



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

June 2025

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 and VIKTORIA-2 clinical trials 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, the estimated costs of our clinical trials, 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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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
- A Phase 3 study in 2L patients is enrolling and a Phase 3 study in 1L patients is expected to begin enrolling in Q2 2025

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 and short-term investments of \$205M as of Q1 2025 expected to fund operations through 2026

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 pathways¹

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

PAM	38%
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 Comprehensively Inhibit the PAM Pathway

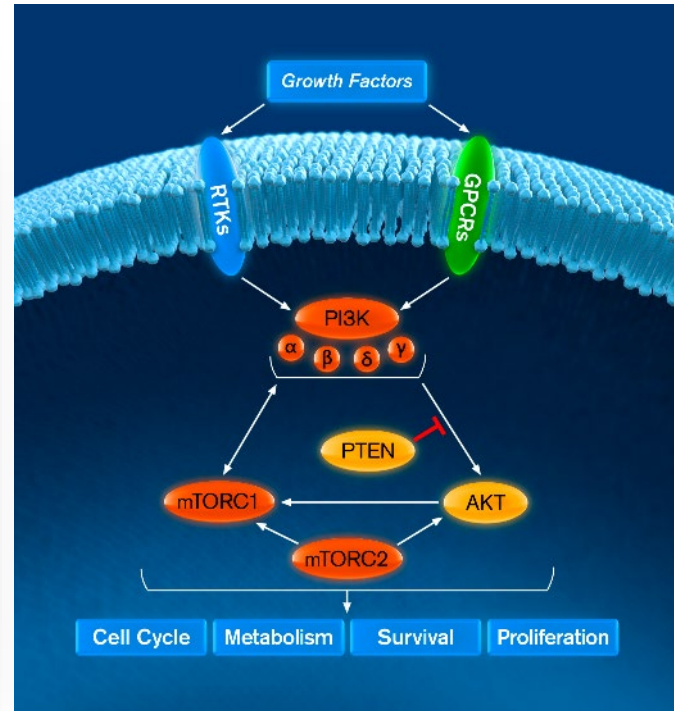
Optimal efficacy may require inhibition of all Class I PI3K isoforms and mTORC1 and mTORC2

Multiple pathway targets provide functional redundancy

If only a single target is inhibited, redundancy ensures pathway function is maintained¹⁻⁹

Feedforward and feedback loops between PI3K isoforms, AKT, and mTOR cross-activates uninhibited targets¹⁻⁹

Explains why 1st generation of PAM inhibitors were pan-PI3K/mTOR inhibitors

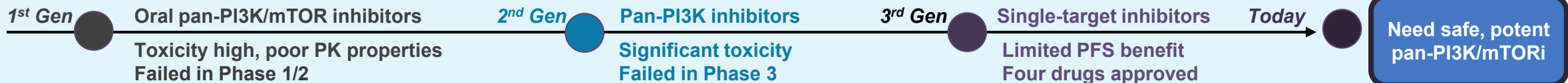


Therapeutic window for oral PI3K/mTOR inhibitors is narrow

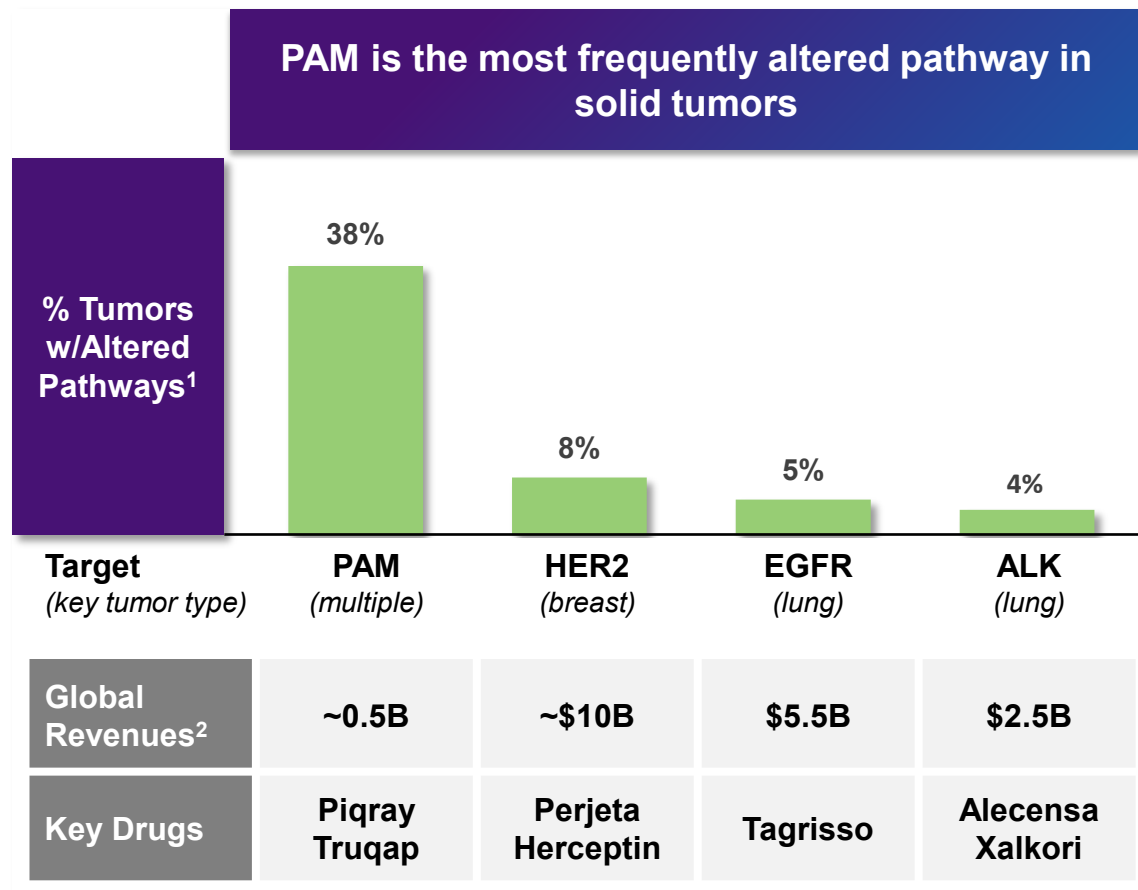
Difficult to optimize pathway inhibition without inducing undue toxicity

Early generations of orally administered pan-PI3K or pan-PI3K/mTOR inhibitors induced unacceptable toxicity¹⁰

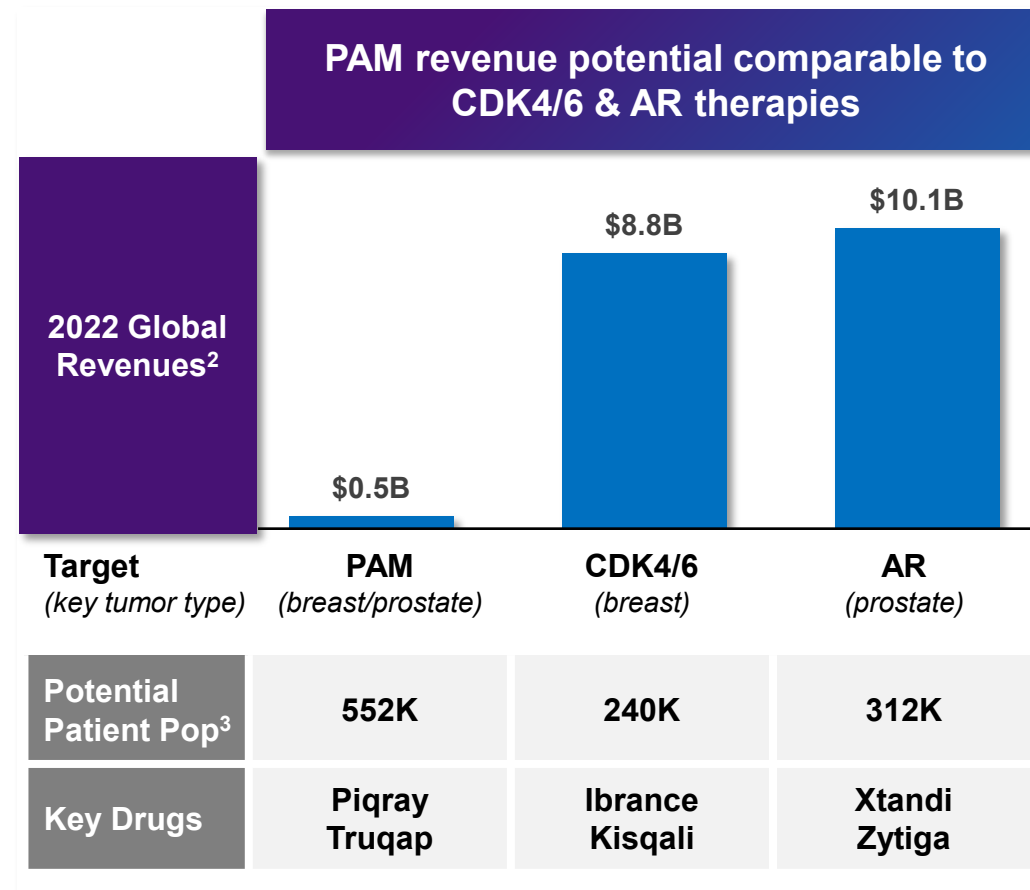
Led to focus on development of single-node PAM inhibitors (e.g. PI3Kα, mTORC1, AKT)



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 PAM (PI3K, AKT, mTOR) Inhibitor

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

Differentiated Mechanism of Action

- Inhibits all PI3K/mTOR nodes at **low or sub-nanomolar** concentrations
- **Nonclinical data suggests more potent & cytotoxic** than the single-node PAM inhibitors approved for breast or prostate cancer

Compelling Preliminary Results

- Gedatolisib + ET + CDK4/6 in HR+/HER2- ABC patients
- **79% ORR, 48.6 months mPFS** in 1L patients (n=41)¹
- **63% ORR, 12.9 months mPFS** in 2L patients (n=27)²

Well-Tolerated

- Nominal Gr 3, no Grade 4 TEAE's as a single agent
- **Only 4% treatment discontinuation** due to AE with Phase 3 dosing in combination with palbociclib and fulvestrant²

Potential to Address Large Unmet Need

- **HR+/HER2- ABC**: Enrolling Phase 3 trials for 2L and 1L³
- **mCRPC**: Enrolling Phase 1b/2 trial for 1L/2L patients³
- **225,000 1L/2L patients** in US, EU5, Japan⁴

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)¹

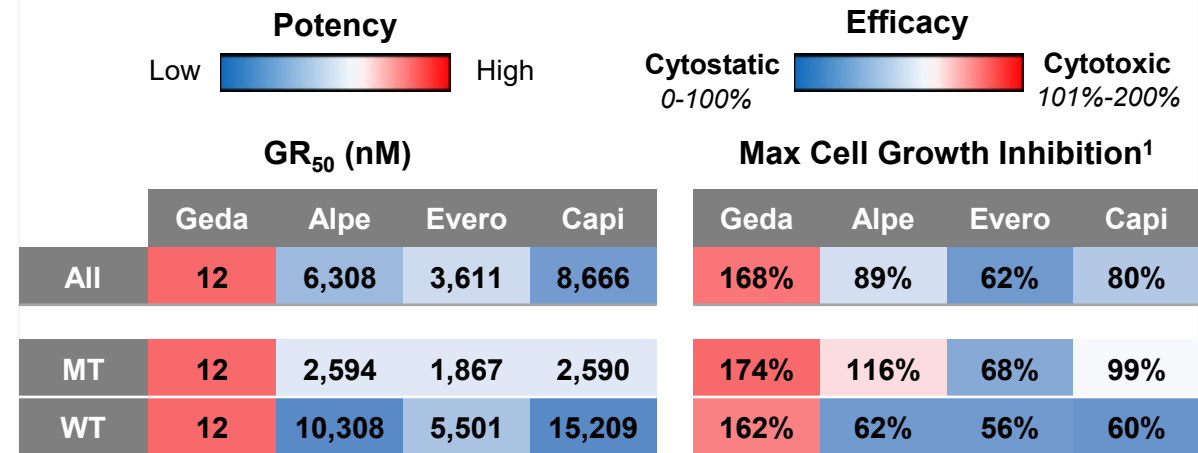
Node	Gedatolisib ²	Alpelisib ³	Everolimus ⁴	Capivasertib ⁵
PI3K-α	0.4	~4.0	-	-
PI3K-β	6.0	1,156	-	-
PI3K-γ	5.4	250	-	-
PI3K-δ	6.0	290	-	-
mTORC1	1.6	-	~2.0	-
mTORC2	1.6	-	-	-
AKT	- ⁶	-	-	3.0

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 AKT⁶
- Comprehensive pathway blockade can induce anti-tumor activity independent of PIK3CA status

Live Cell Proliferation Rate Dose Response Analysis⁷

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 PK Properties and IV Administration Optimize Safety Profile

Lower toxicity vs. approved PI3K inhibitors

	Gedatolisib ¹	Alpelisib ^{2,3}	Copanlisib ³	Duvelisib ³	Idelalisib ³
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)¹

- **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%²**
 - Phase 3 studies prescribe prophylaxis
- **Low incidence of Grade 3 hyperglycemia (1%)**
- **No treatment related neutropenia**
- No Grade 4 or 5 adverse events

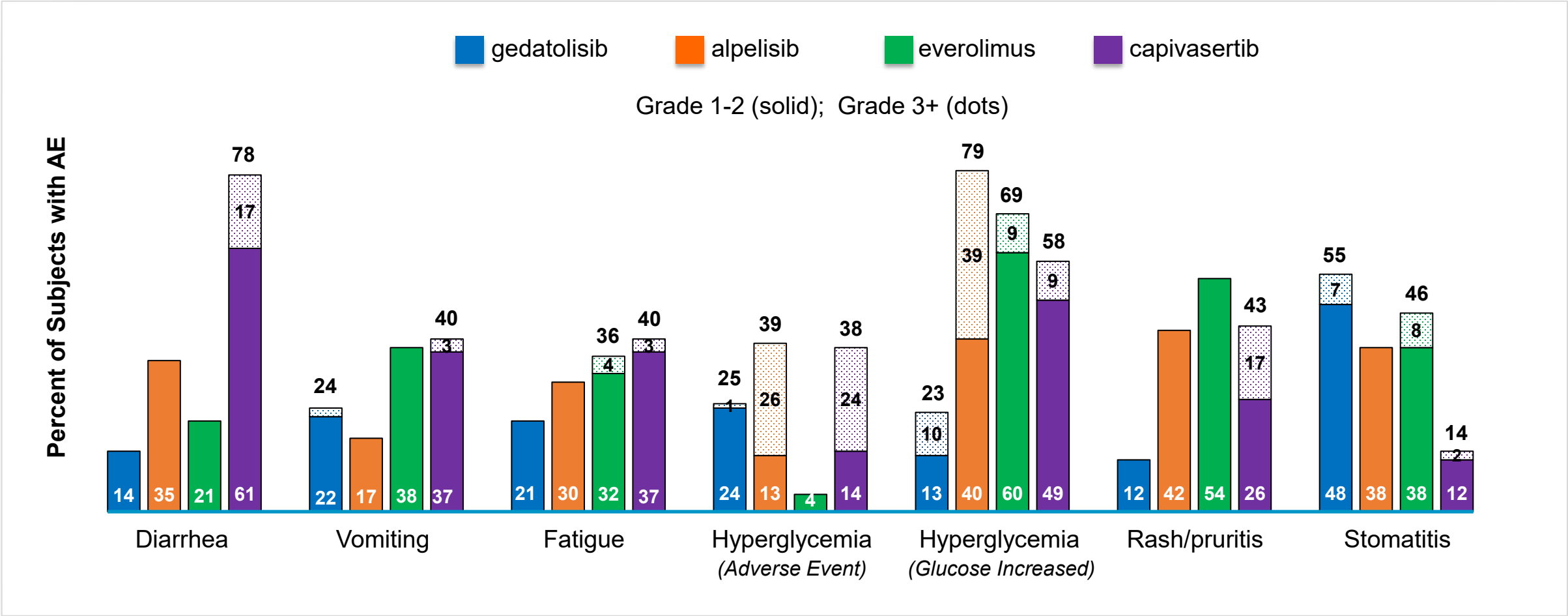
MTD Arm (n=42)

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 Gedatolisib vs. Single Node PAM Inhibitors

Fewer patients reported AE when treated with gedatolisib compared to other PAM inhibitors



Source for all data except Hyperglycemia (Glucose Increased) from single agent studies: Source: (GED) Shapiro 2015, internal data. (ALP) Juric 2018, 300 mg daily dose; (EVE) Tabernero JCO 2008, 10 mg QD or 50 mg QW; (CAP) Hyman JCO 2017; Source for Hyperglycemia (Glucose Increases) data: ALP, EVE, CAP: US Package Insert. GED: Layman Lancet 2024. Note: Hyperglycemia (Glucose Increased) is a laboratory abnormality graded according to specific fasting glucose values whereas Hyperglycemia (Adverse Event) is graded according to a clinical assessment

Clinical Development Programs

Current

2nd Line HR+/HER2- Advanced Breast Cancer

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

- Patients with **HR+/HER2- advanced breast cancer (ABC)** who progressed on CDK4/6 therapy and an AI¹
- All-comer design (*PIK3CA*+/-) includes separate primary endpoints for mutated and non-mutated *PIK3CA* patients
- Breakthrough Therapy Designation was granted by the FDA in July 2022

1st Line HR+/HER2- Advanced Breast Cancer

Phase 3 clinical trial for gedatolisib + CDK4/6i + fulvestrant

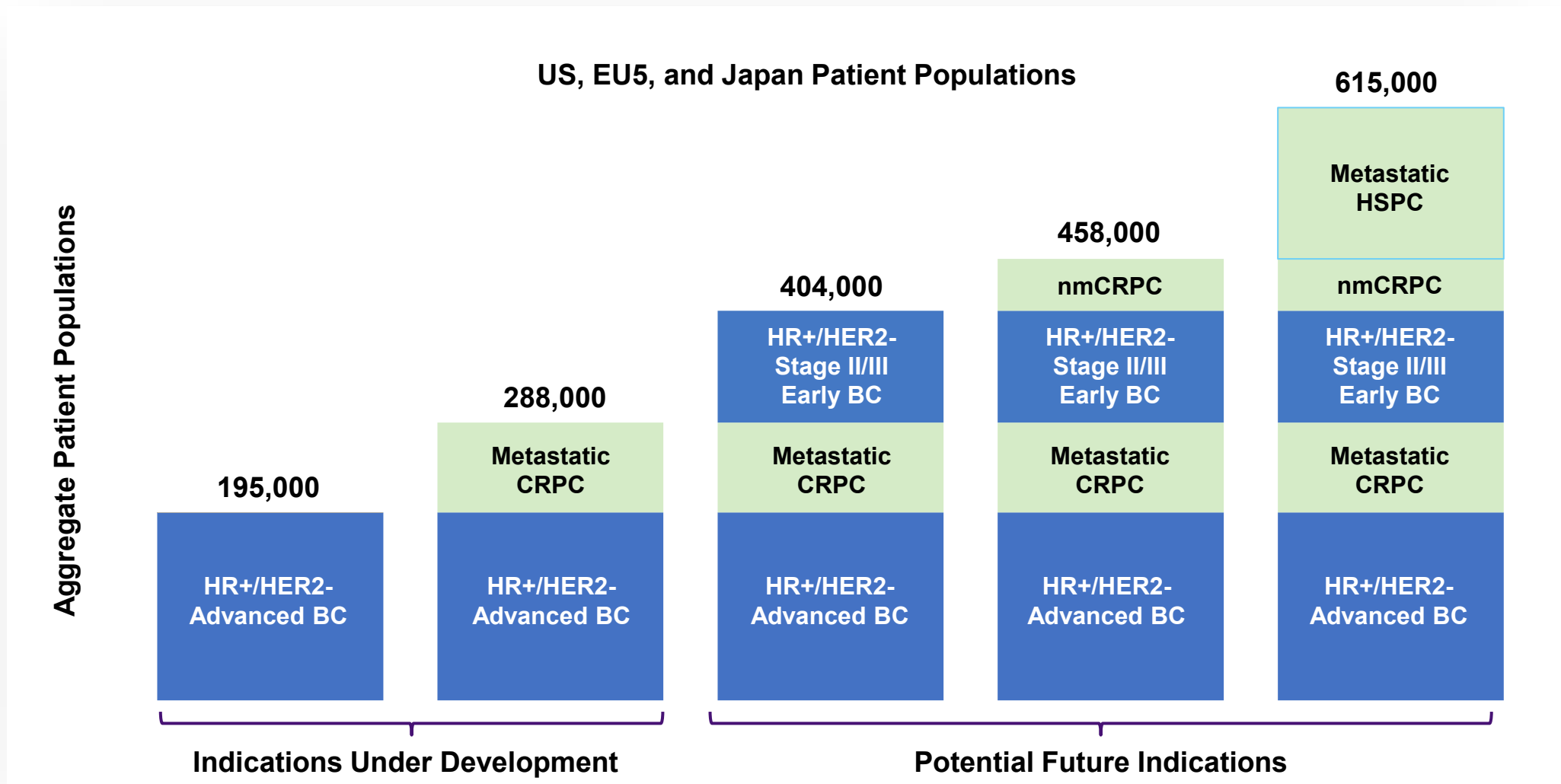
- Patients with HR+/HER2- ABC who are **endocrine therapy resistant (ETR)** and treatment naïve for ABC
- All-comer design (*PIK3CA*+/-) includes separate primary endpoints for mutated and non-mutated *PIK3CA* patients
- Significant unmet need – mPFS with SOC is approximately 7 months¹

2nd Line Metastatic Castration Resistant Prostate Cancer

Phase 1b/2 clinical trial for gedatolisib with darolutamide

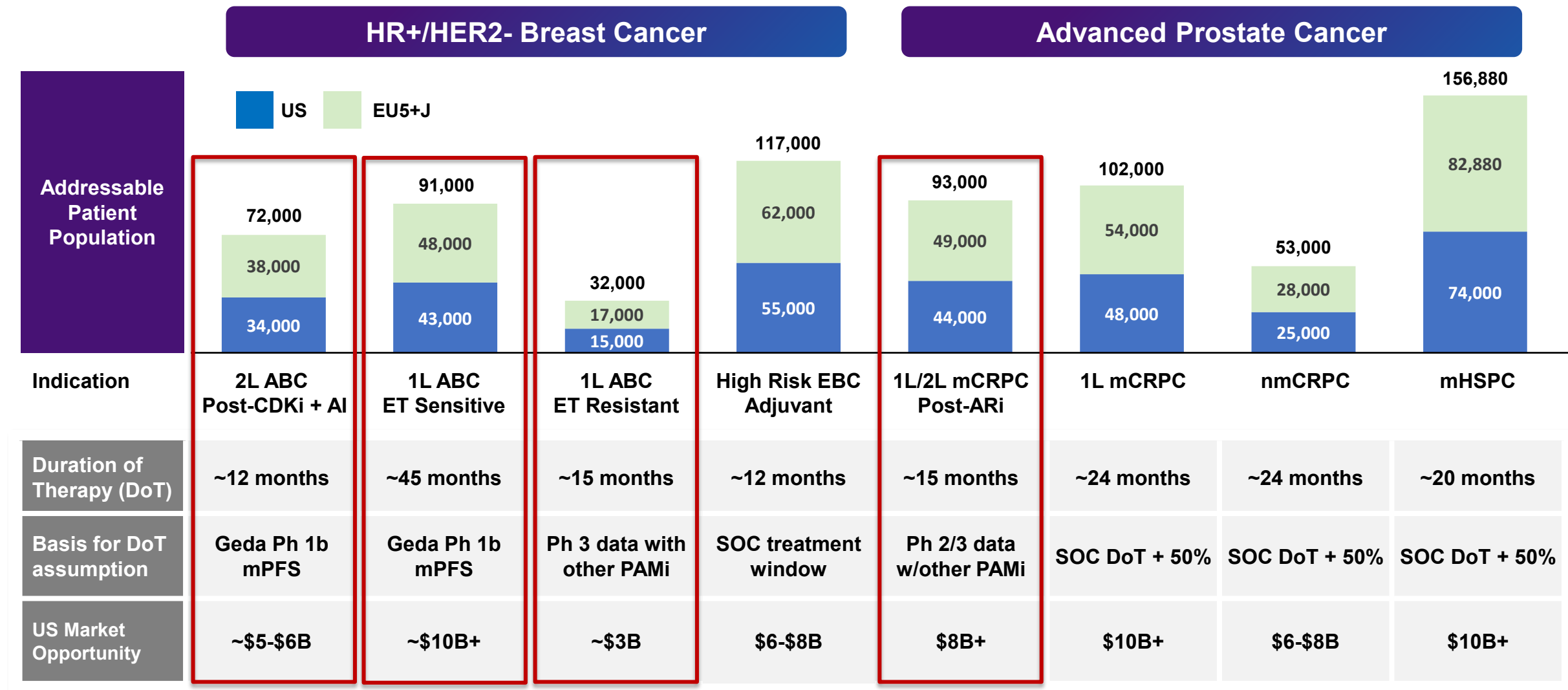
- Extensive literature describes androgen pathway linkage to the PAM pathway
- Gedatolisib demonstrated superior potency and efficacy compared to other PAM inhibitors in nonclinical studies²
- Promising clinical activity with an AR inhibitor when combined with less active PAM inhibitors than gedatolisib³

Addressable Patient Population in Breast and Prostate Cancer



Indications under development include 2L ETS, 1L ETR, 1L ETS, 1L/2L mCRPC. Sources: Internal estimates using data from American Cancer Society, Breast Cancer Statistics 2022; American Cancer Society Facts and Figures 2019-2020; Salvo, E. M. et al. (2021); Scher, et al. 2015; Datamonitor Healthcare; Leith, A. et al. 2022; George, D. J. et al. 2022; EU5 calculated using 112% EU + Japan from Globocan 2020 data; scale up factor Abbreviations: HR, hormone receptor; BC, breast cancer; CRPC, castration resistant prostate cancer; nm, non-metastatic; HSPC, hormone sensitive prostate cancer

Multiple potential blockbuster indications in both tumor types





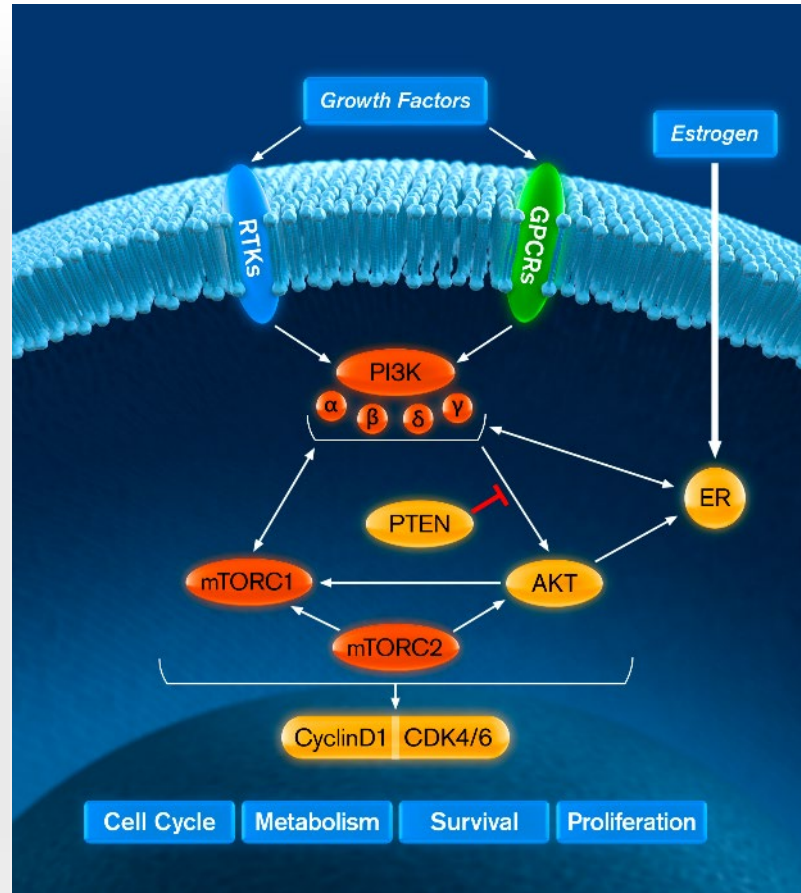
Gedatolisib for Advanced Breast Cancer (ABC)

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 PAM pathway induces estrogen independent ER transcriptional activity ER α phosphorylation^{1,2}
- Conversely, ER target gene expression activates upstream effectors of the PI3K/mTOR pathway³
- ER also activates the PI3K/mTOR pathway by direct binding to PI3K⁴
- **PI3K/mTOR inhibition can increase ER activity and sensitivity to endocrine therapy⁵**

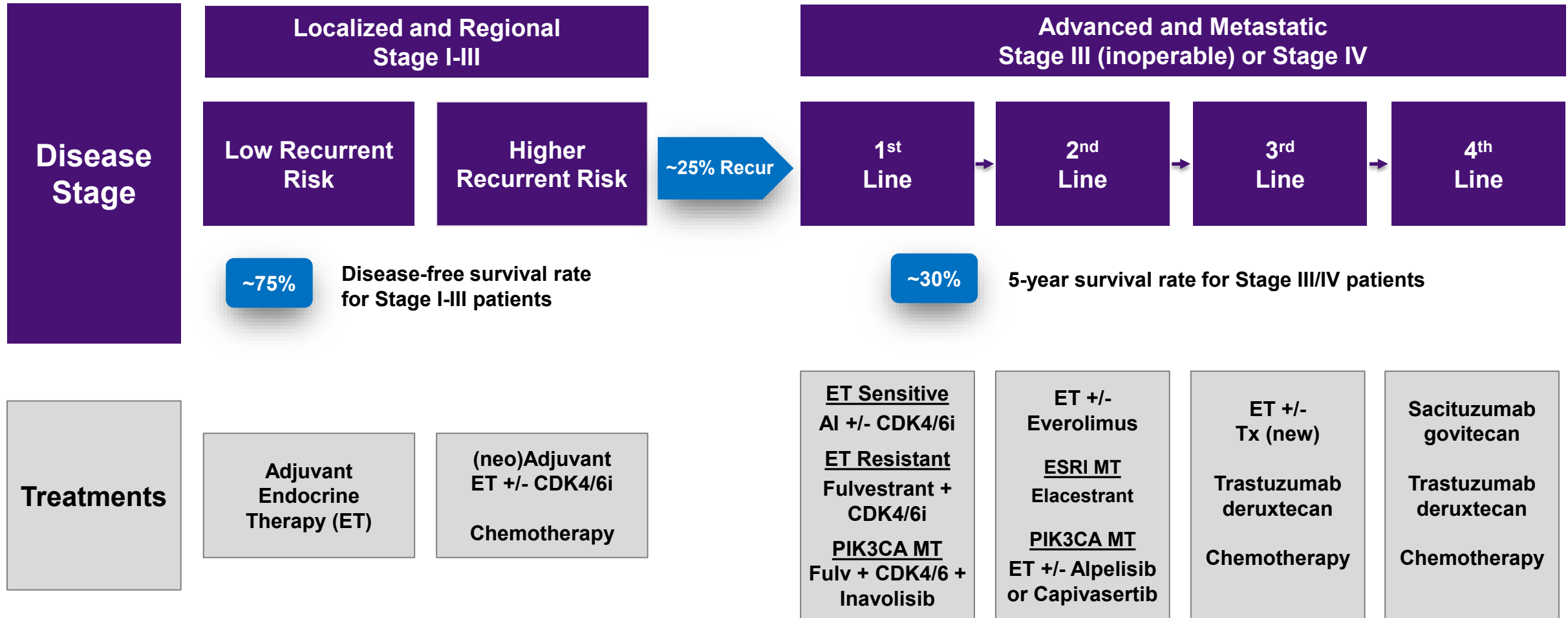


CDK4/6, ER and PI3K/mTOR⁶⁻¹⁰

- 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**

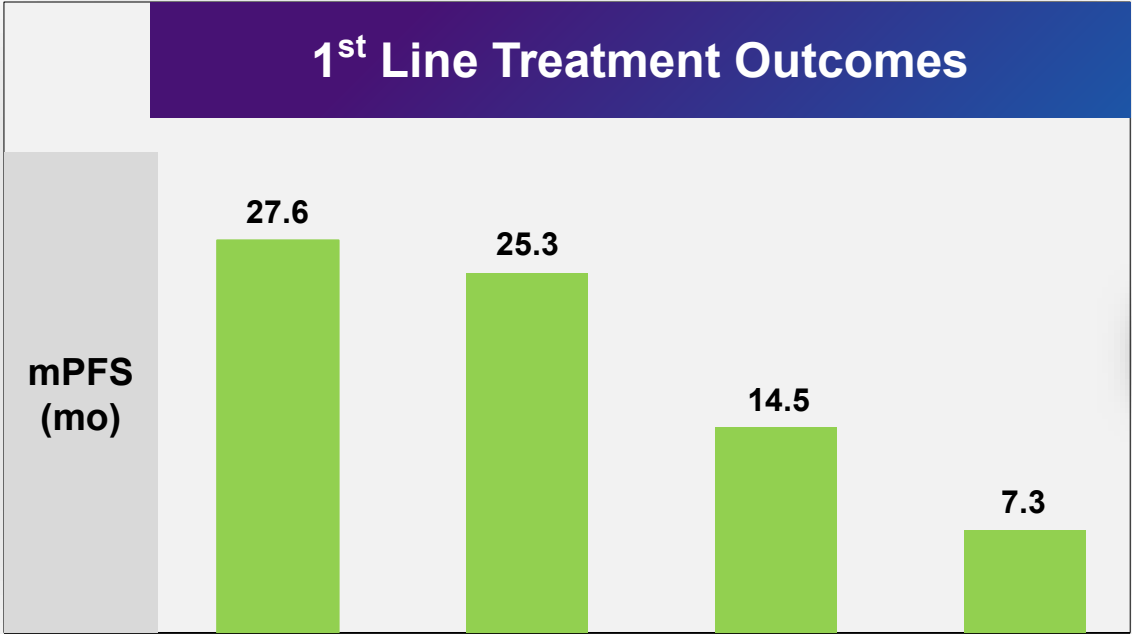
HR+/HER2- Breast Cancer Treatment Landscape¹

~30,000 women in US and ~33,000 women in 5EU and Japan die from breast cancer annually²

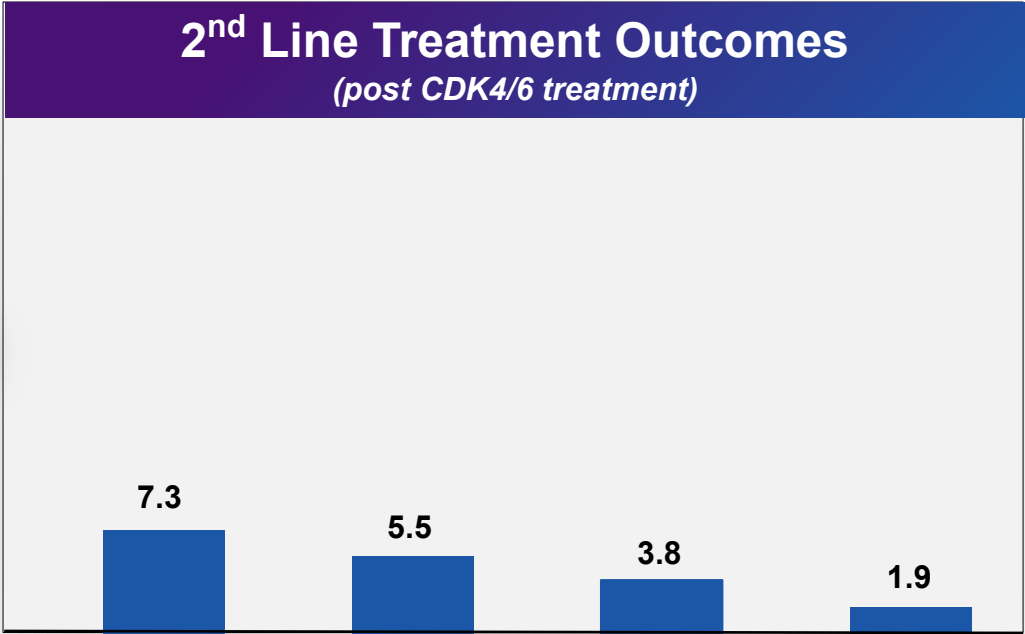


Limited Benefit for 1st Line ET Resistant or 2nd Line HR+/HER2- ABC Patients

Significant need for better therapeutic options



Drugs	Palbociclib + letrozole ¹	Ribociclib + letrozole ²	Letrozole ¹	Palbociclib + Fulvestrant ³
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 ⁴	Capivasertib + fulvestrant ⁵	Elacestrant ⁶	Fulvestrant ⁶
PI3Kα + SERD	AKT + SERD	SERD	SERD
PIK3CA+	PIK3CA/AKT/PTEN+	ESR1+	All
7.3	5.5	3.8	2-4
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

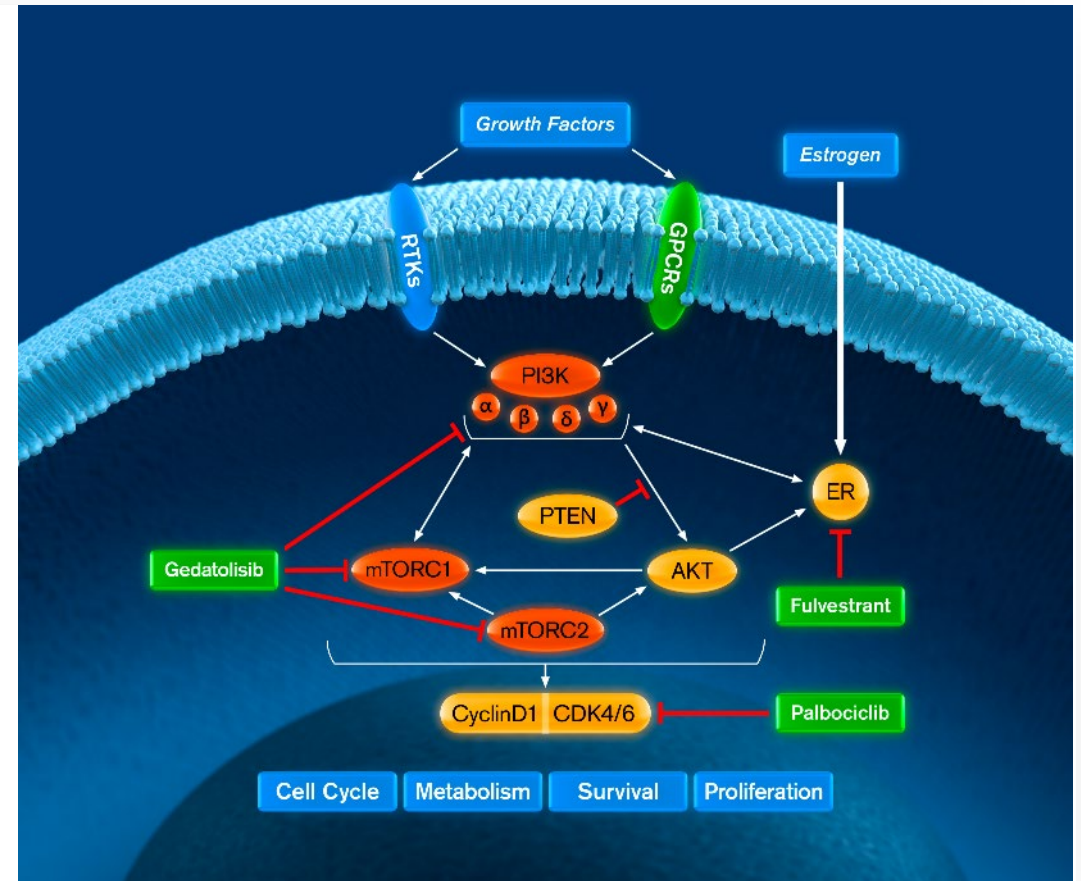
Review of Phase 1b Data

Gedatolisib + Palbociclib + Fulvestrant/Letrozole

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

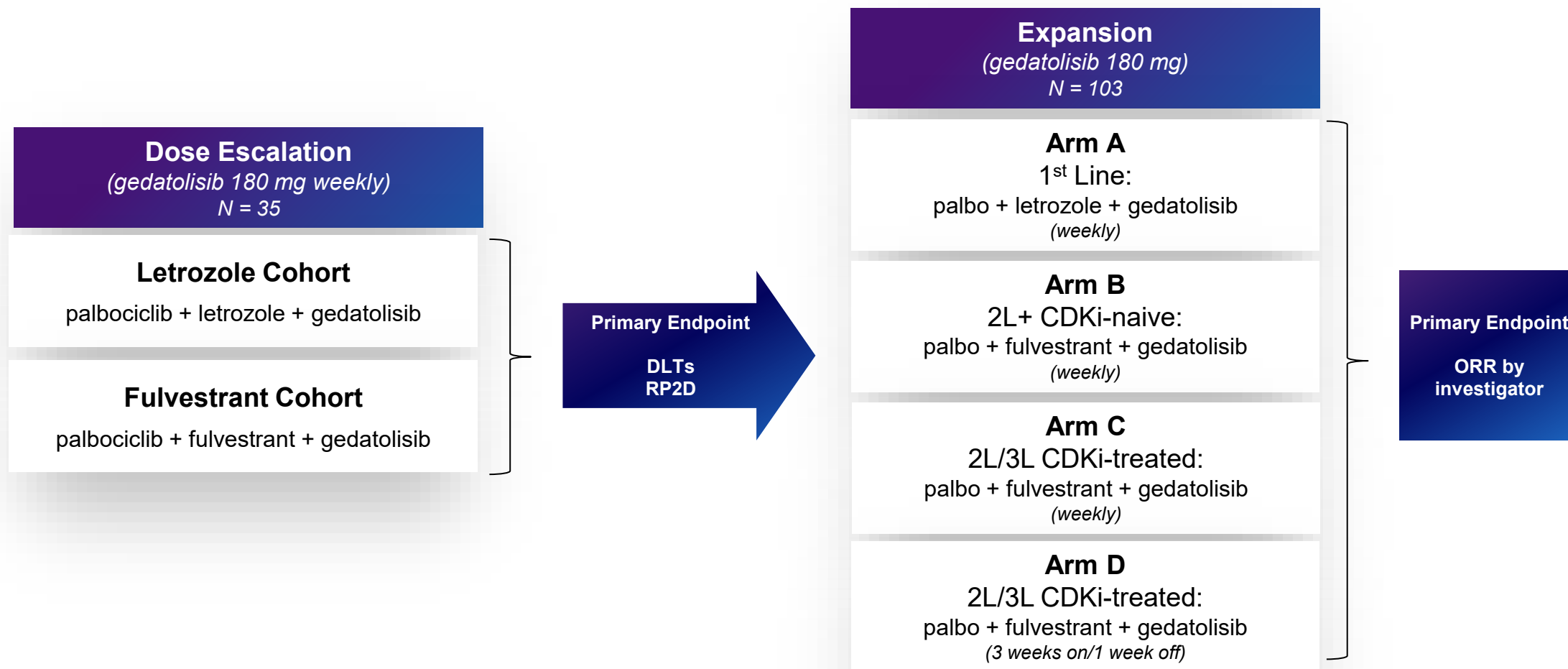
Clinical Hypothesis

- Blockade of interdependent ER, PI3K, mTOR & CDK signaling pathways is required to optimize anti-tumor control
- PAM inhibition:¹⁻⁴
 - Blockades PAM pathway and limits cross-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



Phase 1b Dose Escalation and Expansion Study (B2151009)

Key eligibility criteria: patients with HR+, HER2-, advanced breast cancer



B2151009 Expansion Arms: Baseline Characteristics

	Arm A (N=31)	Arm B (N=13)	Arm C (N=32)	Arm D (N=27)
Tumor, Node, Metastasis (TNM) Current Stage, n (%)				
Stage IV	31 (100)	13 (100)	32 (100)	27 (100)
Prior therapies for ABC, n (%)				
Prior Chemotherapy	1 (3.2)	4 (30.8)	15 (46.9)	5 (18.5)
Prior Endocrine Therapy¹	0	11 (84.6)	31 (96.9)	26 (96.3)
Prior CDK4/6 inhibitor	0	0	32 (100)	26 (96.3)
Number of prior systemic therapies ABC, n (%)				
0	30 (96.8)	2 (15.4)	0	0
1	1 (3.2)	9 (69.2)	15 (46.9)	18 (66.7)
≥2	0	2 (15.4)	17 (53.2)	9 (33.3)
Metastatic disease site involved				
Liver or Lung	20 (64.5)	12 (92.3)	23 (71.9)	22 (81.5)
Liver	14 (45.2)	10 (76.9)	20 (62.5)	17 (63.0)
Lung	7 (22.6)	3 (23.1)	7 (21.9)	6 (22.2)
Bone	18 (58.1)	11 (84.6)	25 (78.1)	18 (66.7)
Bone only	0	0	0	0

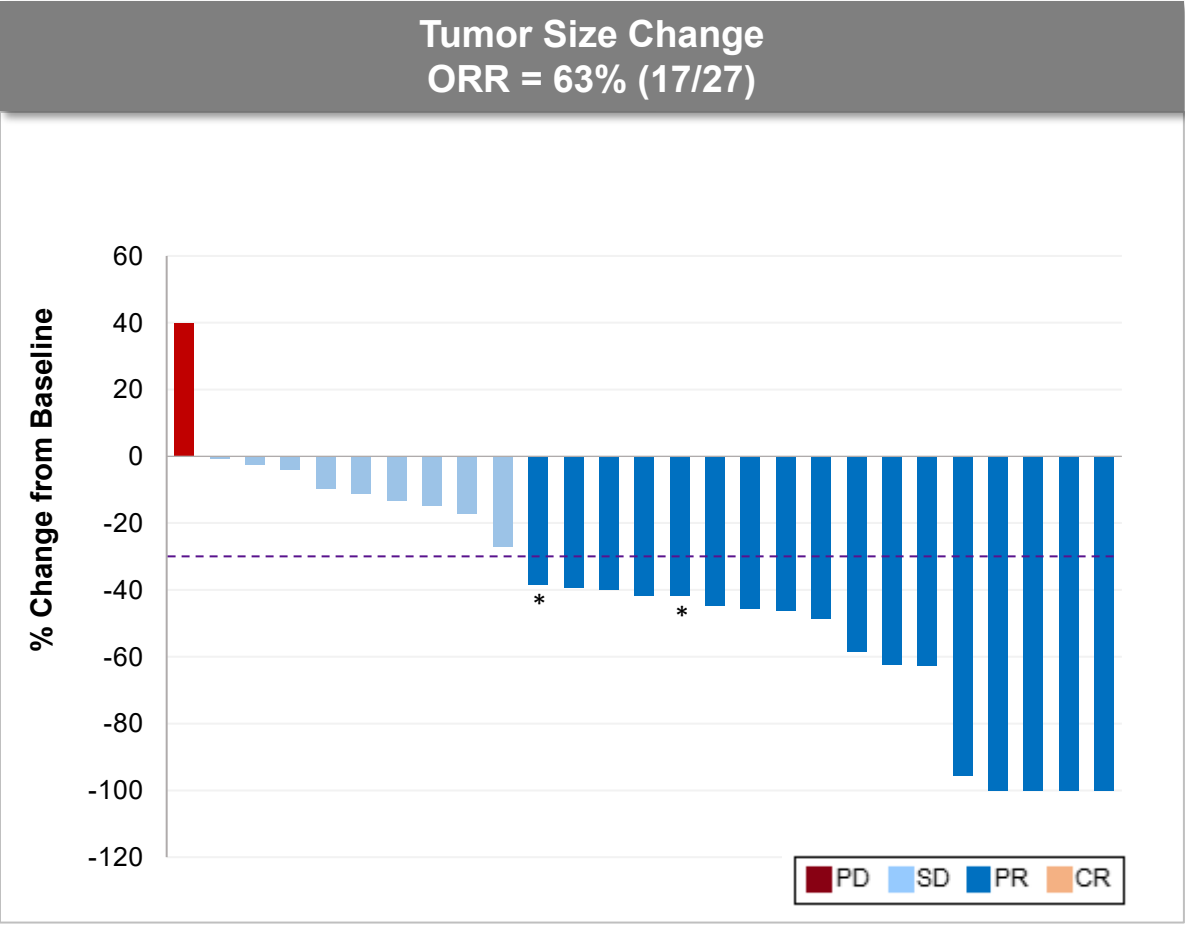
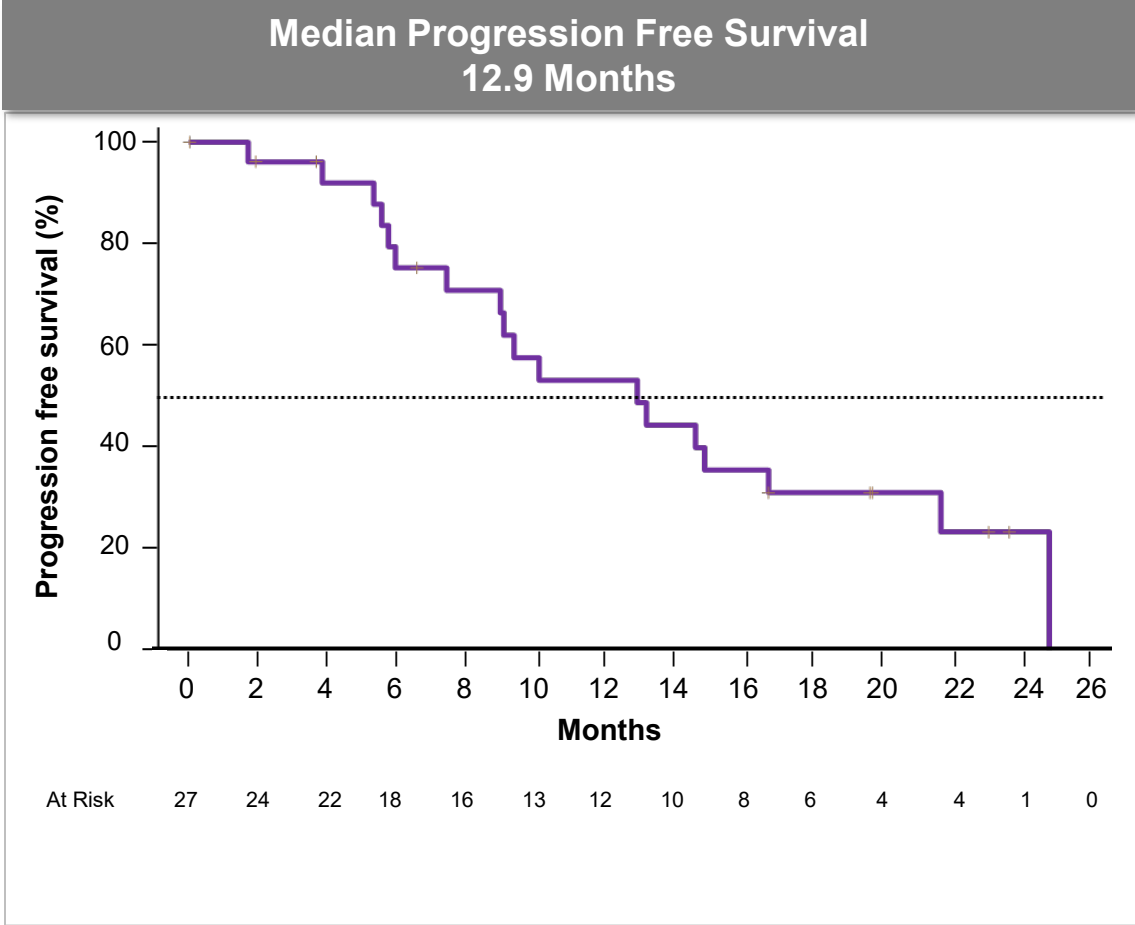
ORR and PFS in Each Expansion Arm Was Superior to SOC

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 ¹ (evaluable)	85%		77%		36%		63%	
mPFS ² , 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 ²	72%		55%		24%		53%	
PIK3CA Status	WT	MT	WT	MT	WT	MT	WT	MT
	81% ³	16%	69%	31%	75%	25%	56% ³	41%
ORR ¹ (evaluable)	81%	100%	78%	75%	25%	63%	60%	73%
PFS % at 12 mos ²	74%	60%	50%	67%	22%	29%	49%	60%

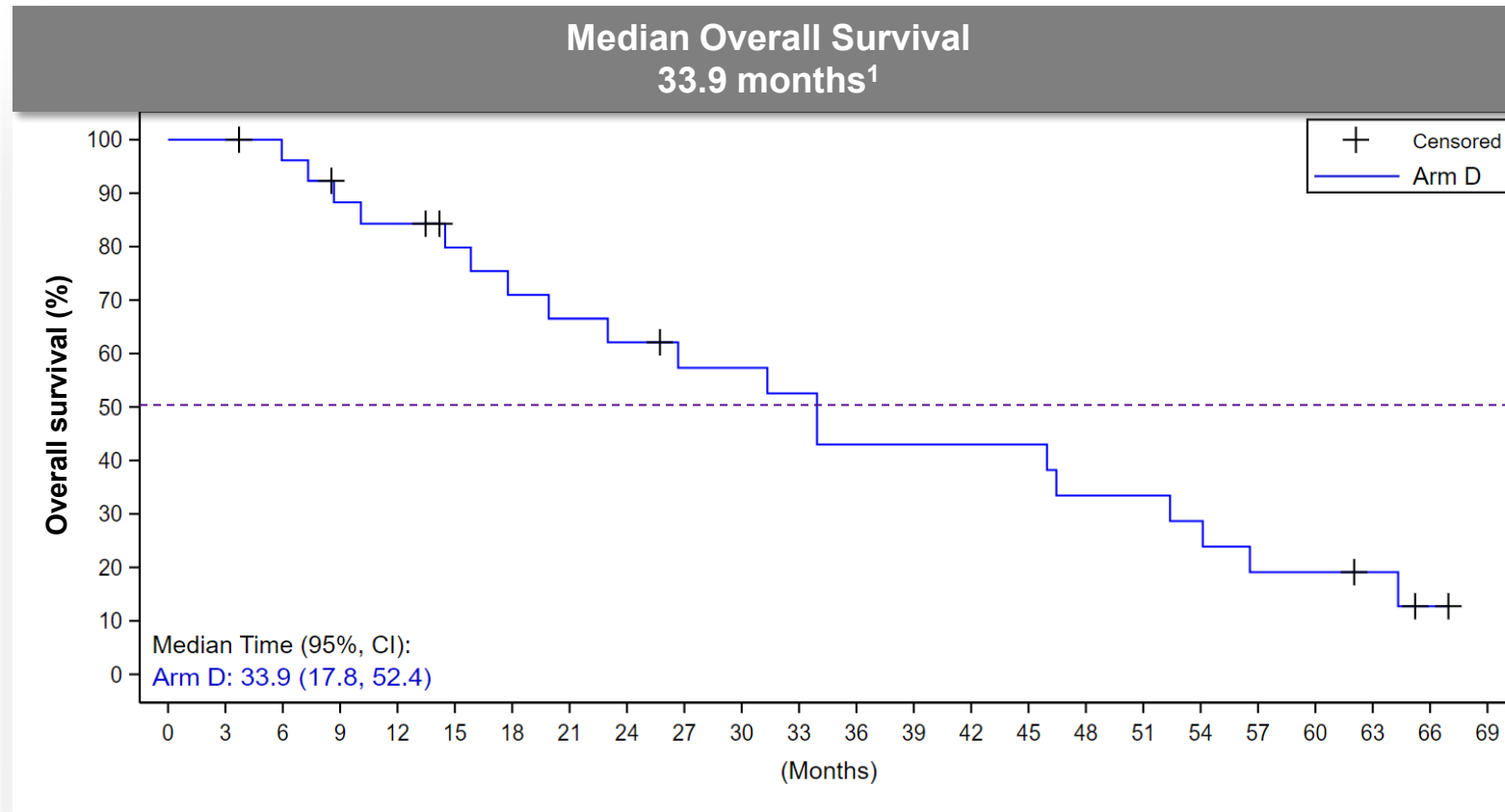
Gedatolisib + Palbociclib + Fulvestrant in 2nd/3rd Line HR+/HER2- ABC Patients

mPFS and ORR from Arm D with Phase 3 regimen compares favorably to published data for current SOC



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

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



Relevant OS data in 2L post-CDK4/6 setting

- Alpelisib + fulvestrant: 27.3 months²
 - BYLieve Cohort A study
 - PIK3CA MT patients
- Endocrine monotherapy: 17.0 months³
 - EMERALD study
 - ESR1 MT patients

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 – 26% discontinued ¹
 - Everolimus – 24% discontinued ²
 - Capivasertib – 10% discontinued ³
- Most TRAE's were Grade 1 or 2
- **Few hyperglycemia adverse events**
 - Gedatolisib - 7% Grade 3/4
 - Alpelisib - 37% Grade 3/4 ¹
- Stomatitis prophylaxis was not utilized in this study
 - **Swish-and-Spit dexamethasone prophylactic mouth rinse reduced Grade 2-4 stomatitis by 90% ⁴**
 - Phase 3 study prescribes 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	%	%	%
Stomatitis⁵	11	56	22
Neutropenia⁶	-	15	67
Nausea	44	30	-
Fatigue	22	37	7
Dysgeusia	44	7	-
Diarrhea	37	-	4
Rash	19	15	7
Leukopenia⁷	-	19	23
Constipation	30	4	4
Vomiting	22	11	4
Anemia⁸	4	15	15
Hyperglycemia	15	4	7

Gedatolisib Combo and SOC Data for 2L HR+ / HER2- ABC Post-CDKi

Gedatolisib Combo Offers Potential for Superior Efficacy Compared to Alternatives

Patient Population	2 nd Line ER+/HER2- ABC	
All	Gedatolisib + Fulvestrant + Palbociclib ¹	mPFS 12.9 months ORR 63%
PIK3CA+	Alpelisib + Fulvestrant ²	mPFS 8.0 months ORR 19%
PIK3CA+	Alpelisib + Fulvestrant ³	mPFS 5.6 months ORR 24%
PIK3CA/AKT1/ PTEN+	Capivasertib + Fulvestrant ⁴	mPFS 5.5 months ORR 23%
ESR1+	Elacestrant ⁵	3.8 months ORR 4%
All	Fulvestrant ⁵	mPFS 1.9 months ORR 6%

(1) Layman 2024, Arm D; (2) Rugo, Lancet Onco, 2024; (3) Rugo, SABCS, 2021;(4) Oliveira, ESMO Breast, 2023, CDK4/6 prior treated patients (5) Bidard, JCO, 2022 and FDA Note: All drugs listed are FDA approved. No head-to-head trials have been conducted; data collected from different trials, in different patient populations and may not be comparable.

Efficacy in Treatment-Naïve Population Superior to SOC

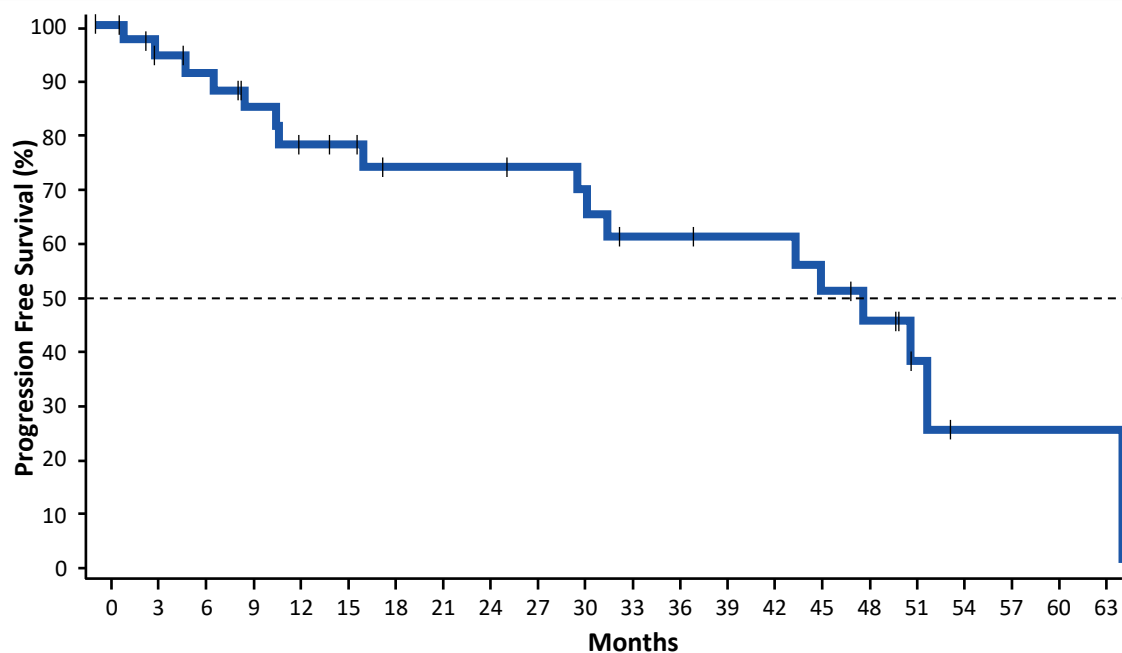
mPFS of 48.6 months, mDOR of 46.9 months, and ORR of 79%

B2151009 Treatment-Naïve Patients (N=41)			
	Escalation Arm A	Expansion Arm A	Total Treatment Naïve
Progression-Free Survival (full analysis set)	n = 11	n = 30	n = 41
Median PFS, mos (95% CI)	45.8 (32.3, NR)	48.6 (11.6, NR)	48.6 (30.4, NR)
Responses (evaluable, measurable disease) ¹, n (%)	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 ¹	4 (57.1)	22 (84.6)	26 (78.8)
Median DOR, mos (95% CI) ²	39.7 (30.5, NR)	46.9 (11.3, NR)	46.9 (24.6, 49.5)

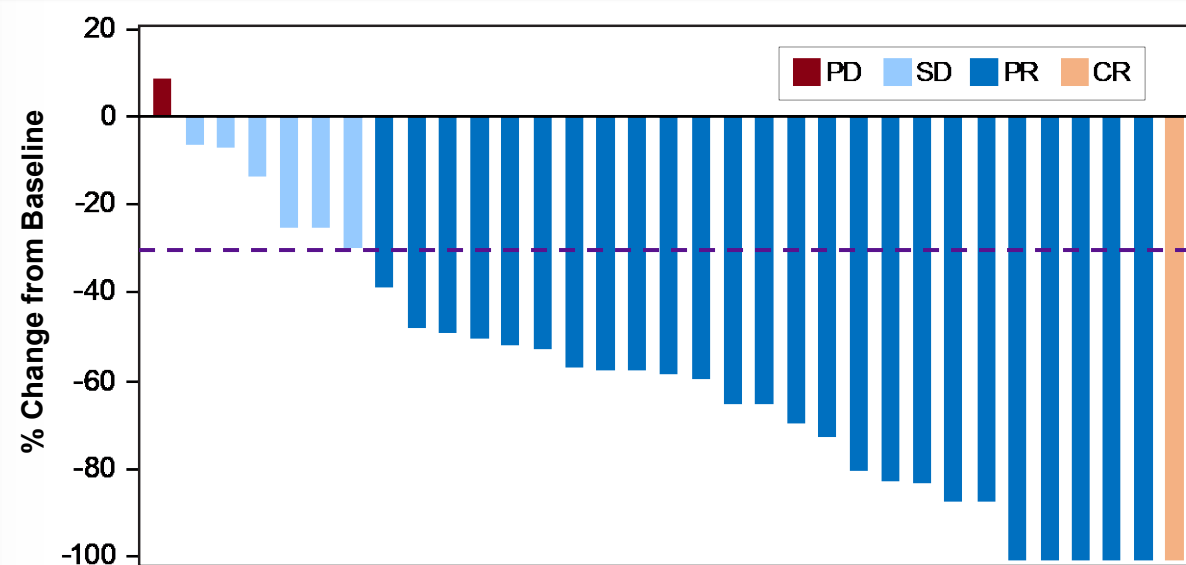
Gedatolisib + Palbociclib + Letrozole in 1st Line HR+/HER2- ABC (N=41)¹

mPFS and ORR for treatment-naïve patients compares favorably to published data for SOC palbociclib + letrozole²

Median Progression Free Survival
48.6 Months

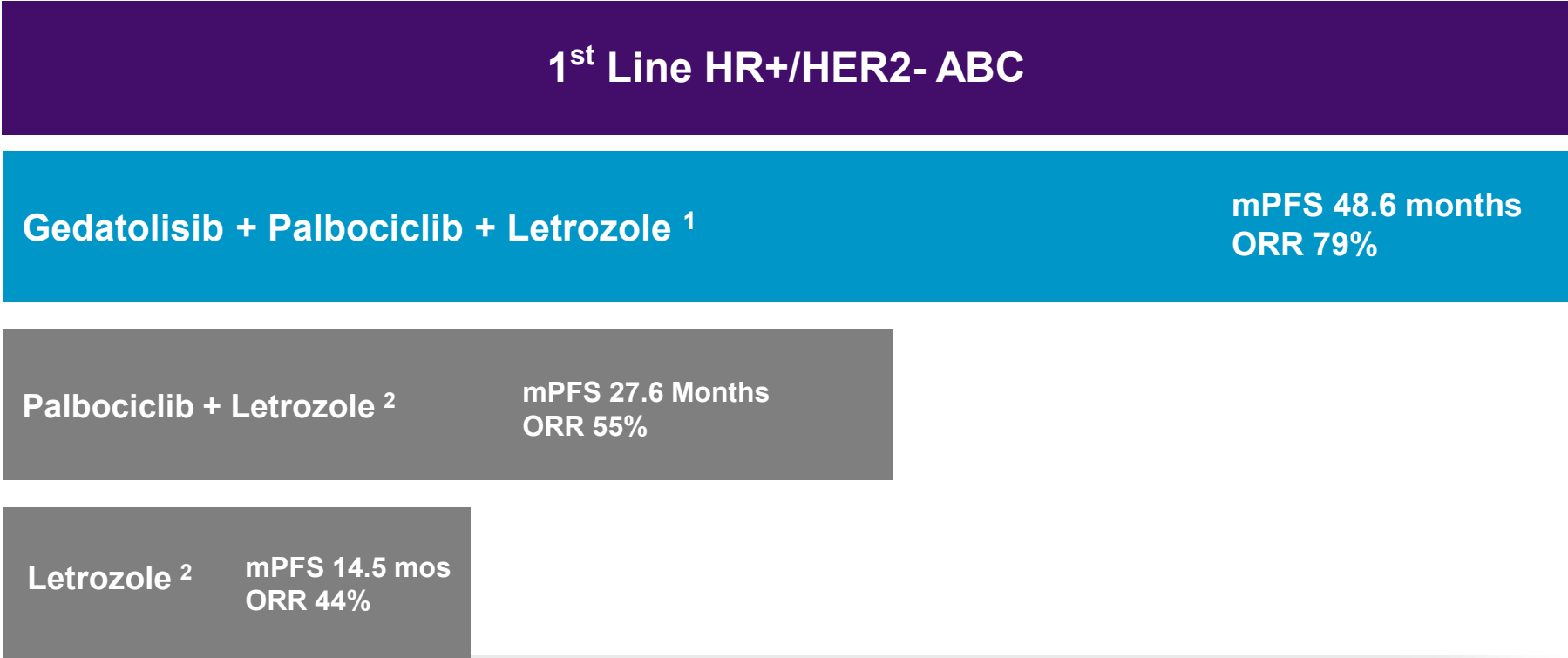


Tumor Size Change
ORR = 79% (26/33)



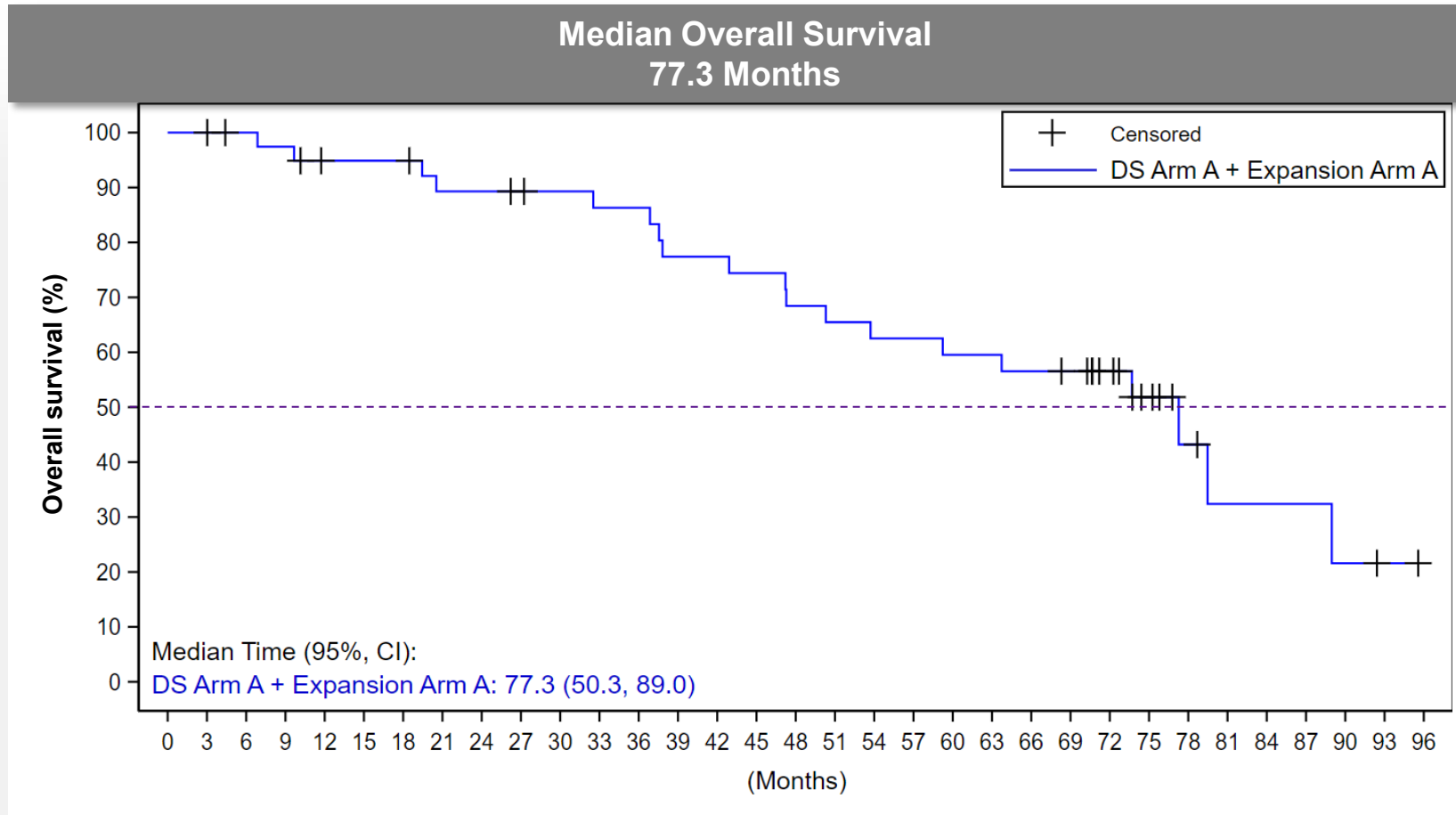
Gedatolisib Combo vs. SOC for 1L HR+ / HER2- ABC

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



Gedatolisib + Palbociclib + Letrozole in 1st Line HR+/HER2- ABC Patients

mOS data for treatment-naïve patients compares favorably to published data for current SOC



Relevant OS data in 1L setting

- Palbociclib + letrozole: 53.8 months²
- PALOMA-2 study

Phase 3 Study Designs VIKTORIA-1 and VIKTORIA-2

VIKTORIA-1: Trial Design Considerations for 2nd Line HR+/HER2- ABC

- Standard-of-care 2nd line treatment is based on *PIK3CA* status
- ~35-40% 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: Phase 3 Study Features for 2L HR+/HER2- ABC

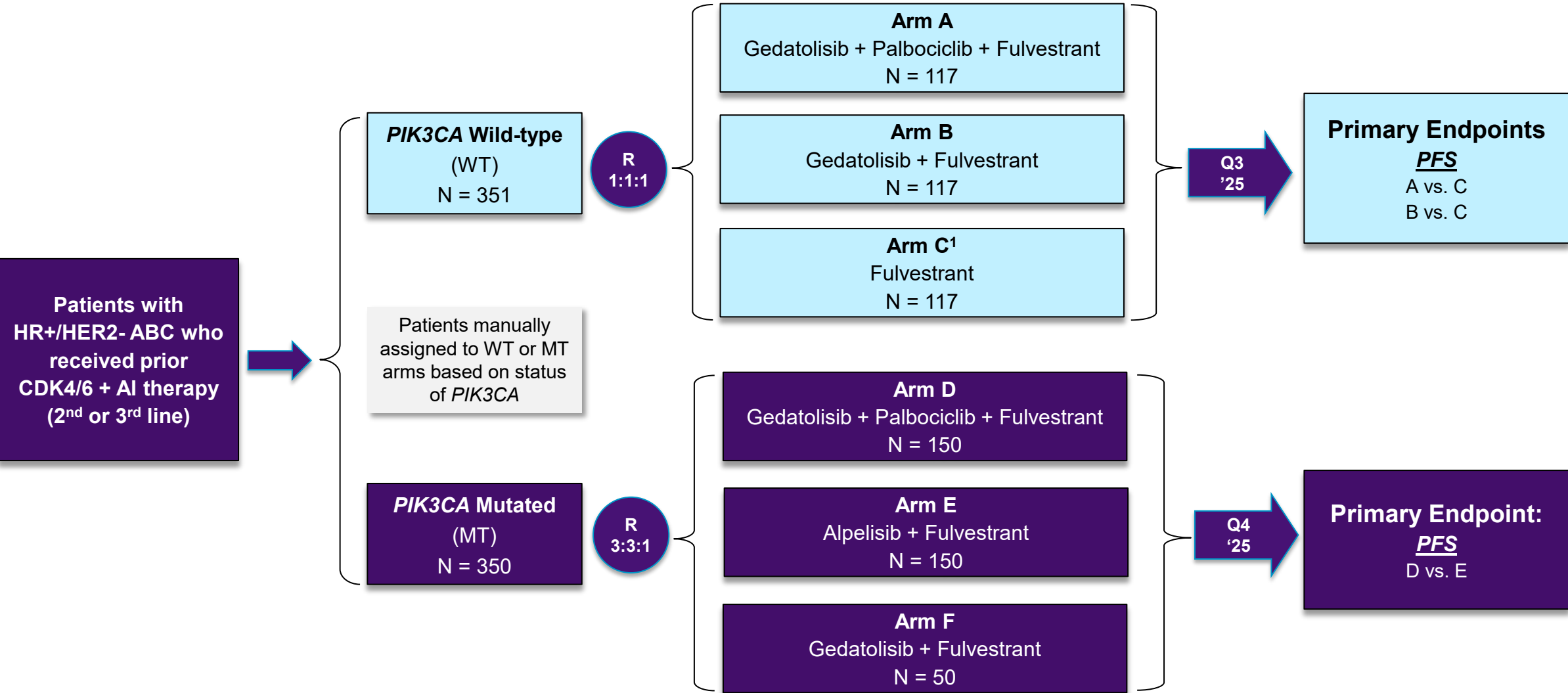
Global open-label randomized study (>200 sites)

- **Key eligibility criteria:**
 - ER+/HER2- advanced or metastatic breast cancer
 - Prior CDK4/6i + NSAI
 - Bone-only with measurable lesions
 - ≤ 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**
- **Stratification by geography, prior treatment response (\leq or $>$ 6 months), presence of liver or lung metastasis (yes/no)**

Phase 3 vs. Phase 1b Arm D Key Eligibility Criteria Differences

- **Prior chemotherapy for ABC**
 - Phase 3: 0% (not eligible)
 - Arm D: 19% had prior chemo
- **Bone-only with measurable lesions**
 - Phase 3: Typically, 15%-20% ABC
 - Arm D: 0% (not eligible)
- **Implications**
 - Bone only and chemo naïve patients typically have better prognosis than those with visceral disease and prior chemo

VIKTORIA-1: Phase 3 Trial Design Overview for 2L HR+/HER2- ABC



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 a prior CDK4/6i

	Gedatolisib + Palbo + Fulvestrant N=27 ^{1,2}	Fulvestrant N=165 ³	Fulvestrant N=37 ⁵	Fulvestrant N=121 ⁶	Alpelisib + Fulvestrant N=126 ⁸	Alpelisib + Fulvestrant N=121 ⁹
Trial	B2151009 – D	EMERALD	SERENA-2	CAPItello-291	BYLieve – C	BYLieve - A
PIK3CA Status	WT / M (56% / 41%)	WT / M (NR)	WT / M (NR)	WT / M	M	M
Line of Therapy (% by line)	2L / 3L+ (67% / 33%)	2L / 3L+ (73% / 27%) ⁴	2L / 3L (NR)	2L / 3L (NR)	2L / 3L+ (37% / 63%)	1L / 2L / 3L+ (2% / 80% / 18%)
mPFS (months)	12.9	1.9	2.1	2.6	5.6	8.0
ORR	63% (overall) ² <u>WT</u> 60% <u>M</u> 73%	NR	12%	14% ⁷	22%	19%
PFS % at 12 months	53% (overall) <u>WT</u> 49% <u>M</u> 60%	10%	10%	12%	22%	27%

Sources: (1) Layman, Lancet Oncol, 2024; (2) Includes 2 unconfirmed PR.(3) Bidard 2022 NEJM – EMERALD trial; (4) 73% of patients had 1 prior line of endocrine therapy and 80% of patients had no prior chemotherapy in the advance setting; (5) Oliveria, Lancet Oncol, 2024, SERENA-2 trial; (6) Turner, NEJM, 2023, CAPItello-291 trial, mPFS only includes WT patients who had prior CDK4/6 treatment; PFS % at 12 months includes all patients who had prior CDK4/6 treatment; (7) ORR includes unconfirmed responses from all patients treated with fulvestrant, including those who had prior CDK4/6i and those who didn't; (8) Rugo 2021 SABCS (9) Rugo Lancet Oncol, 2024. Note: No head-to-head trials have been conducted; data collected from different trials, in different patient populations and may not be comparable.

VIKTORIA-2: Phase 3 Study Features for 1L HR+/HER2- ABC

Global open-label randomized study (~200 sites)

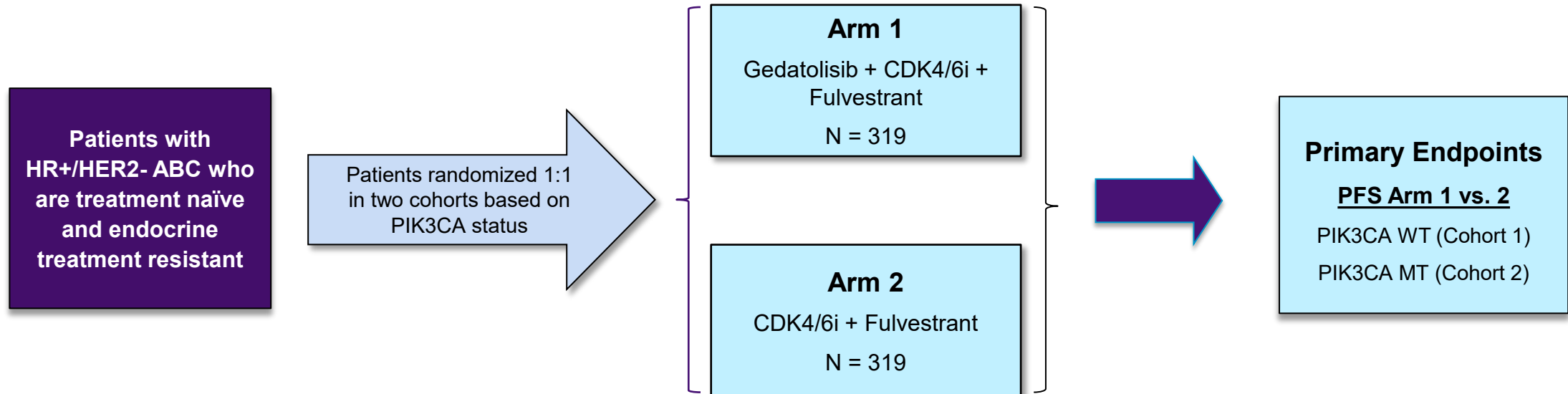
- **Key eligibility criteria:**
 - ER+/HER2- advanced or metastatic breast cancer
 - No prior treatment for advanced or metastatic breast cancer
 - Progression or relapse of disease during or within 12 months of completing adjuvant endocrine treatment
 - Pre-diabetic or patients with controlled diabetes allowed
- Investigator's choice of CDK4/6 inhibitor (ribociclib or palbociclib) for investigational and control arm
- Randomizing patients to cohorts based on PIK3CA status (MT or WT); primary analysis for each cohort is independent
- Stratification by primary vs secondary endocrine treatment resistance, site of metastases (bone-only vs other), geographical area (US vs other)

Key Considerations

- 1L endocrine treatment resistant patients receive limited benefit from CDK4/6 + fulvestrant
 - mPFS = 7.3M in recent study
- Supports potential indication allowing use of either ribociclib or palbociclib
- Minimizes exclusion of patients based on fasting glucose or HbA_{1c} levels
- Independent primary analyses of PIK3CA WT and MT provides two potential opportunities to obtain approval

VIKTORIA-2: Phase 3 Trial Design Overview for 1L HR+/HER2- ABC

Will conduct small safety run-in with gedatolisib plus ribociclib plus fulvestrant prior to Phase 3



Plan to enroll first patient Q2 2025

Relevant Comparisons to VIKTORIA-2 Control

B2151009 study results for 1L patients compares favorably to published data for 1L ETS patients

	Gedatolisib + Palbociclib + Letrozole N=41 ¹	Palbociclib + Letrozole N=441 ²	Palbociclib + Fulvestrant N=164 ³
<i>PIK3CA</i> Status	WT / MT (76% / 22%)	NR	MT (100%)
Endocrine Therapy Sensitivity	Sensitive (ETS)	Sensitive (ETS)	Resistant (ETR)
mPFS (months)	48.6	27.6	7.3
ORR	79%	55%	25%

Sources: (1) Rugo, ESMO-Breast, 2023; (2) Rugo, Palbociclib plus letrozole as 1st Line therapy in ER+/HER2- ABC – PALOMA-2; (3) Jhaveri, SABCS 2023.
Note: No head-to-head trials have been conducted; data collected from different trials, in different patient populations and may not be comparable.

Clinical Trial Results Provide POC in this 1L ABC Patient Population¹

Results for a less potent PAM inhibitor in small fraction of population highlights opportunity for gedatolisib

Study Regimens	Line of Therapy	Patient Population	N	Overall Results (Months rPFS)	Comments
Inavolisib (PI3Kα) + Palbociclib + Fulvestrant vs. Palbociclib + Fulvestrant ¹	1 st Line	PIK3CA MT+ Progressed on prior adjuvant ET w/in 12 months after last treatment Fasting glucose <126 mg/dL and HbA _{1C} <6.0%	325	15.0 vs. 7.3 months (<i>HR = 0.43; P<0.0001</i>)	<ul style="list-style-type: none"> ▪ Inavolisib shows clinical activity despite only targeting PI3Kα ▪ Gedatolisib 5X-10X more potent in vitro than inavolisib² ▪ Indication excludes ~80% of eligible patients <ul style="list-style-type: none"> ▪ No PIK3CA WT (60%-65% of total ABC) ▪ No pre-diabetics or controlled diabetics (40% of PIK3CA MT) ▪ Gedatolisib has reported favorable preliminary results in total eligible population in both 1L and 2L patients

(1) Jhaveri SABCS (INAVO120), 2023; (2) Khan AACR, 2021. Note: No head-to-head trials have been conducted; data collected from different trials, in different patient populations and may not be comparable.



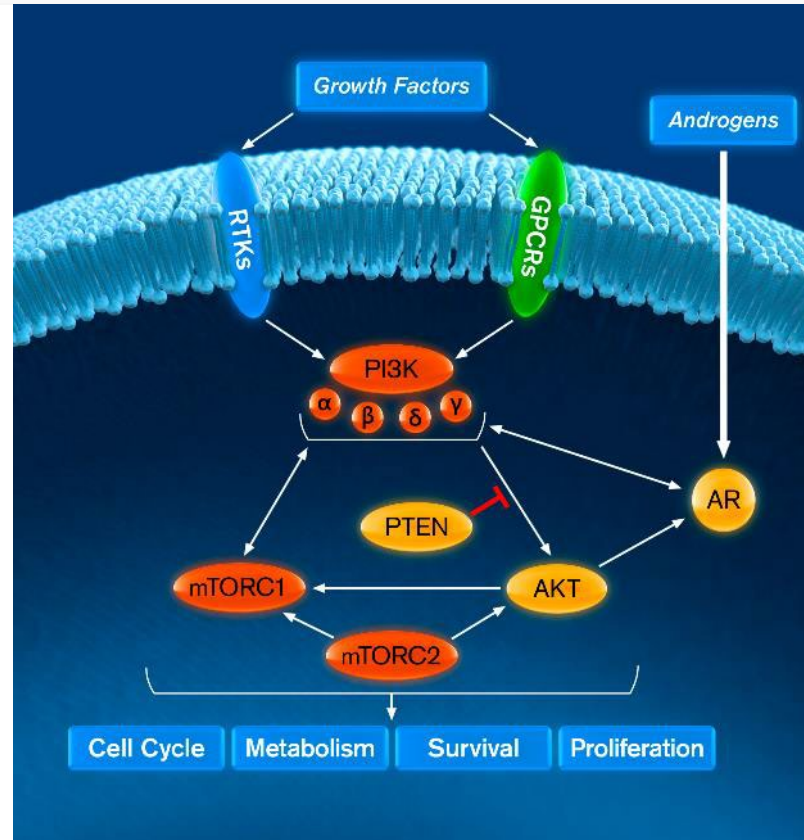
Gedatolisib for Prostate Cancer

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

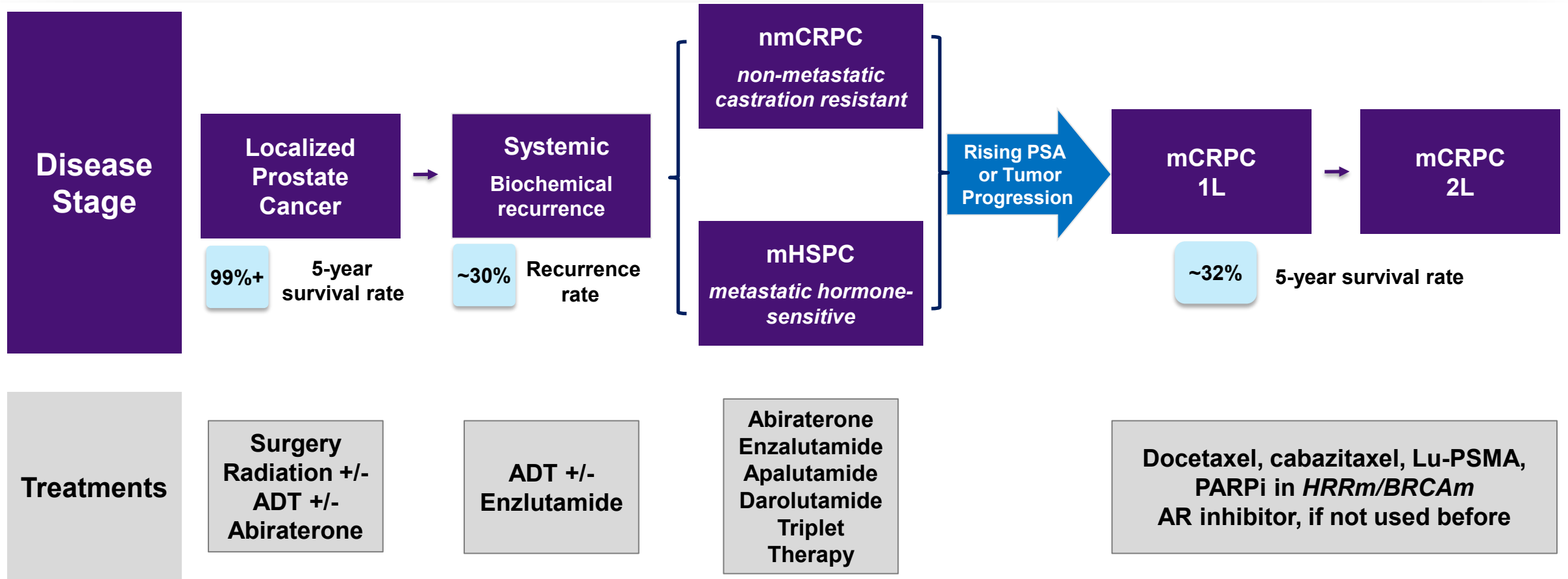


The PAM Pathway Plays a Key Role in mCRPC

- 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

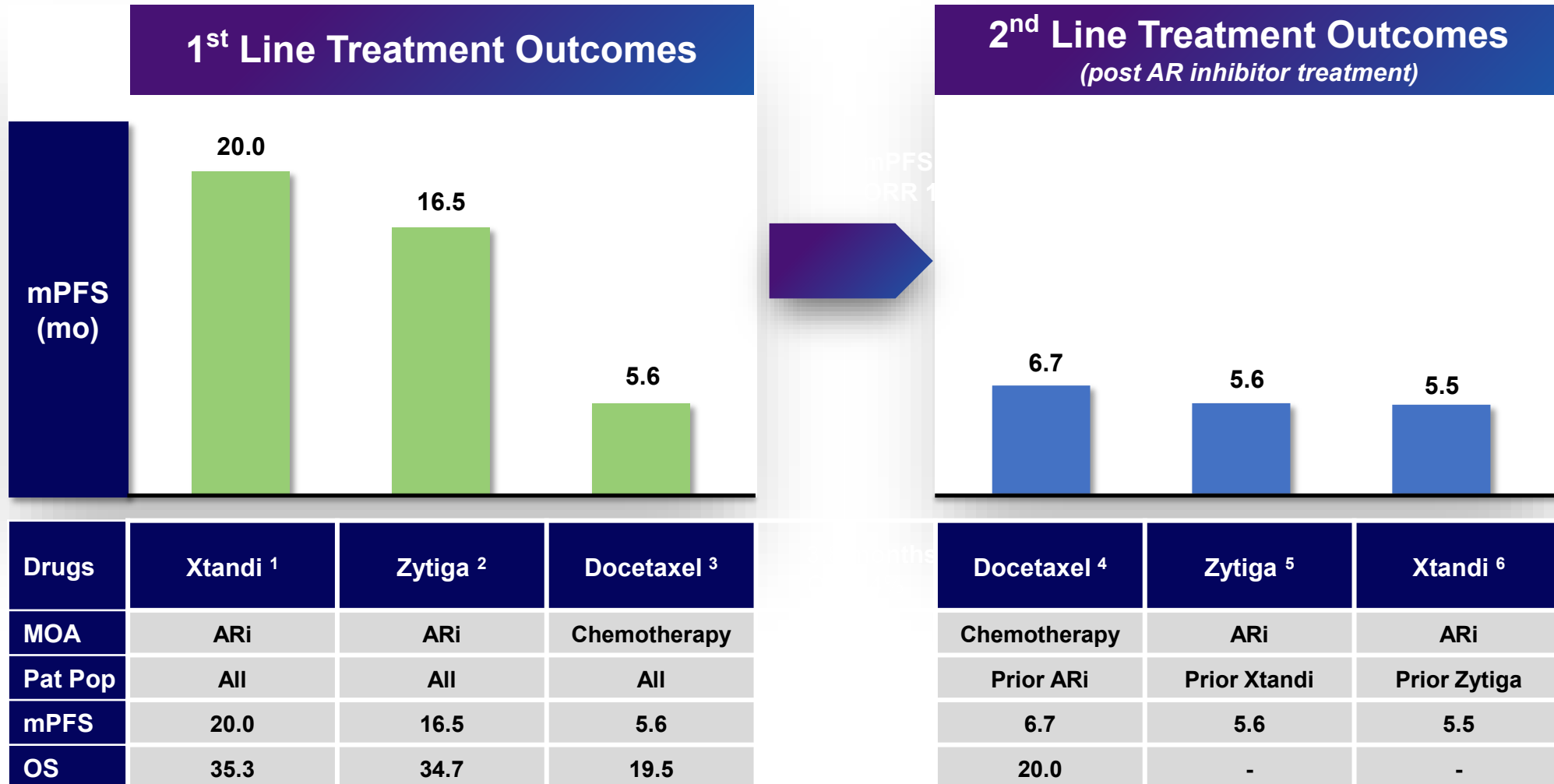
Prostate Cancer Disease and Treatment Landscape^{1,2}

34,700 men in US and 62,400 men in 5EU and Japan die from prostate cancer annually^{3,4}



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

Significant need for better therapeutic options

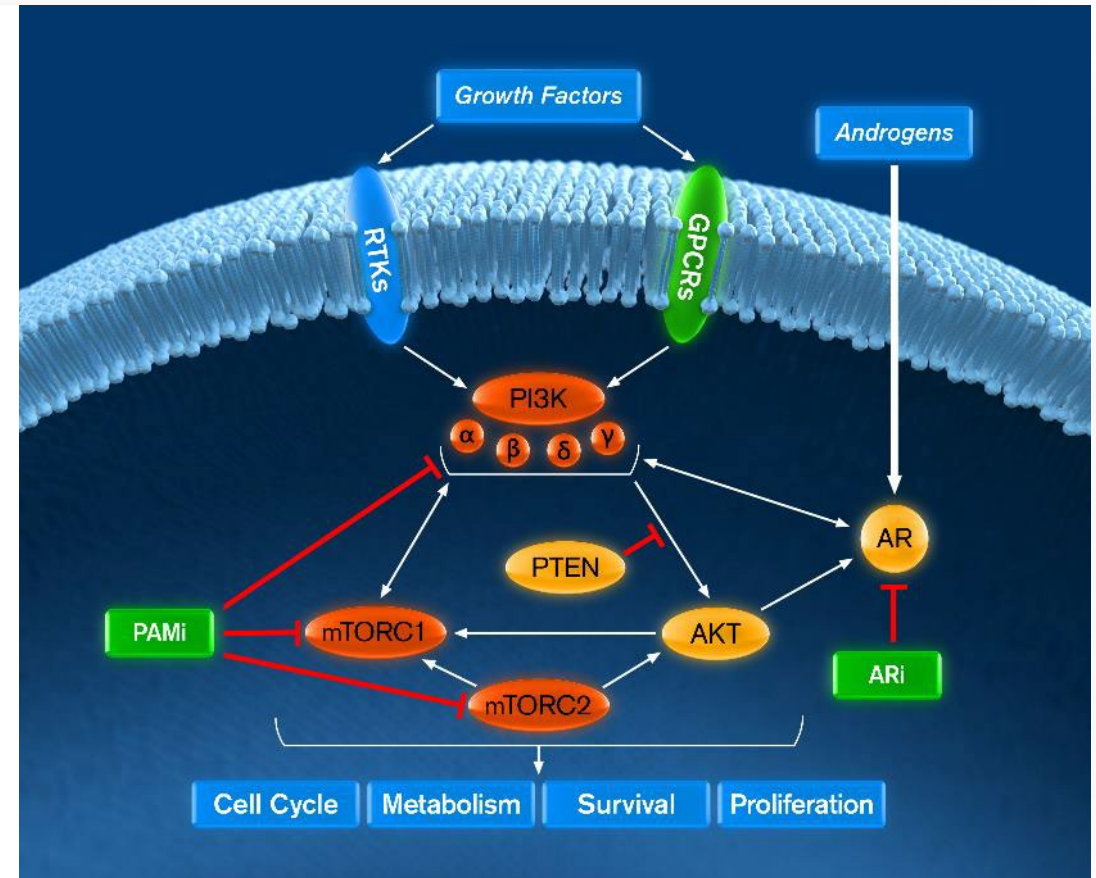


Combining a PAM Inhibitor with an AR Inhibitor has Strong Scientific Rationale

Biological parallels between mCRPC and HR+ ABC – PAM and hormonal pathway drive progression ¹

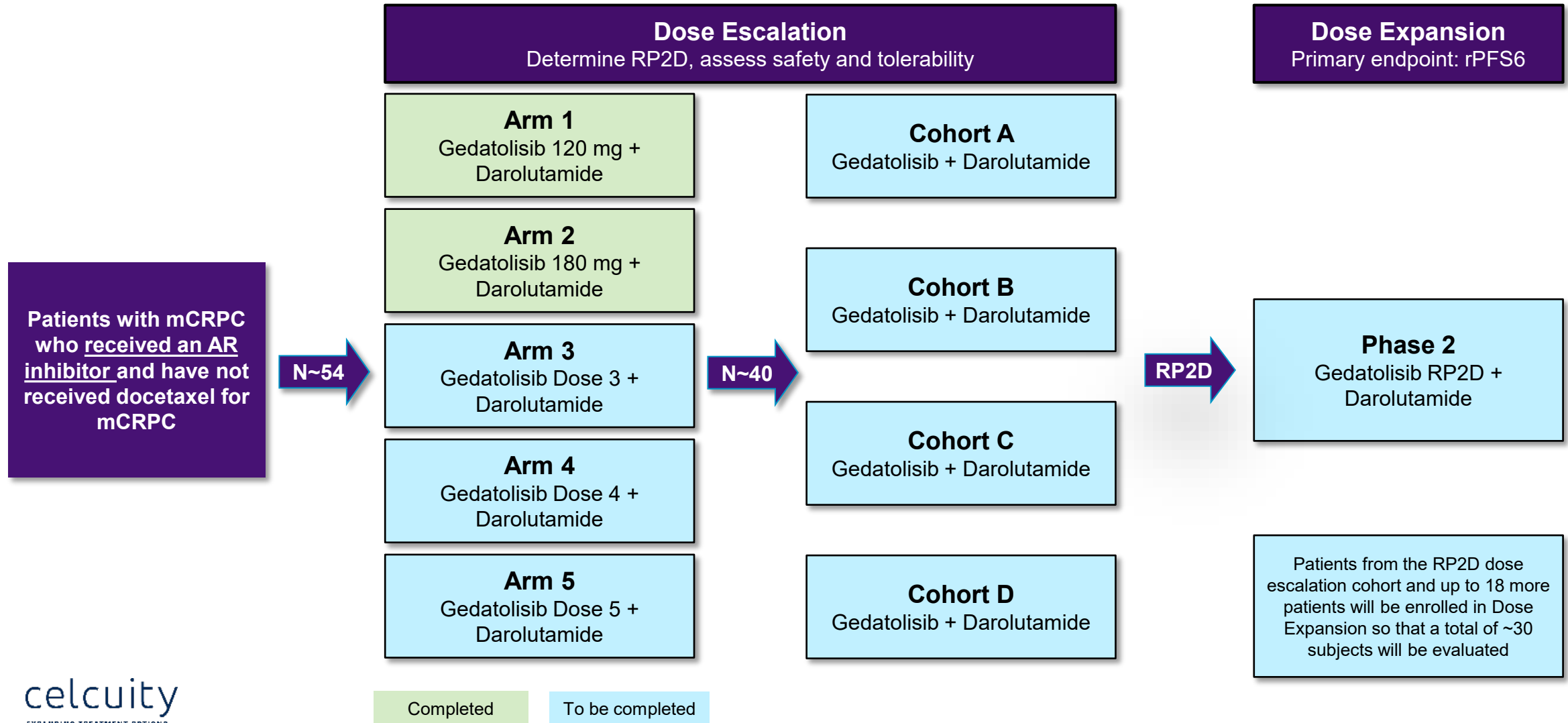
PI3K/mTOR + AR Inhibition *Treatment Rationale*

- 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 results 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



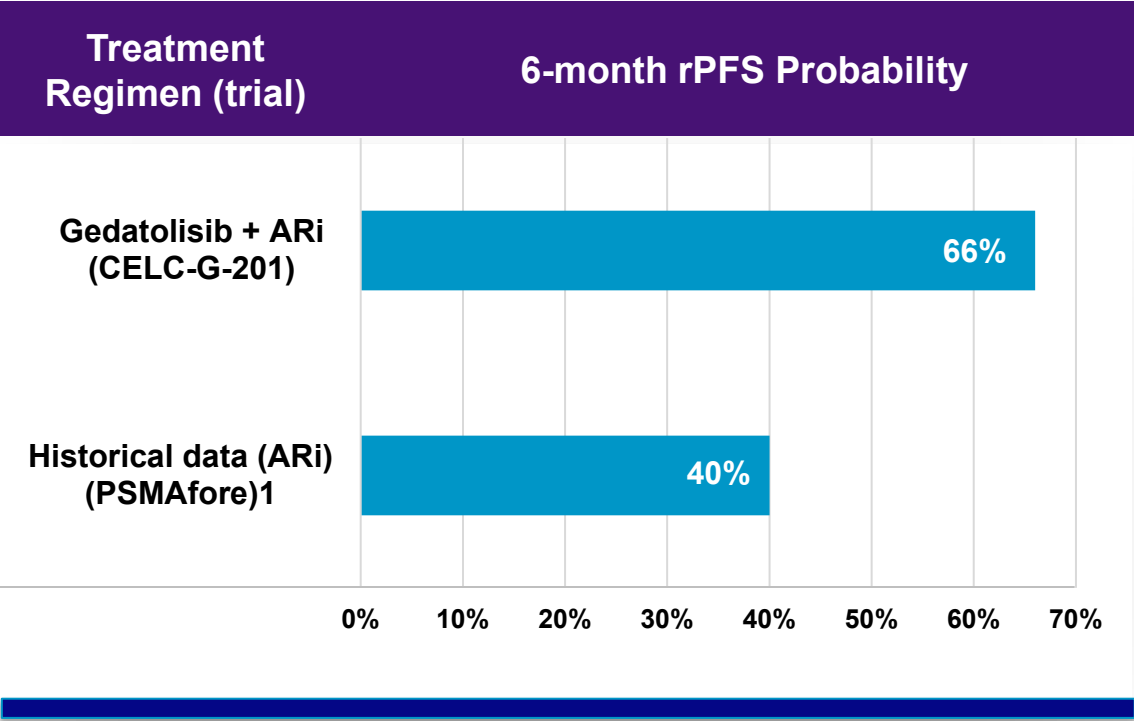
CELC-G-201: Phase 1b/2 Trial Design Overview

Evaluating gedatolisib plus darolutamide to determine preliminary safety and efficacy RP2D



CELC-G-201: Preliminary Topline Data for Gedatolisib + Darolutamide

rPFS6 for G + ARi (darolutamide) compares favorably to historical data for ARi monotherapy



	CELC-G-201 Arms 1 & 2 (N=38)
rPFS6	66%
Discontinuation Rate due to AE	0%
Grade 3 hyperglycemia	0%
Grade 2 stomatitis	7.9%
Grade 3 stomatitis	2.6%

(1) Morris NEJM 2024; Abbreviations: rPFS6 – six-month radiographic progression free survival probability

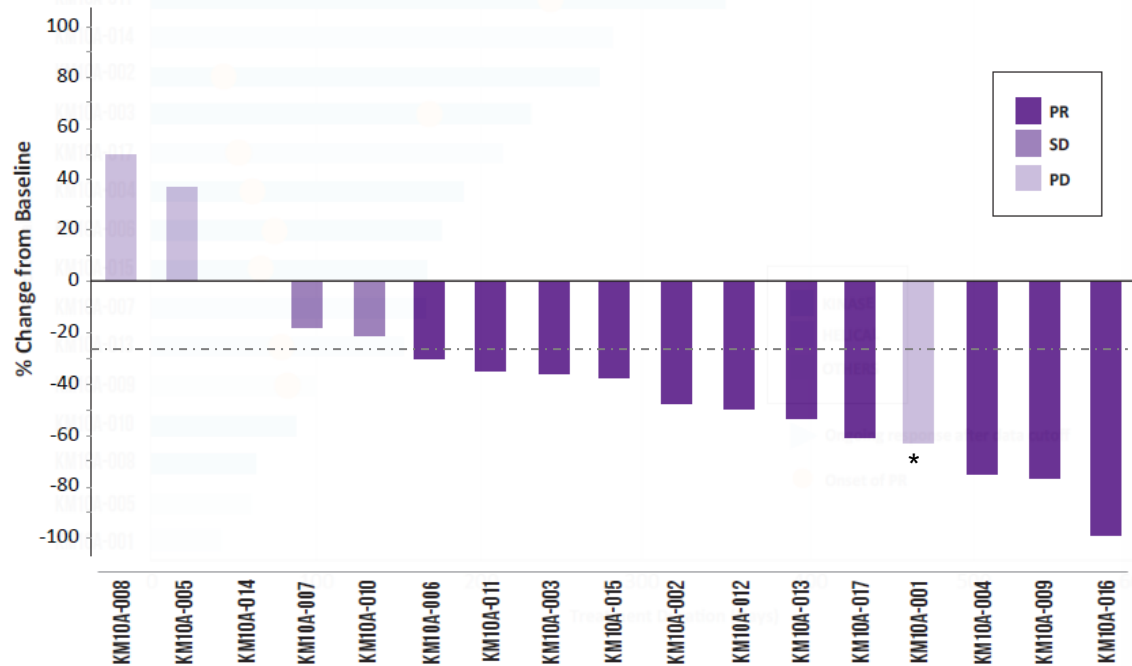


Additional Early Phase Clinical Data

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

59% ORR and 83% clinical benefit rate

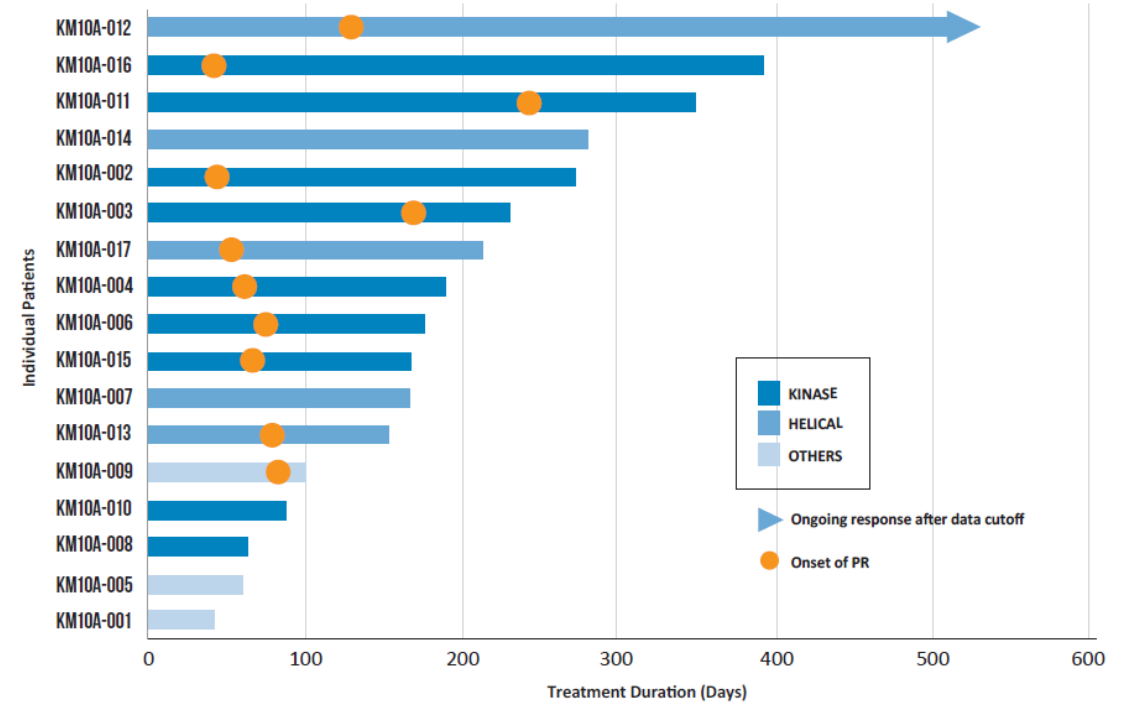
Best Response



* 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)

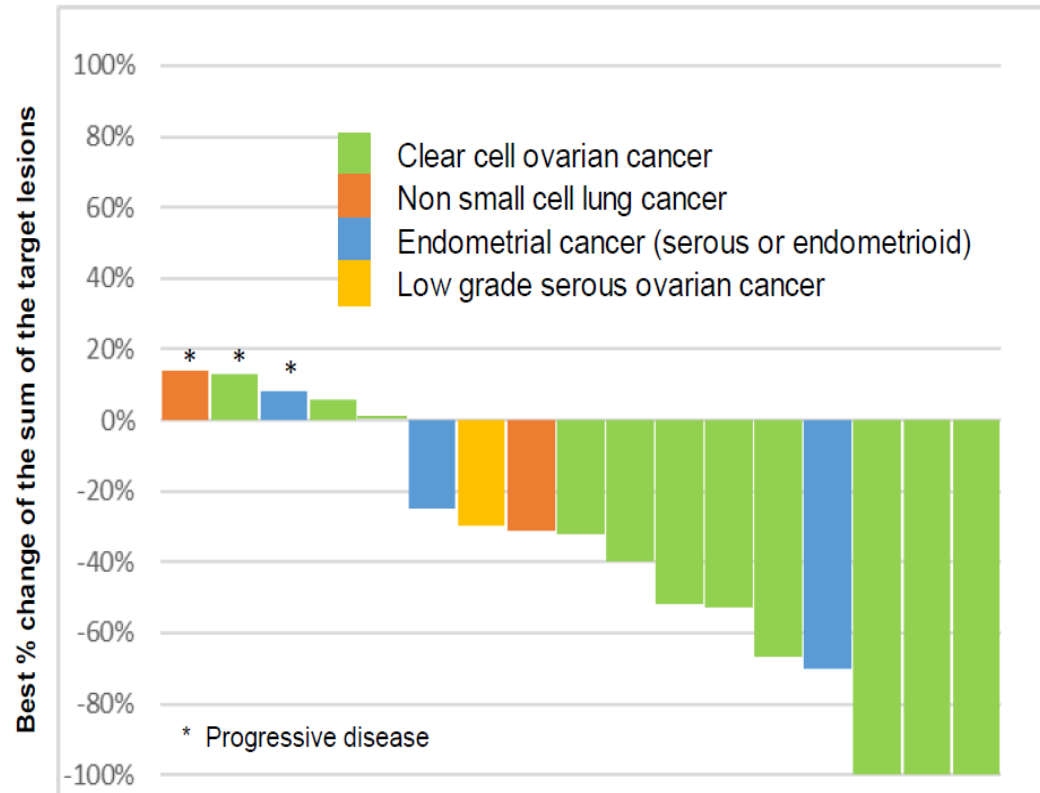
Duration of Response



- Median duration of response 7.1 months

Gedatolisib + Paclitaxel + Carboplatin in Patients with Solid Tumors (N=17)¹

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

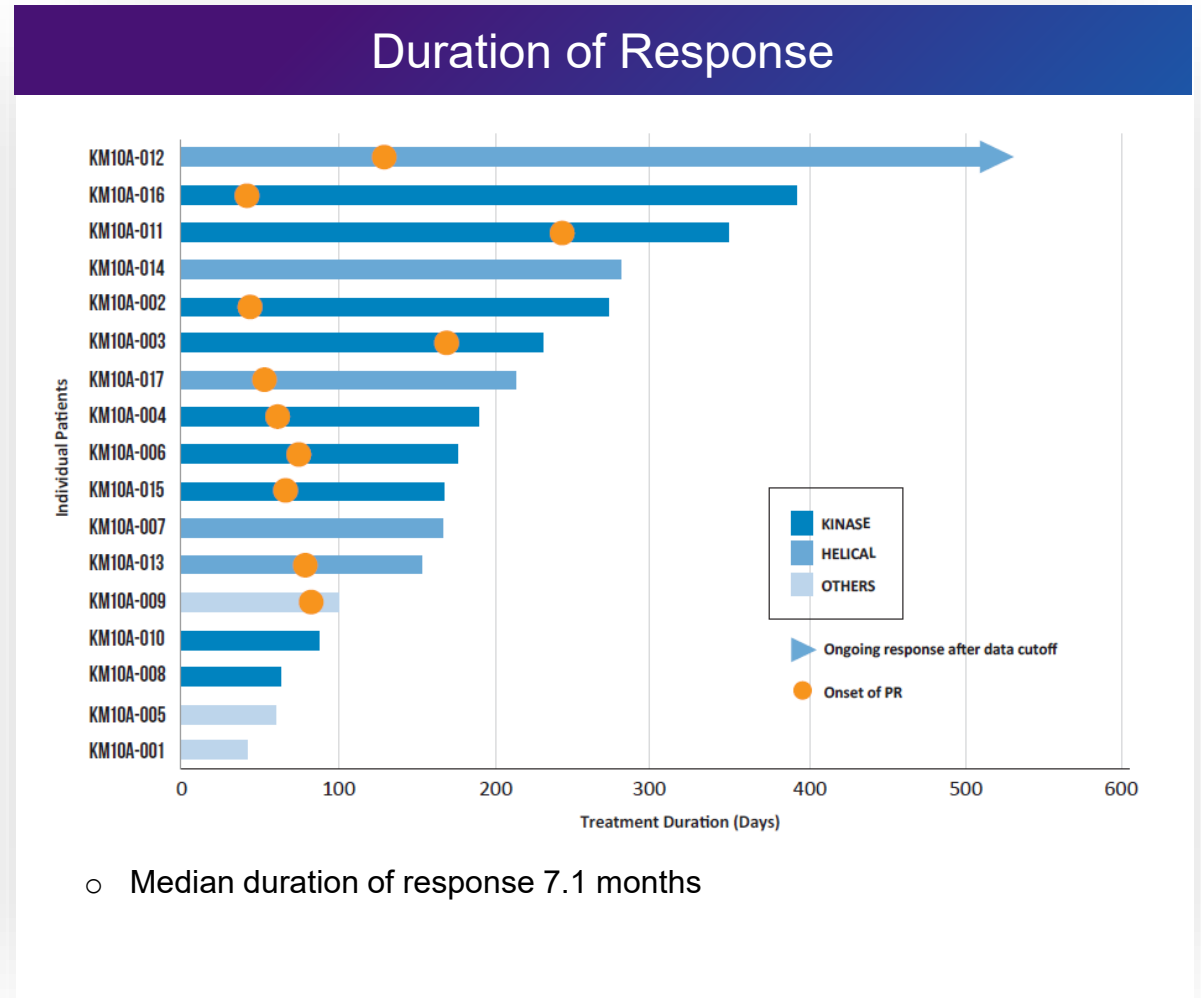


- Ovarian Cancer (N=11)
 - ORR: 82%
 - Clear cell ovarian cancer (CCOC) (N = 10)
 - ORR: 80% - 5/10 PR, 3/10 CR
 - Low grade serous ovarian (N=1)
 - 1/1 PR
- Other solid tumors (N= 6)
 - ORR = 33%
- Median PFS = 6.35 months (95% CI 4.6-11.11)
- Median duration of response = 7.6 months (95% CI 1.9-13.4)

- 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



Leading cancer KOLs are participating in our research

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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
- A Phase 3 study in 2L patients is enrolling and a Phase 3 study in 1L patients is expected to begin enrolling in Q2 2025

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, and short-term investments of \$205M as of Q1 2025 expected to fund operations through 2026

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