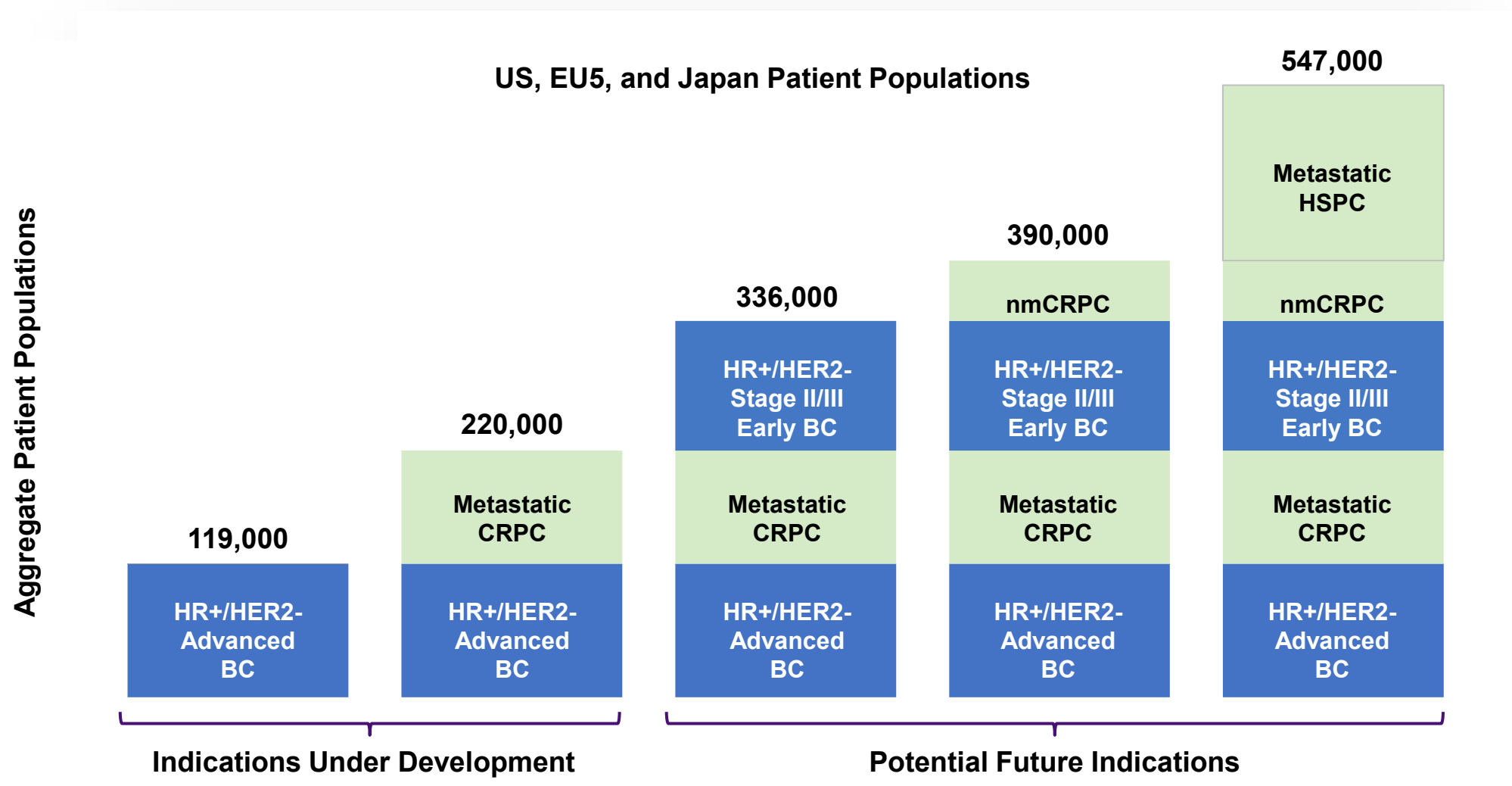
## 2<sup>nd</sup> Line Metastatic Castration Resistant Prostate Cancer

Phase 1b/2 clinical trial for gedatolisib with darolutamide is enrolling

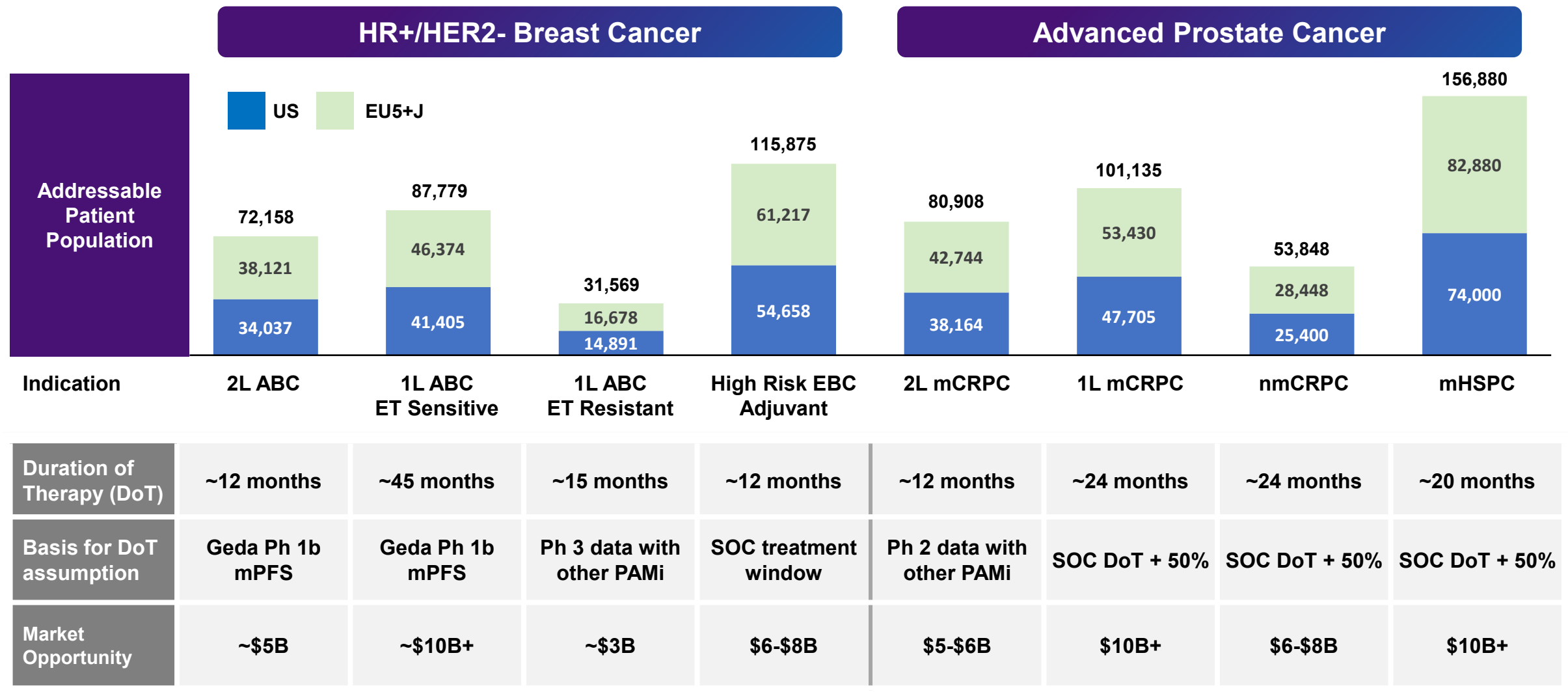
- Extensive literature describes androgen pathway linkage to the PI3K/AKT/mTOR (PAM) pathway
- Gedatolisib demonstrated superior potency and efficacy compared to other PAM inhibitors in nonclinical studies<sup>2</sup>
- Promising clinical activity with an AR inhibitor when combined with less active PAM inhibitors than gedatolisib has been reported in prostate cancer trials<sup>3</sup>



# Addressable Patient Population in Breast and Prostate Cancer



# Multiple potential blockbuster indications in both tumor types





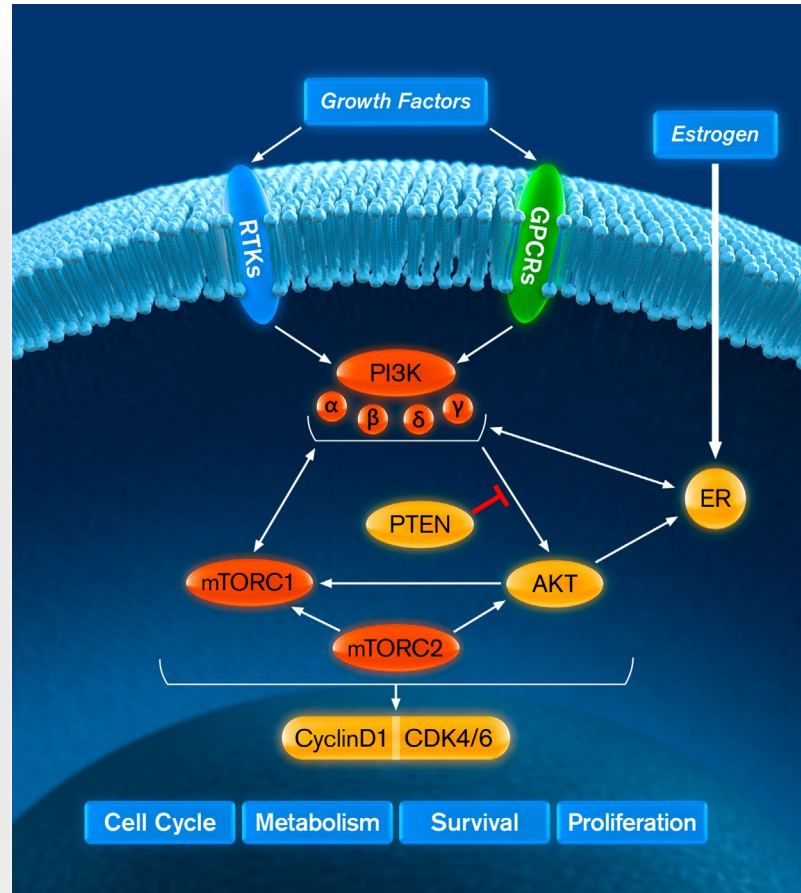
## **Gedatolisib for Advanced Breast Cancer (ABC)**

# ER, CDK4/6, & PI3K/mTOR are Interdependent Drivers of HR+/HER2- ABC

Dysregulation of these pathways promotes excessive cell proliferation and **resistance** to apoptosis

## ER and PI3K/mTOR

- Activation of the PI3K/mTOR pathway induces estrogen independent ER transcriptional activity by mTOR
- Conversely, ER target gene expression activates upstream effectors of the PI3K/mTOR pathway
- ER also activates the PI3K/mTOR pathway by direct binding to PI3K $\alpha$
- **PI3K/mTOR inhibition increases ER activity which increases sensitivity to endocrine therapy**



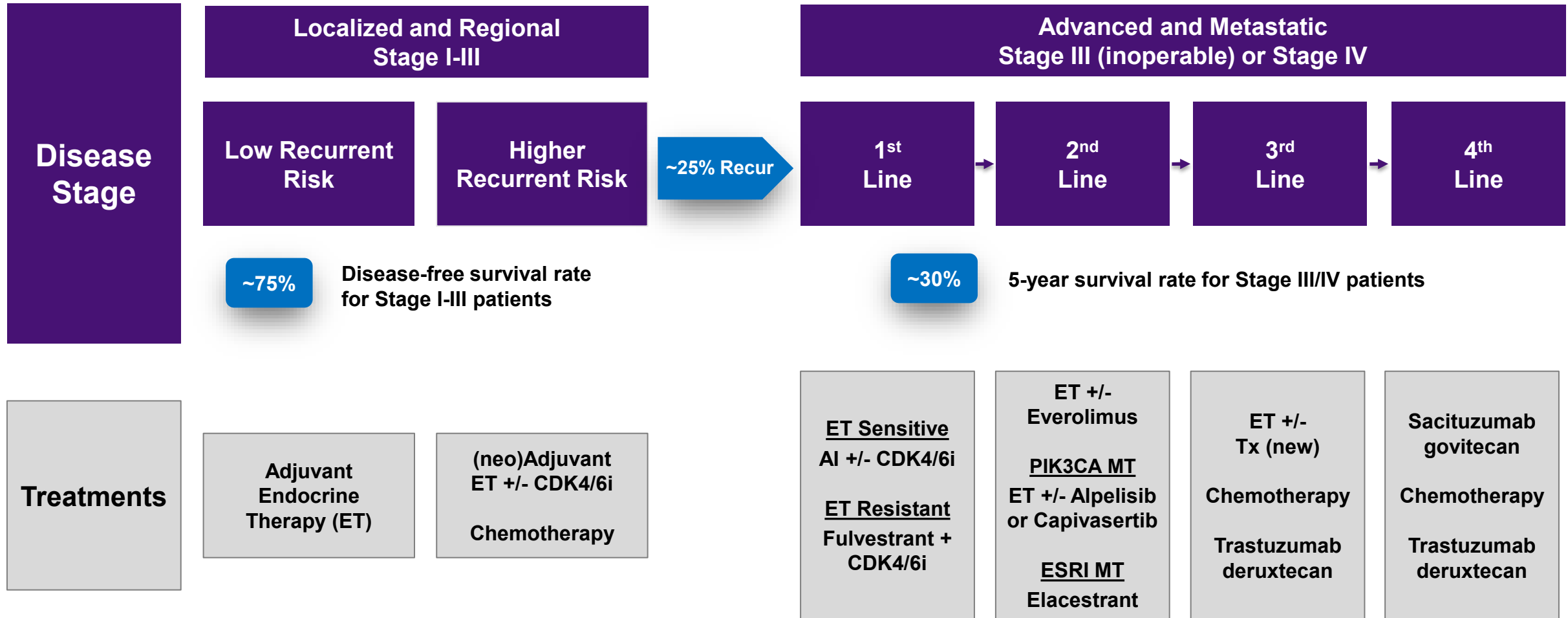
## CDK4/6, ER and PI3K/mTOR

- Estrogen promotes cyclin D1 transcription and cyclin D1 can cause estrogen independent transcription
- Provides rationale for simultaneously inhibiting ER and CDK4/6
- CDK4/6 inhibition causes incomplete cell cycle arrest – addition of PI3K/mTOR inhibition enables more complete arrest
- **PI3K/mTOR inhibition increases cyclin D1 activity which increases sensitivity to CDK4/6 inhibition**

Alves, Int J Mol. Sci. 2023

# HR+/HER2- Breast Cancer Treatment Landscape<sup>1</sup>

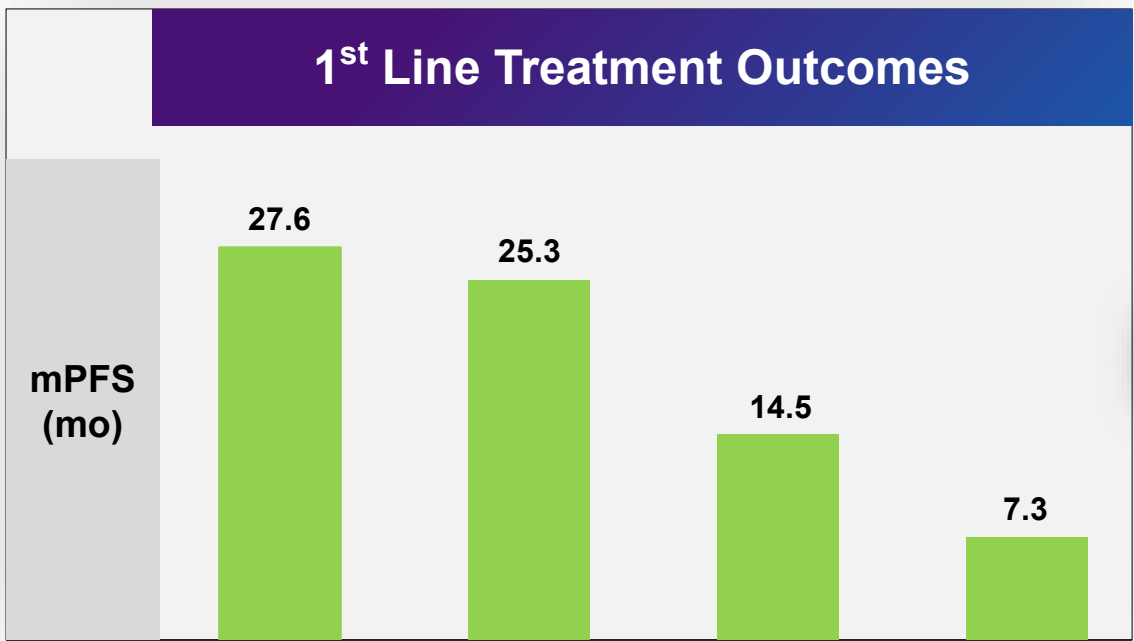
~30,000 women in US and ~33,000 women in 5EU and Japan die from breast cancer annually<sup>2</sup>



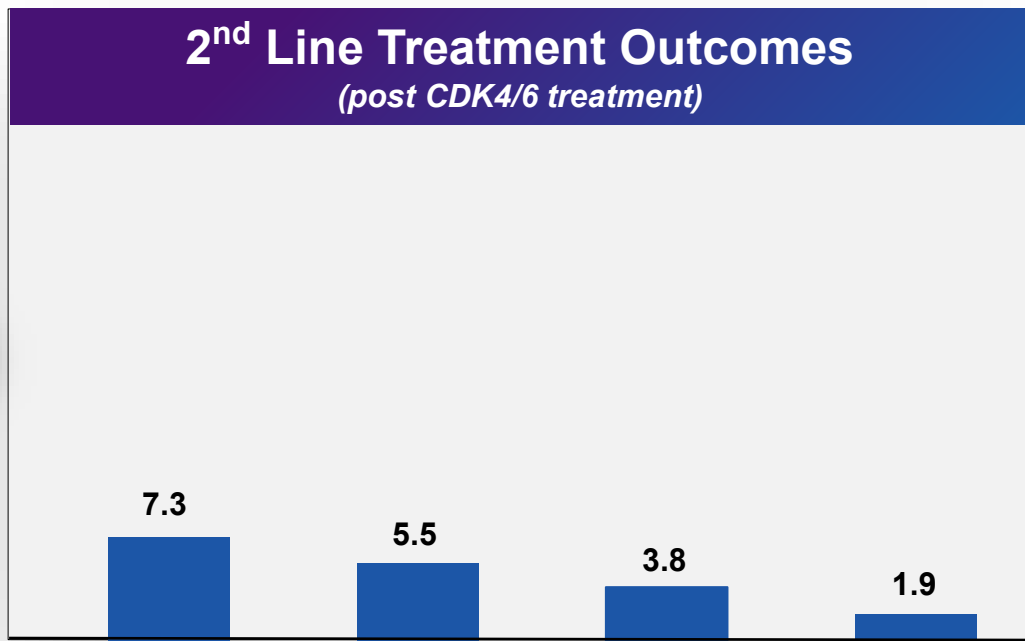


# Limited Benefit for 1<sup>st</sup> Line ET Resistant or 2nd Line HR+/HER2- ABC Patients

Significant need for better therapeutic options



Drugs	Palbociclib + letrozole <sup>1</sup>	Ribociclib + letrozole <sup>2</sup>	Letrozole <sup>1</sup>	Palbociclib + Fulvestrant <sup>3</sup>
MOA	CDK4/6 + AI	CDK4/6 + AI	AI	AI
Pat Pop	ET Sensitive	ET Sensitive	ET Sensitive	ET Resistant
mPFS	27.6	25.3	14.5	7.3
ORR	55%	53%	44%	25%



Alpelisib + fulvestrant <sup>4</sup>	Capivasertib + fulvestrant <sup>5</sup>	Elacestrant <sup>6</sup>	Fulvestrant <sup>6</sup>
PI3Kα + SERD	AKT + SERD	SERD	SERD
PIK3CA+	PIK3CA/AKT/PTEN+	ESR1+	All
7.3	5.5	3.8	1.9
21%	23%	7%	6%

(1) Finn NEJM 2016; Rugo H, et al. Breast Cancer Res Treat, 2019; (2) Hortobagyi NEJM 2016; Hortobagyi Ann Oncol 2018; USPI; (3) Jhaveri SABCS 2023 (4) Rugo Lancet Onco 2021; (5) Oliveira, ESMO Breast, 2023, CDK4/6 prior treated patients (6) Bidard, JCO, 2022 and FDA. Note: All drugs listed are FDA approved

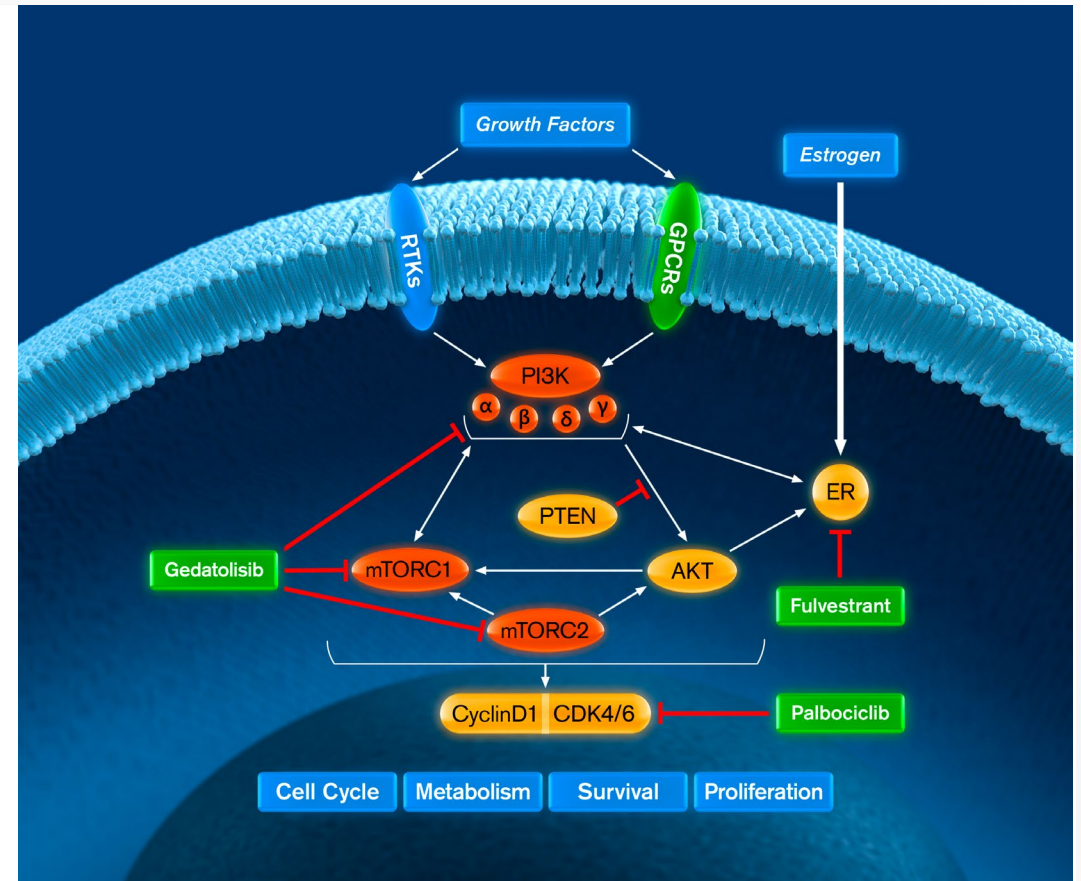
# Review of Phase 1b Data

*Gedatolisib + Palbociclib + Fulvestrant/Letrozole*

# Treatment Strategy: Simultaneous Blockade of PAM, ER, & CDK4/6 Pathways

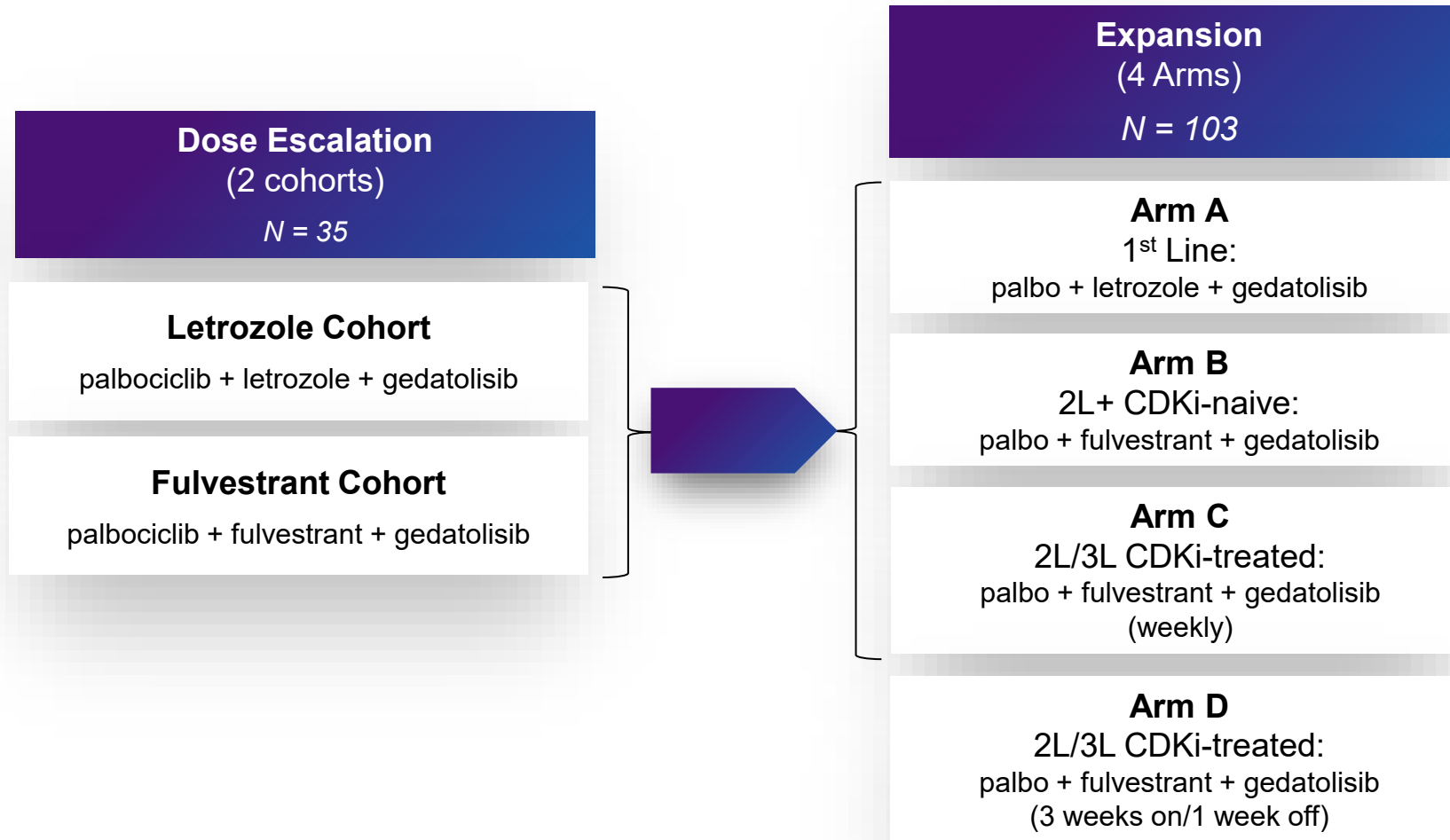
## Treatment Rationale

- Blockade of interdependent ER, PI3K, mTOR & CDK signaling pathways is required to optimize anti-tumor control
- PAM inhibition:
  - Blockades pathway and limits activation when ER or CDK4/6 is inhibited
  - Increases ER activity which increases sensitivity to endocrine therapy
  - Increases cyclin D1 activity which increases sensitivity to CDK4/6 inhibition



# B2151009: Phase 1b Study (138 patients)

Provided Data in Treatment Naïve and Prior CDK4/6 Treated Patients with HR+/HER2- ABC



# B2151009 Expansion Arms: Baseline Characteristics

	Arm A (N=31)	Arm B (N=13)	Arm C (N=32)	Arm D (N=27)
<b>Tumor, Node, Metastasis (TNM) Current Stage, n (%)</b>				
<b>Stage IV</b>	31 (100)	13 (100)	32 (100)	27 (100)
<b>Prior therapies for ABC, n (%)</b>				
<b>Prior Chemotherapy</b>	1 (3.2)	4 (30.8)	15 (46.9)	5 (18.5)
<b>Prior Endocrine Therapy<sup>1</sup></b>	0	11 (84.6)	31 (96.9)	26 (96.3)
<b>Prior CDK4/6 inhibitor</b>	0	0	32 (100)	26 (96.3)
<b>Number of prior systemic therapies ABC, n (%)</b>				
<b>0</b>	30 (96.8)	2 (15.4)	0	0
<b>1</b>	1 (3.2)	9 (69.2)	15 (46.9)	18 (66.7)
<b>≥2</b>	0	2 (15.4)	17 (53.2)	9 (33.3)
<b>Metastatic disease site involved</b>				
<b>Liver or Lung</b>	20 (64.5)	12 (92.3)	23 (71.9)	22 (81.5)
<b>Liver</b>	14 (45.2)	10 (76.9)	20 (62.5)	17 (63.0)
<b>Lung</b>	7 (22.6)	3 (23.1)	7 (21.9)	6 (22.2)
<b>Bone</b>	18 (58.1)	11 (84.6)	25 (78.1)	18 (66.7)
<b>Bone only</b>	0	0	0	0



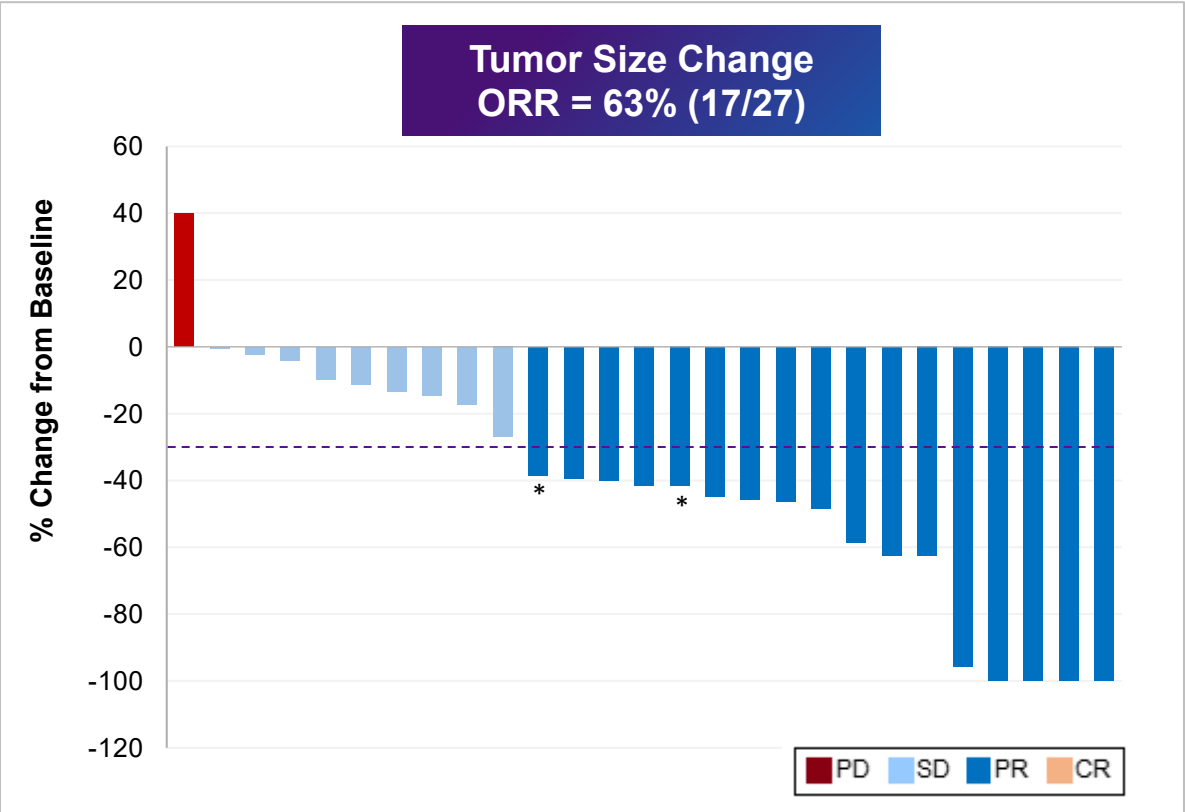
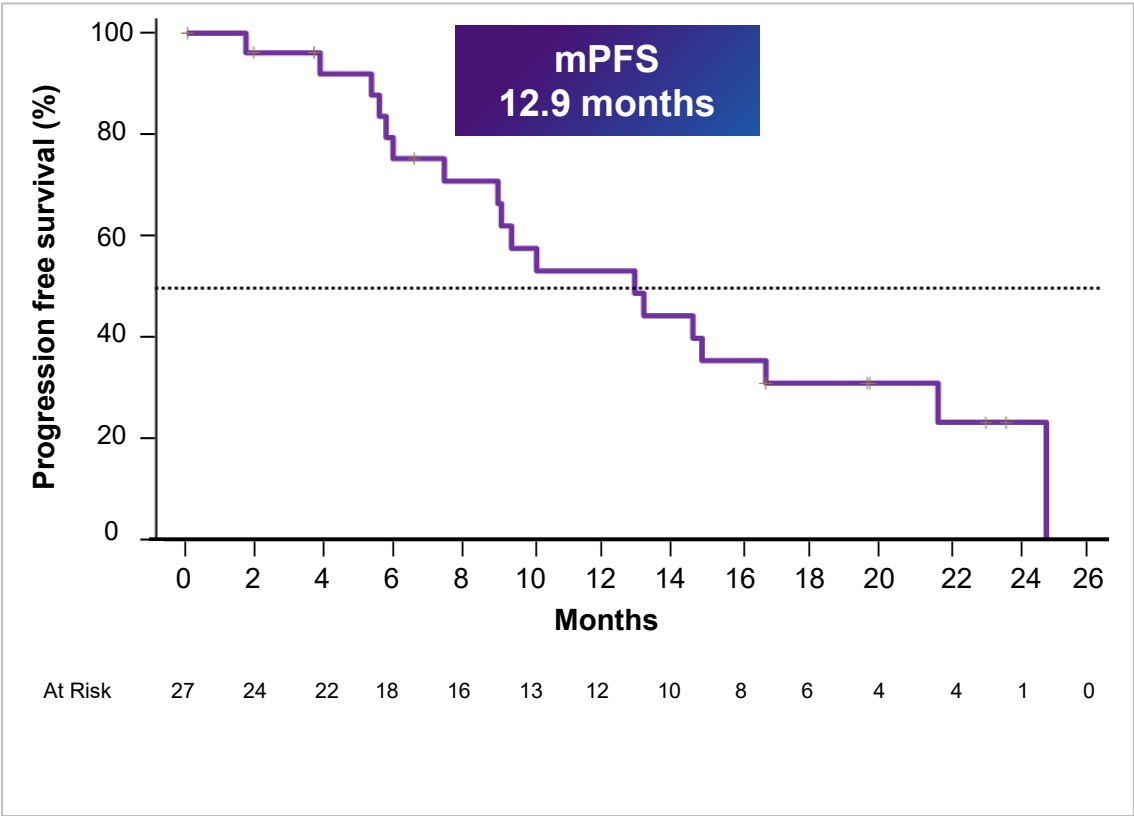
# ORR and PFS in Each Expansion Arm Was Superior to SOC

Results from Arm D - 63% ORR and 12.9 months PFS – provide basis for Phase 3 clinical trial

B2151009 Expansion Arms Efficacy Summary (N=103)								
	Arm A		Arm B		Arm C		Arm D	
Prior Therapy	1L		2L+ CDKi-naïve		2L/3L CDKi-pretreated		2L/3L CDKi-pretreated	
n (Full, response evaluable)	31, 27		13, 13		32, 28		27, 27	
Study Treatment (gedatolisib dosing schedule)	P + L + G (weekly)		P + F + G (weekly)		P + F + G (weekly)		P + F + G (3 weeks on / 1 week off)	
ORR <sup>1</sup> (evaluable)	85%		77%		36%		63%	
mPFS <sup>2</sup> , months (range)	48.4 (16.9, NR)		12.9 (7.6, 38.3)		5.1 (3.3, 7.5)		12.9 (7.4, 16.7)	
PFS % at 12 mos <sup>2</sup>	72%		55%		24%		53%	
PIK3CA Status	WT	MT	WT	MT	WT	MT	WT	MT
	81% <sup>3</sup>	16%	69%	31%	75%	25%	56% <sup>3</sup>	41%
ORR <sup>1</sup> (evaluable)	81%	100%	78%	75%	25%	63%	60%	73%
PFS % at 12 mos <sup>2</sup>	74%	60%	50%	67%	22%	29%	49%	60%

# Gedatolisib + Palbociclib + Fulvestrant in 2<sup>nd</sup>/3<sup>rd</sup> Line HR+/HER2- ABC Patients

Data from Arm D with Phase 3 regimen compares favorably to published data with current SOC



# B2151009 Arm D: Safety Summary for Phase 3 Dosing

G + P + F was well tolerated overall; < 4% discontinuation rate

- Discontinuation of gedatolisib due to AE - <4%
  - Alpelisib – 25% discontinued <sup>1</sup>
- Most TRAE's were Grade 1 or 2
- Few hyperglycemia adverse events
  - 26% all Grades, 7% Grade 3/4
  - Alpelisib (65% all, 37% Grade 3/4) <sup>2</sup>
- Stomatitis prophylaxis was not utilized in this study
  - **Swish-and-Spit dexamethasone prophylactic mouth rinse reduced Grade 2-4 stomatitis by 90%** <sup>3</sup>
  - Phase 3 study will include prophylaxis
- Neutropenia, leukopenia, and anemia AE incidence is nearly identical to PALOMA-3 (palbociclib + fulvestrant)

**Arm D (n=27)**  
**Gedatolisib + Palbociclib + Fulvestrant**  
 (180 mg IV, 3 weeks on, one week off)

Related TEAE's > 30%			
	Grade 1	Grade 2	Grade 3/4
Adverse Event	%	%	%
<b>Stomatitis</b> <sup>4</sup>	11	56	22
<b>Neutropenia</b> <sup>5</sup>	-	15	67
<b>Nausea</b>	44	30	-
<b>Fatigue</b>	22	37	7
<b>Dysgeusia</b>	44	7	-
<b>Diarrhea</b>	37	-	4
<b>Rash</b>	19	15	7
<b>Leukopenia</b> <sup>6</sup>	-	19	23
<b>Constipation</b>	30	4	4
<b>Vomiting</b>	22	11	4
<b>Anemia</b> <sup>7</sup>	4	15	15
<b>Hyperglycemia</b>	15	4	7

# Gedatolisib Combo vs. SOC for 2L HR+ / HER2- ABC Post-CDKi

Gedatolisib Combo Offers Potential for Superior Efficacy Compared to Alternatives

Patient Population	2 <sup>nd</sup> Line ER+/HER2- ABC	
All	Gedatolisib + Fulvestrant + Palbociclib <sup>1</sup>	mPFS 12.9 months ORR 63%
PIK3CA+	Alpelisib + Fulvestrant <sup>2</sup>	mPFS 7.3 months ORR 17%
PIK3CA+	Alpelisib + Fulvestrant <sup>3</sup>	mPFS 5.6 months ORR 24%
PIK3CA/AKT1/ PTEN+	Capivasertib + Fulvestrant <sup>4</sup>	mPFS 5.5 months ORR 23%
ESR1+	Elacestrant <sup>5</sup>	3.8 months ORR 4%
All	Fulvestrant <sup>5</sup>	mPFS 1.9 months ORR 6%

# Efficacy in Treatment-Naïve Population Superior to SOC

mPFS of 48.6 months, mDOR of 46.9 months, and ORR of 79%

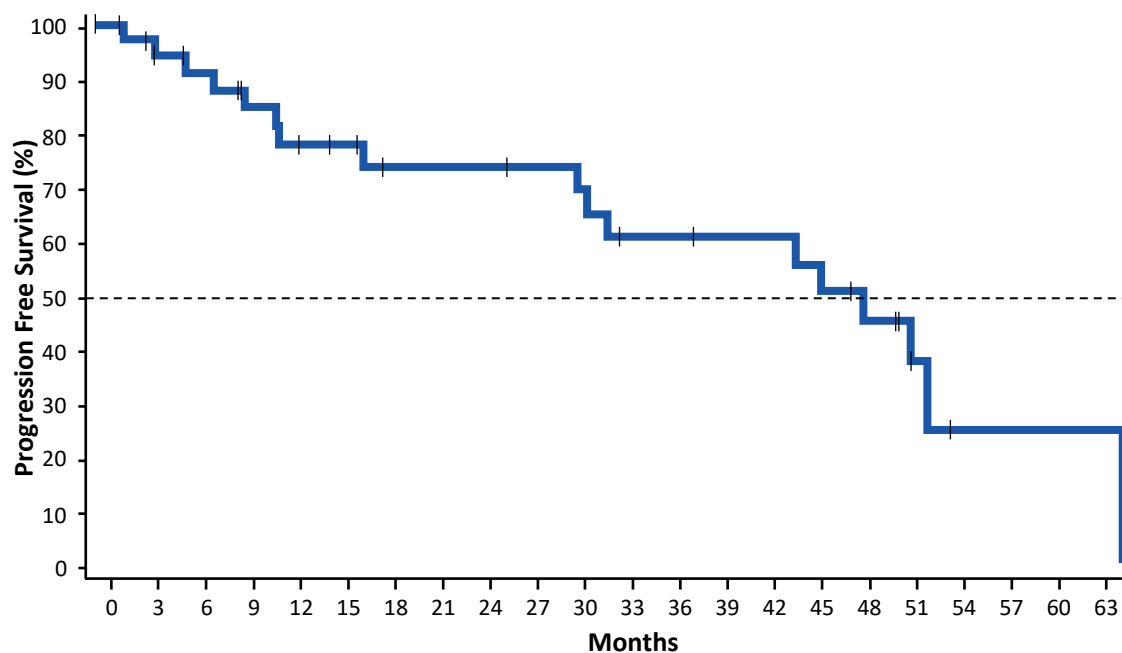
B2151009 Treatment-Naïve Patients (N=41)			
	Escalation Arm A	Expansion Arm A	Total Treatment Naïve
<b>Progression-Free Survival (full analysis set)</b>	n = 11	n = 30	n = 41
Median PFS, mos (95% CI)	<b>45.8</b> (32.3, NR)	<b>48.6</b> (11.6, NR)	<b>48.6</b> (30.4, NR)
<b>Responses (evaluable, measurable disease) <sup>1</sup>, n (%)</b>	n = 7	n = 26	n = 33
CR	0	1 (3.8)	1 (3.0)
PR	4 (57.1)	21 (80.8)	25 (75.8)
SD	3 (42.9)	3 (11.5)	6 (18.2)
Unconfirmed PR	0	0	0
Durable SD (≥24 weeks)	1 (14.3)	2 (7.7)	3 (9.1)
PD	0	1 (3.8)	1 (3.0)
ORR <sup>1</sup>	<b>4 (57.1)</b>	<b>22 (84.6)</b>	<b>26 (78.8)</b>
Median DOR, mos (95% CI) <sup>2</sup>	<b>39.7</b> (30.5, NR)	<b>46.9</b> (11.3, NR)	<b>46.9</b> (24.6, 49.5)



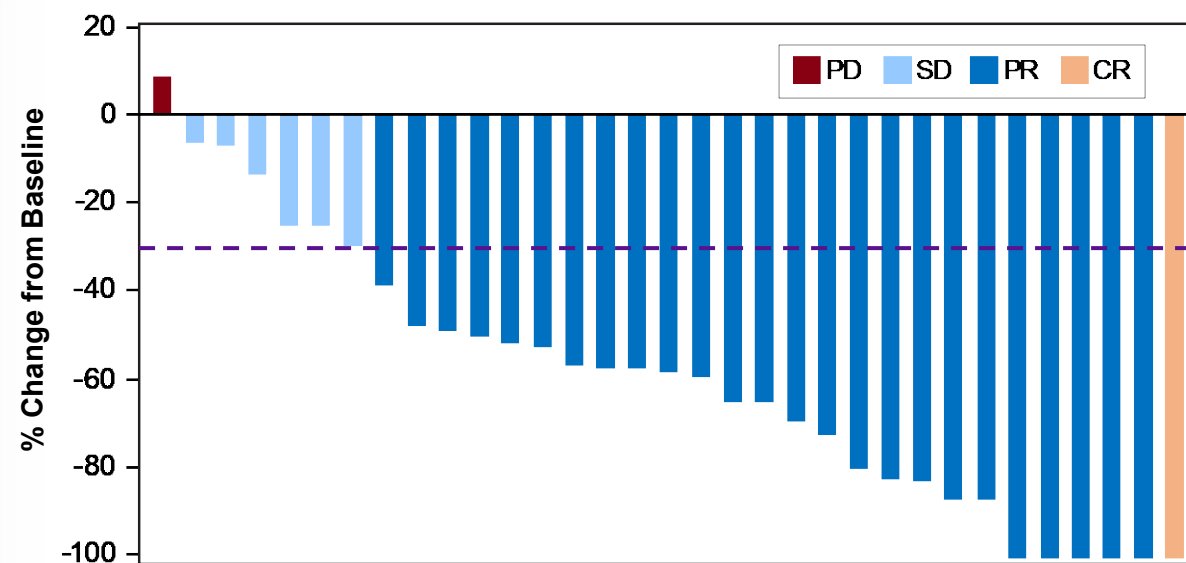
# Gedatolisib + Palbociclib + Letrozole in 1<sup>st</sup> Line HR+/HER2- ABC (N=41)<sup>1</sup>

Combined 1L data from Esc Arm A + Exp Arm A compares favorably to published data for SOC palbociclib + letrozole<sup>2</sup>

mPFS  
48.6 Months

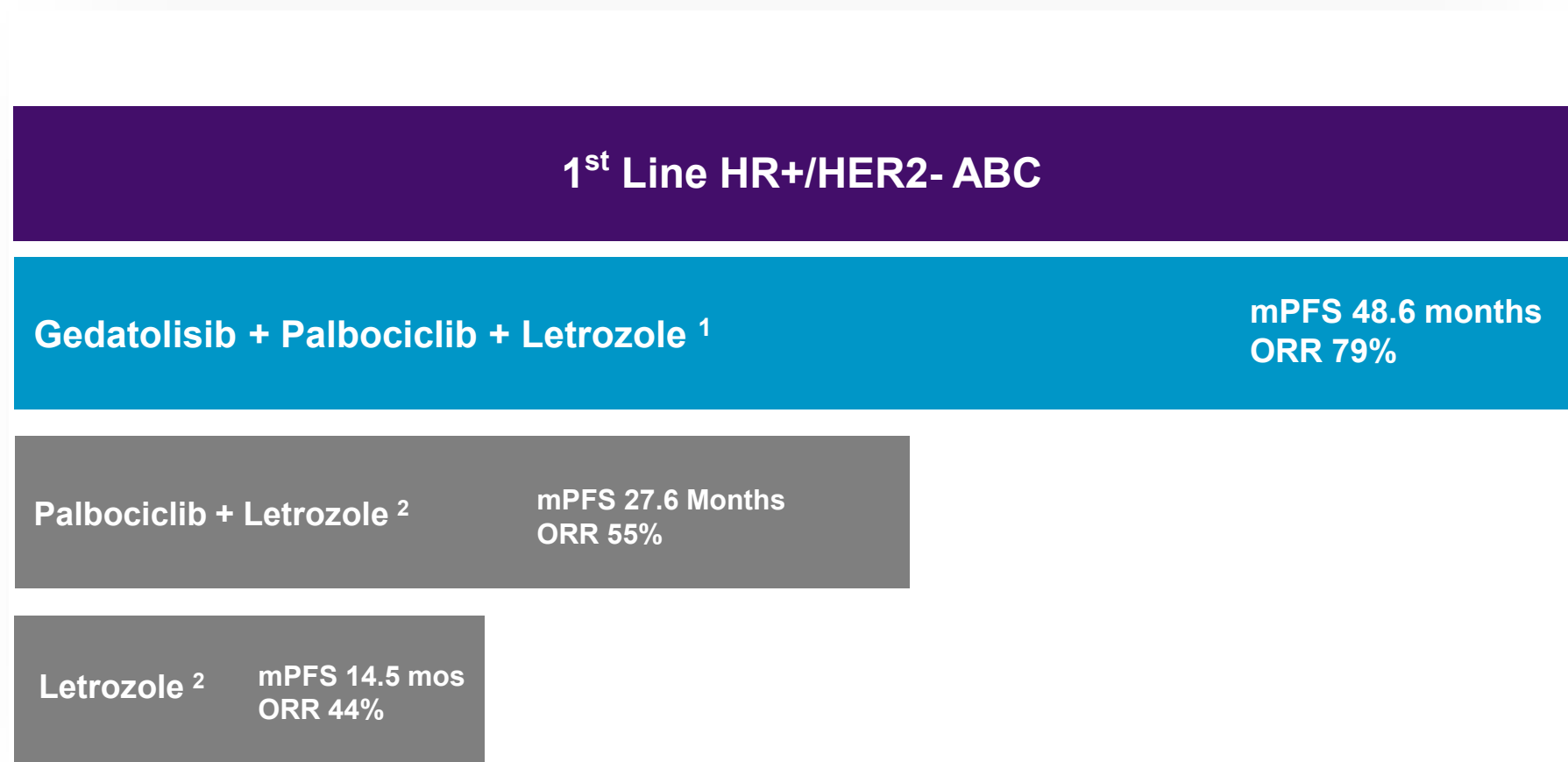


Tumor Size Change  
ORR = 79% (26/33)



# Gedatolisib Combo vs. SOC for 1L HR+ / HER2- ABC

Gedatolisib Combo Offers Potential for Superior Efficacy Compared to 1L SOC



# Phase 3 Study Design

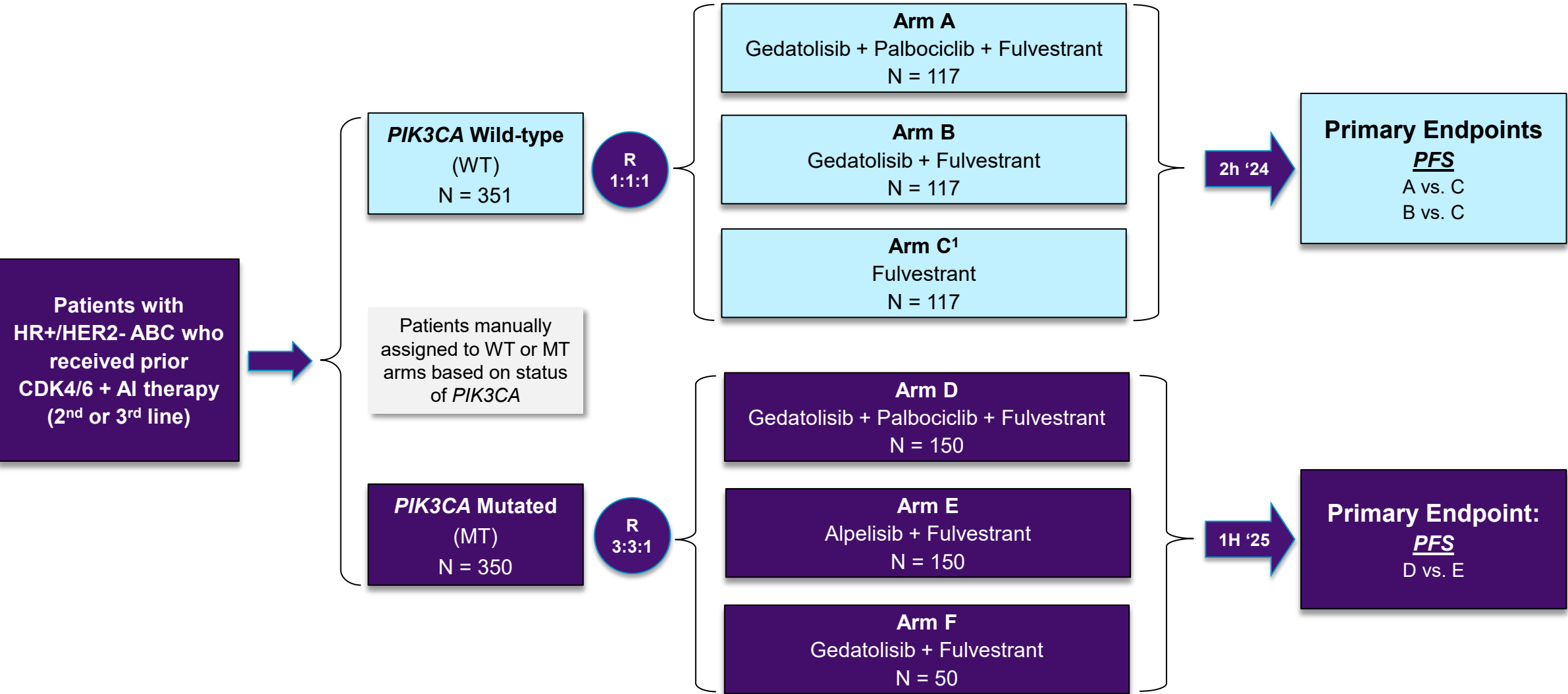
## VIKTORIA-1

# Pivotal Trial Design Considerations for 2<sup>nd</sup> Line HR+/HER2- ABC

- Standard-of-care 2<sup>nd</sup> line treatment is based on *PIK3CA* status
- ~35% of patients have disease with *PIK3CA* mutations
- PFS is accepted primary end point for randomized studies in ABC

Supports design with multiple  
primary endpoints in different  
sub-groups

# VIKTORIA-1 Pivotal Phase 3 Trial Design Overview



1) Optional Cross-over to Arm A or Arm B upon progressive disease; WT = wild type; MT = mutant; PFS = progression free survival

# Relevant Comparisons to VIKTORIA-1 Controls

B2151009 study results compared to published data for patients who received prior CDK4/6i

	Gedatolisib + Palbociclib + Fulvestrant N=27 <sup>1,2</sup>	Fulvestrant N=165 <sup>3</sup>	Fulvestrant N=52 <sup>5</sup>	Alpelisib + Fulvestrant N=126 <sup>6</sup>	Alpelisib + Fulvestrant N=121 <sup>7</sup>
<b>PIK3CA Status</b>	WT / M (56% / 41%)	WT	WT / MT (70% / 30%)	M	M
<b>Line of Therapy (% by line)</b>	2L / 3L+ (67% / 33%)	2L / 3L+ (73%/27%) <sup>4</sup>	2L / 3L+ (83% / 17%)	2L / 3L+ (37%/ 63%)	1L / 2L/ 3L+ (12% / 70% / 19%)
<b>mPFS (months)</b>	12.9	1.9	1.9	5.6	7.3
<b>ORR</b>	63% (overall) <sup>2</sup> <u>WT</u> 60% <u>M</u> 73%	NR	6%	22%	17%
<b>PFS % at 12 months</b>	53% (overall) <u>WT</u> 49% <u>M</u> 60%	10%	12%	22%	27%

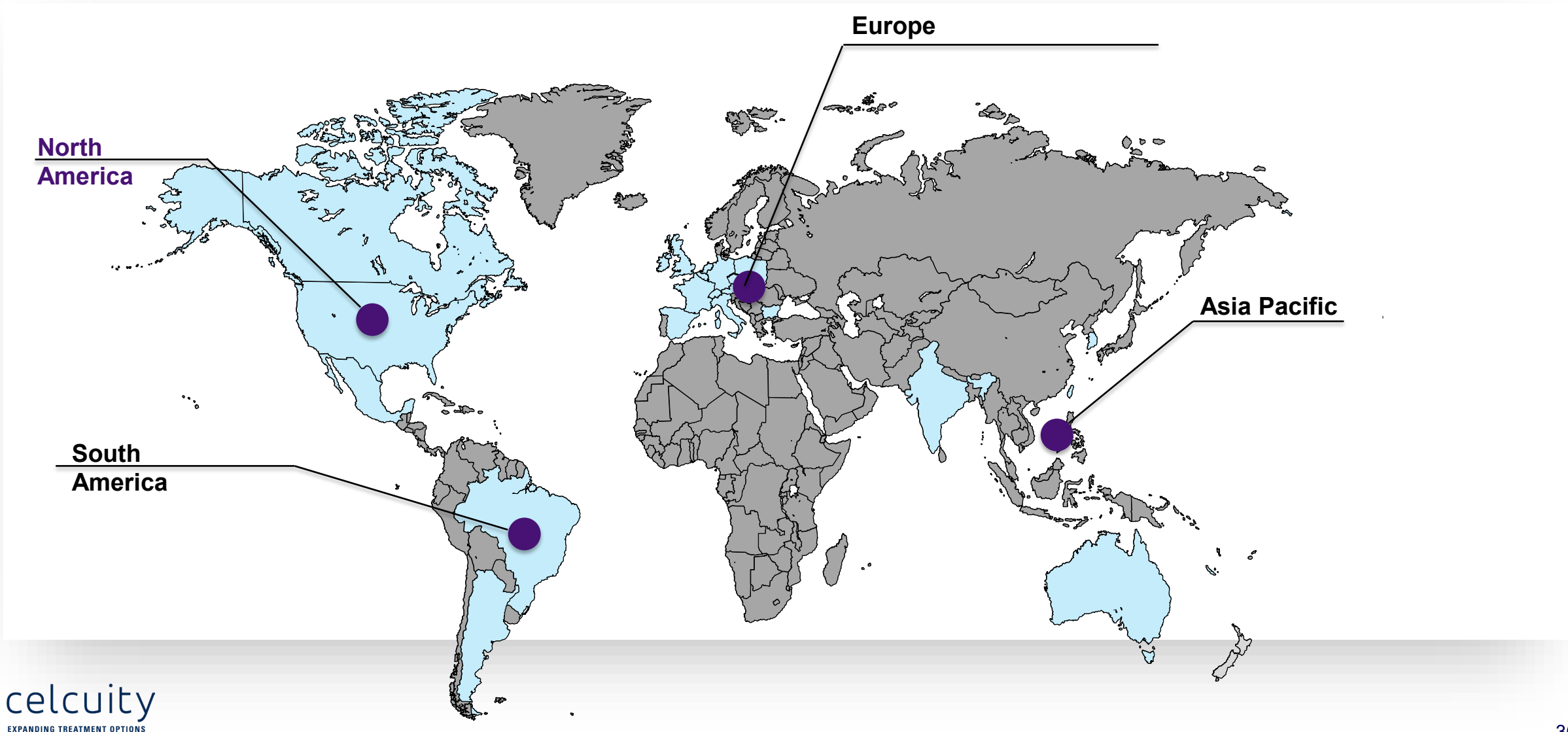


# VIKTORIA-1 Pivotal Study Features

- **Global open-label randomized study**
- **Key eligibility criteria:**
  - Any *PIK3CA* status
  - Prior CDK4/6i + NSAI
  - Any menopausal status
  - $\leq 2$  prior endocrine therapy
  - No prior chemotherapy for ABC
- **Three primary endpoints could support three separate indications**
  - Two co-primary endpoints (PFS) in *PIK3CA* WT patients
  - One primary endpoint (PFS) in *PIK3CA* MT patients
- **Three-arm design for *PIK3CA* WT and MT patients enables evaluation of two different regimens and shows contribution of gedatolisib**
- **Stratification by geography, prior treatment response ( $\leq$  or  $>$  6 months), presence of liver or lung metastasis (yes/no)**

Supports indications for **gedatolisib and fulvestrant with or without palbociclib as second or third treatment for patients with HR+/HER2-advanced or metastatic breast cancer** who have progressed on prior treatment with a CDK4/6 therapy in combination with AI

# 200+ Sites Across 20 Countries





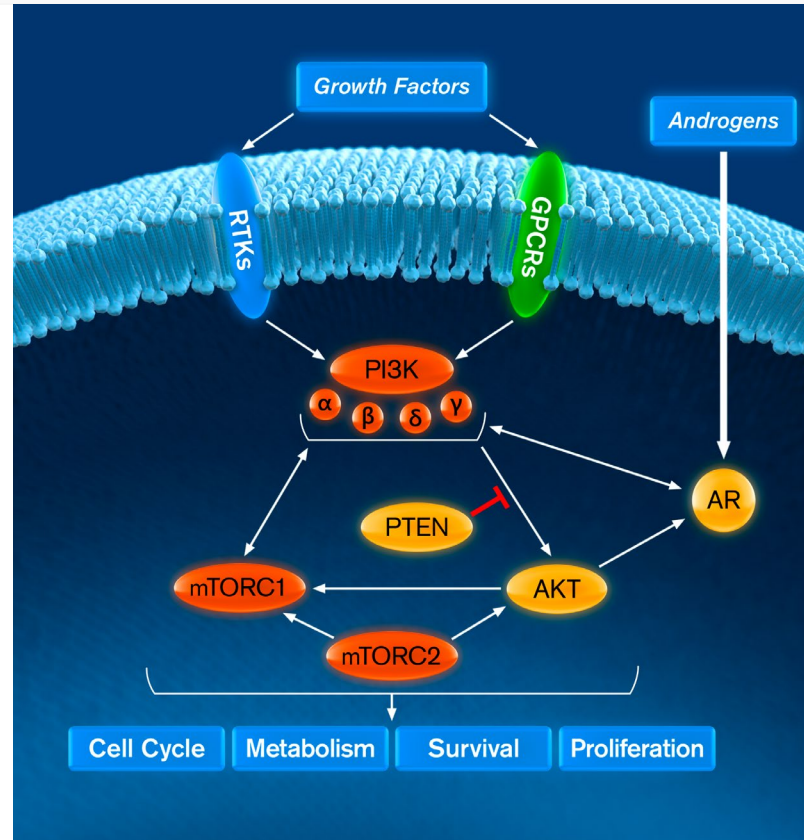
## **Gedatolisib for Prostate Cancer**

# Androgen Signaling is the Key Driver of Prostate Cancer

The PI3K/AKT/mTOR (PAM) pathway helps promote excessive cell proliferation and resistance to apoptosis

## The AR Pathway is the Primary Therapeutic Target

- The androgen receptor (AR) drives the expression of target genes which promote cancer cell survival and growth
- The androgen signaling pathway is the primary therapeutic target for prostate cancer at all stages of disease
- Androgen deprivation therapies (ADT) are used primarily for localized disease
- Second generation AR inhibitors are used for advanced disease

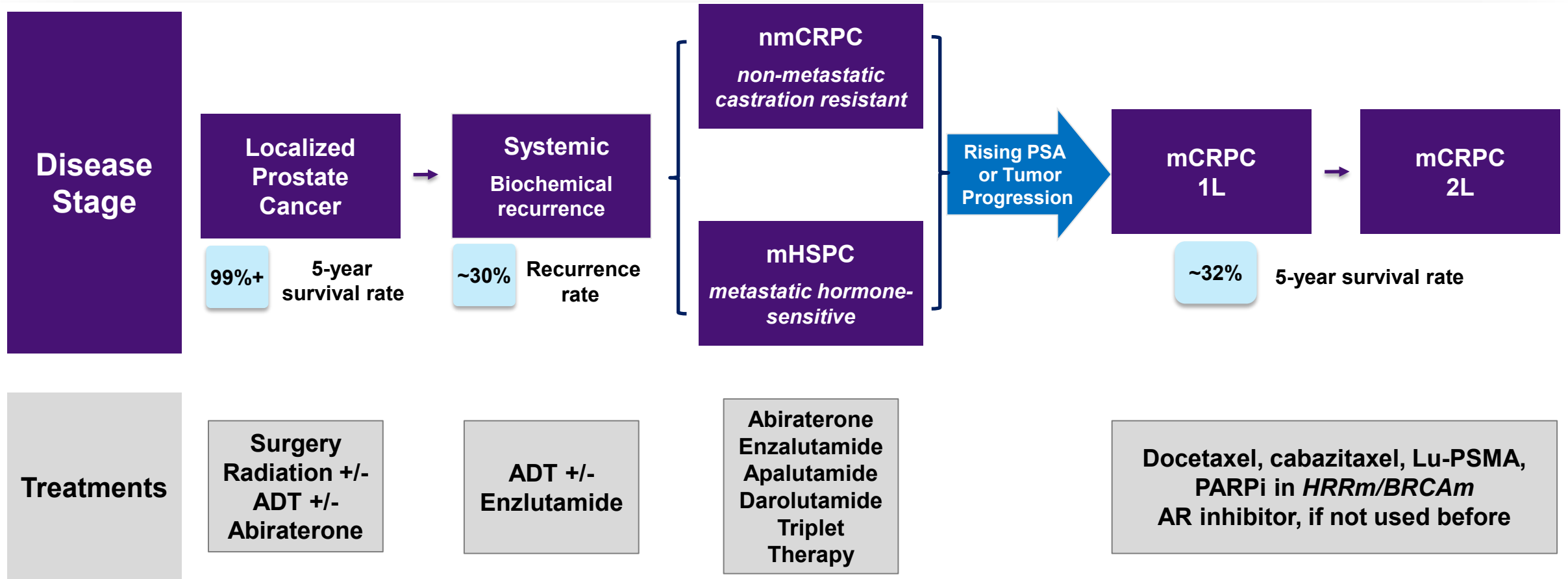


## The PAM Pathway Plays a Key Role in mCRPC

- AR and PI3K-AKT-mTOR pathways cross-regulate each other.
- 70% - 100% of mCRPC tumors have PI3K/AKT/mTOR related pathway alterations.
- Mutations dispersed across PTEN, PI3K, AKT, and mTOR sub-units

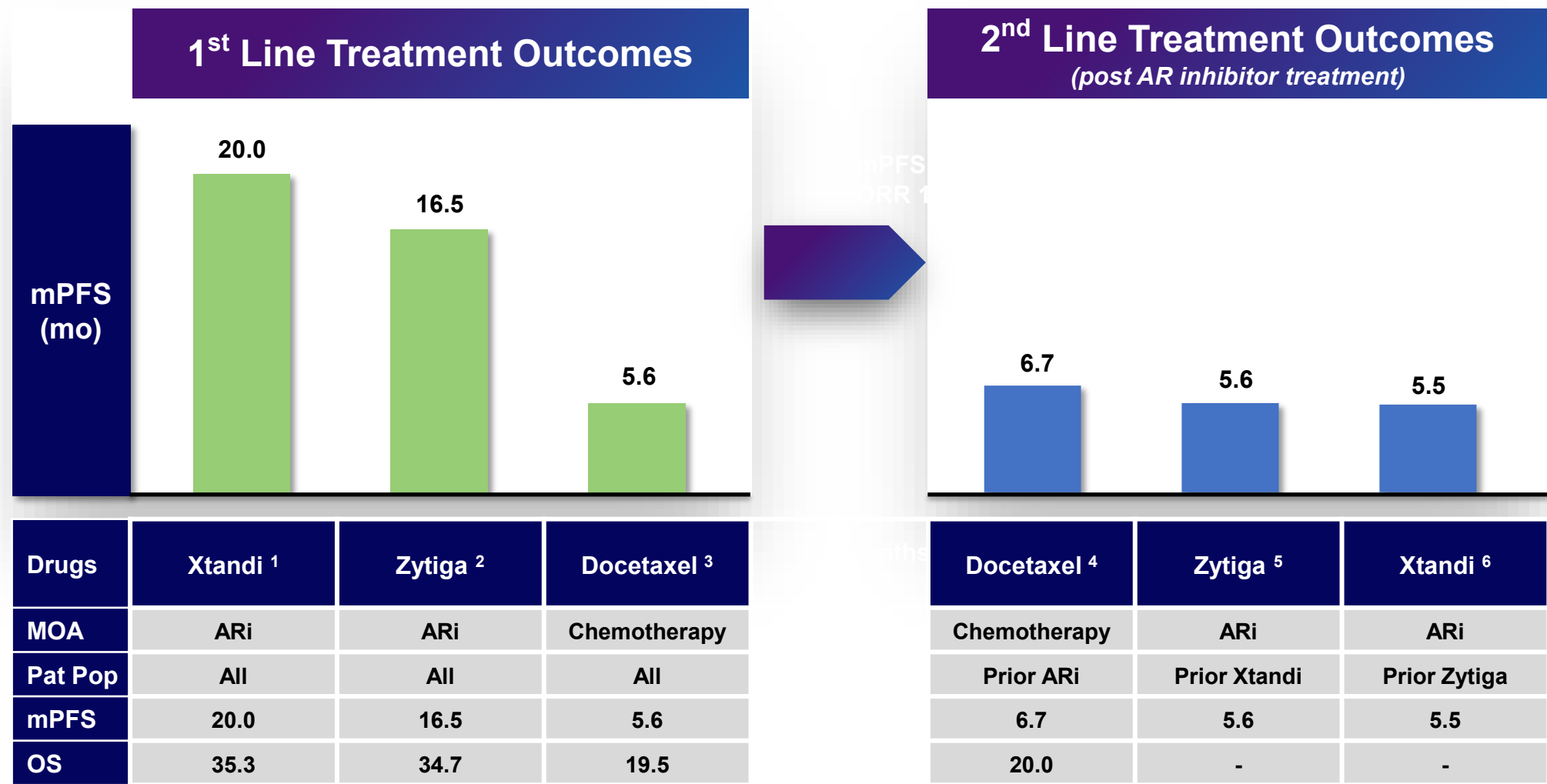
# Prostate Cancer Disease and Treatment Landscape<sup>1,2</sup>

34,700 men in US and 62,400 men in 5EU and Japan die from prostate cancer annually<sup>3,4</sup>



# Limited Benefit for 2L HRR- mCRPC Patients After Treatment with AR Inhibitor

Significant need for better therapeutic options



(1) Beer Eur Urol. 2017; (2) Ryan NEJM 2013; Ryan Lancet Oncol 2015 (3) Kellokumpu-Lehtinen Lancet Oncol. 2013, time-to-treatment failure reported; (4) Crabb J Clin Oncol 2021; (5) Attard J Clin Oncol 2018; (6) Sweeny Clin Cancer Res 2022. Abbreviations: HRR = homologous recombination repair; AR = androgen receptor

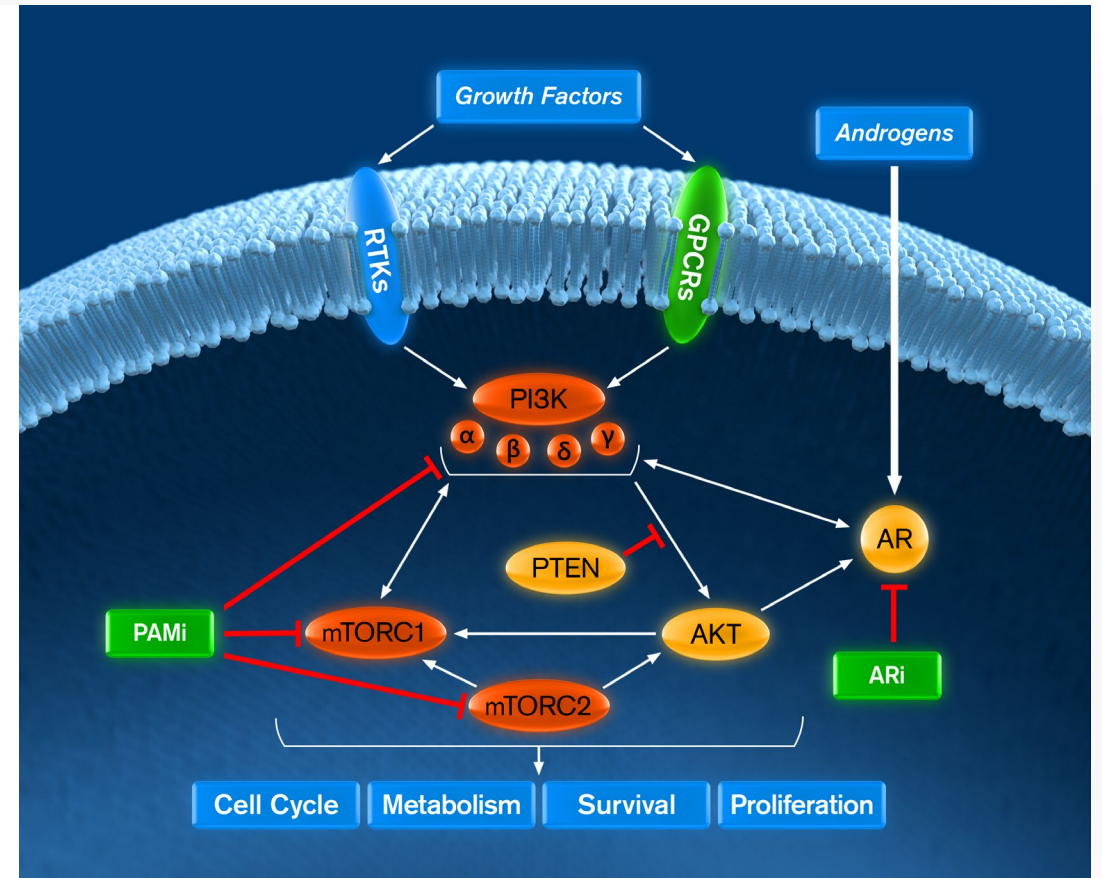


# Combining a PAM Inhibitor with an AR Inhibitor has Strong Scientific Rationale

Biological parallels between mCRPC and HR+ ABC – PAM and hormonal pathway drive progression <sup>1</sup>

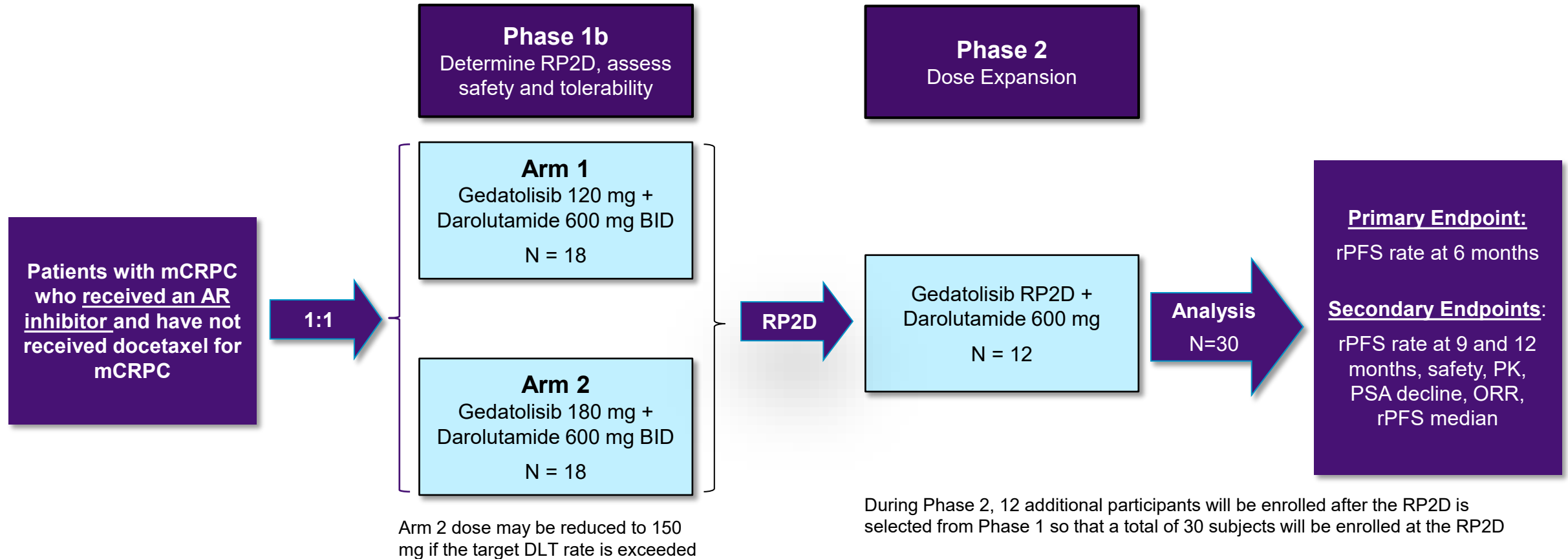
## PI3K/mTOR + AR Inhibition *Treatment Rationale*

- Favorable clinical data in mCRPC with PAM inhibitors provides “proof-of-concept” of benefit of combining a PAM and AR inhibitor in 2L setting
- Gedatolisib’s clinical efficacy in breast cancer correlated with strong activity in nonclinical tumor models
- Gedatolisib exhibits similar potency and efficacy in prostate cancer cell lines as those reported in breast cancer cell lines
- Xenograft data in PR models is consistent with in vivo data – gedatolisib exhibits anti-tumor effects independent of PTEN or AR status



# CELC-G-201: Phase 1b/2 Trial Design Overview

Evaluating gedatolisib combined with darolutamide, a potent next generation androgen receptor inhibitor



Expect to enroll first patient Q1 2024 and announce initial data 1H 2025

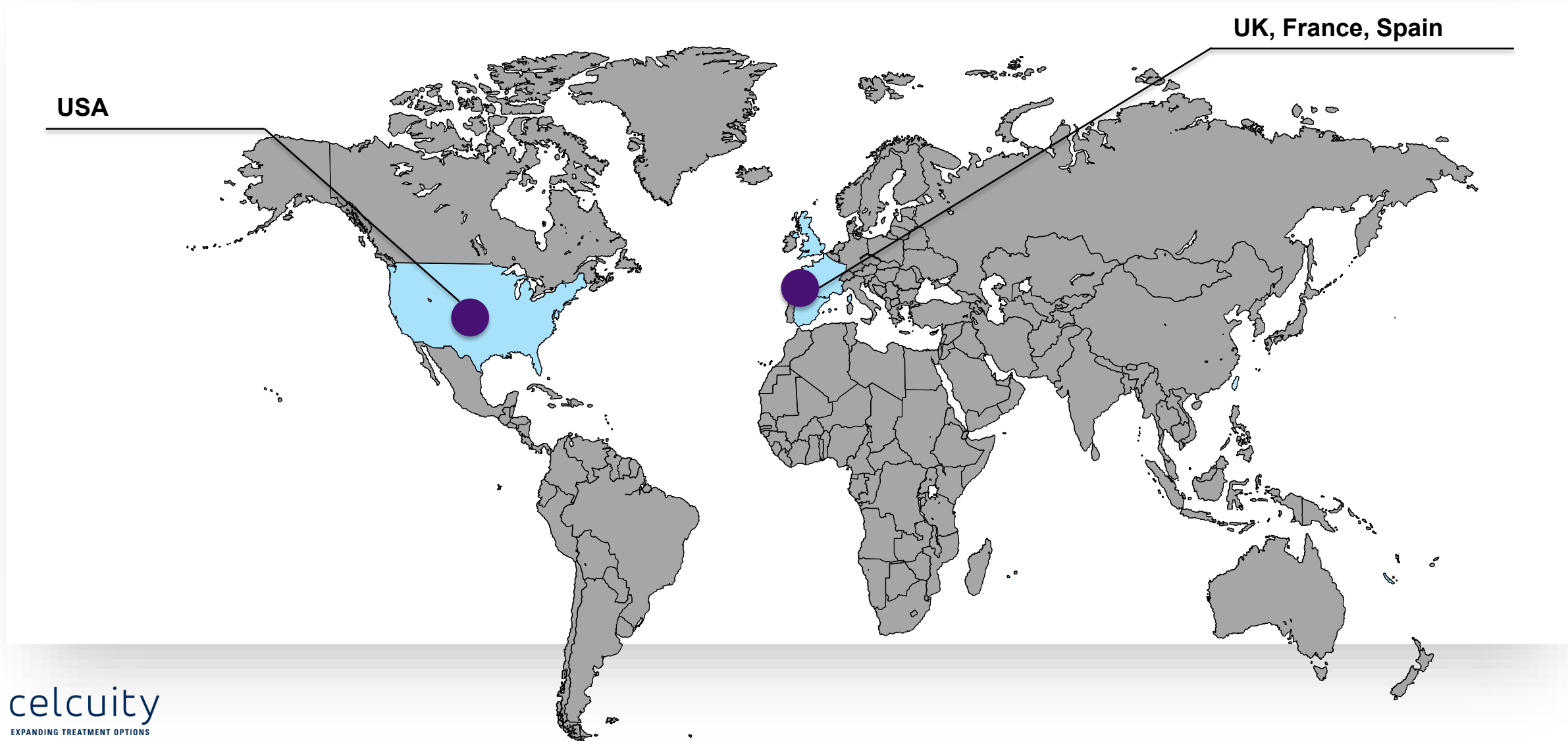
# Darolutamide is More Potent and Better Tolerated than SOC 1L AR Inhibitors

Bayer is collaborating with Celcuity and will supply darolutamide for the trial

	Darolutamide		Abiraterone		Enzalutamide	
Approved Indications	nmCRPC, mHSPC		mCRPC, mHSPC		mCRPC, nmCRPC, mHSPC	
IC <sub>50</sub> <sup>1</sup>	11 nM <sup>2</sup>		72 nM <sup>3</sup>		86 nM <sup>2</sup>	
Most Common AE's (%) <sup>4</sup>	All Grades	Grade 3/4	All Grades	Grade 3/4	All Grades	Grade 3/4
Fatigue	16	1	39	2	51	9
Pain in extremities	6	0	30	2	21	3
Edema	<2	0	25	0.4	15	1
Constipation	<2	0	23	0.4	<2	0
Diarrhea	<2	0	23	1	22	2
Hot Flush	<2	0	22	0.2	20	0
Hypertension	<2	0	22	4	<2	1
Back Pain	<2	0	<5	0	26	5

# ~12 Sites Across US and Europe

Expect to enroll first patient Q1 2024 and announce initial data 1H 2025

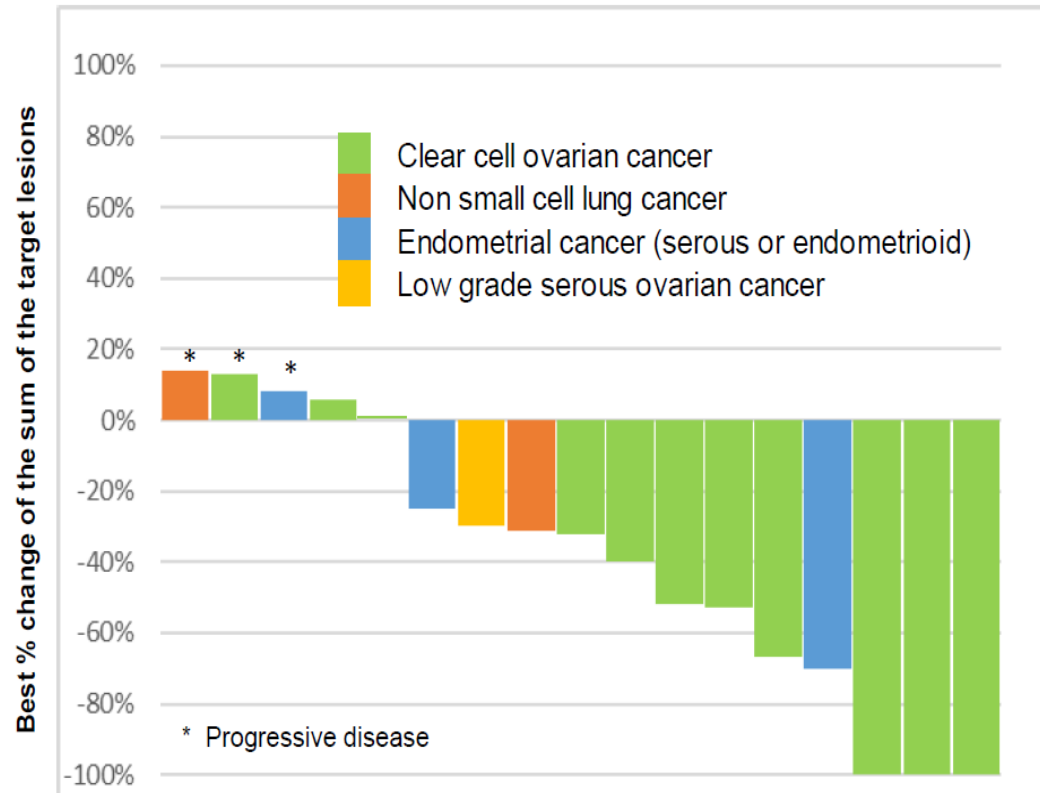




## **Additional Early Phase Clinical Data**

# Gedatolisib + Paclitaxel + Carboplatin in Patients with Solid Tumors (N=17)<sup>1</sup>

65% ORR in all patients, 82% ORR in patients with ovarian cancer



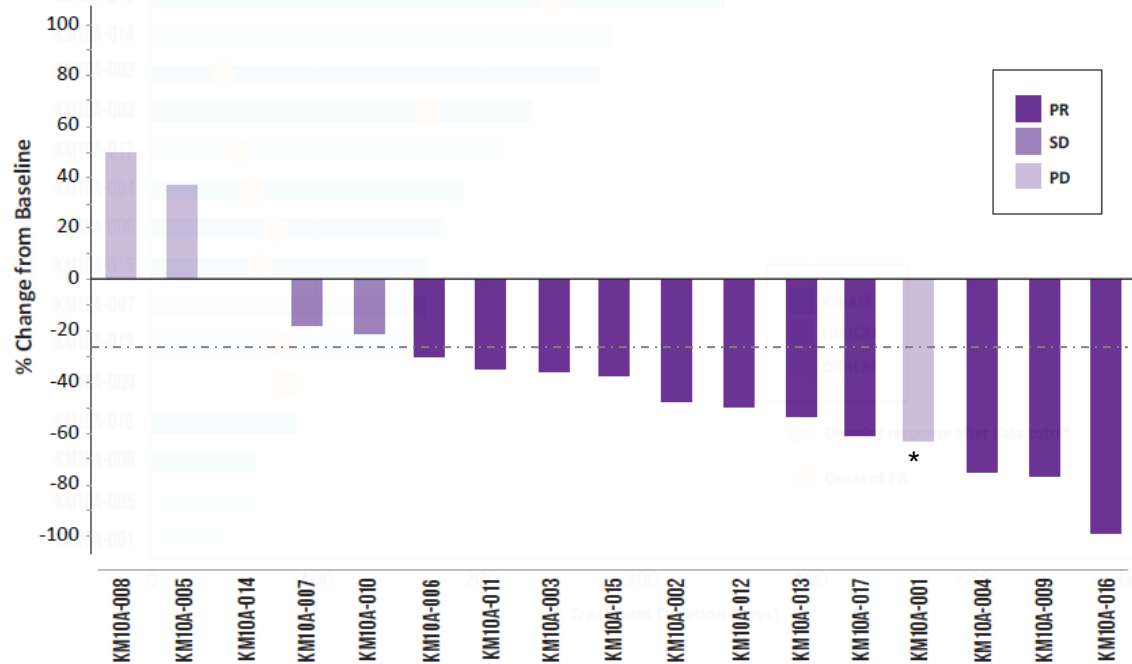
- Ovarian Cancer (N=11)
  - ORR: 82%
    - Clear cell ovarian cancer (CCOC) (N = 10)
      - ORR: 80% - 5/10 PR, 3/10 CR
    - Low grade serous ovarian (N=1)
      - 1/1 PR
- Other solid tumors (N= 6)
  - ORR = 33%
- Median PFS = 6.35 months (95% CI 4.6-11.11)
- Median duration of response = 7.6 months (95% CI 1.9-13.4)

- The CCOC data compares very favorably to ORR for platinum therapy reported in platinum-naïve CCOC patients - 25%-50%
- CCCO accounts for ~15% ovarian cancers in Asia
- Will assess likelihood other ovarian sub-types may benefit from gedatolisib + platinum therapy

# Gedatolisib + Trastuzumab Biosimilar in 3L+ HER2+ ABC Patients (N=17)

59% ORR and 83% clinical benefit rate

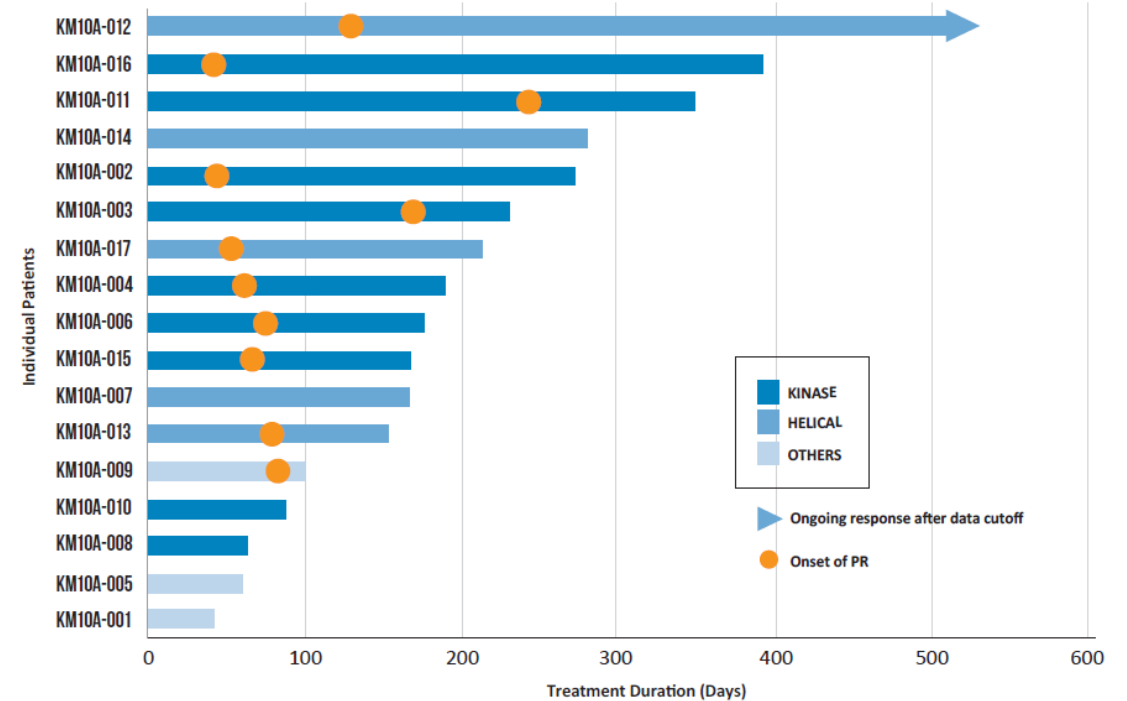
## Best Response



\* Target lesion decreased by 63% but a new leptomeningeal seeding occurred.

- 10 of 17 (59%) showed partial response (PR)
- 4 of 17 (24%) had stable disease (SD)

## Duration of Response



- Median duration of response 7.1 months



# Leading cancer KOLs are participating in our research

## Clinical Advisory Board



**Mark Pegram M.D. Ph.D.**



**Sara Hurvitz M.D.**



**Ben Ho Park M.D., Ph.D.**



**Adam Brufsky M.D., Ph.D.**



**Lee Schwartzberg M.D.**



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**Carol Lange Ph.D.**



**Manfred Auer Ph.D.**



**John Katzenellenbogen Ph.D.**



**Ron McGlennen M.D.**



**Benita Katzenellenbogen Ph.D.**



# Leadership Team: Track Record of Developing Approved Therapies and Building Companies



**Brian Sullivan**

Chief Executive Officer  
Co-Founder



**Igor Gorbachevsky, MD**

Chief Medical Officer



**Fred Kerwood**

VP, Program Management



**Lance Laing, PhD**

Chief Scientific Officer  
Co-Founder



**Bernhard Lampert, PhD**

VP, Pharmaceutical  
Development



**Nadene Zack**

VP, Clinical Operations



**Vicky Hahne**

Chief Financial Office



**David Bridge**

VP, Quality Assurance and  
Process Development



**Pratima Nayak, MD**

VP, Medical Affairs



**Eldon Mayer**

Chief Commercial Officer



**Charlotte Moser, PhD**

SVP, Clinical Development



**Sunni Miller**

VP, Regulatory Affairs

# The Celcuity Opportunity

Significant untapped potential to effectively treat PAM pathway involved cancers

1

- Gedatolisib's differentiated MOA and PK profile result in a highly potent, cytotoxic, and well tolerated PAM inhibitor

2

- Very compelling data in 1L (mPFS 48 months) and 2L (mPFS 12.9 months) patients with HR+/HER2- ABC
- Potential to replace currently available standard-of-care

3

- Strong scientific rationale to develop gedatolisib for prostate cancer indications
- Parallels between breast and prostate cancer – interdependent activity between PAM pathway and hormonal pathways

4

- Uniquely positioned to advance multiple potential blockbuster indications in breast and prostate cancer
- Cash & cash equivalents of \$181M as of YE 2023 expected to fund operations through data readouts in ABC and mCRPC



Live tumor cells contain infinitely more data than the fragmented cells current cancer diagnostics use

**CEL**signia

The CELsignia platform captures this data

# Researchers recognize need for alternatives to genomic analysis

Complexity of signaling pathway networks requires much greater data to characterize than genomics can provide

**“It is becoming increasingly clear that pathways rather than individual genes govern the course of tumorigenesis.”**

Kornelia Polyak, MD, PhD  
Professor of Medicine  
Harvard Medical School



**“In order to fully understand aberrant signaling, the systematic perturbation of the entire network is required.”**

Neal Rosen, MD, PhD  
Director, Center for Mechanism-Based Therapy  
Memorial Sloan Kettering Cancer Institute



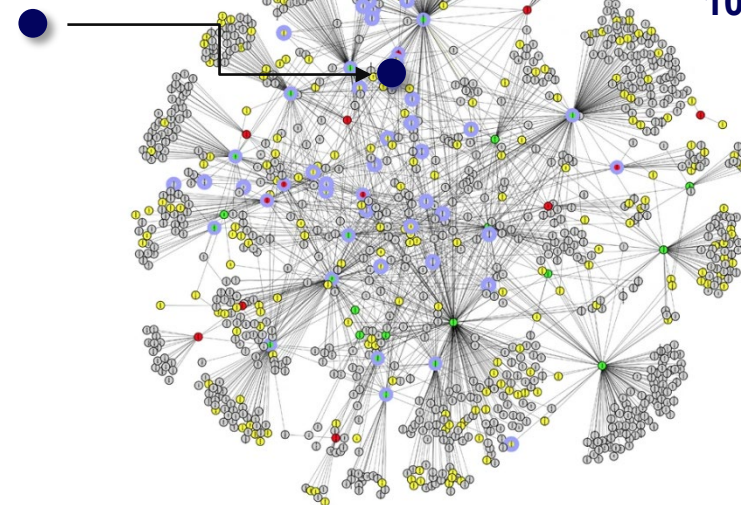
Memorial Sloan Kettering  
Cancer Center

**“Sequencing alone cannot definitively determine whether a specific gene actually contributes to tumor formation.”**

Ben Ho Park, MD, PhD  
Co-Leader Breast Cancer Research Program  
Vanderbilt University Medical Center



**Single gene mutation**



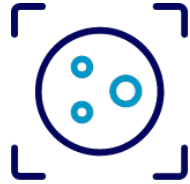
**Signaling Pathway  
Network:  
 $10^{20}$  cascading  
events**



# CEL<sub>signia</sub> – the first 3rd generation diagnostic

Measures dynamic cell signaling activity to identify cancer drivers genomic tests cannot detect

## Live Tumor Cells Isolated



>100,000 patient tumor cells are isolated in a **proprietary cell microenvironment**

## Cell Signaling Quantified



Cell pathways are activated to generate **data from  $>10^{20}$  cellular events** at 240 time points to create a “movie” of the signaling activity<sup>1</sup>

## Algorithmic Analysis

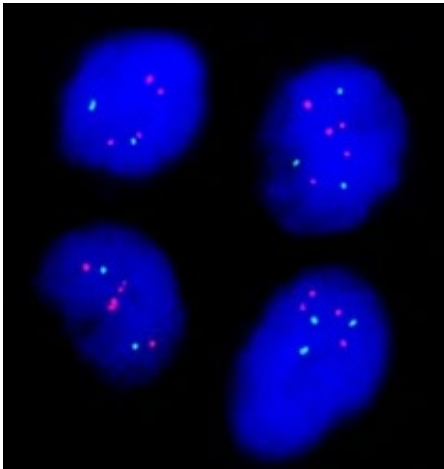


A **proprietary algorithm analyzes this “big data”** set to identify signaling activity 5 standard deviations from normal

# Current Molecular Diagnostics vs. CELsignia – HER2 Example

CELsignia identifies new sub-group of patients with HER2 driven cancer

**FISH HER2 Dx**  
(1 pathway gene )



\$9 billion  
anti-HER2 drug annual revenue<sup>1</sup>

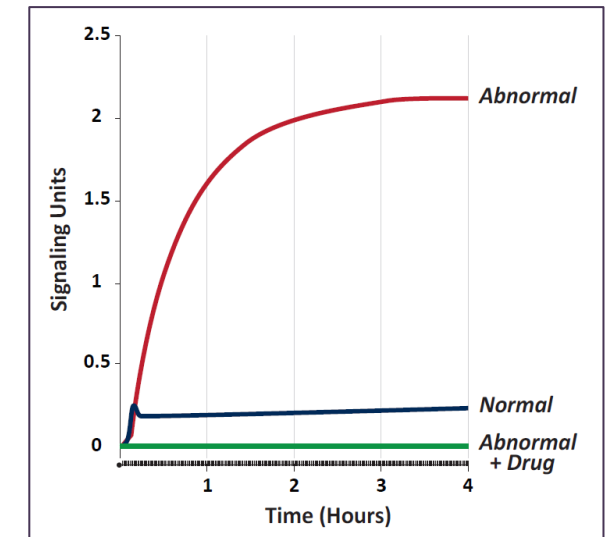
**FISH+**  
15%

**CELsignia+**  
15%-20%



CELsignia identifies new  
patients for anti-HER2 drugs

**CELsignia HER2 Activity**  
(4 hours of pathway signaling events)



\$Billions additional  
anti-HER2 drug revenue potential



# Key research discoveries drive test development

CELsignia platform provides powerful tool to discover new cancer sub-types and mechanisms

## Specific target mutations (e.g. HER2+) not required for oncogenic signaling

- Discovered 16 cancer sub-types that genomic tests cannot detect
- Confirms mutational status is not sufficiently specific

### Implications

- May miss 50% of HER2, EGFR, PI3K, c-Met driven cancers

## Mutations often don't lead to oncogenic signaling

- Demonstrated that target specific mutations often do not drive aberrant signaling
- Further confirms mutational status is not sufficiently specific

### Implications

- Explains low response rates of many targeted therapies

## Drug resistance mechanisms characterized

- Linkages identified between:
  - c-Met, HER3, HER2, & EGFR
  - LPA, S1PA, PI3K, MEK
- Untreated cooperative pathways drive drug resistance

### Implications

- May miss 50% of HER2, EGFR, PI3K, c-Met driven cancers

**Celcuity is focused on  
unlocking the potential  
of treating cancers that  
involve the PI3K/mTOR  
pathway**



Our third-generation cellular analysis platform unravels complex oncogenic activity molecular tests can't detect.



We harvest these insights to develop new targeted therapies for cancer patients