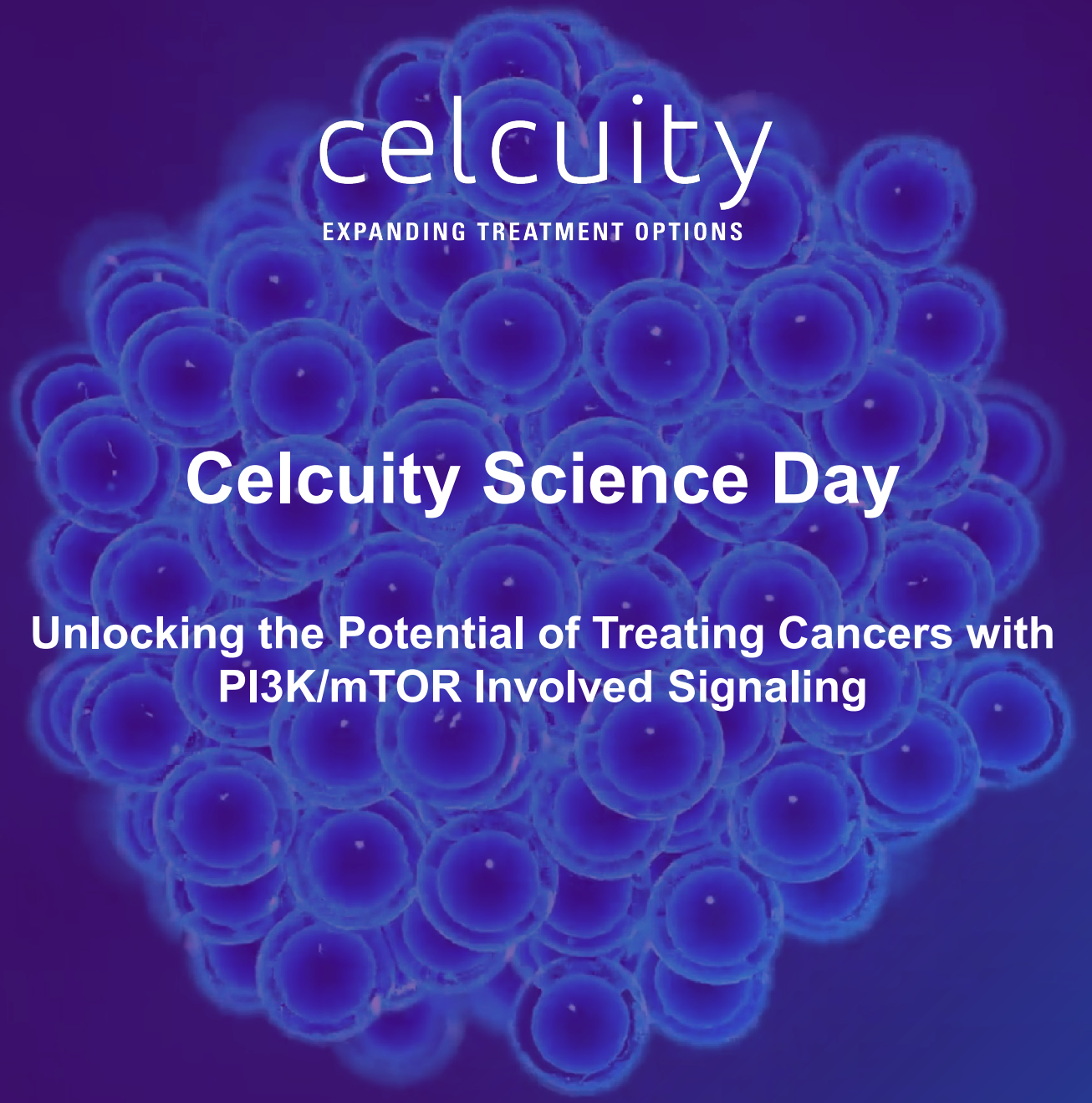

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Celcuity Science Day

Unlocking the Potential of Treating Cancers with PI3K/mTOR Involved Signaling

September 21, 2023

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. Forward-looking statements include but are not limited to statements based on 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, and the anticipated market opportunity at that time, our plans to research, discover and develop additional product candidates, our planned milestones and timing of achieving such milestones, the scope, protocol, and costs of our clinical development program and upcoming clinical trials for gedatolisib, including but not limited to our VIKTORIA-1 Phase 3 clinical trial and our Phase 1b/2 CELC-G-201 clinical trial, the expected results of VIKTORIA-1 and CELC-G-201, including but not limited to the anticipated efficacy of gedatolisib in combination with fulvestrant and with or without palbociclib, the anticipated efficacy of gedatolisib in combination with darolutamide, the expected timing of funding of tranches under the Company’s debt financing facility, any potential benefits resulting from Breakthrough Therapy designation for gedatolisib, and other expectations with respect to Celcuity’s lead product candidate, gedatolisib, 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, “may,” “will,” “would,” “should,” “could,” “look forward to,” “believe,” “predict,” “expect,” “anticipate,” “intend,” “continue”, “ongoing,” “target,” “goal,” “plan,” “potential,” or “estimate,” and similar expressions or words, identify forward-looking statements.

Any forward-looking statements in this presentation are based on management’s current expectations and beliefs and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this presentation, including, without limitation, risks relating to: (i) unforeseen delays in clinical trial enrollment or other activities that may affect the timing and success of our ongoing gedatolisib and CELsignia trials, (ii) the fact that preliminary data from a clinical study may not be predictive of the final results of such study or the results of other ongoing or future studies, (iii) unforeseen challenges in developing and continuing partnership opportunities with pharmaceutical companies, (iv) our ability to obtain and maintain FDA approval to commercialize gedatolisib, and the market acceptance of a commercialized product, (v) our ability to raise additional capital for further product development and other activities, (vi) the development of products or services competitive with our products, including without limitation, other effective drug candidates, diagnostic tests and treatment options, (vii) our dependence on intellectual property licenses and other third-party relationships, and (viii) uncertainties and assumptions regarding the impact of macro-economic conditions and global risks, such as the COVID-19 pandemic or a government shutdown, on our business, operations, clinical trials, supply chain, strategy, goals and anticipated timelines.

Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond our control, you should not rely on these forward-looking statements as predictions of future events. In our reports and filings with the SEC, including our Annual Report on Form 10-K for the year ended December 31, 2022, we present more information about the risks and uncertainties applicable to our business. New risks and uncertainties may emerge from time to time, and it is not possible to predict all risks and uncertainties. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

The information in this presentation does not provide full disclosure of all material facts relating to Celcuity or its securities. This presentation shall not constitute an offer to sell or the solicitation of an offer to buy any securities.

Celcuity Leadership Team and External Speakers Participating Today

Celcuity Participants

Brian Sullivan
Chief Executive Officer
Co-Founder

Lance Laing, PhD
Chief Scientific Officer
Co-Founder

Igor Gorbatchevsky, MD
Chief Medical Officer

External Key Opinion Leaders

Sara Hurvitz, MD
Professor of Medicine
Head, Division of Hematology & Oncology
Sr. Vice President, UW Medicine,
Fred Hutch Cancer Center

Karim Fizazi, MD, PhD
Professor of Medicine
GETUG President
Head, GU Group,
Institute Gustav Roussy
University of Paris Saclay

Agenda

Topic	Session	Presenter
	Overview of Gedatolisib's Potential	Brian Sullivan
Scientific Overview	Importance of PI3K/mTOR as an Anti-Cancer Target	Lance Laing, PhD
	Gedatolisib Differentiation – Nonclinical	Lance Laing, PhD
	Gedatolisib PK and Safety Overview	Igor Gorbatchevsky, MD
Prostate Cancer	KOL Presentation: 2L SOC and PI3K/mTOR in Prostate Cancer	Karim Fizazi, MD, PhD
	Gedatolisib for Prostate Cancer	Igor Gorbatchevsky, MD
Breast Cancer	KOL Presentation: SOC and Future Landscape in HR+/HER2- ABC	Sara Hurvitz, MD
	Gedatolisib for Breast Cancer	Igor Gorbatchevsky, MD
	Wrap-up Q&A	Brian Sullivan

Introduction and Overview

Brian Sullivan

CEO and Co-Founder

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Focused on Treating Cancers Involving the PI3K/mTOR Pathway

One of the most important oncogenic pathways

PI3K/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[1]

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

PI3K/mTOR	**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

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(1) cBioPortal References:Cerami et al., Cancer Discov. 2012, and Gao et al., Sci. Signal, 2013;

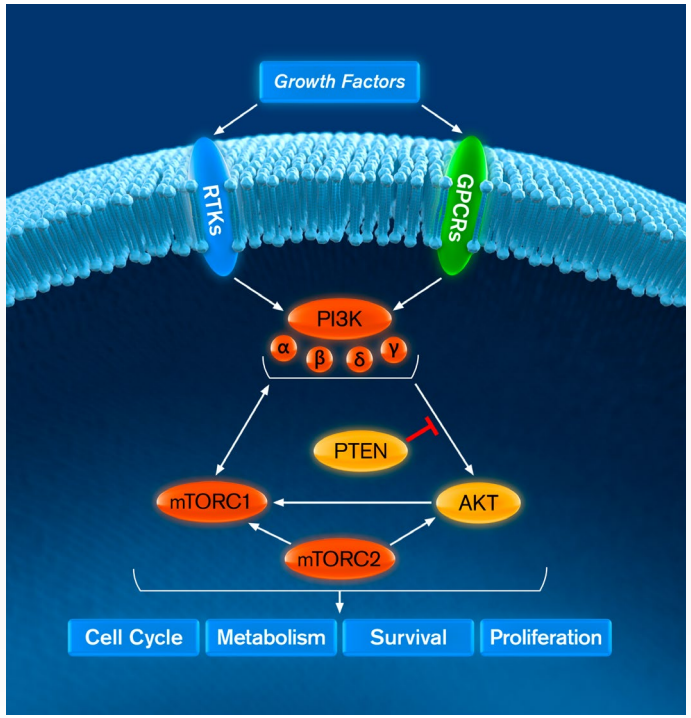
Difficult to Safely and Efficaciously Inhibit PI3K/mTOR

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 administrated pan-PI3K or pan-PI3K/mTOR inhibitors induced unacceptable toxicity

1st Gen	Oral pan-PI3K/mTOR inhibitors Toxicity high, poor PK properties Failed in Phase 1/2	*2nd Gen*	Pan-PI3K inhibitors Significant toxicity Failed in Phase 3	*3rd Gen*	Node-specific inhibitors Limited PFS benefit Two drugs approved	*Today*	Need safe, potent pan-PI3K/mTORi

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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[1]
- **63% ORR, 12.9 months mPFS** in 2L patients[2]

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[2]

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[3]

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(1) Combined data from treatment-naïve patients enrolled in Escalation Arm A and Expansion Arm A of the B2151009 Phase 1b clinical trial (Rugo 2023); (2) Data from Expansion Arm D of the B2151009 clinical trial (Wesolowski 2022); includes 2 unconfirmed partial responses; (3) Salvi, The Breast, 2021; Globocan 2020; Abbreviations: ORR = objective response rate; mPFS = median progression free survival; 1L = 1st line; 2L = 2nd line; TEAE = Treatment emergent adverse event; AE = adverse events; ABC = advanced breast cancer; mCRPC = metastatic castration resistant prostate cancer; 5EU = France, Germany, Italy, Spain, UK

Current Clinical Development Programs

2nd Line HR+/HER2- Advanced Breast Cancer (ABC)

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
- Breakthrough Therapy Designation for this indication
- Expect to report top-line primary analysis data for:
  - PIK3CA WT patients in 2H 2024
  - PIK3CA MT patients in 1H 2025

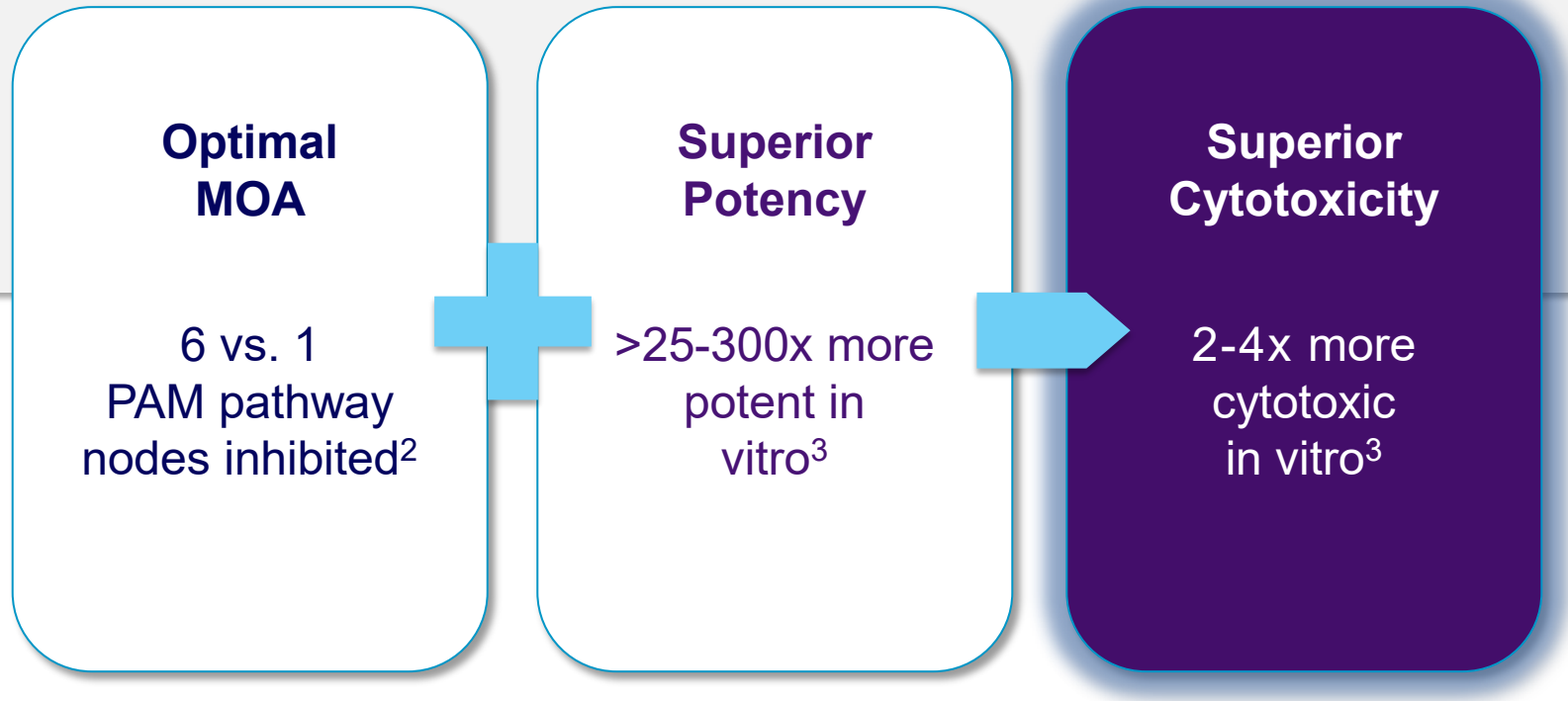
2nd Line Metastatic Castration Resistant Prostate Cancer (mCRPC)

Phase 1b/2 clinical trial for gedatolisib with darolutamide

- Will enroll patients with who progressed on androgen receptor (AR) therapy
- Entered into Clinical Trial Collaboration Agreement with Bayer to provide darolutamide for Phase 1b/2 study
- Expect to enroll first patient in Q1 ’24
- Expect to report initial data in 1H ‘25

Mechanism of Action (MOA) & Potency Induce Superior Cytotoxicity

Gedatolisib vs. approved PAM inhibitors assessed in 34 breast and prostate cancer cell lines[1]



(1) Approved PAM inhibitors are alpelisib and everolimus (2) Gedatolisib inhibits four class I PI3K isoforms and two mTOR sub-complexes. Currently approved PAM therapies, alpelisib and everolimus, are single node PAM inhibitors. (3) Internal data on file.

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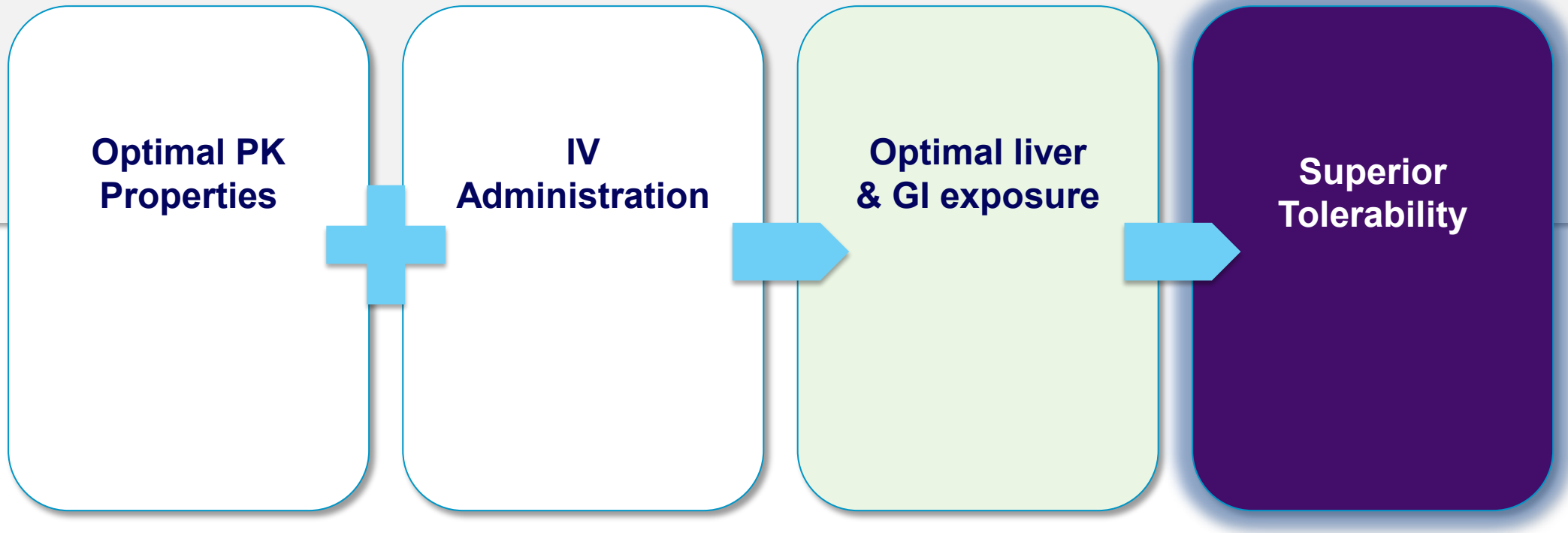
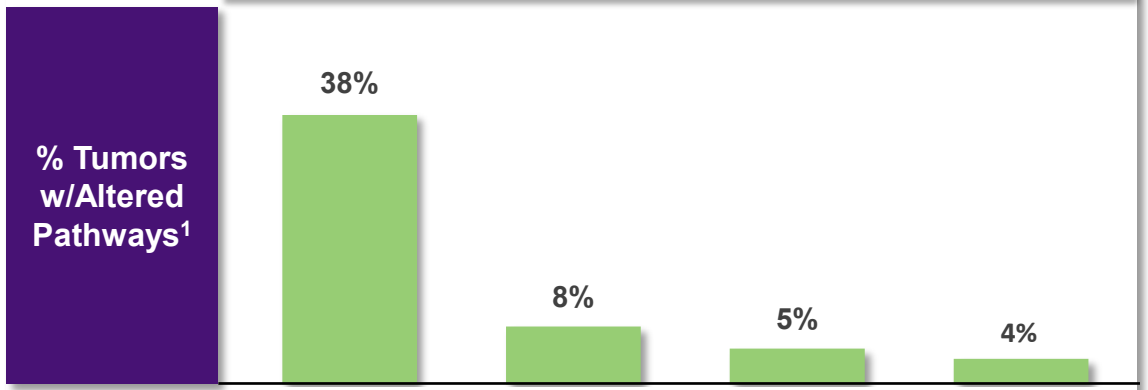
Gedatolisib Is Well Tolerated - Unlike Earlier PI3K/mTOR or Pan-PI3K Inhibitors



The PAM Pathway is the Most Underdeveloped Target in Solid Tumors

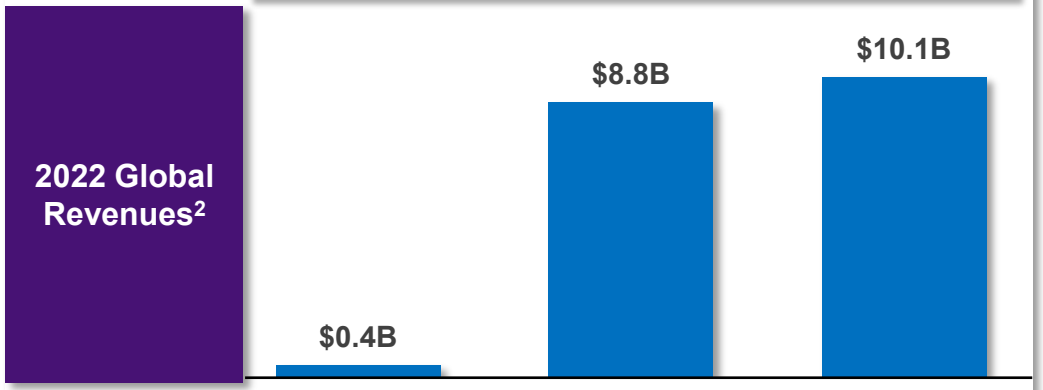
PAM is the most frequently altered pathway in solid tumors



Target *(key tumor type)*	PAM *(breast)*	HER2 *(breast)*	EGFR *(lung)*	ALK *(lung)*
Global Revenues[2]	~0.4B	~$10B	$5.5B	$2.5B
Key Drugs	Piqray	Perjeta Herceptin	Tagrisso	Alecensa Xalkori

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

Gedatolisib has revenue potential comparable to CDK4/6 & AR therapies



Target *(key tumor type)*	PAM *(breast/prostate)*	CDK4/6 *(breast)*	AR *(prostate)*
Potential Patient Pop	539K	227K	312K
Key Drugs	Piqray	Ibrance Kisqali	Xtandi Zytiga

Gedatolisib's potential patient population is not tumor specific like CDK4/6 or AR inhibitors

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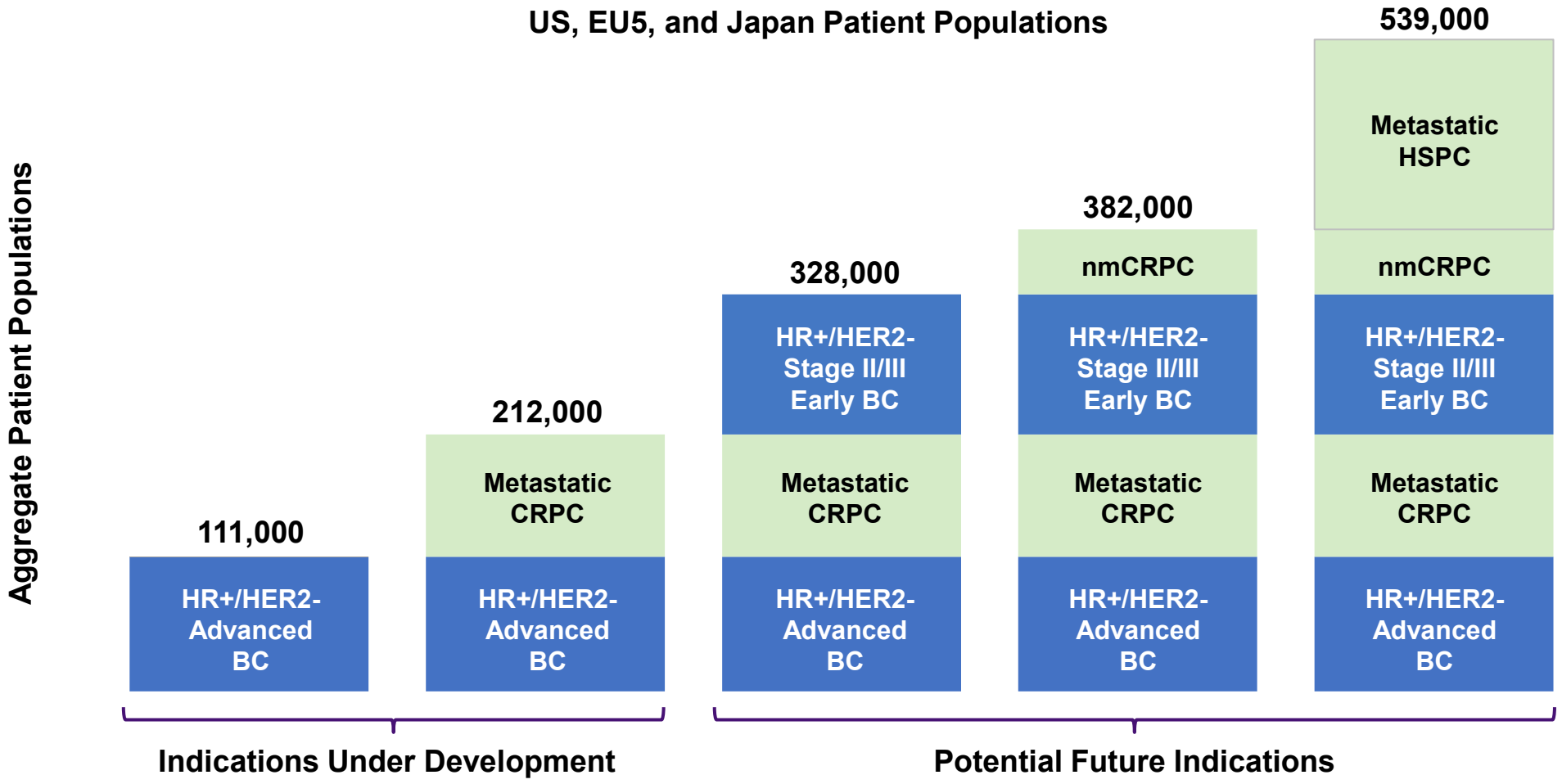
(1) cBioPortal References:Cerami et al., Cancer Discov. 2012, and Gao et al., Sci. Signal, 2013; (2) Annual Reports for Novartis, Pfizer, Astellas, Roche, AstraZeneca, Johnson & Johnson

Addressable Patient Population in Breast and Prostate Cancer



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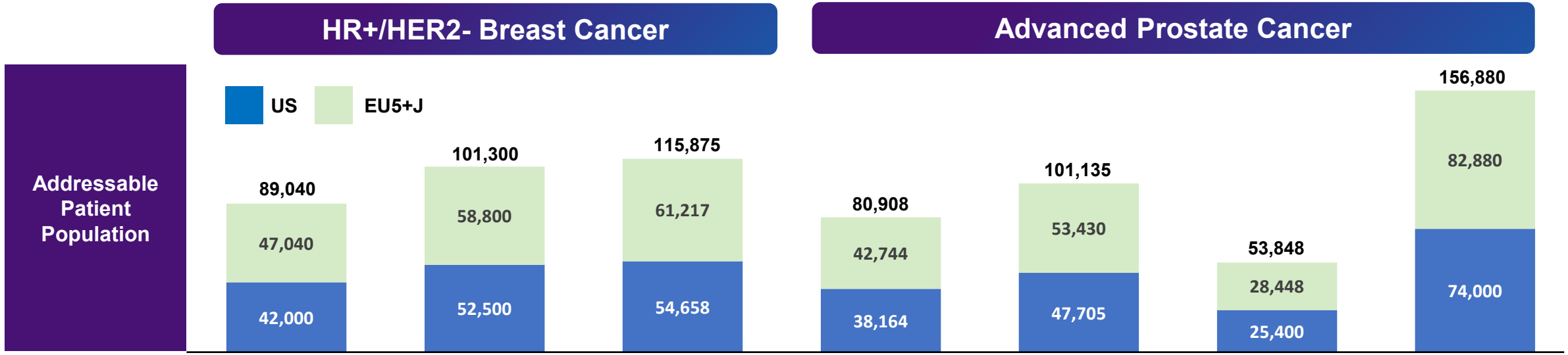
Sources: American Cancer Society, Breast Cancer Statistics 2022; American Cancer Society Facts and Figures 2019-2020; Salvo, E. M. et al. (2021); Scher, et al. 2015; Datamonitor Healthcare; Leith, A. et al. 2022; George, D. J. et al. 2022; EU5 + Japan calculated using 112% scale up factor Abbreviations: 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



Indication	2L ABC	1L ABC	High Risk EBC Adjuvant	2L mCRPC	1L mCRPC	nmCRPC	mHSPC
Duration of Therapy (DoT)	~12 months	~45 months	~12 months	~12 months	~24 months	~24 months	~20 months
Basis for DoT assumption	95% Gedatolisib Phase 1b mPFS	95% Gedatolisib Phase 1b mPFS	SOC treatment window	Phase 2 data with other PI3K/mTOR	SOC DoT + 50%	SOC DoT + 50%	SOC DoT + 50%
Market Opportunity	~$5-$6B	~$10B+	$6-$8B	$5-$6B	$10B+	$6-$8B	$10B+

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Sources: 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+Japan calculated using 112% scale up factor; Celcuity internal estimates Abbreviations: HR, hormone receptor; BC, breast cancer; CRPC, castration resistant prostate cancer; nm, non-metastatic; HSPC, hormone sensitive prostate cancer

Key Themes for Today's Meeting

Significant untapped potential to effectively treat PAM pathway involved cancers

1

- **The PAM pathway is one of the most important, yet underdeveloped, targets in cancer**

2

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

3

- **Very compelling data in 1L and 2L patients with HR+/HER2- ABC**
- Gedatolisib combined with CDK4/6i + hormonal therapy has potential to replace currently available standard-of-care

4

- **Uniquely positioned to advance multiple potential blockbuster indications in breast and prostate cancer**
- Cash & cash equivalents of $146M at end of Q2 '23 expected to fund operations through data readouts in ABC and mCRPC

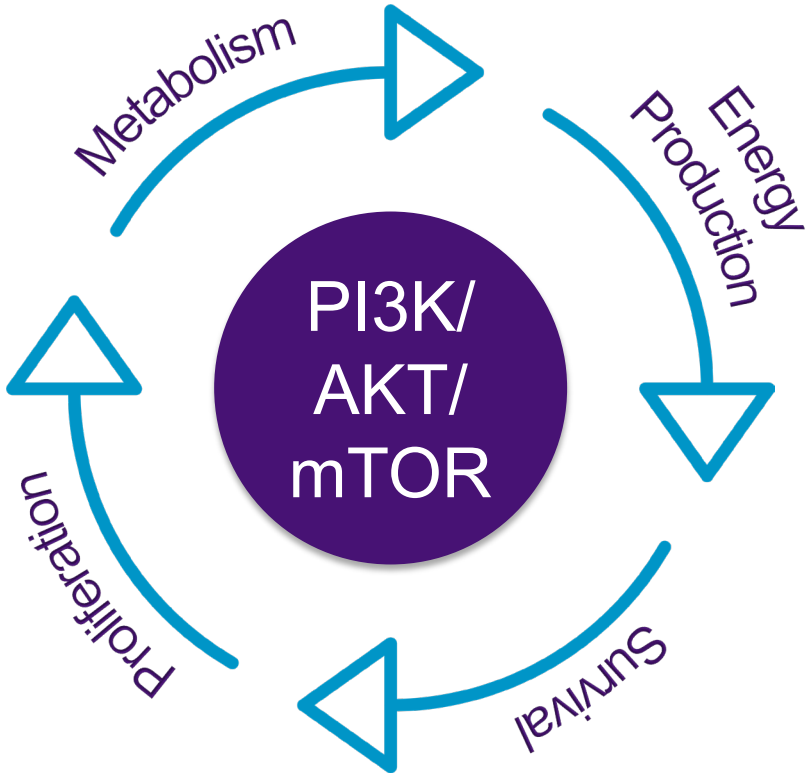
The Importance of the PI3K/mTOR Pathway as a Cancer Driver

Lance Laing, PhD
Chief Science Officer and Co-Founder

The PAM Pathway Regulates Critical Cell Functions

PAM – PI3K/AKT/mTOR pathway

PAM is a "command and control" center of critical cellular processes.



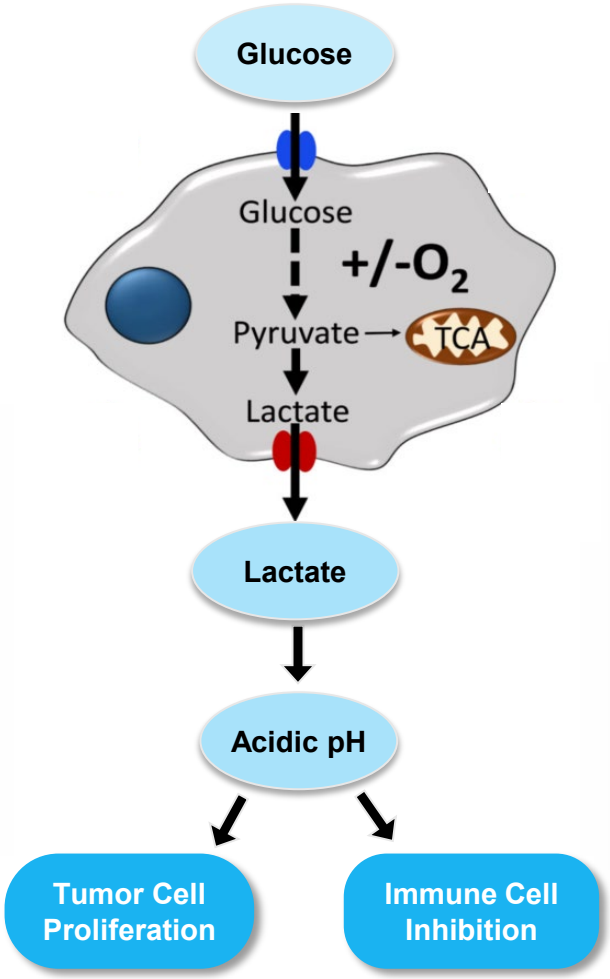
Hoxhaj et al. 2020, Nat Rev Cancer. 20(2):74-88; Fruman et al. 2017 Cell 170(4): 605–635; Manning and Toker 2017 Cell 169(3): 381–405; Khatpe et al. 2021 Cancers 13(3):369; Tortorella et al. 2023 Int J Mol Sci 24(3):2046

Tumors Rely on Metabolic Changes Controlled by PAM Pathway

Activity controlled by the PAM pathway creates a pro-tumor microenvironment

Tumor cells require tremendous amounts of glucose relative to normal cells

- **High glucose consumption causes excess** extracellular lactate, low pH, and low oxygen
- Creates a tumor microenvironment **that can promote** tumor cell proliferation and inhibit normal immune cell function



The PAM pathway regulates glucose consumption, which makes it a fundamental tumor driver

- PAM's role as regulator of glucose consumption cells is a feature of all tumor types
- Makes PAM a therapeutic target regardless of a tumor's mutational status

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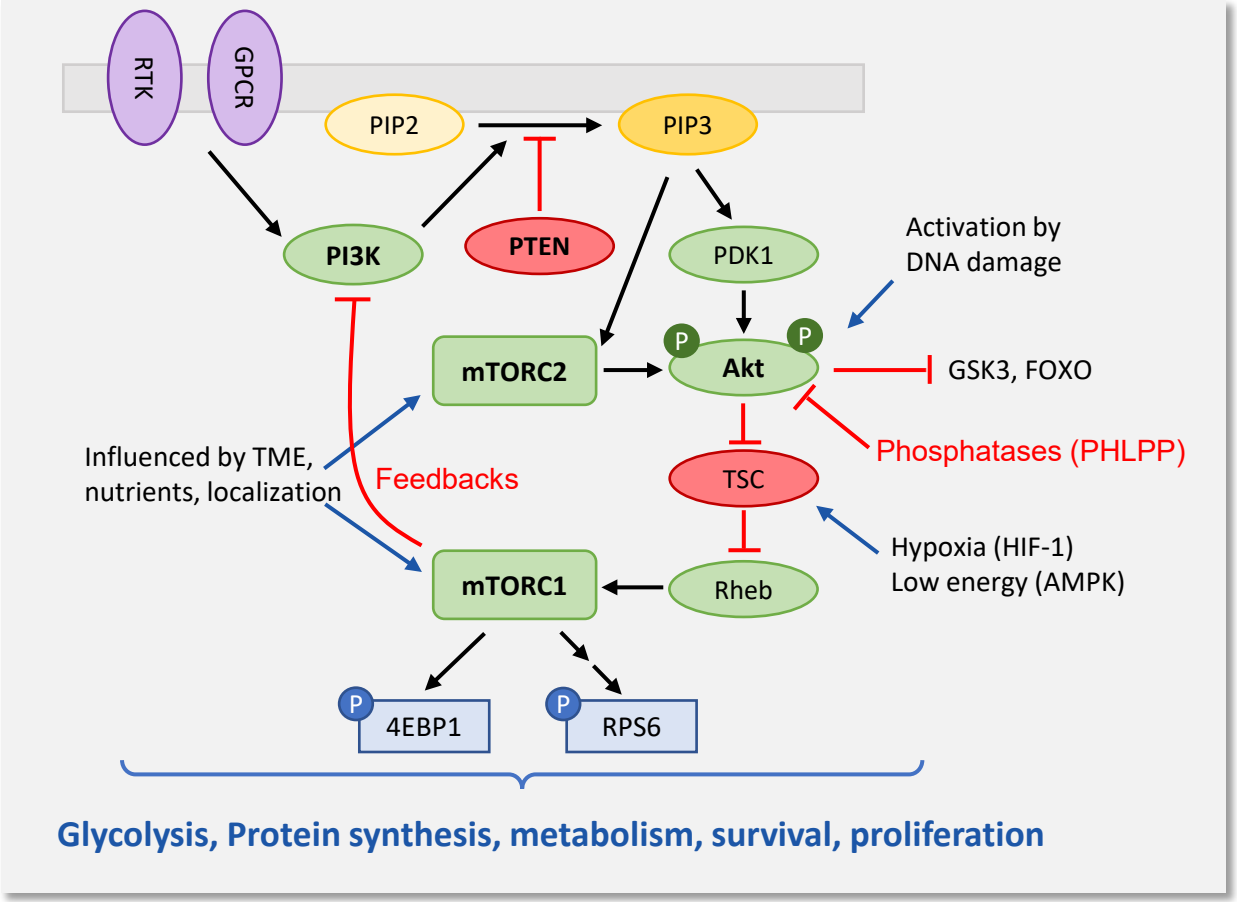
PAM has Multiple Signaling Nodes that Provide Functional Redundancy

Redundancy ensures pathway function is maintained if a single node becomes disrupted

- **PAM pathway primary signaling nodes**
  - PTEN
  - Class I PI3K isoforms – α,β,γ,δ
  - mTORC1 and mTORC2
  - AKT
- **Redundancy in PAM signaling nodes** ensures tumor can maintain metabolic dysfunction under variety of conditions
  - Enables the tumor to be resilient
- To overcome this redundancy, **must target multiple nodes of the PAM pathway**



Juric 2015 Nature. 518:240-244; Castel 2016 Nat Cancer. 2:587-597; Mao 2021 Nat Commun. 12:5053; Schwatrz 2015 Cancer Cell. 27:109-122. Chandarlapaty 2011, Cancer Cell. 19:58-71; Bago 2016, EMBO J. 35:1902-1922; Manning 2017, Cell. 169:381-405.; Mukherjee 2021, Mol Cell. 81:708-723 e705.

Node Redundancy Requires PI3Kα/β/γ/δ and mTORC1/2 Inhibition

Intrinsic pathway complexity challenges single node control therapeutic approach

- **Each PAM node has a critical role in maintaining viability**
- **Inhibition of individual nodes results in adaptive/resistance signaling**
- **Partial or imbalanced inhibition results in compensatory resistance**
- **Feedforward and feedback loops between PI3K isoforms and mTOR cross-activate uninhibited sub-units**
- **Multiple pathway components must be targeted**

Adaptive response of PAM nodes when a single PAM node inhibited		
PI3Kα inhibition	→	Reduces PTEN tumor suppression Increase PI3Kβ activity[1,2,3,4]
PI3Kβ inhibition	→	Reduces PTEN tumor suppression Increase PI3Kα activity [3,4]
AKT inhibition	→	Activates RTK's[5] and mTOR [6]
mTOR inhibition	→	Reactivates PAM nodes [7,8]

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(1) Juric 2015 Nature. 518:240-244; (2) Castel 2016 Nat Cancer. 2:587-597; (3) Mao 2021 Nat Commun. 12:5053; (4) Schwatrz 2015 Cancer Cell. 27:109-122. (5) Chandarlapaty 2011, Cancer Cell. 19:58-71; (6) Bago 2016, EMBO J. 35:1902-1922; (7) Manning 2017, Cell. 169:381-405.; (8) Mukherjee 2021, Mol Cell. 81:708-723 e705.

Gedatolisib Differentiation

Nonclinical Data Review

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Gedatolisib Has a Highly Differentiated Mechanism of Action

Inhibits six different PAM nodes to induce comprehensive pathway blockade

Gedatolisib is Potent Against all Class I PI3K Isoforms and mTORC1/2

- More potent against these targets than single node inhibitors
- Pan-PI3K/mTOR inhibition limits cross-activation that occurs with node-specific drugs
- MOA creates potential to induce anti-tumor activity independent of PIK3CA status

Gedatolisib vs PAM Node Inhibitors IC50 (nM)[1]

Node	Gedatolisib[2]	Alpelisib[3]	Everolimus[4]	Capivasertib[5]
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	-	-	-	3.0

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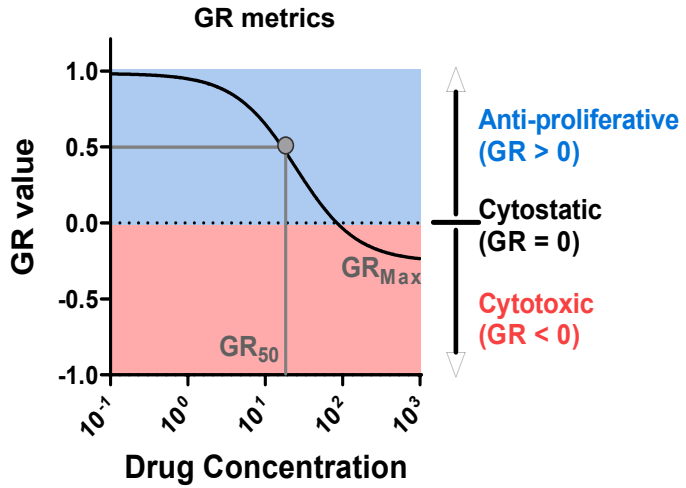
(1) IC50 derived from cell-free biochemical dose response analysis; (2) Venkatesan 2010 J Med Chem 53(6):2636-45. (3) Fritsch 2014, Mol Cancer Ther. 13(5):1117-29. (4) Schuler 1997; Transplantation, 64(1):36-42. (5) Davies 2012, Mol Cancer Ther 11(4):873-87.

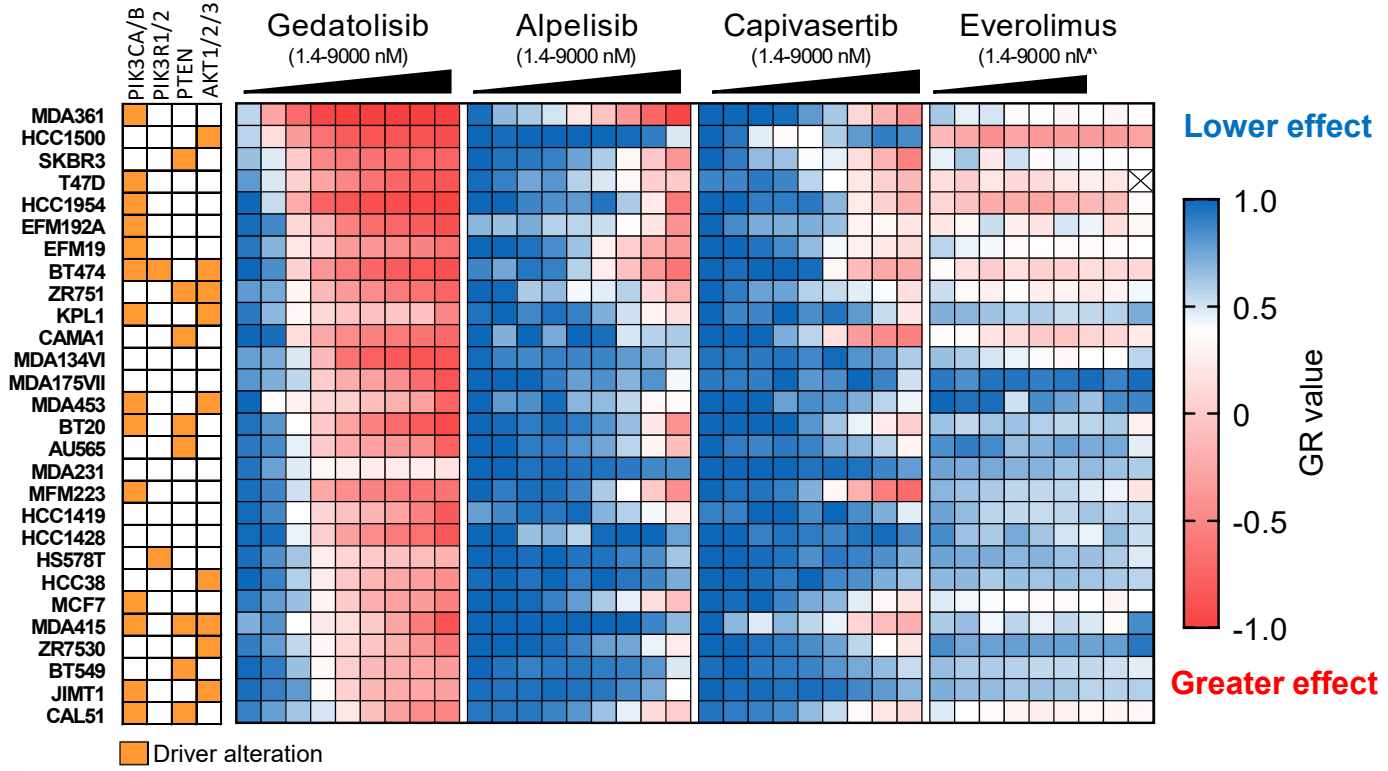
Breast Cancer Cell Lines: Evaluated Gedatolisib and Node-Specific Inhibitors

Gedatolisib exerts superior cytotoxic effects at all concentrations relative to other PAM inhibitors

- **Assessed cytotoxic and cytostatic effects using growth rate metric**
- **Avoids the confounding effects of individual cell line proliferation rates**



28 Cell Lines Evaluated



Source: Internal data on file; Footnote: Growth rate (GR) was assessed by measuring live cells reducing potential with Real Time-Glo MT luciferase assay before and after 72h drug treatment. GR metrics allow to assess drugs cytotoxic and cytostatic effects without the confounding effects of individual cell line proliferation rates. GR_{50} (conc required to inhibit growth rate by 50%) is a measure of potency. GR_{Max} (GR at highest drug conc. tested) is a measure of efficacy. Hafner et al, Nat. Methods, 2016 (Sorger lab, Harvard); NIH LINCS program.

Breast Cancer Cell Lines: Gedatolisib is >300x more potent, 2X more cytotoxic

Average Values for 28 Breast Cancer Cell Lines

Potency: Low — High

Efficacy: Cytostatic *0-100%* — Cytotoxic *101%-200%*

GR_{50} (nM)

	Geda	Alpe	Capi	Evero
All cell lines (n=28)	12	6308	8666	3611
PIK3CA MT (n=14)	12	2594	2590	1867
PIK3CA WT (n=14)	12	10308	15209	5501

Max Cell Growth Inhibition[1]

	Geda	Alpe	Capi	Evero
All cell lines (n=28)	168%	89%	80%	62%
PIK3CA MT (n=14)	174%	116%	99%	68%
PIK3CA WT (n=14)	162%	62%	60%	56%

% Cell Lines Sensitive[2]

	Geda	Alpe	Capi	Evero
	<100nM	*<3000nM*	*<3000nM*	*<3000nM*
All cell lines (n=28)	100%	57%	54%	50%
PIK3CA MT (n=14)	100%	86%	79%	71%
PIK3CA WT (n=14)	100%	29%	29%	29%

% High Efficacy in Cell Lines[3]

	Geda	Alpe	Capi	Evero
All cell lines (n=28)	96%	43%	29%	7%
PIK3CA MT (n=14)	100%	64%	43%	7%
PIK3CA WT (n=14)	93%	21%	14%	7%

Gedatolisib vs. Other PAM Inhibitors

- **~ 2x higher in vitro efficacy** than other PAM inhibitors
  - Alpelisib, capivasertib, everolimus mostly not cytotoxic
- **More potent** than other PAM inhibitors
  - **> 300X** more potent than alpelisib, capivasertib, & everolimus on average
- Same potency and efficacy regardless of PIK3CA/PTEN status unlike other PAM inhibitors

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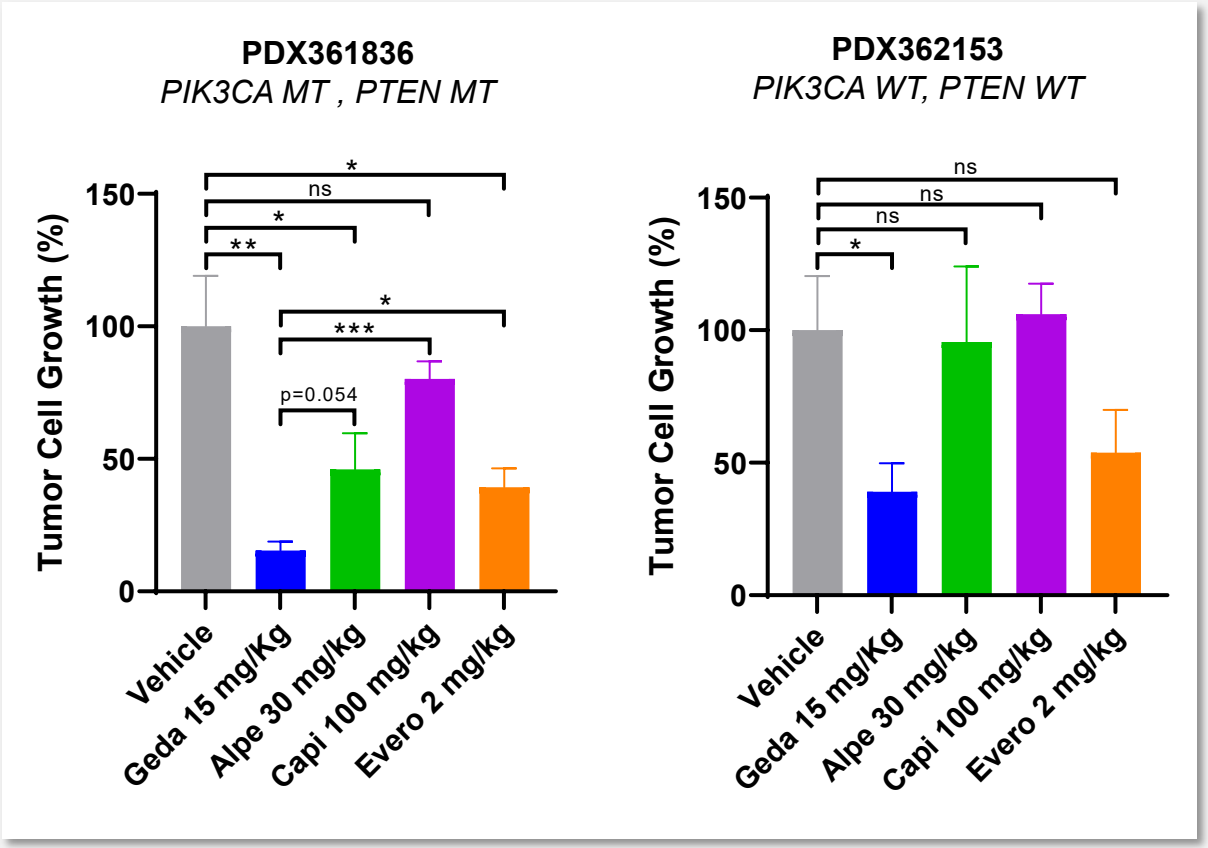
Source: Internal data on file; Footnotes: (1) Based on GR_{Max}; (2) Sensitive: GR50 < 100 nM for gedatolisib; GR_{50} < 3 uM for alpelisib, capivasertib, and everolimus; (3) High Efficacy: >100% cell growth inhibition

Breast Cancer Mini-PDX Models: Compared PAM Inhibitors

Gedatolisib induced higher tumor growth inhibition than node specific inhibitors in PIK3CA WT and MT models

- **Gedatolisib induced significant tumor growth inhibition (TGI) in both wild type and mutant PI3K/PTEN PDX models**
  - Only agent effective in both wild-type and mutant models
- **Results**
  - 85% TGI in PIK3CA/PTEN mutant model
  - 61% TGI in PIK3CA/PTEN wild-type model



Souce: Internal data on file: Footnotes: Mini-PDX tumor capsules (n=6) injected in the flank of BALB/c nude mice. 7 day treatment with gedatolisib (iv Q4D), alpelisib (p.o. QD), capivasertib (p.o. BID 4 days on/3 days off) or everolimus (p.o. QD). Data represent tumor cell growth mean +/- SEM at the end of treatment. * $p<0.05$; ** $p<0.01$; *** $p<0.001$; ns = not significant

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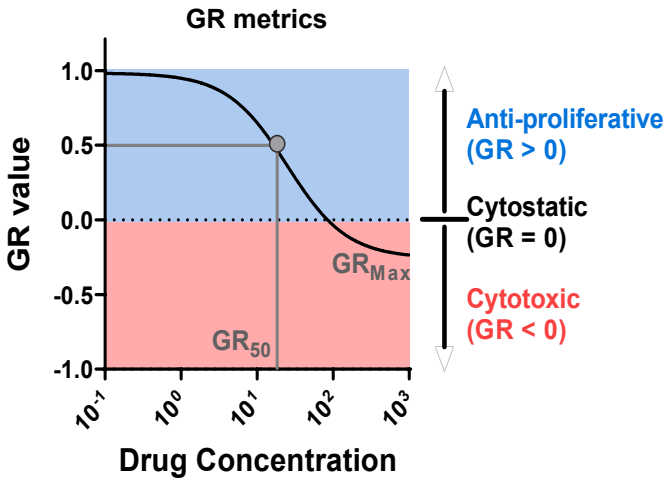
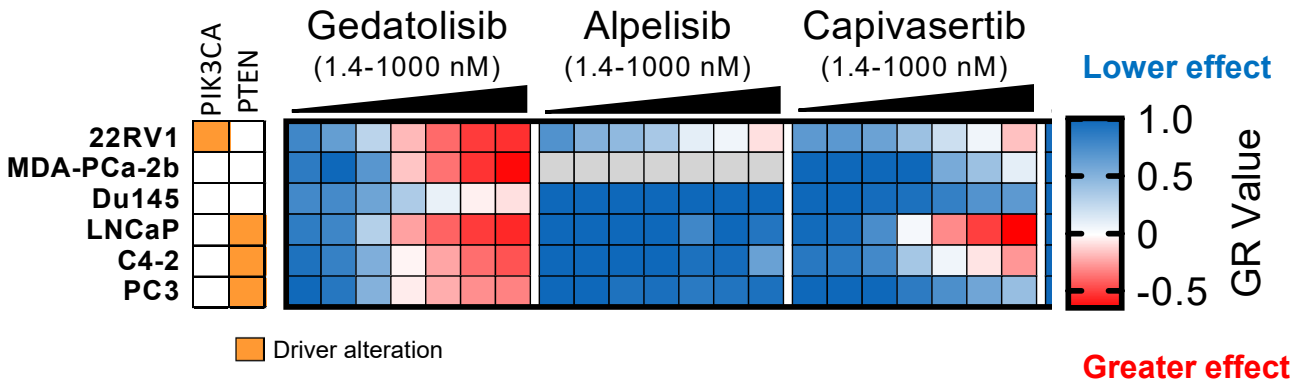
Prostate Cancer Cell Lines: Compared PAM Inhibitors

Gedatolisib exerts superior cytotoxic effects at all concentrations relative to other PAM inhibitors

- Assessed cytotoxic and cytostatic effects using growth rate metric
- Avoids the confounding effects of individual cell line proliferation rates





Source: Sen, ASCO-GU, 2023; Footnote: (1) Based on GR_{Max}

Prostate Cancer Cell Lines: Gedatolisib is ~20-65x more potent, more cytotoxic

Average Values for Six Prostate Cancer Cell Lines
(22RV1, MDA-PCa-2b, DU145, LNCaP, C4-2, PC3)

Potency

Low — High

Efficacy

Cytostatic *0-100%* — Cytotoxic *101%-200%*

	GR50 (nM)			Max Cell Growth Inhibition[1]		
	Gedatolisib *PI3K/mTOR*	**Alpelisib** *PI3K-α*	**Capivasertib** *AKT*	**Gedatolisib** *PI3K/mTOR*	**Alpelisib** *PI3K-α*	**Capivasertib** *AKT*
Average all	**12**	**802**	**290**	**143%**	**30%**	**98%**
PTEN WT	**13**	**504**	**383**	**141%**	**38%**	**79%**
PTEN altered	**11**	**1000**	**197**	**144%**	**24%**	**116%**

Gedatolisib vs. Other PAM Inhibitors

- **More cytotoxic** than other PAM inhibitors on average
  - Alpelisib and capivasertib are <u>not</u> cytotoxic
- **More potent** than other PAM inhibitors on average
  - **65x** more potent than alpelisib
  - **24x** more potent than capivasertib
- Gedatolisib has same potency and efficacy regardless of PTEN status unlike other PAM inhibitors.

Source: Sen, ASCO-GU, 2023; Footnote: (1) Based on GR_{Max}

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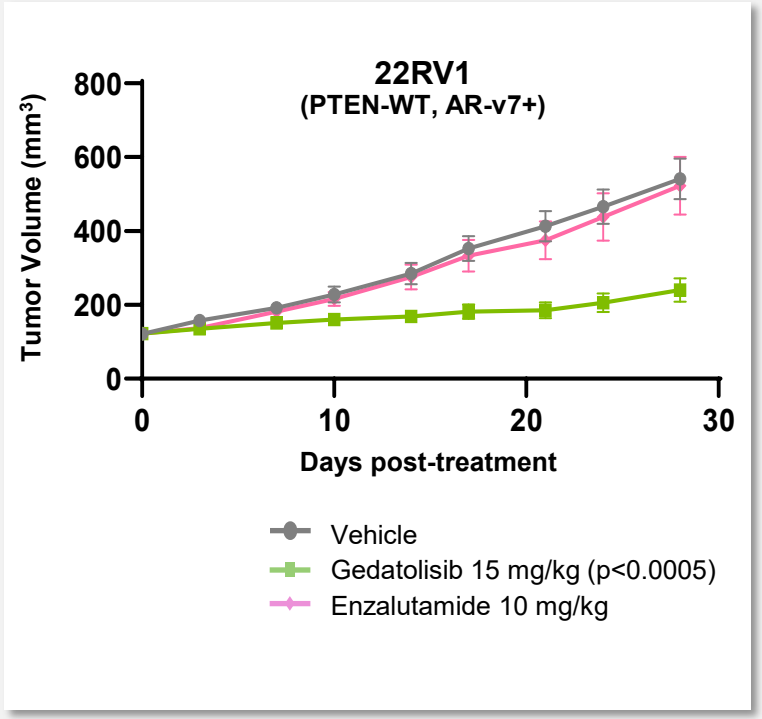
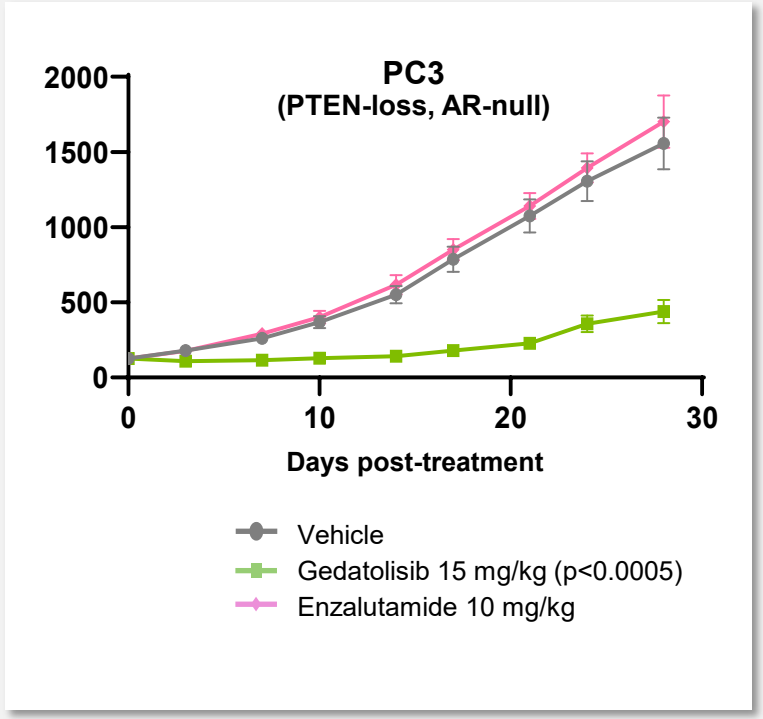
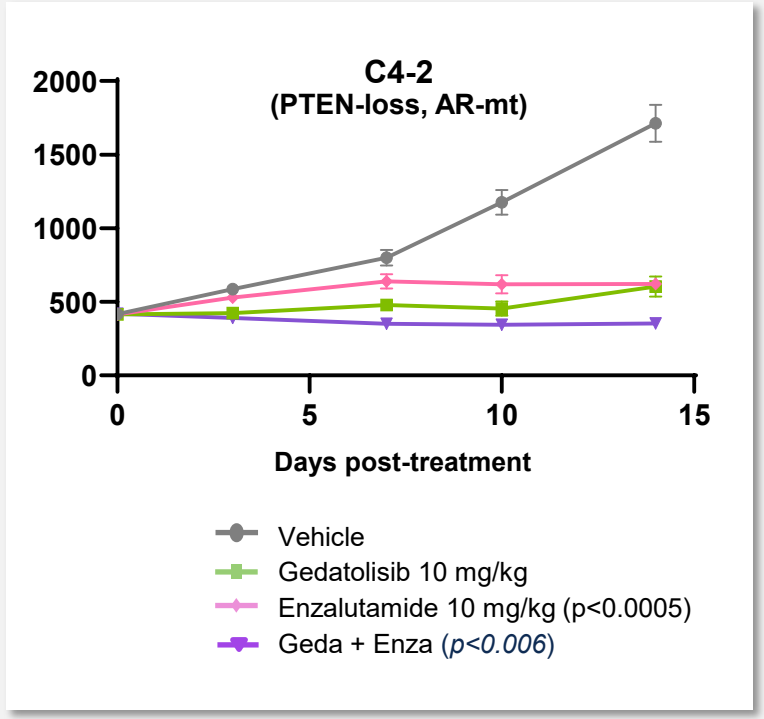
In Vivo Activity of Gedatolisib in Prostate Cancer Xenograft Models

Gedatolisib induced >80% tumor growth inhibition (TGI) regardless of PTEN or AR status







- **Robust single-agent TGI in PC xenograft models regardless of sensitivity to enzalutamide (ARi) and PTEN status**
- **Gedatolisib + enzalutamide induced significantly greater TGI than enzalutamide alone in enzalutamide sensitive model**

Source: Sen, ASCO-GU, 2023

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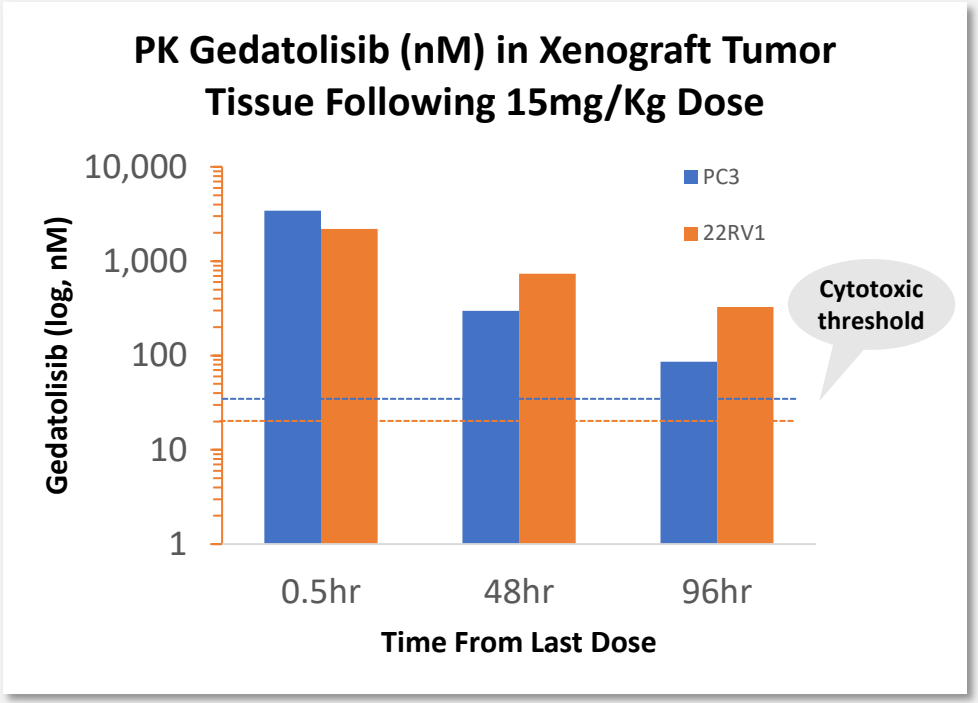
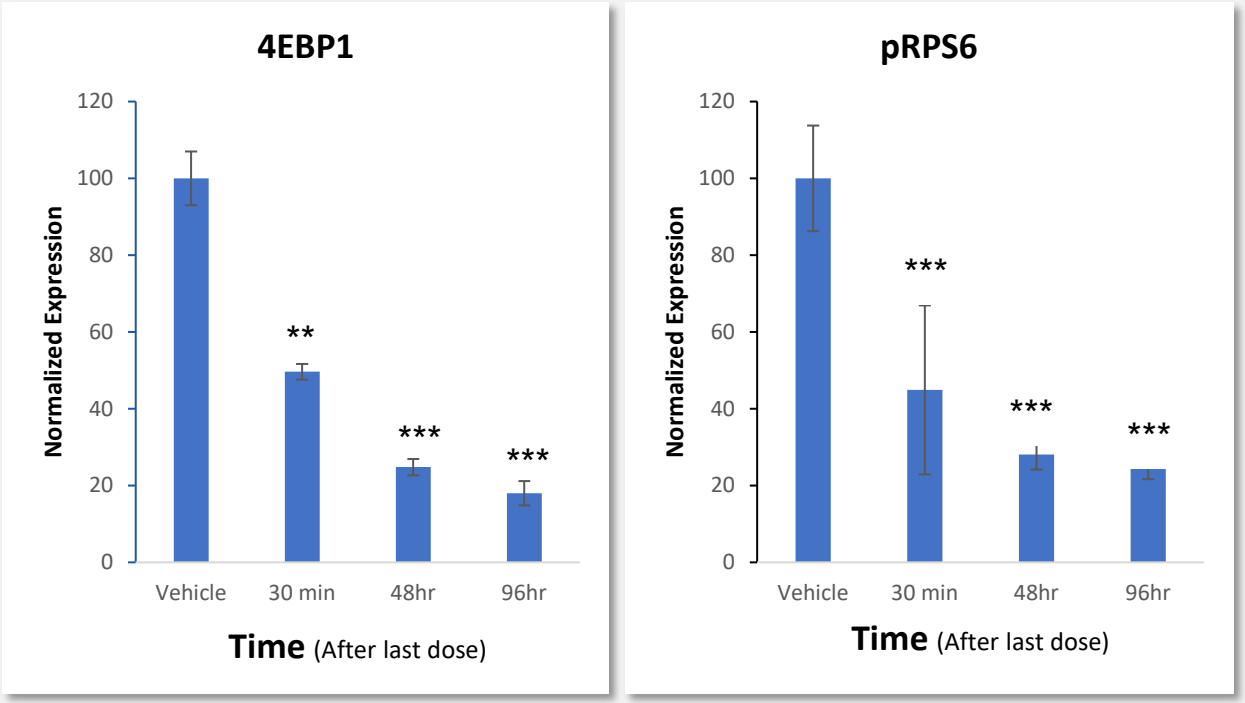
PK/PD Xenograft Tumor Tissue Analysis During Dosing Interval

Gedatolisib concentration remains above cytotoxic and pathway inhibition threshold during dosing interval



Dosing every 4 days in mice comparable to once per week in patients; Cytotoxic threshold equivalent to in vitro IC_{80} for each cell line

Effect of gedatolisib on PAM pharmacodynamic markers in PC3 xenograft tissue



Total protein production and active translation suppressed between doses

Pharmacokinetics

- Plasma $T_{1/2}$ = 4.9 hours mice
- Plasma $T_{1/2}$ = 37 hours human

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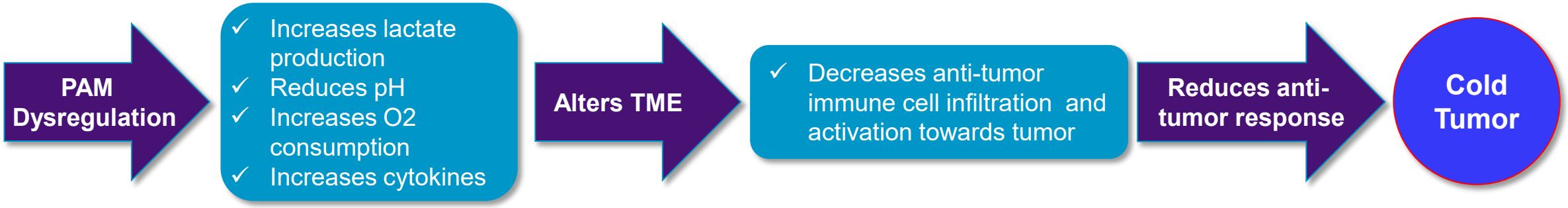
Source: Internal data on file. Abbreviations: PK, pharmacokinetic; PD, pharmacodynamic

PAM Reduces Immune System Function in Tumors

Causes tumor cells to generate biochemical factors that negatively affect tumor microenvironment (TME)

PAM pathway impact on TME is likely a major factor that causes breast and prostate tumors to be immunologically "cold"



Inhibition of PAM improves the TME which can increase anti-tumor immune response

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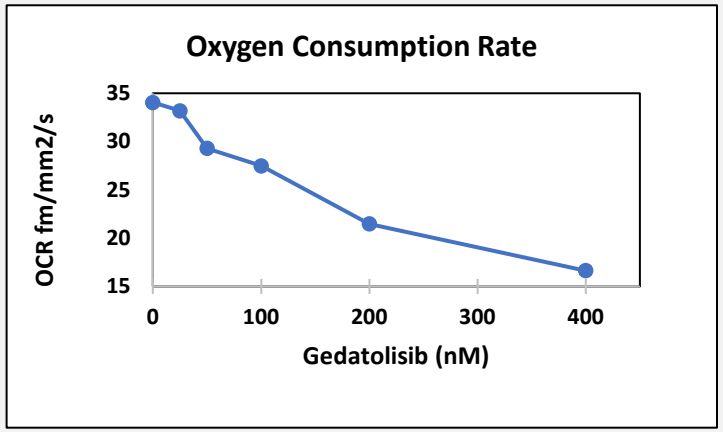
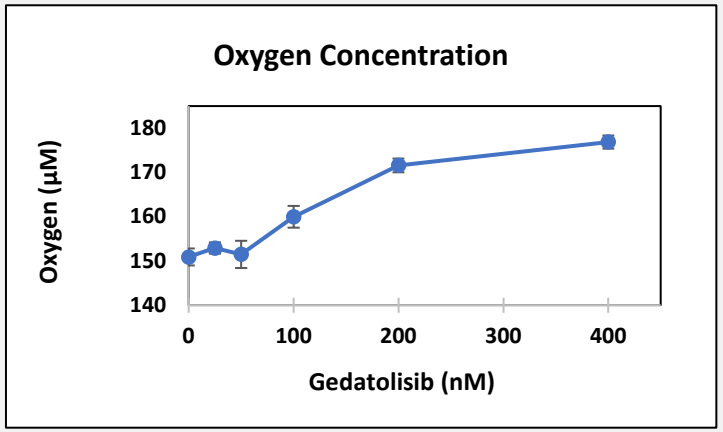
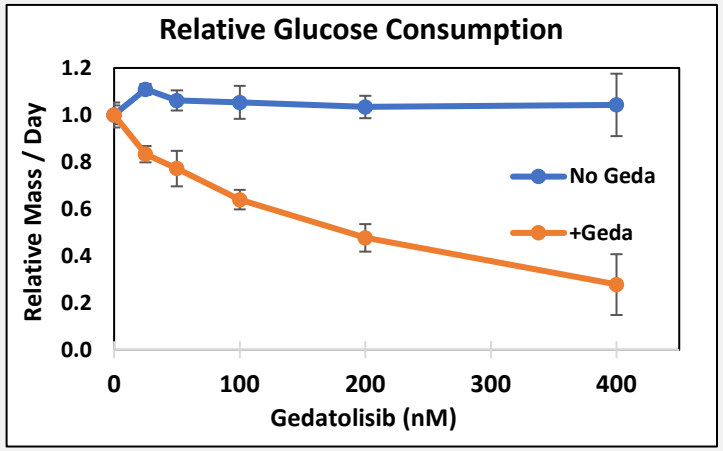
DePeaux 2021, Nat Rev Immunol 21(12):785:797; Jayaprakash 2018, J Clin Invest.128(11):5137-5149; Semenza 2021 Physiology 36: 73-83; Thomas 2023, Front. Oncol. 13:1063051

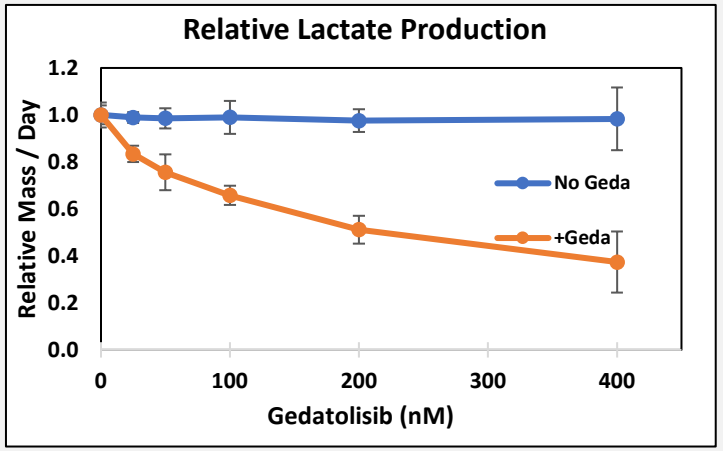
Gedatolisib Favorably Impacts Tumor Microenvironment

PAM inhibition decreases O2 and glucose consumption and lactate production









A TME with low O2, low glucose, and high lactate is correlated with immuno-suppression, low anti-tumor activity[1, 2,3,4]

Gedatolisib's dose-dependent reduction of O_2 consumption leads to an increase in O_2 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

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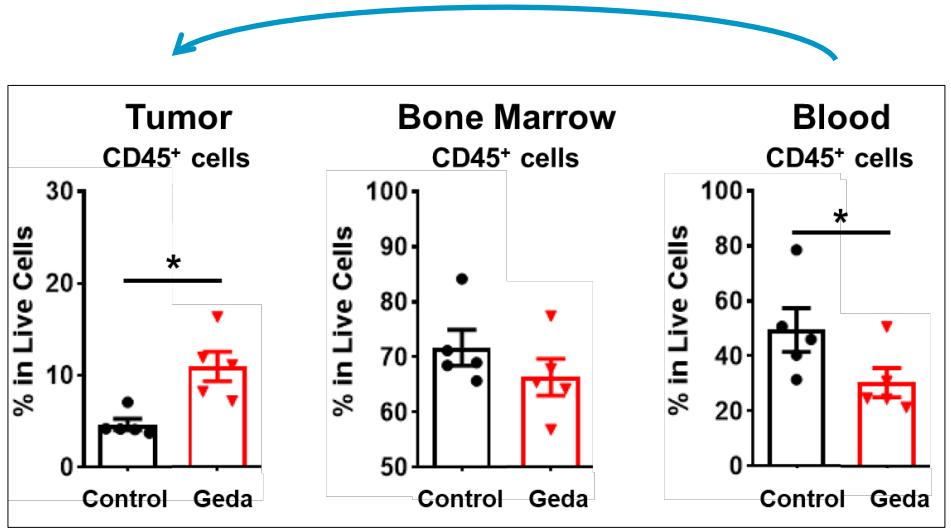
(1) DePeaux 2021, Nat Rev Immunol 21(12):785:797. (2) Jayaprakash 2018, J Clin Invest.128(11):5137-5149. (3) Semenza 2021 PHYSIOLOGY 36: 73-83. (4) Thomas 2023, Front. Oncol. 13:1063051

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



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

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+

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

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Source: Yan, C.et al. Int. J. Mol. Sci. 2021, 22, 5207.
Abbreviations; DC = dendritic cell; NA = not available

Key Takeaways: Non-clinical

Gedatolisib is highly potent and cytotoxic; controls factors that induce immunosuppression in TME

PAM is Complex Pathway	• PAM pathway is an important driver of metabolic activities that support tumor cell proliferation • Multi-node inhibition is required to address pathway complexity and effectively block PAM activity
Comprehensive MOA	• Gedatolisib equipotently antagonizes major PAM signaling nodes • Reduces tumor glucose and oxygen consumption and lactate production
Superior Potency and Cytotoxicity	• Superior potency and cytotoxicity in vitro and in vivo vs single node PAM inhibitors • Gedatolisib remains above IC_{80} threshold throughout dosing interval in PK/PD xenograft studies
Reduces Immuno-suppression	• Gedatolisib's control of tumor glucose and oxygen reduce TME potential to support tumor cell proliferation • Data suggests gedatolisib may improve infiltration and activation of anti-tumor immune cells in TME

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PK and Safety Overview of Gedatolisib

Igor Gorbatchevsky, MD
Chief Medical Officer

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Gedatolisib's PK and Metabolic Profile

Stable chemical structure leads to optimized PK profile

PK characteristics in humans

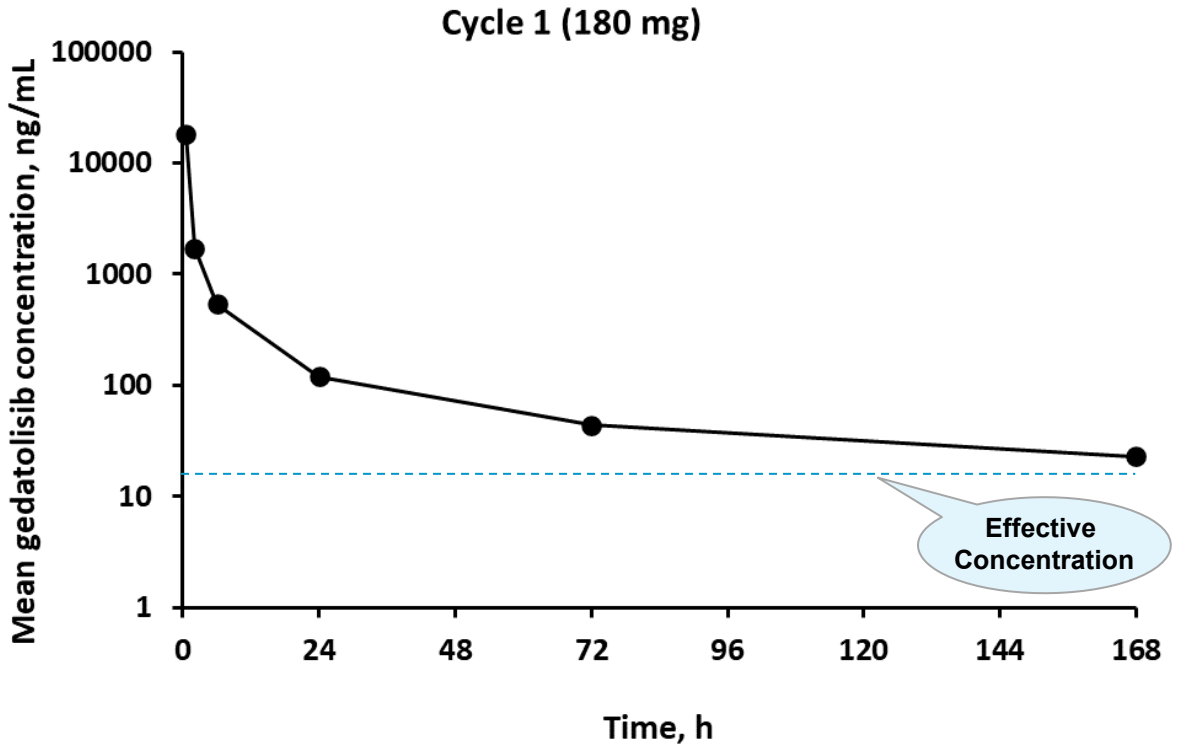
- T ½ ≈ 37 hours
- Dose-proportional and predictable PK exposure
- No accumulation after multiple doses
- Minimal inter-patient variability in PK parameters

Metabolism

- Minimal metabolic turnover in in-vitro and in-vivo studies
- No metabolites have been identified (<1%)
- Main route of elimination for unchanged gedatolisib in human: feces and urine

PK Drug Interactions

- No impact on metabolic clearance of drugs that are substrates of CYP enzymes
- Potentially low or no risk for clinically significant CYP-pathway mediated DDI



Gedatolisib remains above its effective concentration threshold throughout dosing interval

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Gedatolisib Key PK Properties and Safety Metrics vs. Approved PI3Ki

Differentiated favorable PK profile leads to lower toxicity

	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

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(1) Shapiro 2015, internal data on file; 154 mg weekly dose (MTD); all AE refers to related AEs; (2) Juric 2018, hyperglycemia from 300 mg daily dose arms (MTD); SAE and related treatment related discontinuation data from all arms; (3) US Package Insert; Note: No head-to-head trials have been conducted; data collected from different trials, in different patient populations and may not be comparable. Abbreviations: G, Grade; SAE, serious adverse event; mmol = miliimolar; L = liter

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 study will include 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	-

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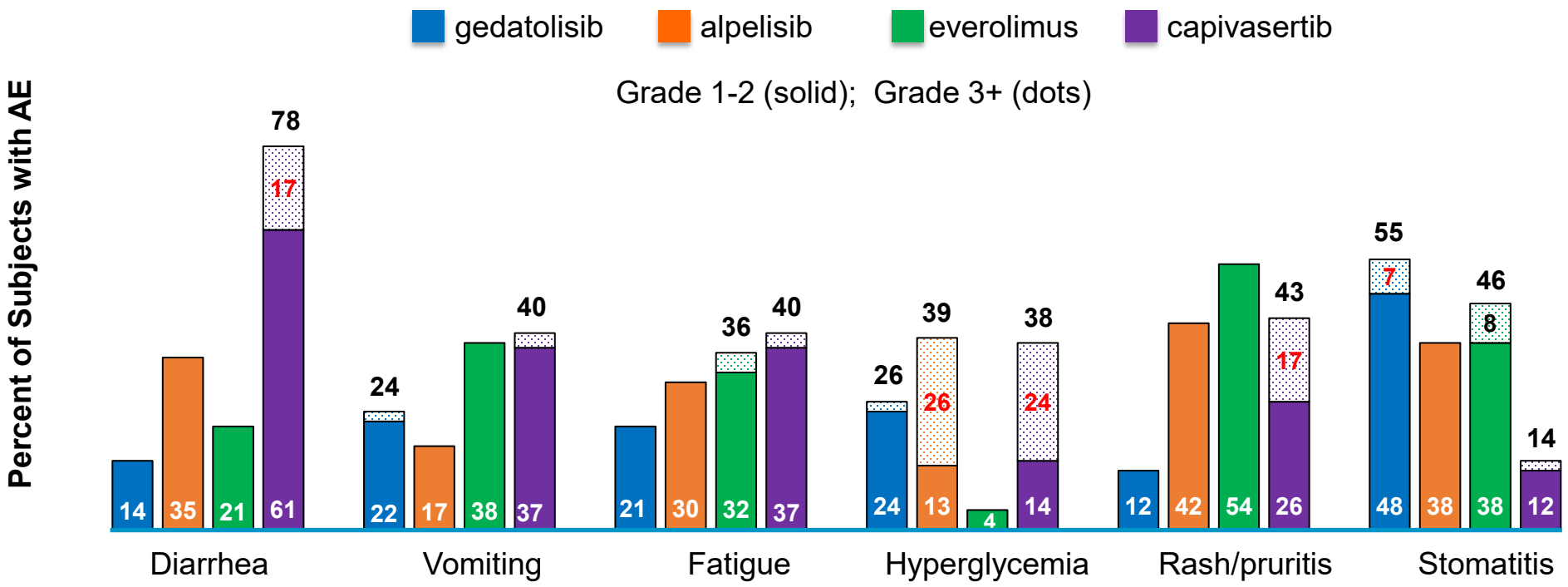
Source: (1) Shapiro 2015; (2) Rugo 2017; TEAE = treatment emergent adverse events; AE = adverse event.

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



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

Prostate Cancer

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Current Standards of Care in mCRPC and Unmet Clinical Needs

Karim Fizazi, MD, PhD

Professor of Medicine, University of Paris-Saclay

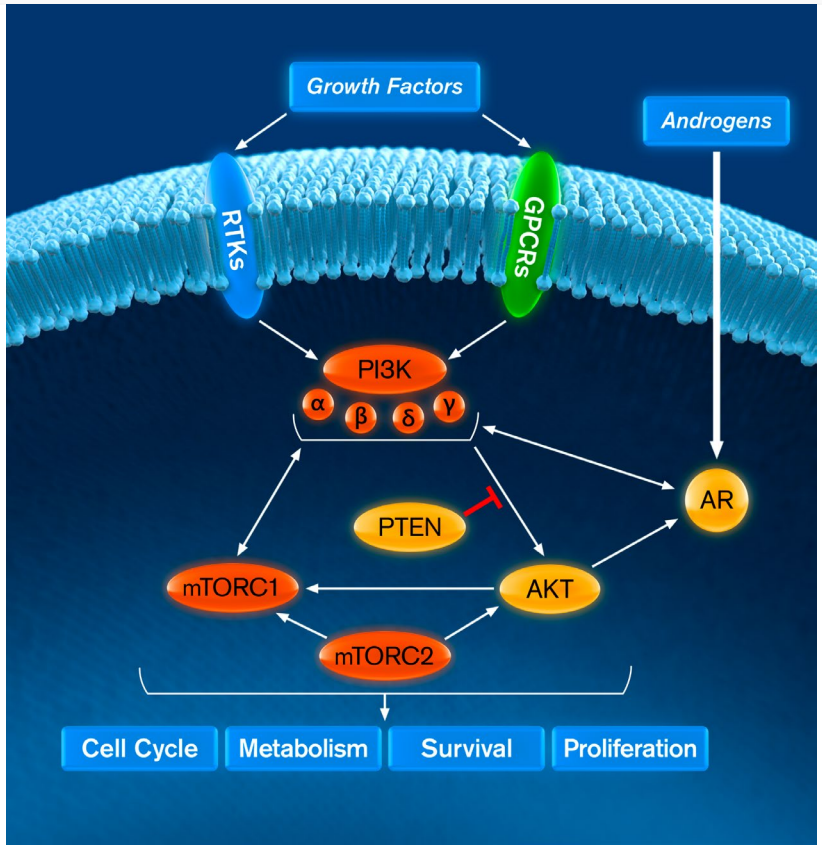
GETUS President
Head, GU Group, Institute Gustav Roussy
University of Paris Saclay

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

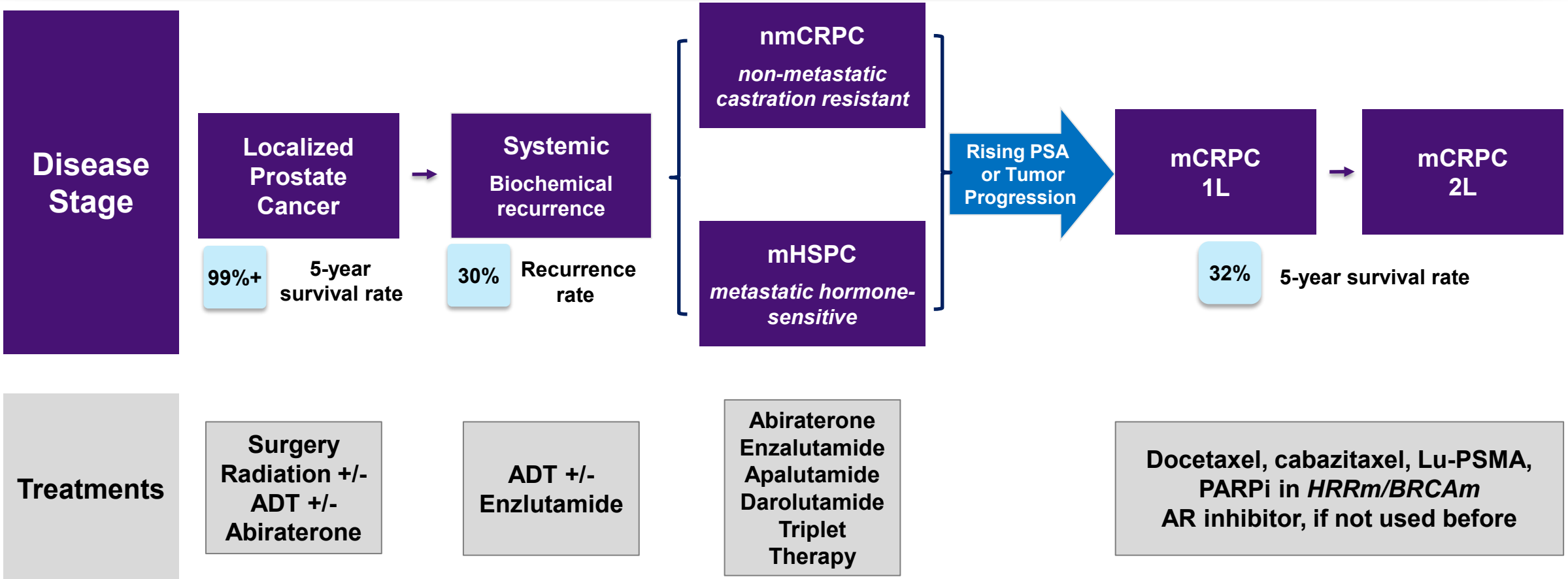
- AR and PI3K-AKT-mTOR pathways cross-regulate each other.
- 70% - 100% of mCRPC tumors have PI3K/AKT/mTOR related pathway alterations.
- Mutations dispersed across PTEN, PI3K, AKT, and mTOR sub-units

Karim Fizazi, MD, PhD
Gustave Roussy

Source: Alves, Int J Mol. Sci. 2023

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]



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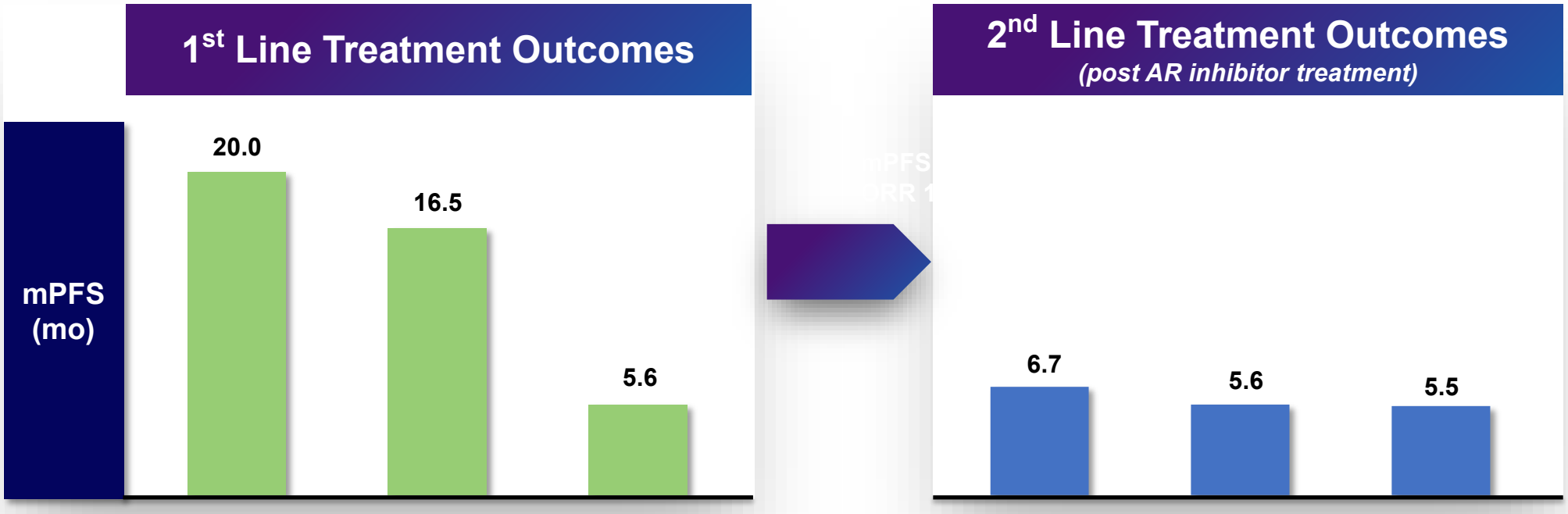
(1) Saad, Prostate Cancer Prostatic Dis. 2021; (2) Scher, Plos One 2015; Leith, A. et al. 2022; George, D. J. et al. 2022; NCCN Guidelines for Prostate Cancer Version 1.2023; (3) American Cancer Society, Cancer Facts & Figures 2023; (4) Wang, Front. Public Health, 2022; Abbreviations: mCRPC = metastatic castration resistant prostate cancer; HRR = homologous recombination repair 1L = first line of therapy; 2L = second line of therapy; ADT = androgen deprivation therapy; AR = androgen receptor

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

Significant need for better therapeutic options



Drugs	Xtandi [1]	Zytiga [2]	Docetaxel [3]	Docetaxel [4]	Zytiga [5]	Xtandi [6]
MOA	ARi	ARi	Chemotherapy	Chemotherapy	ARi	ARi
Pat Pop	All	All	All	Prior ARi	Prior Xtandi	Prior Zytiga
mPFS	20.0	16.5	5.6	6.7	5.6	5.5
OS	35.3	34.7	19.5	20.0	-	-

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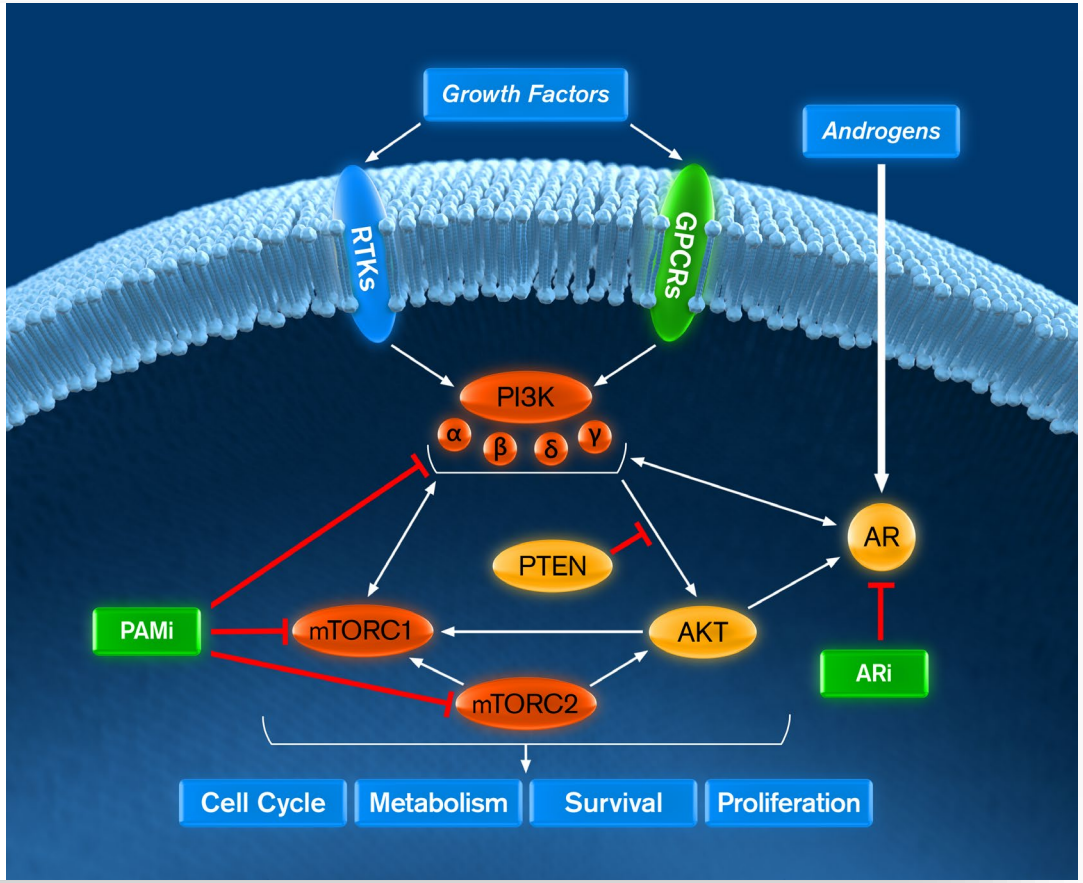
(1) Beer Eur Urol. 2017; (2) Ryan NEJM 2013; Ryan Lancet Oncol 2015 (3) Kellokumpa-Lehtinen Lancet Oncol. 2013, time-to-treatment failure reported; (4) Crabb J Clin Oncol 2021; (5) Attard J Clin Oncol 2018; (6) Sweeny Clin Cancer Res 2022. Abbreviations: HRR = homologous recombination repair; AR = androgen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

PI3K/mTOR + AR Inhibition
Treatment Rationale

- AR inhibition increases PAM pathway signaling [2]
- For patients who progressed on an AR inhibitor, PI3K inhibition may resensitize them to an AR inhibitor
- PI3K inhibition increases AR protein levels and activation [3]
- mTOR inhibition is particularly critical in patients when the tumor suppressor, PTEN, is functional
- Strong rationale to combine an AR inhibitor with a PAM inhibitor in patients who progressed on an AR inhibitor



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(1) Carver et al, Cancer Cell 2011; (2) Mulholland et al, Cancer Cell 2011; (3) Crumbaker et al, Cancers 2017

PAM Inhibitor Development Efforts for mCRPC Have Focused on AKT

Reflects high incidence of PTEN alterations in mCRPC that AKT inhibition can address

- **The AKT inhibitor, ipatasertib, has been extensively evaluated in prostate cancer**
  - AKT inhibition can lead to reactivation of the PAM pathway through various resistance mechanisms [1,2,3,4]

- **When PTEN is altered**, AKT inhibition can overcome some resistance mechanisms
  - Feedback mechanisms through mTORC1/2 are still functional and likely limit potential effect of AKT inhibition[1,4]

- **When PTEN is not altered, AKT inhibition has limited effect likely due to resistance feedback loops[1,4]**
  - Resistance mechanisms include relief of negative feedback loops between PI3K and mTORC1/2 [4]

- **Signaling feedback loops between PI3K and mTORC1/2 may limit efficacy for AKTi to PTEN loss patients**

(1) Mao 2021. Nat Commun. 2021; (2) Chandarlapaty 2011, Cancer Cell; (3) Bago 2016, EMBO J; (4) Manning 2017, Cell

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Clinical Trial Results for PAM Inhibitors After Progression on AR Therapy

Evidence of PAM pathways involvement and sensitivity to PAM inhibitors in mCRPC

Study Regimens	Line of Therapy	Patient Population	N	Overall Results (Months rPFS)	Comments

Samotolisib (PI3K/mTOR) + Enzalutamide vs. Enzalutamide [1]	2nd Line prior abiraterone	All	129	**10.5 vs. 5.5 months** *(HR = 0.64; P = 0.03)*	▪ Samotolisib efficacious despite only modest PI3K-α and mTOR potency
					▪ Results in PTEN wild-type patients reflect benefit of mTOR inhibition
					▪ Gedatolisib vs. samotolisib [3]
					  ▪ 7X more potent overall; 100x for mTOR
					  ▪ More cytotoxic
					▪ Drug is not under active development

		AR-v7-negative	103	**13.2 vs. 5.3 months** *(HR = 0.52; P = 0.03)*	
		PTEN wild-type	60	**13.2 vs. 3.6 months** *(HR = 0.49; P = 0.07)*	
Ipatasertib (AKT) + Abiraterone vs. Abiraterone [2]	1st Line	All	1101	**19.2 vs. 16.6 months** *(HR = 0.84; P = 0.04)*	▪ Efficacy limited to PTEN loss patients ▪ Limited response in PTEN functional patients demonstrates role mTOR plays as resistance mechanism to AKT inhibition
		PTEN loss by NGS	209	**19.1 vs. 14.2 months** *(HR = 0.65; P = 0.02)*	

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(1) Sweeney Clin Cancer Res 2022; (2) De Bono, Lancet, 2021; (3) Sen, ASCO-GU, 2023

Key Takeaways

Strong scientific rationale to combine a pan-PI3K/mTOR inhibitor with a next generation AR inhibitor

1

- **Efficacy of current 2L therapies for mCRPC post-ARi is limited; new therapeutic approaches are needed**
- Docetaxel mPFS: 6-7 months
- AR inhibitors mPFS: 5-6 months

2

- **Extensive nonclinical data has characterized the role the PI3K/mTOR pathway plays as a driver of mCRPC**
- The challenge has been finding the right PI3K/mTOR drug to address this disease mechanism

3

- **The limited efficacy gains reported to date for AKT inhibitors in mCPRC suggest more comprehensive blockade of the PAM pathway may be required**

4

- **Evaluating a PAM inhibitor in combination with a next generation AR is an important priority for mCRPC research**

Karim Fizazi, MD, PhD
Gustave Roussy

Clinical Overview of Gedatolisib for mCRPC

Igor Gorbatchevsky, MD
Chief Medical Officer

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Strong Scientific Rationale to Evaluate Gedatolisib in mCPRC

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

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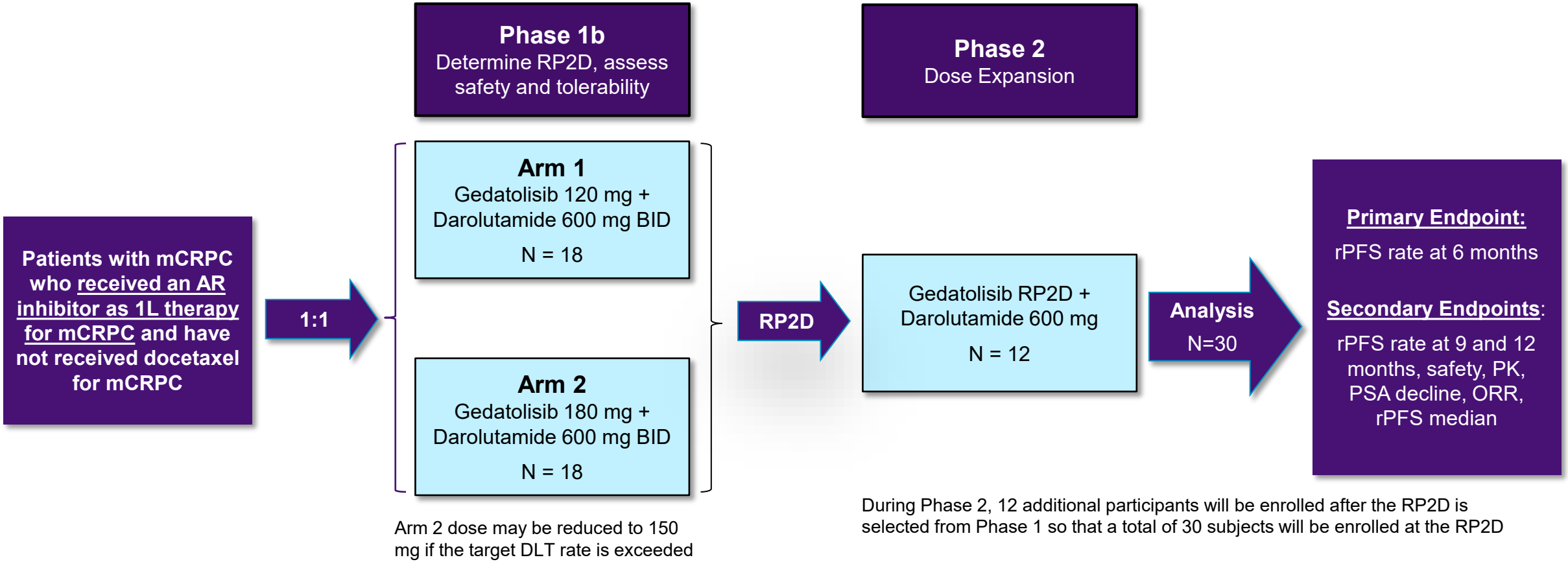
CELC-G-201: Phase 1b/2 Trial Design Overview

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



Arm 2 dose may be reduced to 150 mg if the target DLT rate is exceeded

During Phase 2, 12 additional participants will be enrolled after the RP2D is selected from Phase 1 so that a total of 30 subjects will be enrolled at the RP2D

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

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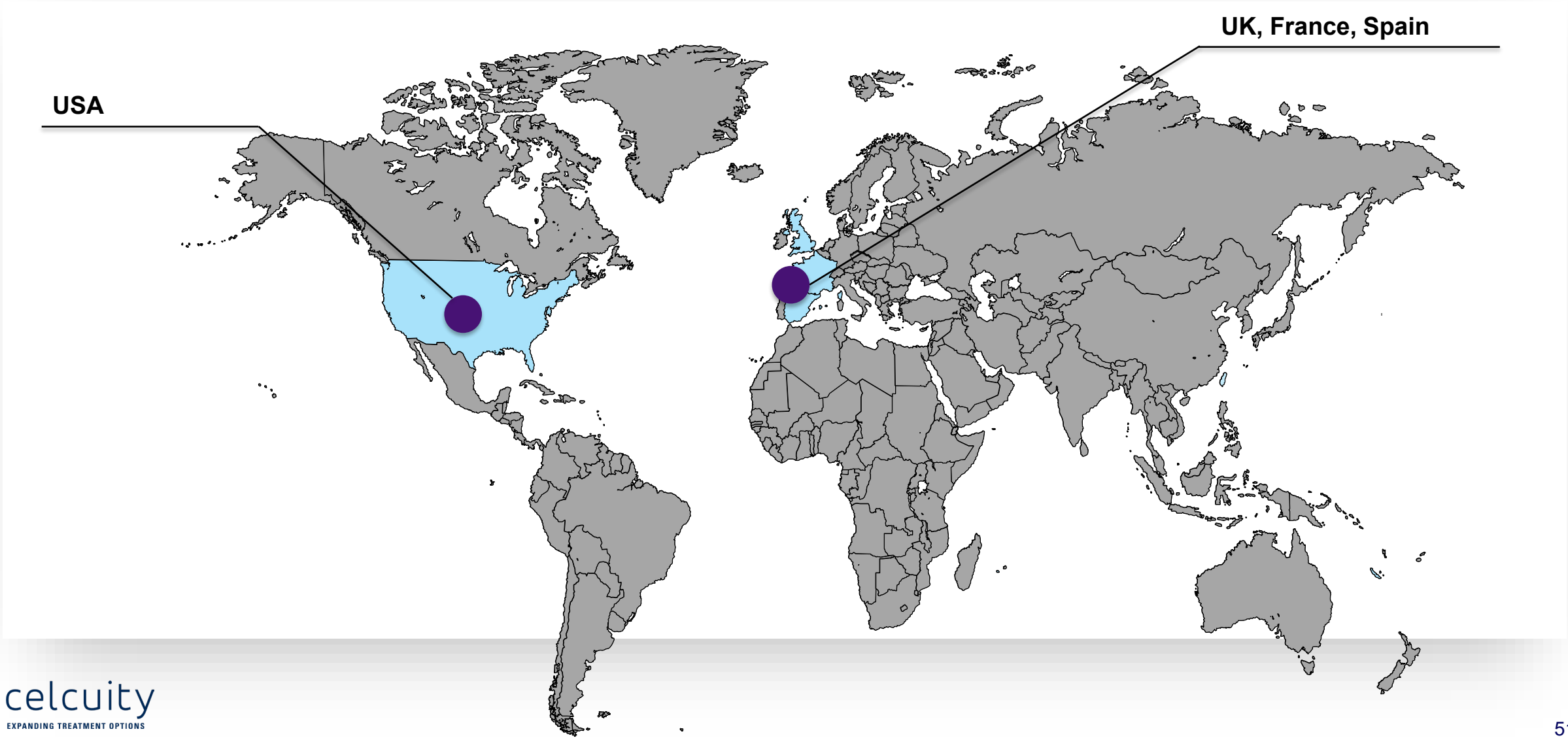
~12 Sites Across US and Europe

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



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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_{50} [1]	**11 nM [2]**		**72 nM [3]**		**86 nM [2]**	
Most Common AE's (%) [4]	**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

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(1) IC50 derived from cell-free biochemical dose response analysis; (2) Moilanen, et al. Sci Rep 2015; (3) Pinto-Bazurco Mendieta et al. J Med Chem 2008. (4) US Package Inserts. Abbreviations: mCRPC = metastatic castration resistant prostate cancer; nm = non-metastatic; HSPC = hormone sensitive prostate cancer

Breast Cancer

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Current Standards of Care in HR+/HER2- Advanced Breast Cancer and Unmet Clinical Needs

Sara A. Hurvitz, MD, FACP

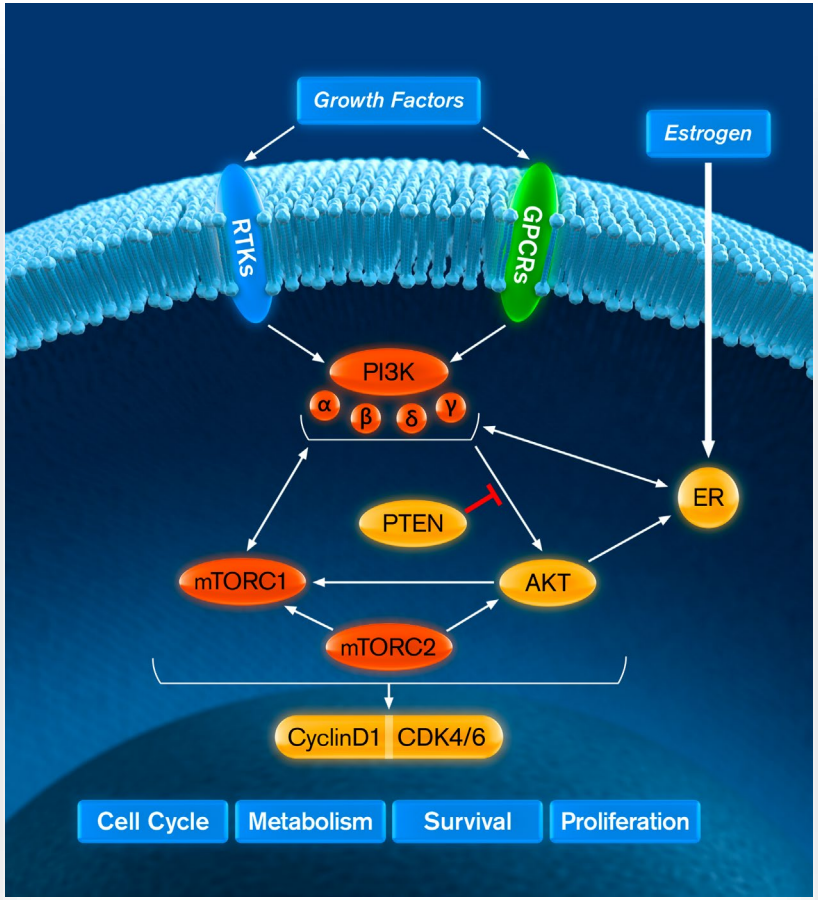
Professor of Medicine
Head, Division of Hematology and Oncology
Senior Vice President, Clinical Research Division
Department of Medicine, UW Medicine
Fred Hutchinson Cancer Center

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 PI3Kα
- 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

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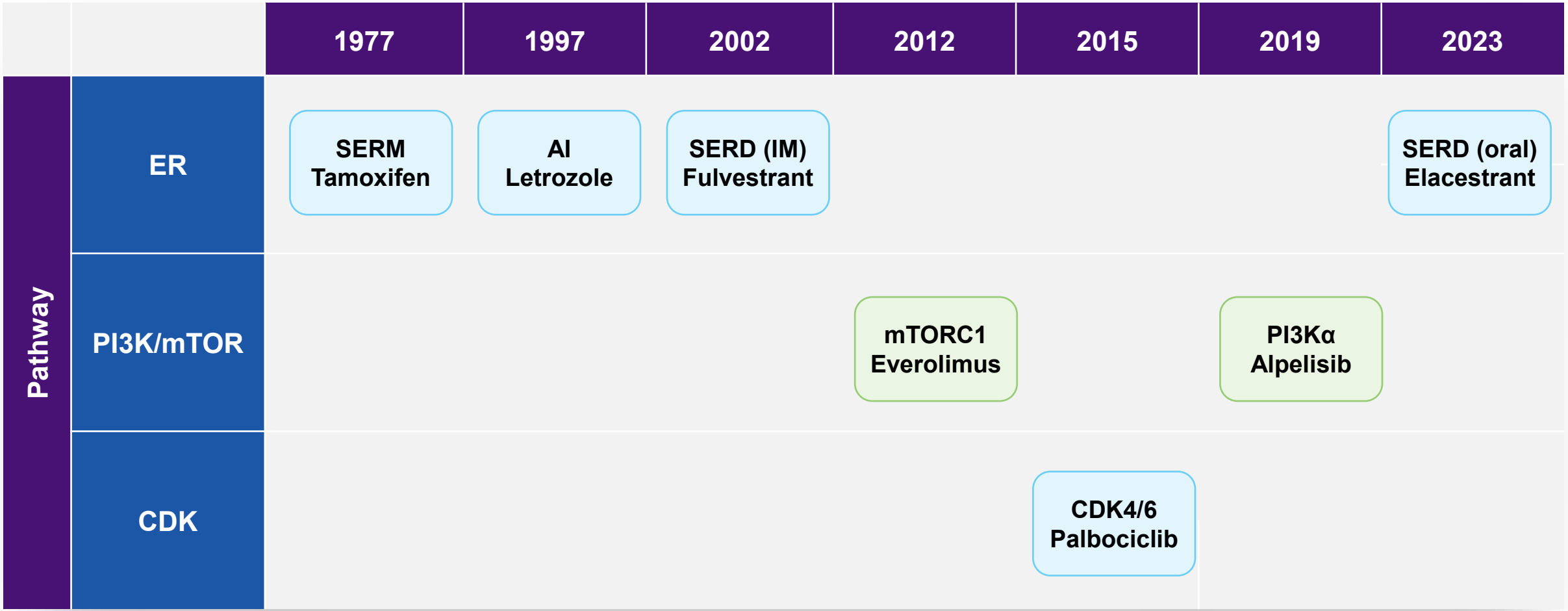
Abbreviations: ER = estrogen receptor; ABC = advanced breast cancer

Drug Development Activities Reflect Important Role of ER, CDK4/6 and PAM

Key targeted therapy approval milestones for HR+/HER2- ABC



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Abbreviations: ER = Estrogen receptor; SERM = selective estrogen receptor modulator; SERD = selective estrogen receptor degrader

HR+/HER2- Breast Cancer Treatment Landscape

Local and Regional
Stage I-III

~200,000 Cases diagnosed annually in USA

Low Recurrent Risk Adjuvant Tx	Higher Recurrent Risk (neo)Adjuvant Tx
Endocrine Therapy (ET)	ET +/- CDK4/6
	Chemotherapy

~75% Disease-free survival rate for Stage I-III patients

25% Recur

Advanced and Metastatic
Stage III (inoperable) or Stage IV

~50,000 Cases diagnosed annually in USA

1st Line	2nd Line (post CDK4/6)	3rd Line	4th Line
ET +/- CDK4/6i	ET +/- Everolimus	ET +/- Tx (new)	Sacituzumab govitecan
	PIK3CA MT ET + Alpelisib	Chemotherapy	
	ESRI MT Elacestrant	Trastuzumab deruxtecan	

~30% 5-year survival rate for Stage III/IV patients

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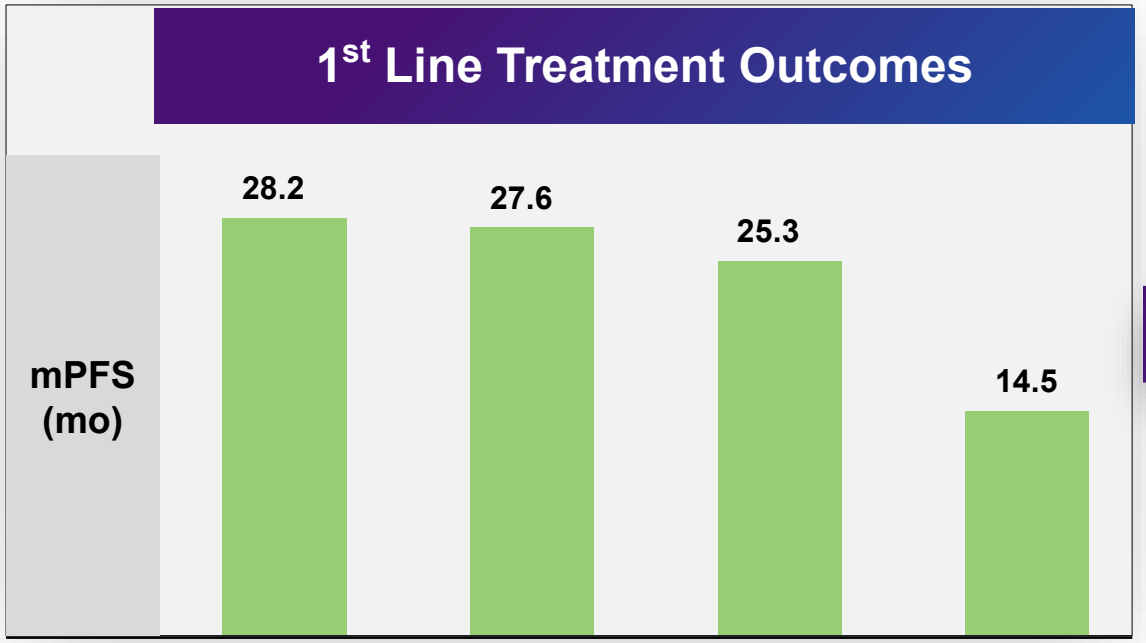
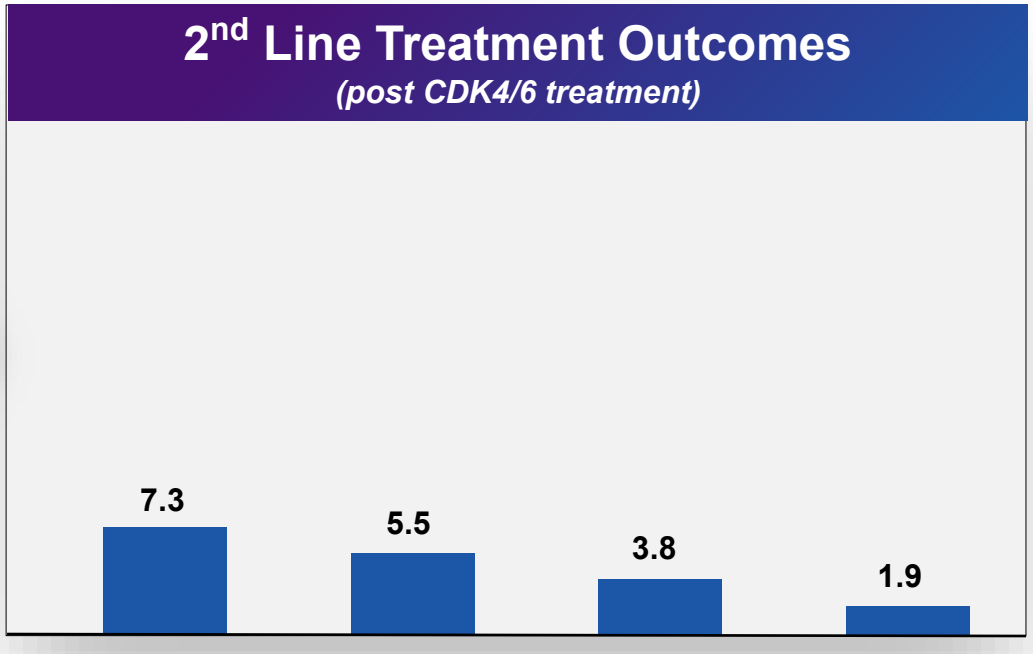
Limited Benefit for 2nd Line HR+/HER2- ABC Patients Post-CDK4/6 Treatment

Significant need for better therapeutic options





Drugs	Abemaciclib + letrozole [1]	Palbociclib + letrozole [2]	Ribociclib + letrozole [3]	Letrozole [2]
MOA	CDK4/6 + AI	CDK4/6 + AI	CDK4/6 + AI	AI
Pat Pop	All	All	All	All
mPFS	28.2	27.6	25.3	14.5
ORR	55%	55%	53%	44%

Alpelisib + fulvestrant [4]	Capivasertib + fulvestrant [5]	Elacestrant [6]	Fulvestrant [6]
PI3Kα + SERD	AKT + SERD	SERD	SERD
PIK3CA MT	All	ESRI MT	All
7.3	5.5	3.8	1.9
21%	23%	7%	6%

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(1) Goetz JCO 2017; Johnson S, et al. npj Breast Cancer 2019; (2) Finn NEJM 2016; Rugo H, et al. Breast Cancer Res Treat, 2019; (3) Hortobagyi NEJM 2016; Hortobagyi Ann Oncol 2018; USPI; (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, except for capivasertib

Key Unmet Needs for Patients with HR+/HER2- ABC

Key Unmet Needs

- Improve mPFS after progression on CDK4/6 inhibitors
  - PIK3CA WT patients: 2 – 5.5 months
  - PIK3CA MT patients: 5.5 – 7.3 months
- Extend period before patients are treated with chemotherapy and antibody drug conjugates (ADC's)

Key Questions

- What role can PI3K/mTOR inhibitors play?
- Is retreatment with CDK4/6 inhibitors beneficial?
- What role will new oral SERDs play?
- What role will new ADC's play?

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Initial PAM Drug Development in ABC Focused on PI3K/mTOR Inhibitors

Toxicity, PK, and efficacy limitations resulted in shift towards PAM single-node inhibitors

1st Gen PI3K/mTOR →		2nd Gen Pan-PI3K →		3rd Gen Single Node →		PI3K/mTOR
Programs halted at Phase 1/2		Programs halted at Phase 3		Approved	Phase 3	Phase 3
PF-04691502 PKI-402 Dactolisib BGT226 Apitolisib	Pictlisib Omipalisib GSK01059615 Samotolisib	Buparlisib	Taselisib	Everolimus *(mTORC1)* Alpelisib *(PI3Kα)*	Capivasertib *(AKT)* Inavolisib *(PI3Kα)*	Gedatolisib
Orally administered Too toxic to proceed Poor PK properties		Orally administered High toxicity Limited efficacy		Orally administered Limited PFS benefit Tolerable to difficult to tolerate safety profiles		IV administered Promising preliminary PFS Well-tolerated Excellent PK properties

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Clinical Trial Results for PAM Inhibitors After Progression on CDK4/6 Therapy

Evidence of PAM pathways involvement and sensitivity to PAM inhibitors in HR+/HER2- ABC

Therapies	Patient PIK3CA Status	N	ORR	mPFS (months)	Comments
Gedatolisib + Palbociclib + Fulvestrant [1]	WT and MT	27	63%	**12.9**	• Data for pan-PI3K/mTOR, AKT, and mTOR inhibitors suggest efficacy is independent of PIK3CA status • PI3Kα inhibitors have only demonstrated efficacy in patients with PIK3CA MT • ORR was 0% for PIK3CA WT patients treated with alpelisib + fulvestrant in a Phase 1b study [8] • Alpelisib is poorly tolerated
Everolimus + Ribociclib + Exemestane [2]	WT and MT	46	7%	**8.0**	
Alpelisib + Fulvestrant [3]	MT	127	21%	**7.3**	
Alpelisib + Letrozole [4]	MT	126	NR	5.7	
Capivasertib + Fulvestrant vs. Fulvestrant [5]	WT and MT	496	NR	5.5 vs. 2.6	
Everolimus + Fulvestrant [6]	WT and MT	25	NR	4.9	

(1) Wesolowski SABCS 2022, Arm D; includes 2 unconfirmed partial responses; (2) Hurvitz JCO 2022, TRINITI-1; Group 1 patients; (3) Rugo Lancet 2021, BYLieve Cohort A; (4) Juric SABCS 2021, BYLieve Cohort B; (5) Oliveira SABCS 2022, CAPItello-292; (6) Nichette ESMO 2020; retrospective analysis; (8) Juric Jama 2019, Phase 1b
Abbreviations: WT, wild-type; MT, mutant; NR, not reported
Note: No head-to-head trials have been conducted; data collected from different trials, in different patient populations and may not be comparable.

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Therapy after Progression on a CDK4/6i

Is there a benefit to retreating with CDK4/6i with a different ET or different CDK4/6i or both?

Therapies (Study)	Patient Population	N	Results	Comments

Ribociclib + Switched ET vs. Switched ET (MAINTAIN) [1]	Prior palbociclib	103	**5.3 vs. 2.8 months HR = 0.58 (0.38-0.89)**	• MAINTAIN suggests ribociclib after palbo with a different ET may be beneficial
				  • Benefit reported is comparable to treatment with a PI3Kαi or AKTi + ET
				• PACE showed no benefit continuing palbociclib treatment with a different ET after progression on palbociclib
				  • Sub-group of endocrine resistant patients (25% of total) reported encouraging results
				• **Unknown whether switching from palbociclib or abemaciclib to a different CDK4/6i is beneficial**

	Prior ribociclib	14	2.8 vs. 2.8 months HR = 0.50 (0.15-1.70)	
Palbociclib + fulvestrant vs. Fulvestrant (PACE) [2]	Prior palbociclib	154	4.6 vs. 4.8 months HR = 1.15 (0.81-1.63)	
	Endocrine Resistant	42	**HR = 0.41 (0.20-0.82)**	

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(1) Kalinsky K, JCO, 2023, (2) Mayer E, SABCS, 2022,

Therapy after Progression on a CDK4/6i

What role should oral SERD's play?

Therapies (Study)	Prior CDK4/6i	Prior Fulvestrant	mPFS ESR1 MT	Comments

Elacestrant vs ET (EMERALD)[1]	100%	30%	**3.8 vs 1.9 months HR = 0.65, P=0.005**	• **Data to date not as promising as expected when development of this drug class began**
				• mPFS benefit of oral SERD's as single agents evaluated to date has been limited to patients with ESR1 mutations
				  • Magnitude of mPFS benefit ~2 months
				• Several studies underway to evaluate oral SERD's with CDK4/6 inhibitors
				  • Given extended mPFS for current CDK4/6i + ET regimens, an oral SERD must add substantially greater mPFS benefit than 2 months to demonstrate efficacy

Camizestrant vs fulvestrant (Serena-2)[2]	100% (sub-group)	0%	**3.8-5.5 vs 2.1 months HR = 0.49-68**	
Giredestrant vs ET (acelERA)[3]	42%	19%	5.3 vs 3.5 months HR = 0.60, P=0.06	
Amcenestrant vs. ET (AMEERA-3)[4]	80%	10%	3.7 vs 2.0 months HR = 0.90	

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(1) Bidard F, JCO 2022; (2) Oliviera, SABCS 2022; (3) Martin M, ESMO 2022, (4) Tolaney S, ESMO 2022

Therapy after progression on a CDK4/6i

When should an ADC be used?

Therapies (Study)	Patient Population	Prior Therapy	N	mPFS	Comments

Trastuzumab Deruxtectan
 	
(DB-04)
	Progressed on prior chemotherapy
	
	HR+
	HER2 IHC 1+ or 2+
		70% prior CDK4/6i
		
		1-2 prior lines of chemo in ABC (median 1)
			480	**10.1 vs 5.4 months**
				HR = 0.51; *P*<0.001
					• **Goal is to utilize endocrine backbone therapy as long as possible**
					• **ADC's should be used after exhausting endocrine based regimens**
					• Adverse event profiles are similar to chemotherapy
					  • Alopecia
					  • Neutropenia
					  • Nausea/vomiting (especially T-DX)
					  • Diarrhea (especially SG)
					  • ILD (especially T-DX)

Sacituzumab Govitecan **(TROPiCS-02)**	Progressed on prior chemotherapy HR+/HER2-	99% prior CDK4/6i 2-4 prior lines of chemo in ABC (median 3)	543	**5.5 vs 4.0 months** **HR = 0.66; *P*=0.003**	

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(1) (2)

Key Takeaways

A more effective PAM inhibitor may offer best opportunity to improve outcomes for HR+/HER2- ABC

1

- **The PAM pathway is key driver of breast cancer and is linked to ER and CDK4/6 pathways**
  - Approval of multiple PAM inhibitors confirm relevance of pathway

2

- **The two approved PAM therapies and one likely to be approved have shortcomings**
  - Limited efficacy: 5.5 – 7.3 months
  - Suboptimal safety profile in the case of alpelisib; leads to high discontinuation rate and limits utilization

3

- **Oral SERD's offer greater convenience than fulvestrant, but efficacy has not been as significant as was hoped**
  - ~2 months mPFS improvement has only been demonstrated in patients with ESR1 mutants
  - Obtaining approvals in combination with other agents will require greater mPFS improvement

4

- **Developing an effective and well tolerated PAM inhibitor is an important research priority**
  - Gedatolisib's early phase results are promising, and, if replicated in VIKTORIA-1 study, regimen could be new SOC

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Fred Hutch CC

Clinical Data for Gedatolisib in Breast Cancer

Igor Gorbatchevsky, MD
Chief Medical Officer

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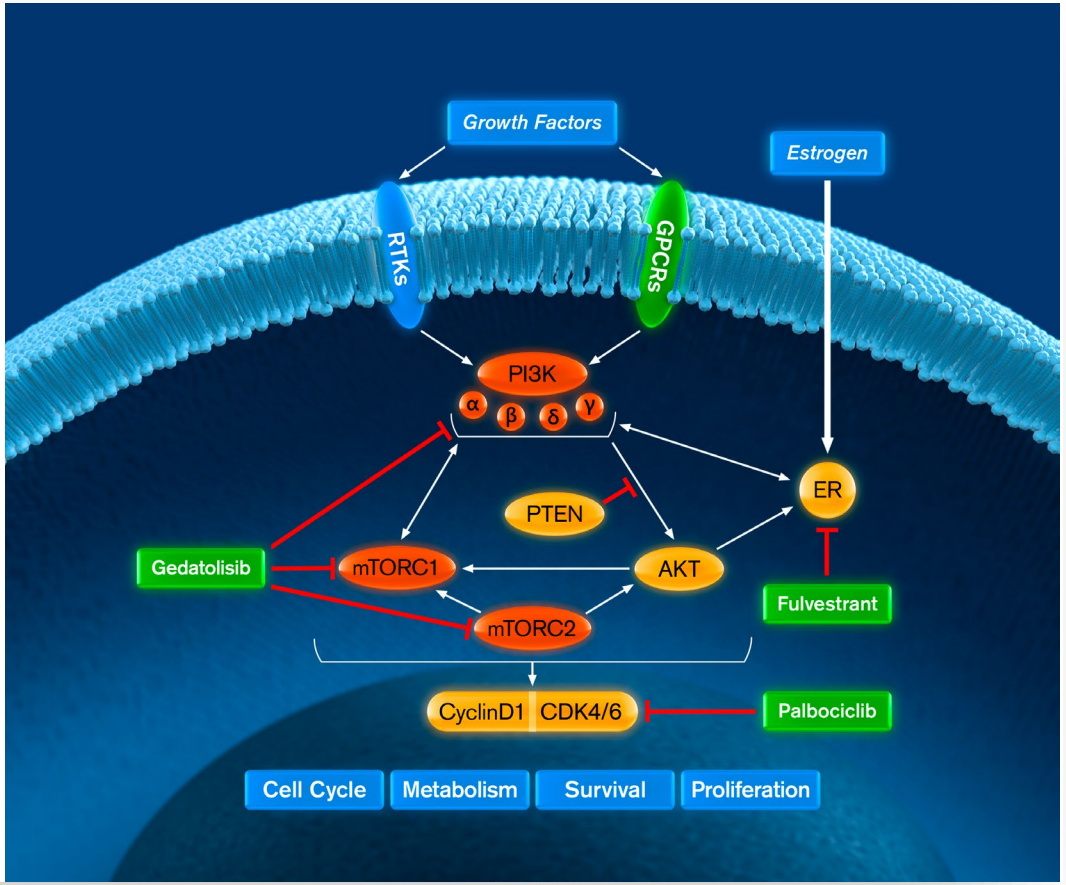
PI3K/mTOR, ER, and CDK4/6 are Interdependent Signaling Pathways

PI3K/mTOR is a key resistance mechanism to estrogen and CDK4/6 therapies

PI3K/mTOR + ER + CDK4/6 Inhibition *Treatment Rationale*

- Simultaneously blocking interdependent ER, PI3K, mTOR & CDK signaling pathways in ER+ breast cancer addresses ER and CDKi resistance mechanisms
- Inhibiting all PI3K isoforms and mTORC1/2 prevents resistance mechanisms that occur when only PI3K-α or mTOR are inhibited
- Leads to improved response rates and duration of response



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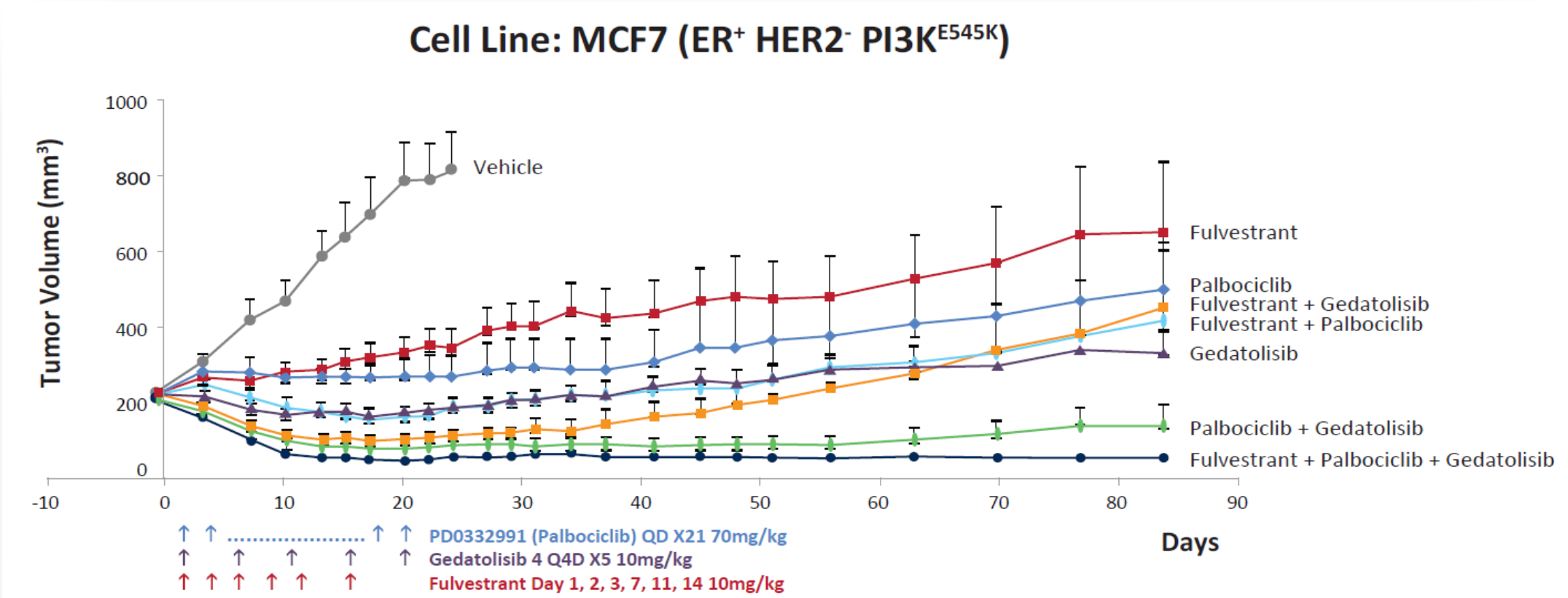
Non-Clinical Data Consistent with Treatment Hypothesis

Gedatolisib with palbociclib and fulvestrant in ER+/PIK3CA mutated breast cancer mouse xenograft



Tumor Growth Inhibition *(during dosing)*	**Maintenance of Tumor Suppression** *(65 Days post-dosing)*
G+P+F, G+P, G+F > 120%	G+P+F and G+P

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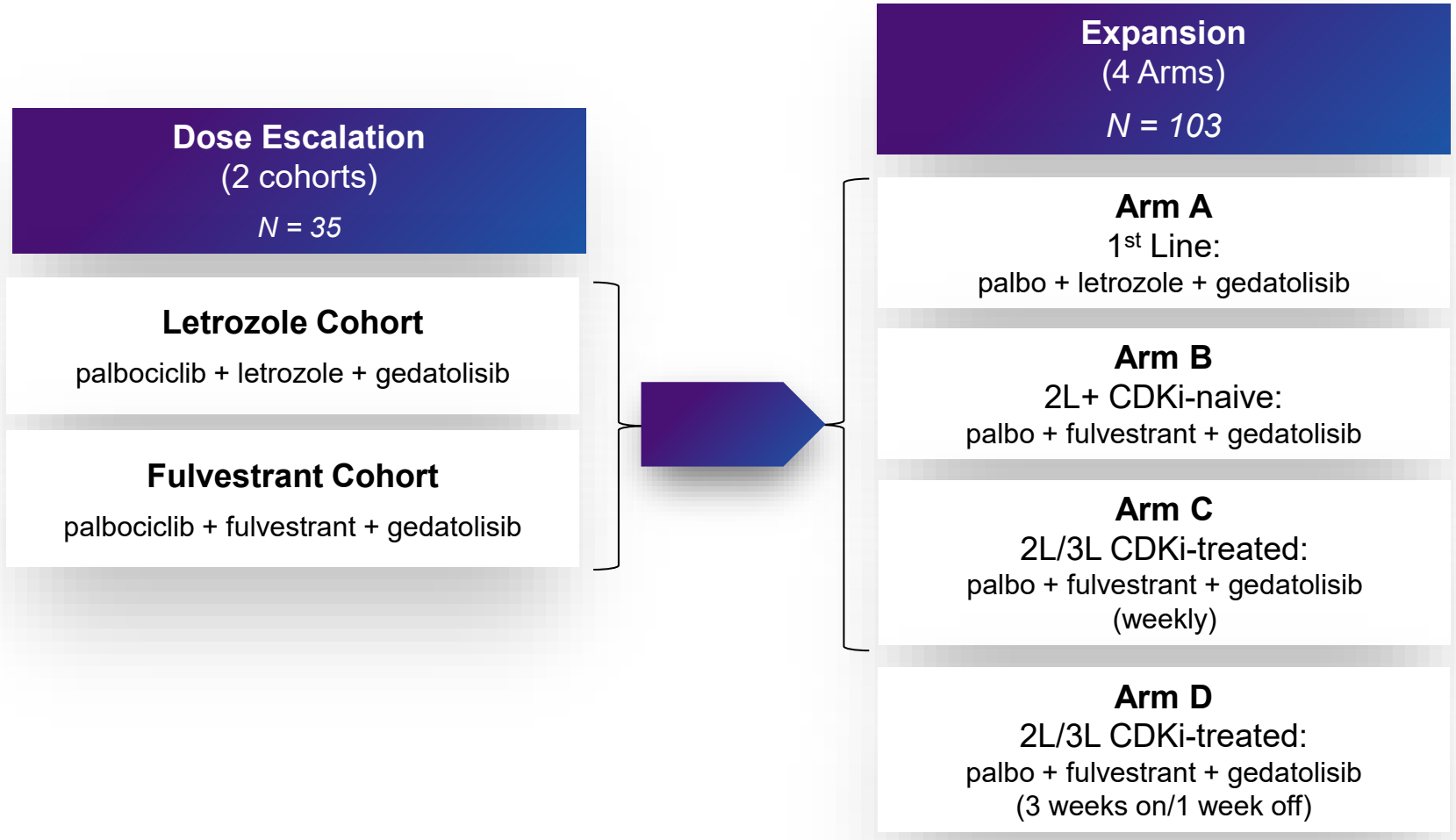
B2151009: Phase 1b Study (138 patients)

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



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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 Therapy[1]	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

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(1) SERD, SERM, or aromatase inhibitor

B2151009 Expansion Arms: Patient Treatment Discontinuation

Reasons for treatment discontinuation, n (%)	Arm A (N=31)	Arm B (N=13)	Arm C (N=32)	Arm D (N=27)
Progression or relapse	12 (38.7)	10 (76.9)	24 (75.0)	20 (74.1)
Global Deterioration	2 (6.5)	0	1 (3.1)	2 (7.4)
Death [a]	0	0	0	1 (3.7)
Adverse Event [b]	3 (9.7)	2 (15.4)	3 (9.4)	1 (3.7)
Protocol Violation	1 (3.2)	0	0	0
No Longer willing to participate in study	4 (12.9)	0	4 (12.5)	0
Study Terminated by sponsor [c]	8 (25.8)	1 (7.7)	0	2 (7.4)
Other [d]	1 (3.2)	0	0	1 (3.7)

a) One subject died of septic shock, which was reported as due to disease in the liver and not related to treatment.
b) Overall discontinuation rate due to AE <10%; stomatitis was the only AE that led to more than one patient discontinuing treatment (4%); no discontinuations due to hyperglycemia
c) Celcuity terminated the study and transitioned subjects who were still receiving study therapy to either expanded access protocol CELC-G-001 or a single subject investigational new drug (IND) to continue therapy.
d) Arm A: new diagnosis of renal cell carcinoma; Arm D: too many missed visits and assessments due to transportation issues/COVID-19 pandemic.

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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-naive		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%

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Source: Wesolowski 2022 SABCS; Rugo 2023 ESMO-Breast. Footnotes: (1) Response evaluable analysis set per RECIST v1.1 including uPR (n=2, Arm B; n=3, Arm C; n=2, Arm D); (2) full analysis set, mPFS updated with data cutoff 29-May-2023; (3) Baseline *PIK3CA* mutation status missing for one patient. Abbreviations: 1L, first line, 2L, second line; mos, months; MT, *PIK3CA* mutation; NR, Not reached; ORR, objective response rate; mPFS, median progression free survival; SOC, standard of care; WT, wild type

2nd Line HR+/HER2- Advanced Breast Cancer

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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 [1]
- 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) [2]
- Stomatitis prophylaxis was not utilized in this study
  - **Swish-and-Spit dexamethasone prophylactic mouth rinse reduced Grade 2-4 stomatitis by 90%** [3]
  - 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	%	%	%
Stomatitis[4]	11	56	22
Neutropenia[5]	-	15	67
Nausea	44	30	-
Fatigue	22	37	7
Dysgeusia	44	7	-
Diarrhea	37	-	4
Rash	19	15	7
Leukopenia[6]	-	19	23
Constipation	30	4	4
Vomiting	22	11	4
Anemia[7]	4	15	15
Hyperglycemia	15	4	7

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Source: (1) Andre 2019; (2) USPI Alpelisib; (3) Rugo 2017. (4) Stomatitis category includes mucositis; (5) Neutropenia includes neutrophil count decrease; (6) Leukopenia includes white blood cell decrease; (7) Anemia includes hemoglobin decrease; Abbreviations: G = gedatolisib; P = palbociclib; F = fulvestrant; TEAE = treatment emergent adverse events; AE = adverse event

Arm C and D Had Significant Differences in Baseline Characteristics

Both arms enrolled patients who had received prior CDK4/6 therapy

Baseline Characteristics That Differed Significantly Between Arm C and D

	Arm C (N=32)	Arm D (N=27)
Gedatolisib (dosing schedule)	Weekly	3 weeks on / 1 week off
Duration of Immediate Prior Therapy (DIPT)	5.2 months	13.5 months
Prior Chemotherapy (%)	47%	19%
Median Lines of Prior therapy	2	1
Participants with ≥3 metastatic disease site	59.4%	44.4%

- 61% shorter duration on immediate prior therapy in Arm C vs. D
  - 5.2 vs. 13.5 months
  - 2L patients whose prior treatment was 1L CDK4/6 + aromatase inhibitor, would expect DIPT to be 18-22 months
- 2.5 times more patients received prior chemotherapy for ABC in Arm C vs. D
  - 47% vs. 19%
- 2X more median number of prior therapies in Arm C compared to Arm D
  - 2 vs 1
- More metastatic patients with ≥ 3 metastatic sites in Arm C vs. D
  - 59.4% vs. 44.4%

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Source: Wesolowski 2022 SABCS; Rugo 2023 ESMO-Breast. Footnotes: (1) Finn, NEJM, 2016; Hortobagyi, Ann Oncol, 2018; Johnston, NPJ Breast Cancer, 2018

Analysis of Arm C and D Patients with Similar Prior Treatment Durations

Enables isolation of effect of the different dosing schedules used in each arm

Duration of Immediate Prior Treatment (DIPT)

	DIPT <180 Days		DIPT <365 Days	
	Arm C	Arm D	Arm C	Arm D
# Evaluable patients with DIPT <185 or 365 days (% of evaluable)	12 (44%)	7 (27%)	20 (74%)	11 (42%)
Gedatolisib Dosing Schedule	Weekly	3 weeks on / 1 week off*	Weekly	3 weeks on / 1 week off*
Median DIPT (months)	3.2	3.5	4.8	5.1
Median Duration of Study Treatment (DST, months)	2.7	8.9	4.3	9.2
Ratio of median DST vs. DIPT	0.8	2.6	0.9	1.8
ORR (95% CI)	**0%** *(0%-26%)*	**71%** *(29%-96%)*	**15%** *(3%-38%)*	**73%** *(39%-94%)*

Key Finding

Patients remained on gedatolisib 2-3X longer on a 3 weeks on/one week off vs. weekly schedule

when they had similar time on their prior therapy

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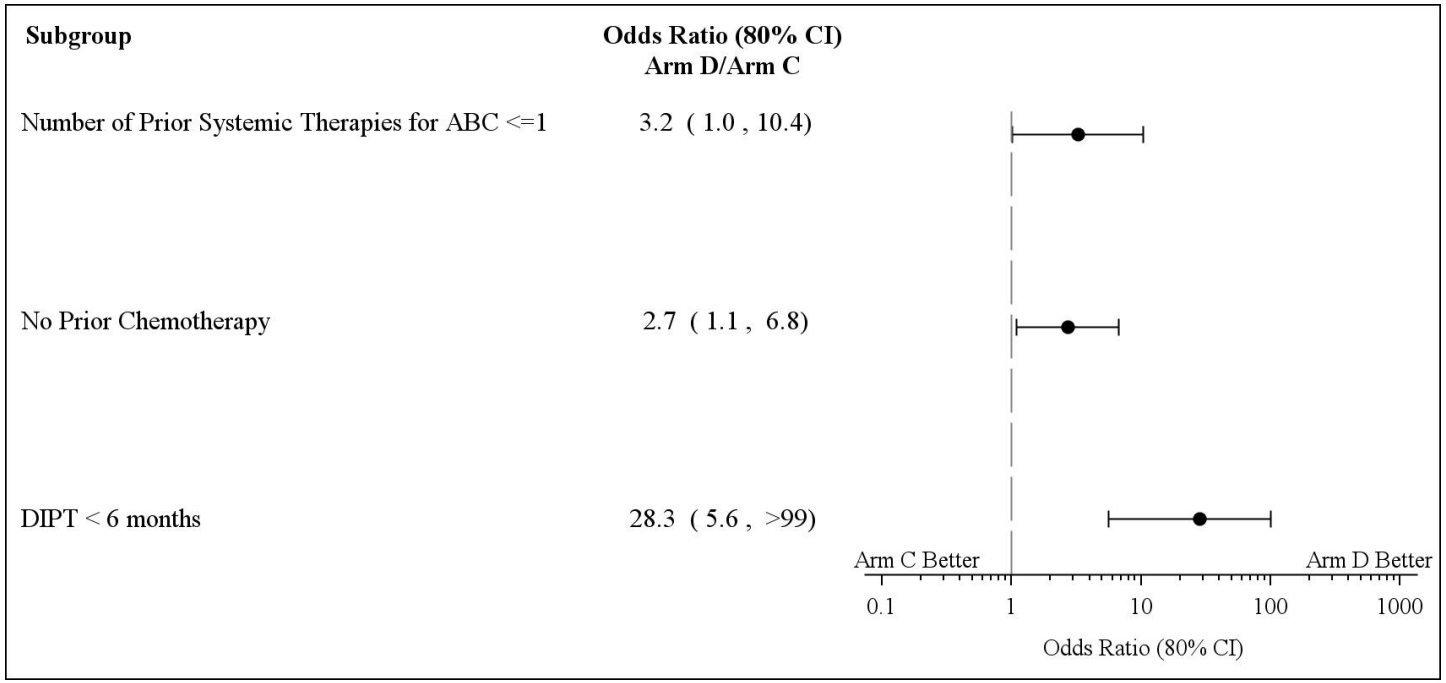
Source: Layman, SABCS, 2021; IPT: Duration of Immediate Prior Therapy; DST: Duration of Study Treatment; Responses by Physician Assessment per RECIST 1.1; 2 by 2 contingency table using Fisher's exact test for ORR p-value; *gedatolisib and palbociclib dosing synchronized at 3 weeks on/1 week off

Forest Plot for Model-Selected Subgroups

Dose schedule effect (Arm D over C) is observed in all critical subgroups selected by a logistic regression model



Approach

- Tested 8 factors to identify ones affecting ORR
- Of the 8 factors tested, 3 met significance criteria
  - Duration of immediate prior therapy
  - Number of prior therapies
  - Prior chemotherapy (yes or no)

Conclusions

- Effect of dose schedule on efficacy (ORR) remained robust when controlled for all 3 factors
- Provide strong evidence that intermittent dose schedule is associated with enhanced efficacy

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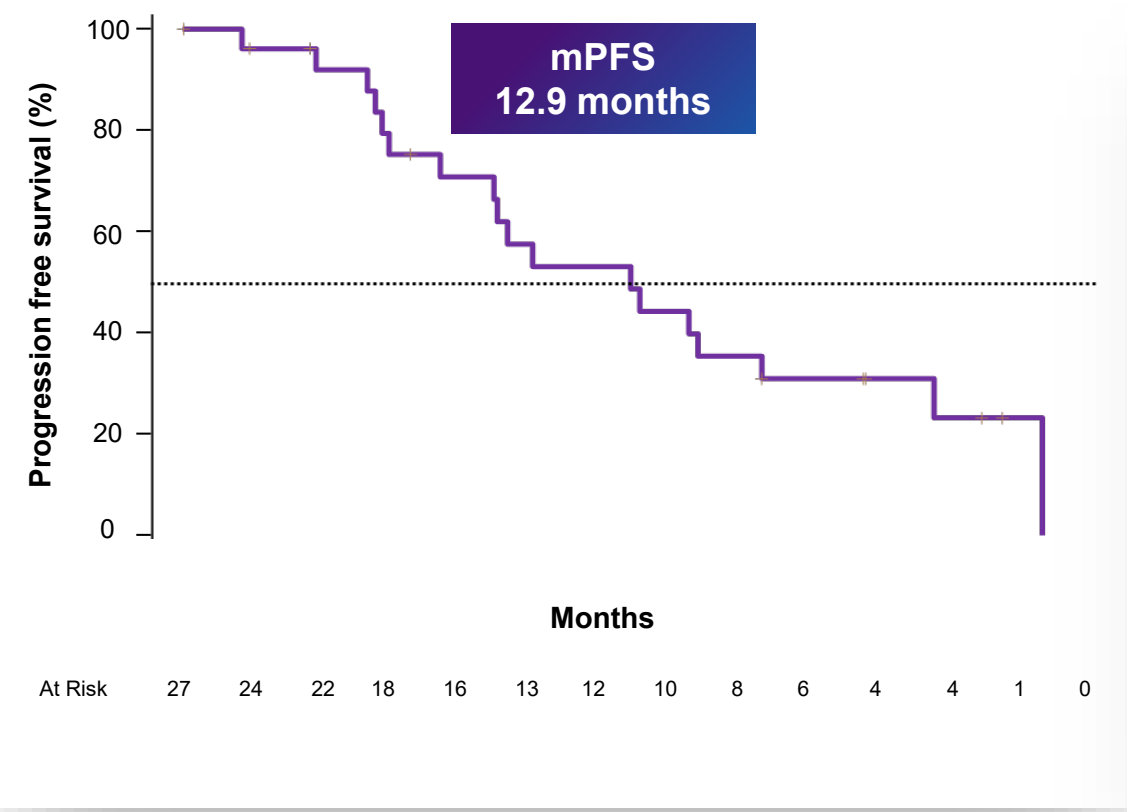
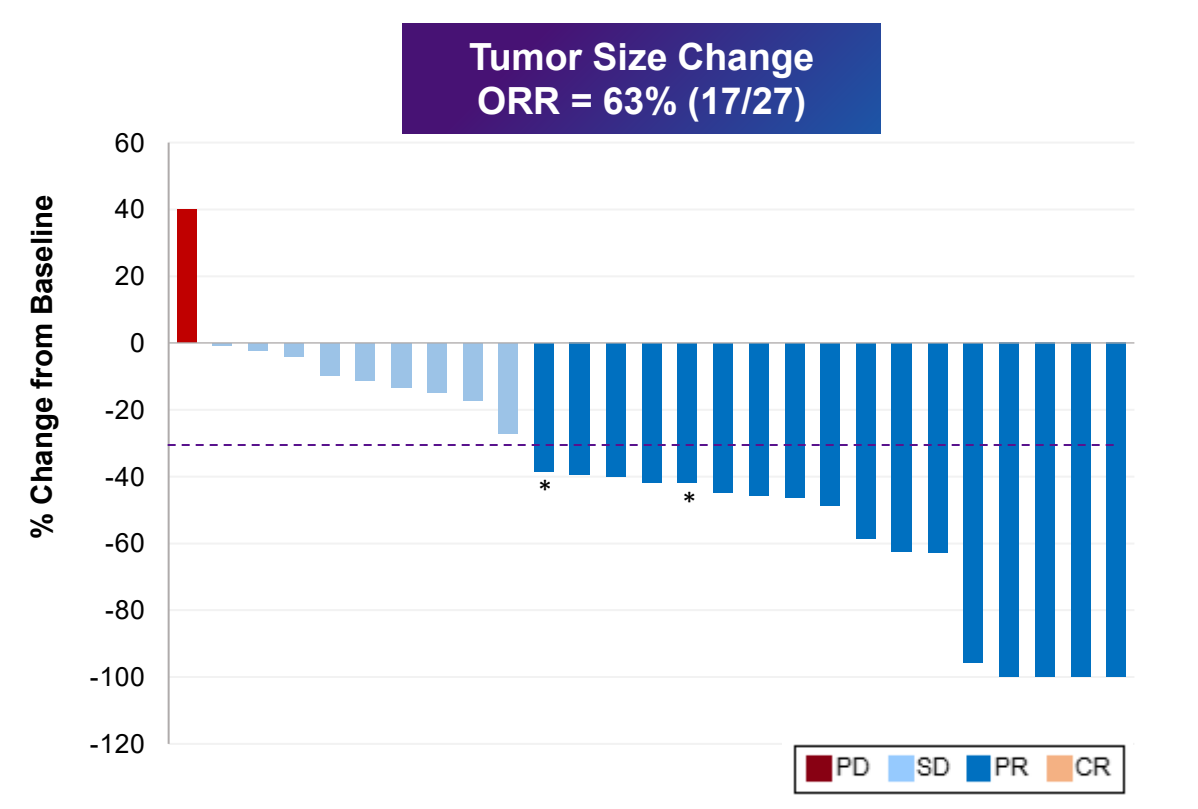
Gedatolisib + Palbociclib + Fulvestrant in 2nd/3rd Line HR+/HER2- ABC Patients

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





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Source: Layman 2021 SABCS, Wesolowski 2022 SABCS - Arm D data from B2151009 study. ORR includes 2 unconfirmed PRs; *unconfirmed PR. Data presented is from a data analysis cutoff as of June 29, 2022

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

Gedatolisib Combo Offers Potential for Superior Efficacy Compared to Alternatives

Patient Population	2nd Line ER+/HER2- ABC	
All	Gedatolisib + Fulvestrant + Palbociclib [1]	mPFS 12.9 months ORR 63%
PIK3CA+	Alpelisib + Fulvestrant [2]	mPFS 7.3 months ORR 17%
PIK3CA+	Alpelisib + Fulvestrant [3]	mPFS 5.6 months ORR 24%
All	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%

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(1) Wesolowski SABCS 2022, Arm D; (2) Rugo, Lancet Onco, 2021; (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, except for capivasertib. No head-to-head trials have been conducted; data collected from different trials, in different patient populations and may not be comparable.

Phase 3 Study Design
VIKTORIA-1

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Pivotal Trial Design Considerations for 2nd Line HR+/HER2- ABC

- Standard-of-care 2nd 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

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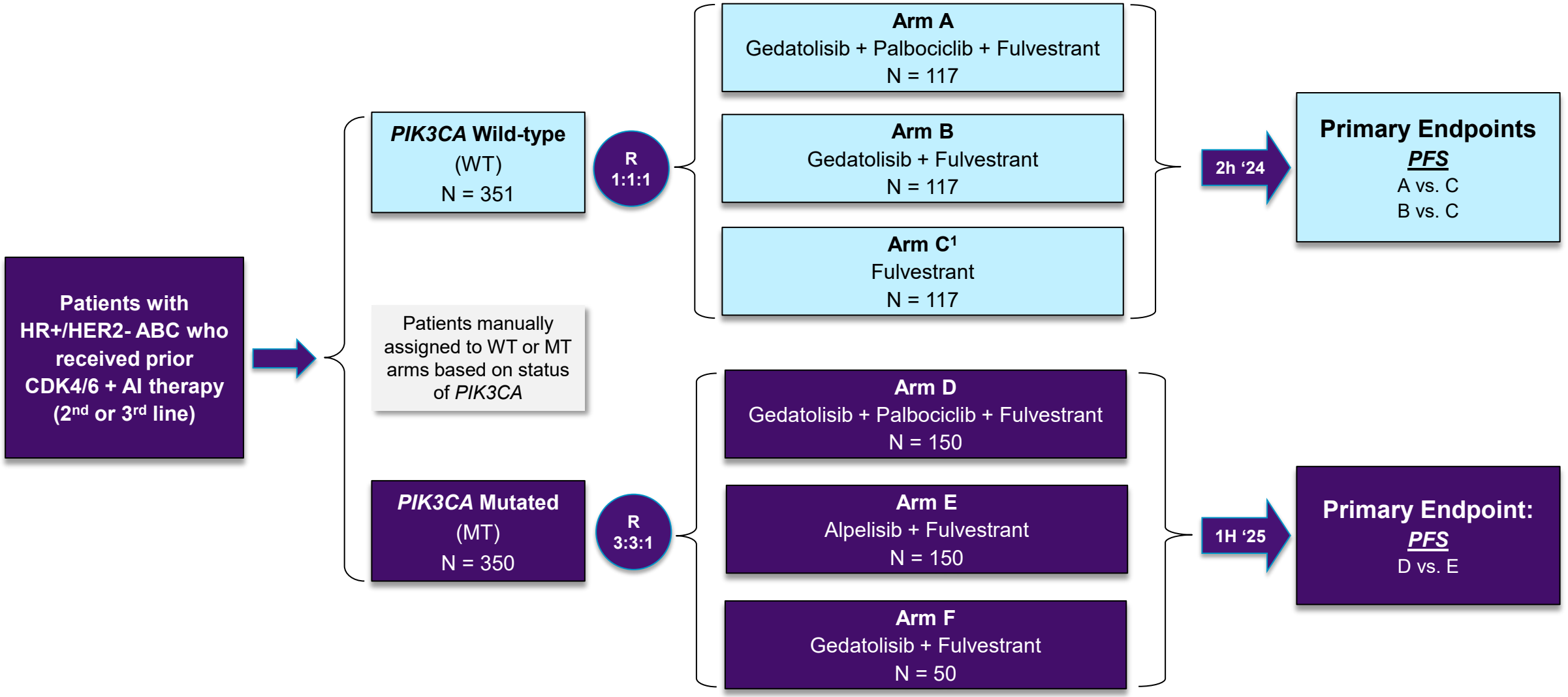
VIKTORIA-1 Pivotal Phase 3 Trial Design Overview



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

VIKTORIA-1 Pivotal Study Features

- **Global open-label randomized study**
- **Key eligibility criteria:**
  - Any *PIK3CA* status
  - Prior CDK4/6i + NSAI
  - Any menopausal status
  - ≤ 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 (≤ 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

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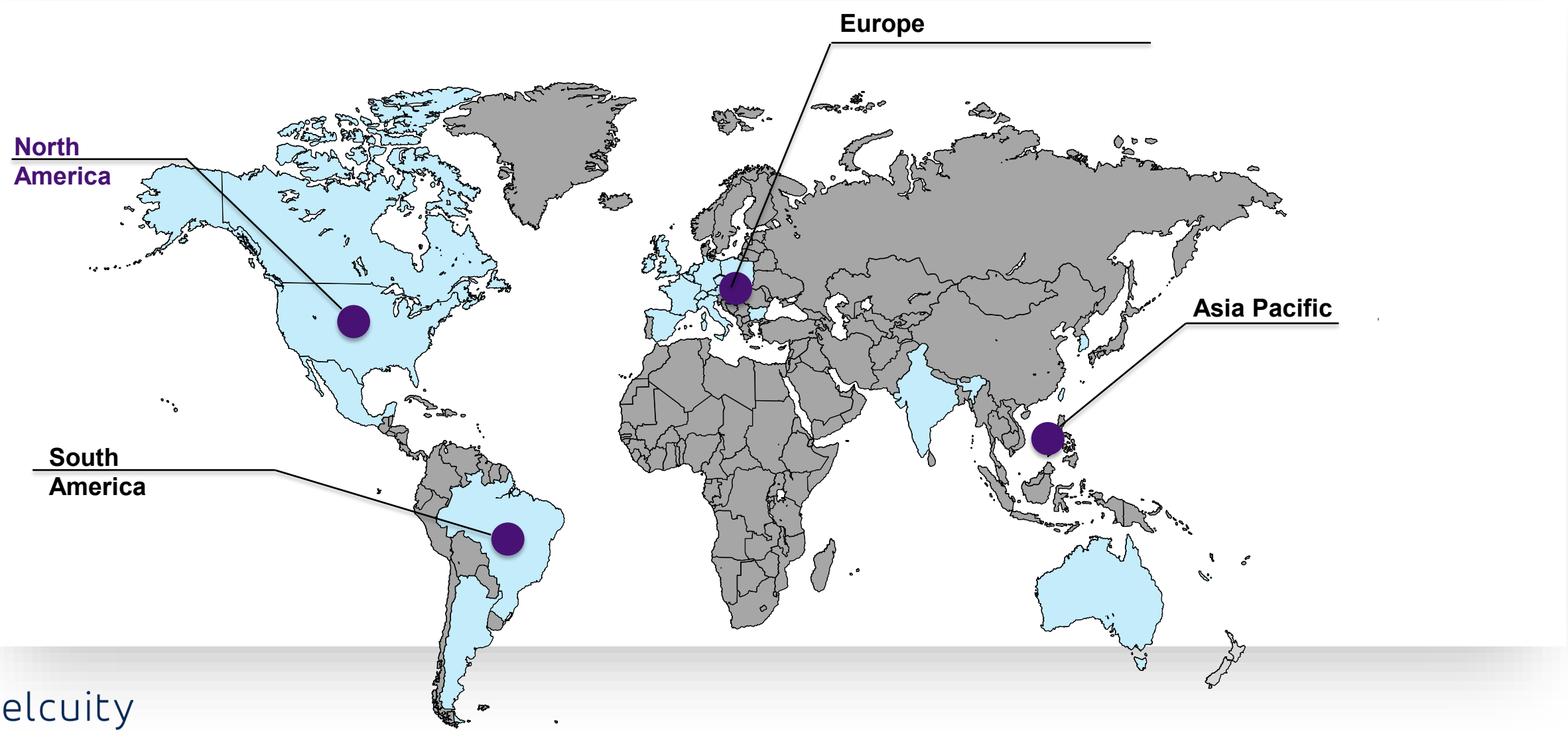
200+ Sites Across 20 Countries



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Relevant Comparisons in CDK4/6i Pretreated Patients with ABC

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

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

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Sources: (1) Wesolowski, SABCS, 2022; (2) Includes 2 unconfirmed PR.(3) Bidard 2022 – 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) Lindeman 2021, VERONICA trial; (6) Rugo 2021 SABCS (7) Rugo 2021 Lancet. Note: No head-to-head trials have been conducted; data collected from different trials, in different patient populations and may not be comparable. Data presented for gedatolisib is from a preliminary data analysis as of a cutoff date of June 29, 2022.

1st Line HR+/HER2- Advanced Breast Cancer

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B2151009 Treatment Naïve Patients: Baseline Characteristics

	Escalation Arm A (n=11)	Expansion Arm A (N=30)	Total Treatment-Naïve (n=41)
Tumor, node, metastasis (TNM) stage, n (%)			
Stage IV	11 (100.0)	30 (100.0)	41 (100.0)
Number of Prior Therapies - Advanced Breast Cancer, n (%)			
0	11 (100.0)	30 (100.0)	41 (100.0)
Disease Site Involved, n (%)			
Liver or Lung	1 (9.1)	20 (66.7)	21 (51.2)
Liver	1 (9.1)	14 (46.7)	15 (36.6)
Lung	0	7 (23.3)	7 (17.1)
Bone	9 (81.8)	17 (56.7)	26 (63.4)
Bone Only	1 (9.1)	0	1 (2.4)
Prior Adjuvant Endocrine Therapy, n (%)			
Yes	2 (18.2)	16 (53.3)	18 (43.9)
No	9 (81.8)	14 (46.7)	23 (56.1)

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Source: Rugo 2023 ESMO Breast

B2151009 Treatment Naïve Patients: Treatment Discontinuation

Patients who discontinued treatment, n (%)	Total Treatment-Naïve Patients (n=41)
Reasons other than AE's	36 (87.8)
Progression or relapse	15 (36.6)
Study terminated by sponsor [1]	9 (22.0)
Withdrawal by Subject	6 (14.6)
Global Deterioration	2 (4.9)
Protocol Violation	1 (2.4)
Lost to Follow-up	1 (2.4)
Other [2]	2 (4.9)
Adverse Events [3]	
Treatment related	4 (9.8)
Unknown	1 (2.4)

Source: Rugo 2023 ESMO Breast; internal data on file; (1) After study termination, nine pts in this subgroup rolled over to an expanded access protocol (EAP) and continued treatment. As of March 16, 2023, 5 of these pts remain enrolled in the EAP. (2) Other includes: withdrawal by subject, lost to follow up, global deterioration, PI decision, new diagnosis-renal cell carcinoma; (3) Treatment related AEs: 1 each of four different AE's

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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)**

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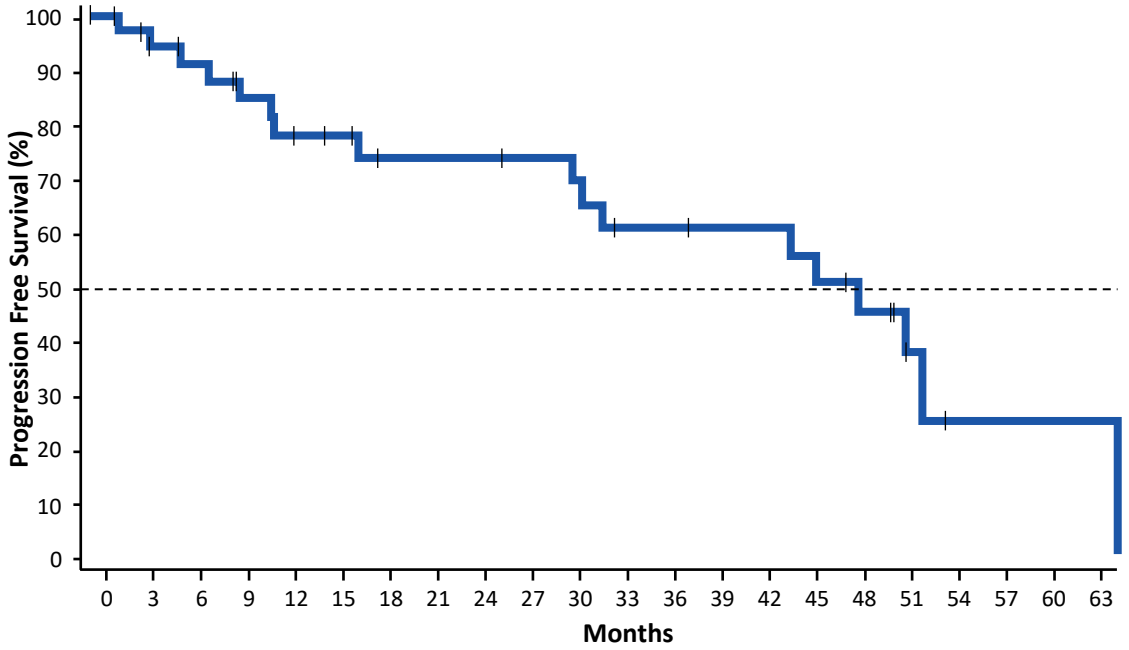
Source: Rugo 2023 ESMO Breast. (1) Subjects with measurable disease in response evaluable analysis set per RECIST v1.1;(2) Confirmed responders in the full analysis set. Abbreviations: CR, complete response; DOR, duration of response; mos, months; NR, Not Reached; ORR, objective response rate; PD, progressive disease; PFS, progression free survival; PR, partial response; SD, stable disease

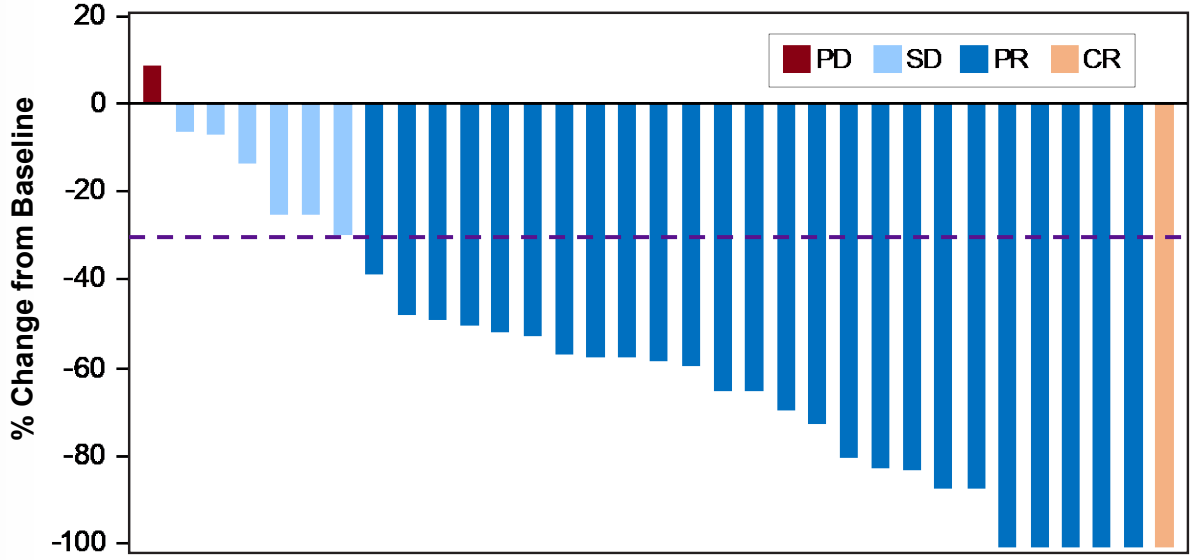
Gedatolisib + Palbociclib + Letrozole in 1st Line HR+/HER2- ABC (N=41)[1]

Combined 1L data from Esc Arm A + Exp Arm A compares favorably to published data for SOC palbociclib + letrozole[2]

mPFS
48.6 Months



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



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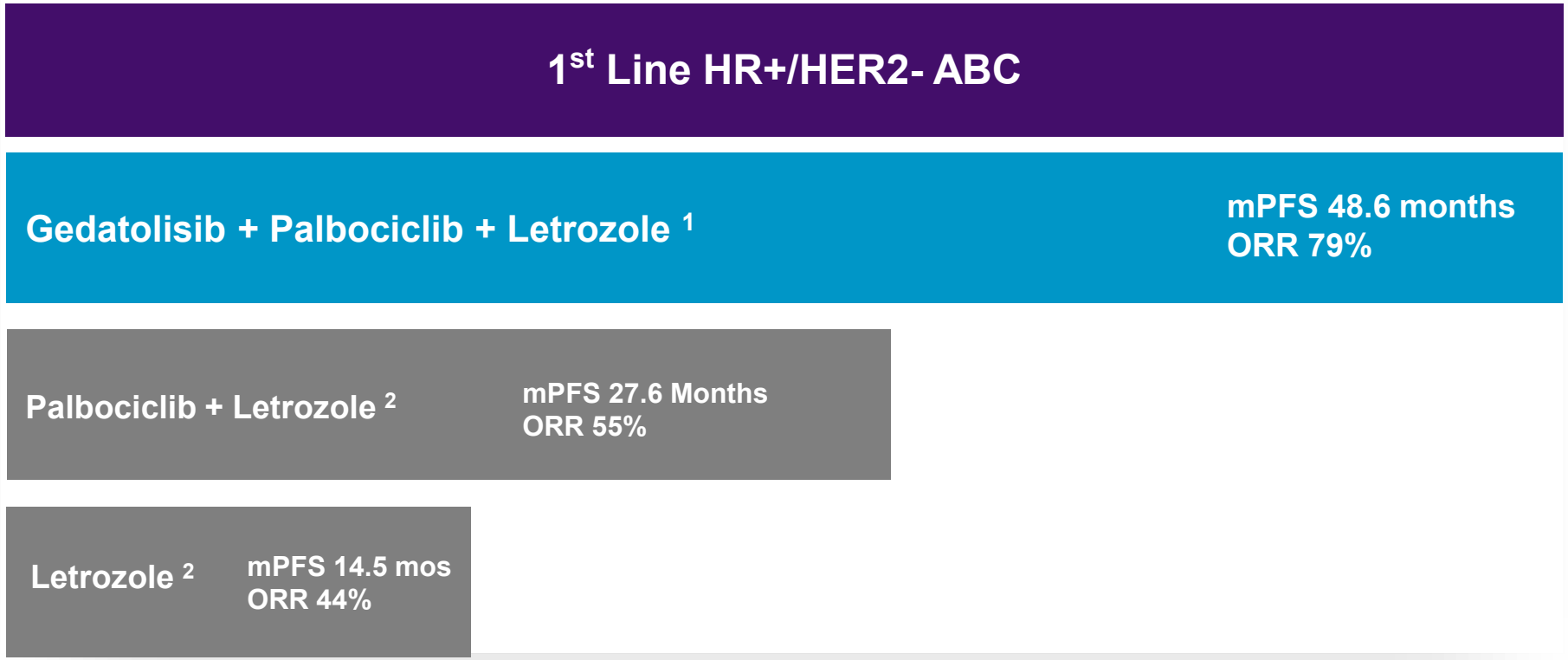
(1) Rugo 2023 ESMO-Breast; Escalation Arm A & Expansion Arm A data from B2151009 study; (2) Finn 2016 NEJM – PALOMA-2; (3). Note: (a) ORR reported is for patients with measurable disease of a target lesion. (b) No head-to-head trials have been conducted; data collected from different trials, in different patient populations and may not be comparable. (c) Data presented is from data analysis as of a cutoff date of June 29, 2022.

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

Gedatolisib Combo Offers Potential for Superior Efficacy Compared to SOC



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Sources: (1) Rugo 2023 ESMO-Breast. (2) Rugo H, et al. Breast Cancer Res Treat, 2019; Finn 2016. Abbreviations: mPFS = median progression free survival; ORR = objective response rate. SOC = standard of care. Note: No head-to-head trials have been conducted; data collected from different trials, in different patient populations and may not be comparable.

B2151009: 1L and 3L Patient Overview

1L patient on therapy for 5.1 years; 3L on therapy for 4.3 years; both remain on treatment

- 62-year-old female
- Initial diagnosis of BC: 2008
- Recurrence with Stage 4 (lung metastases) on May 2018
- Start of treatment: May 2018 (Geda + Palbo + Letrozole)
- Best Overall response: PR
- **Remains on treatment**
- **Completed 67 cycles of treatment as of August 2023**

- 61-year-old female
- Initial diagnosis of BC: 2000
- Prior treatment for BC:
  - Radical mastectomy 2000
  - Adjuvant chemotherapy 2000
  - Hormonal therapy: 2001-2006
- Recurrence with stage 4 (metastases in lung) Feb 2016
- Two prior lines of therapy for ABC:
  - Chemotherapy: May - Aug ’16
  - Palbociclib + Fulvestrant: Oct ’16 - Mar ’19
- Start of treatment: March 2019
  - Geda + Palbo + Fulvestrant
- Best Overall response: PR
- **Remains on treatment**
- **Completed 57 cycles of treatment as of August 2023**

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The Celcuity Opportunity

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Don’t blame the pathway for limited efficacy and tolerability of PAM inhibitors

Blame the drugs

Significant untapped potential to treat PAM pathway involved cancers

- Failures, limited efficacy, and lack of tolerability of other PAM inhibitors reflect limitations of the drugs, not irrelevance of pathway
  - MOA of single node PAM inhibitors have limited potential to achieve potency or cytotoxicity necessary to optimize efficacy
  - Oral route of administration challenging

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 and cytotoxic PAM inhibitor**

2

- **Very compelling data in 1L and 2L 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**

Q&A

Instructions

- Submit questions using the Q&A feature on the event page

Participants in Today's Q&A Session

Brian Sullivan
Chief Executive Officer and Co-Founder

Lance Laing, PhD
Chief Scientific Officer and Co-Founder

Igor Gorbatchevsky, MD
Chief Medical Officer

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