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Corporate Overview

# Advancing medicines for breast cancer and beyond

# — Forward-looking statements

This presentation contains forward-looking statements made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Statements in this presentation that are not statements of historical fact are forward-looking statements. Words such as “anticipate,” “believe,” “estimate,” “expect,” “goal,” “intend,” “may,” “plan,” “potential,” “project,” “will,” and similar expressions are intended to identify forward-looking statements, though not all forward-looking statements necessarily contain these identifying words. Such forward-looking statements include, without limitation, statements regarding our research and clinical development plans, the scope, progress, results and costs of developing our product candidates or any other future product candidates, strategy, market size and opportunity, clinical trial designs, regulatory matters, including the timing and likelihood of success of obtaining drug approvals, the timelines for potential initiation of clinical trials and the result of any such clinical trials of palazestrant (OP-1250) as a monotherapy and in combination trials, including OPERA-01, the Company’s pivotal Phase 3 monotherapy clinical trial, and OPERA-02, the Company’s potential pivotal Phase 3 clinical trial of palazestrant in combination with ribociclib, the timelines for potential commercial launch and related preparatory work, the sufficiency and potential beneficial characteristics, profile, safety, tolerability, efficacy and therapeutic effects of palazestrant as a monotherapy and in combination trials, the progression-free survival rate under palazestrant in combination trials, the potential of palazestrant to become a therapeutic leader and a best-in-class treatment option for ER+/HER2- metastatic breast cancer and a backbone therapy for women living with breast cancer and beyond, the combinability of palazestrant with other drugs, the timelines for initiation of potential clinical trials for and the results of any such clinical trials in connection with our KAT6 inhibitor program, including OP-3136, the potential value and impact of our KAT6 inhibitor program, the best-in-class potential for OP-3136, including for breast and other solid tumor cancers, the potential beneficial characteristics, profile, safety, efficacy, tolerability, and therapeutic effects of OP-3136, our opportunity in breast, other solid tumor cancers, and beyond, our ability to impact treatment for endocrine-driven cancers, our financial condition, cash position, runway and the sufficiency of our financial resources, and the sufficiency and expertise of our management team. These forward-looking statements are based on the beliefs of the Company’s management as well as assumptions made by and information currently available to the Company. Such statements reflect the current views of the Company with respect to future events and are subject to known and unknown risks, including business, regulatory, economic and competitive risks, uncertainties, contingencies and assumptions about the Company, including, without limitation, risks inherent in developing products and technologies, future results from the Company’s ongoing and planned clinical trials, the Company’s ability to obtain adequate financing to fund its planned clinical trials and other expenses, trends in the industry, the legal and regulatory framework for the industry and future expenditures, and other risks and uncertainties affecting the Company, including those described under the caption “Risk Factors” and elsewhere in the Company’s Quarterly Reports on Form 10-Q, Annual Report on Form 10-K, and other filings and reports the Company files with the Securities and Exchange Commission from time to time. In light of these risks and uncertainties, the events or circumstances referred to in the forward-looking statements may not occur. The actual results may vary from the anticipated results and the variations may be material. These forward-looking statements should not be taken as forecasts or promises nor should they be taken as implying any indication, assurance or guarantee that the assumptions on which such forward-looking statements have been made are correct or exhaustive or, in the case of the assumptions, fully stated in this presentation. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date this presentation is given.

**This presentation discusses product candidates that are under clinical study and which have not yet been approved for marketing by the U.S. Food and Drug Administration. No representation is made as to the safety or effectiveness of these product candidates for the use for which such product candidates are being studied.**

This presentation incorporates publicly-available third-party data that we have not independently verified. There are risks inherent in conducting cross-trial comparisons and the results should be interpreted with caution. The presentation of such third-party data does not represent a head-to-head comparison of how palazestrant, in monotherapy or in combination, or OP-3136 performed against any other third-party drug candidate or study. Rather, such third-party data has been pulled by us from publicly-available sources for supplemental informational purposes, only. We caution you that any comparisons against third-party data set forth herein should not be viewed as a side-by-side comparison, and you should not rely on the completeness or accuracy of our presentation of the results of any third-party drug candidate in these slides, due to differences in study design, how other companies quantify or qualify eligibility criteria, and how results are recorded, among other distinguishing factors and uncertainties. Because we may be unaware of or may not adequately present various distinguishing factors and uncertainties, the comparisons set forth herein may not properly present such third-party data, which may differ materially from the data as presented here. Investors are encouraged to independently review third party data and should not rely on our presentation of such data (including any such data placed in comparison with the performance of palazestrant) as a single measure to evaluate our business.

The trademarks included herein are the property of the owners thereof and are used for reference purposes only. Such use should not be construed as an endorsement of such products.

# - We are on a mission to elevate patient care in breast cancer and beyond

Olema is a leader in developing therapies for endocrine driven-cancers with a mechanistically superior scientific approach that fully inactivates estrogen receptor signaling

## STRATEGIC PRIORITIES



### Palazestrant

Establish palazestrant as the best-in-class backbone therapy for ER+/HER2- breast cancer both as a monotherapy and in combination with other targeted anti-tumor agents



### OP-3136

Advance the clinical development of OP-3136, a potential best-in-class KAT6 inhibitor, in breast and other solid tumor cancers



### Pipeline

Further expand capabilities through drug discovery and development partnerships

Headquartered  
in San  
Francisco, CA

Offices in  
Cambridge, MA

Leadership with  
Deep Oncology  
Experience

~100  
Employees  
and Growing

Collaborations  
in Place with  
Key Strategic  
Partners

Potential  
Commercial  
Launch in 2027

Strong Capital  
Position with  
\$434.1M<sup>1</sup>

<sup>1</sup> Estimated cash, cash equivalents, and marketable securities as of December 31, 2024 (unaudited).

ER = estrogen receptor; HER2 = human epidermal growth factor receptor 2; KAT6 = lysine acetyltransferase 6

# — Strategy driven by leaders positioned to go the distance

Oncology and industry experts with track record of advancing programs from clinical to commercial

## Executive Committee



Sean Bohlen, M.D., Ph.D.  
President and CEO



Shane Kovacs  
Chief Operating and  
Financial Officer



Naseem Zojwalla, M.D.  
Chief Medical Officer



David Myles, Ph.D.  
Chief Discovery and  
Non-Clinical  
Development Officer



Julie Dexter  
Senior Vice President  
and Head of People

## Board of Directors

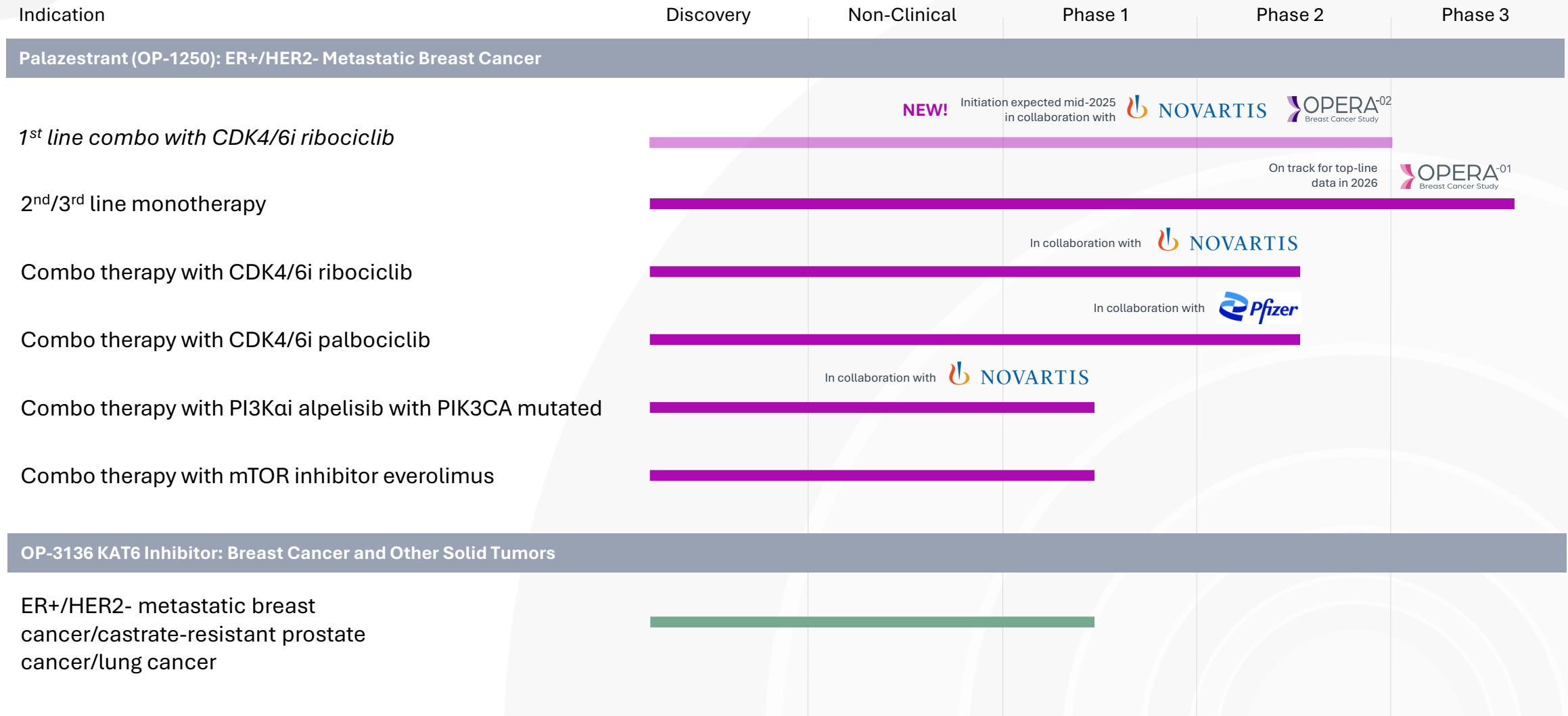
- Ian Clark  
Chairman of the Board
- Sean Bohlen, M.D., Ph.D.  
President and CEO
- Sandra Horning, M.D., FACP, FASCO
- Cindy Butitta
- Scott Garland
- Cyrus Harmon, Ph.D.
- Gorjan Hrustanovic, Ph.D.
- Yi Larson
- Andy Rappaport
- Graham Walmsley, M.D., Ph.D.

## Experience



# — Rapidly advancing clinical pipeline

Actively accruing patients in palazestrant mono and combo trials as OP-3136 enters the clinic





## 2024 ACHIEVEMENTS AND ANTICIPATED MILESTONES IN 2025 AND BEYOND

2024

- Continued accruing patients in the pivotal Phase 3 OPERA-01 clinical trial of palazestrant as a monotherapy in 2/3L metastatic breast cancer
- Presented OP-3136 non-clinical data at ENA 2024
- Announced new Novartis collaboration
- Presented palazestrant + ribociclib combination data at SABCS
- Received FDA clearance for OP-3136 Investigational New Drug application
- Initiated OP-3136 Phase 1 clinical trial

2025

- Advance patient accrual in the pivotal Phase 3 OPERA-01 clinical trial
- Initiate the pivotal Phase 3 OPERA-02 clinical trial of palazestrant in combination with ribociclib in 1L metastatic breast cancer
- Present new non-clinical data for OP-3136
- Present mature Phase 1b/2 palazestrant + ribociclib combination data at major medical meeting

2026

- Present initial data from the Phase 1 clinical trial of OP-3136
- Announce top-line results from the pivotal Phase 3 OPERA-01 clinical trial
- Submit New Drug Application for the potential approval of palazestrant as a monotherapy in 2/3L metastatic breast cancer
- Prepare for the potential U.S. commercial launch of palazestrant

2027

- Anticipated U.S. commercial launch of palazestrant



OUR PHASE 3 ASSET

# — Palazestrant

“Palazestrant is not an endocrine therapy where you need to wait six months to see a patient begin to derive benefit. We’ve seen some not only nice responses, but pretty quick responses—significant reduction of disease burden. And you know, **the patients feel great.**”

– Virginia Borges, M.D.  
Professor, Medicine-Medical Oncology  
University of Colorado  
Principal Investigator

# — What drives us: we are all impacted by breast cancer

The most common cancer diagnosed and the second leading cause of cancer death among women

1 in 8\*

Women in the U.S. will be diagnosed with  
invasive breast cancer in her lifetime

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~311k\*

Estimated women in the U.S. who were  
diagnosed with breast cancer in 2024

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~42k\*

Estimated women in the U.S. who died  
of metastatic breast cancer in 2024

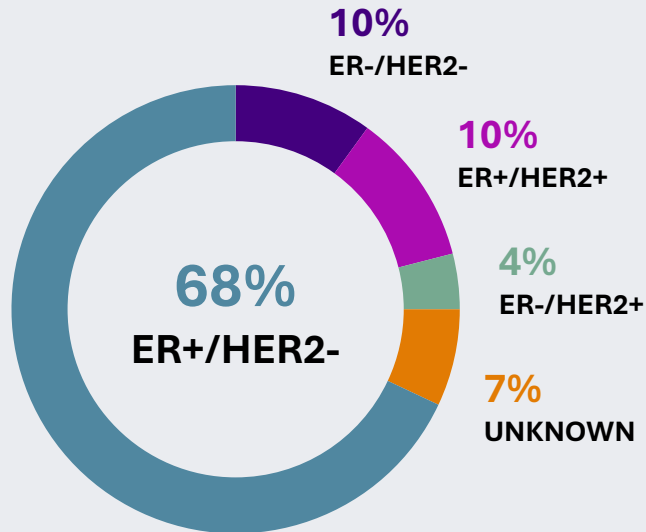




# — Today's therapies are insufficient to meet patient needs

Patient outcomes reflect limitations and discontinuations of currently available therapies

A majority of all breast cancers are estrogen receptor positive (ER+)\*



Current ER targeting agents have significant deficiencies

**AIs**  
**SERMs**  
**SERDs**

Common targeted therapies used in combination with an endocrine agent

- abemaciclib (CDK4/6i)
- palbociclib (CDK4/6i)
- ribociclib (CDK4/6i)
- alpelisib (PI3Kai)
- everolimus (mTORi)
- capivasertib (AKTi)
- inavolisib (PI3Kai)

- Incomplete ER antagonism
- Sub-optimal PK profile
- Limited CNS penetration
- Tolerability issues

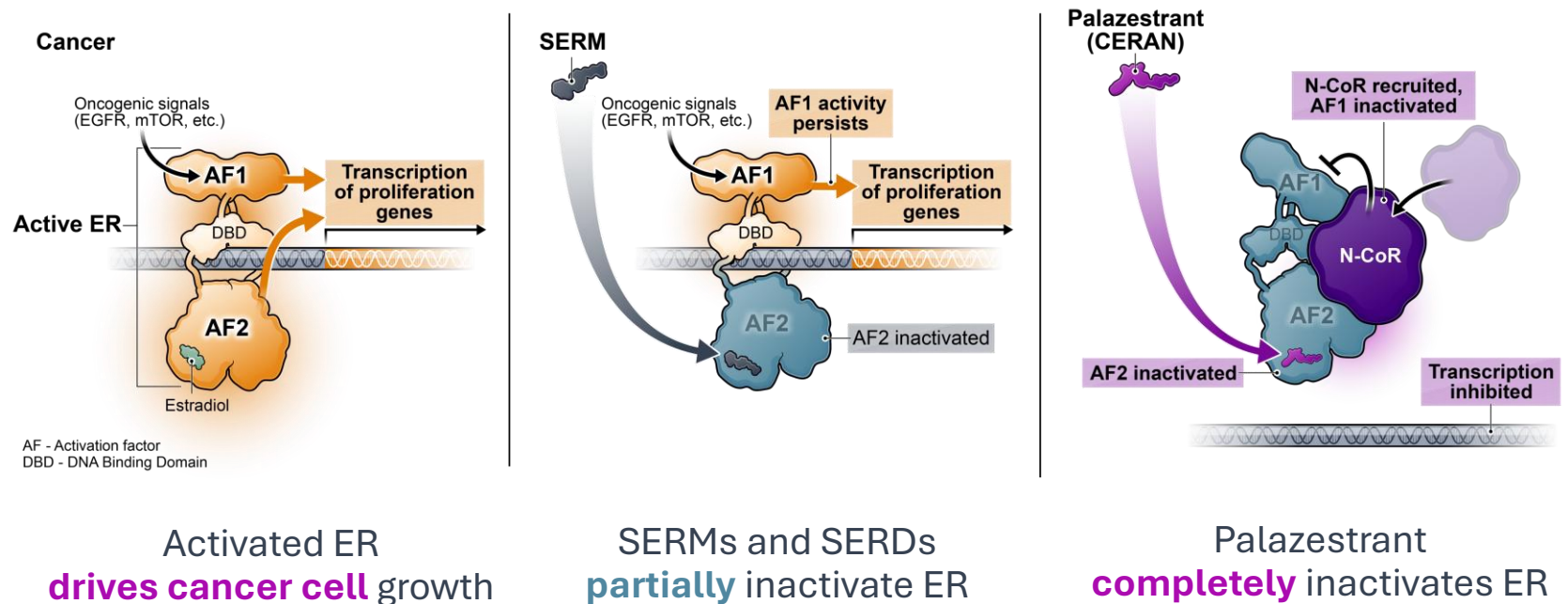
“Aromatase inhibitors are **life-saving** ... but **life-eroding** and really difficult to be on.”

– ER+/HER2- Stage 3A patient

# Palazestrant has the attributes of a potential therapeutic class leader

A differentiated oral CERAN/SERD targeting metastatic breast cancer with experience in over 400 patients to date

## Growth and Proliferation Mechanism Driving ER+ Breast Cancer



Palazestrant delivers what patients need

- Complete ER antagonism
- Once-daily oral delivery
- Favorable tolerability
- Combinability
- Robust tumor shrinkage
- Attractive PK profile
- CNS penetration

Our goal: help patients **feel better, longer**

# — Significant opportunity for palazestrant across the spectrum of care

Estimated >\$20B ER+/HER2- global metastatic breast cancer market<sup>1</sup>

2L/3L+  
ER+/HER2- MBC



Patients<sup>2</sup>

~150K



Duration of Therapy<sup>3</sup>

~2-12+ months



Global Market Potential<sup>4</sup>

\$5B+

1L  
ER+/HER2- MBC



Patients<sup>2</sup>

~115K



Duration of Therapy<sup>3</sup>

~6-36+ months



Global Market Potential<sup>4</sup>

\$10B+

# — Clinical development strategy to unlock the potential of palazestrant

Potential best-in-class backbone therapy designed to preserve and prolong a higher quality of life

## Establishing palazestrant as the backbone endocrine therapy of choice across the metastatic setting

2/3L+

### OPERA-01

- Ongoing 510-patient pivotal Phase 3 trial
- Monotherapy trial vs. SOC
- Phase 1/2 monotherapy data support potentially differentiated opportunity
- Top-line results expected 2026

1L

### OPERA-02

- Proposed ~1,000 patient pivotal Phase 3 trial
- Palazestrant in combination with ribociclib vs. SOC
- Phase 1/2 palazestrant + ribociclib combination data demonstrate no significant DDI and tolerability profile consistent with the FDA-approved label of ribociclib; efficacy maturing
- Successfully conducted FDA interactions
- Preparing for initiation in 2025

# — Palazestrant monotherapy Phase 2 data supports ongoing Phase 3 trial

Data demonstrate palazestrant is well-tolerated with favorable PK and differentiated efficacy profile



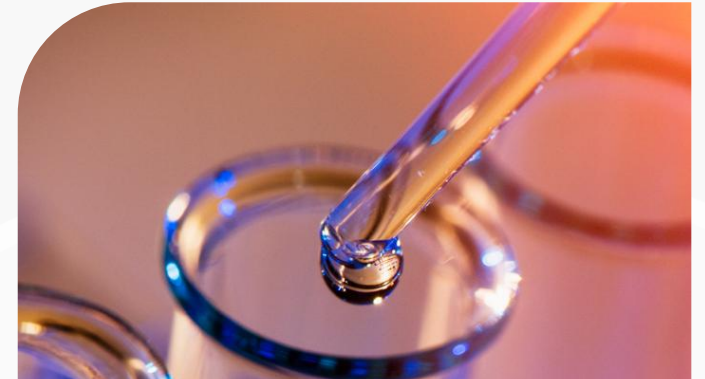
## Differentiated Efficacy Profile

- Median PFS of:
  - 7.3 months in 2/3L ±CT *ESR1*-mutant
  - 5.5 months in 2/3L ±CT *ESR1*-wild-type



## Favorable Pharmacokinetics

- High oral bioavailability with daily dosing
- Dose proportional exposure
- Long half-life supports once-daily dosing



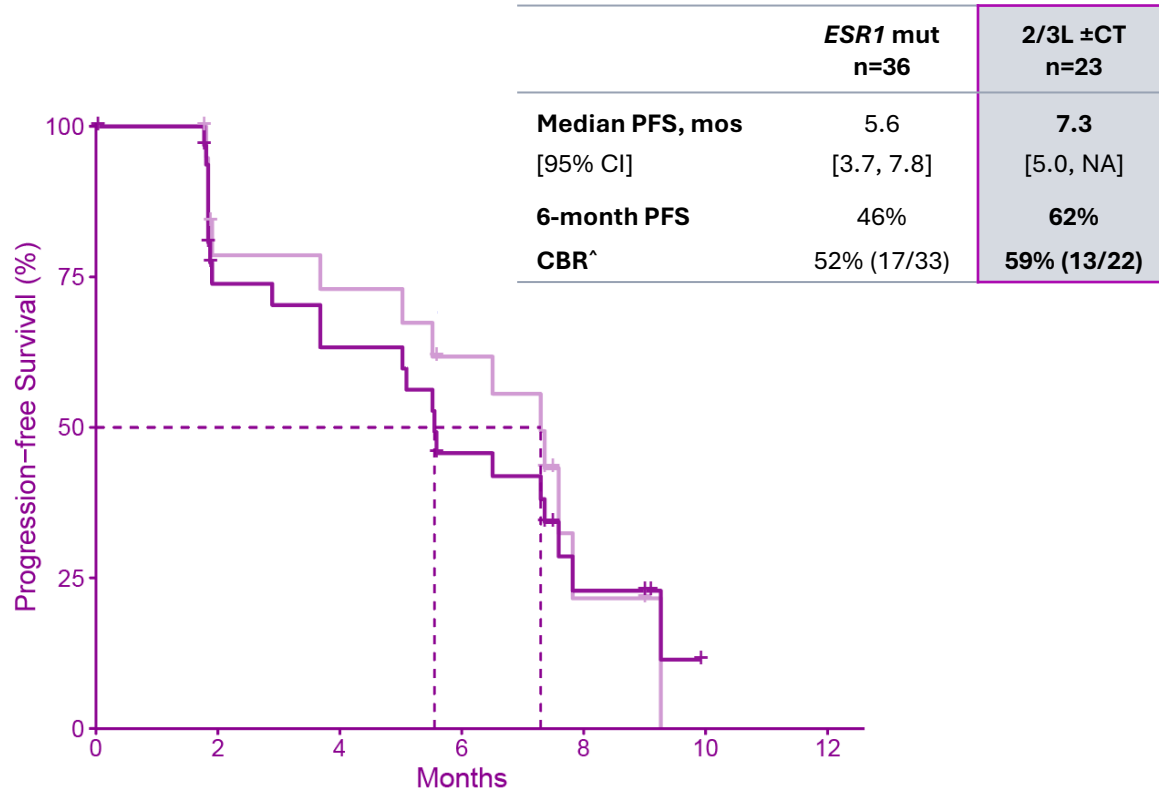
## Summary Safety

- Well-tolerated
- Most AEs were low grade (1/2)

# – Compelling palazestrant Phase 2 data supports ongoing OPERA-01 trial

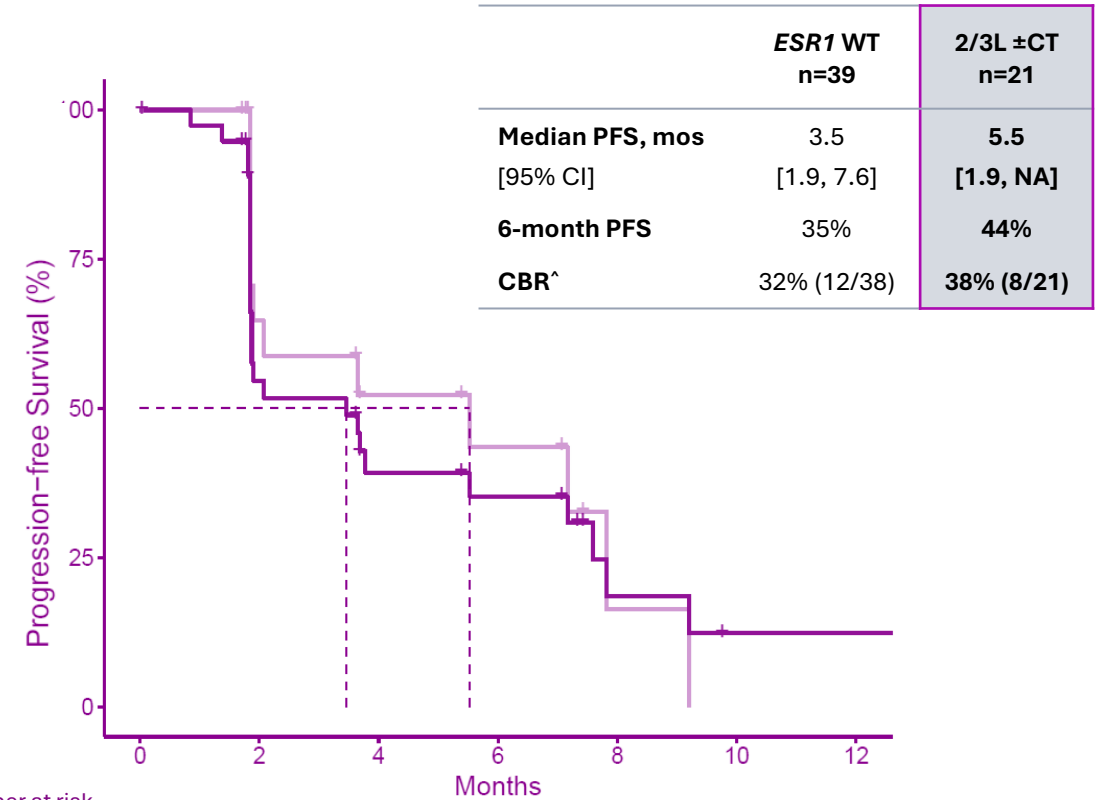
7.3 months mPFS in *ESR1*-mutant; 5.5 months in wild-type for EMERALD-eligible 2/3L ± CT Patients\*

**Patients with *ESR1* Mutation<sup>1</sup>**



Number at risk		0	2	4	6	8	10	12
All	36	21	18	12	4	0	0	
2/3L ±CT	23	14	13	10	2	0	0	

**Patients with *ESR1* Wild-Type<sup>2</sup>**



Number at risk		0	2	4	6	8	10	12
All comers	39	19	11	9	3	1	1	
2/3L+/-CT	21	11	7	5	1	0	0	

\* **NOTE: This analysis is the aggregation of results across independent studies. There are risks inherent in conducting cross-trial comparisons. Refer to further disclaimers on slide 2.**

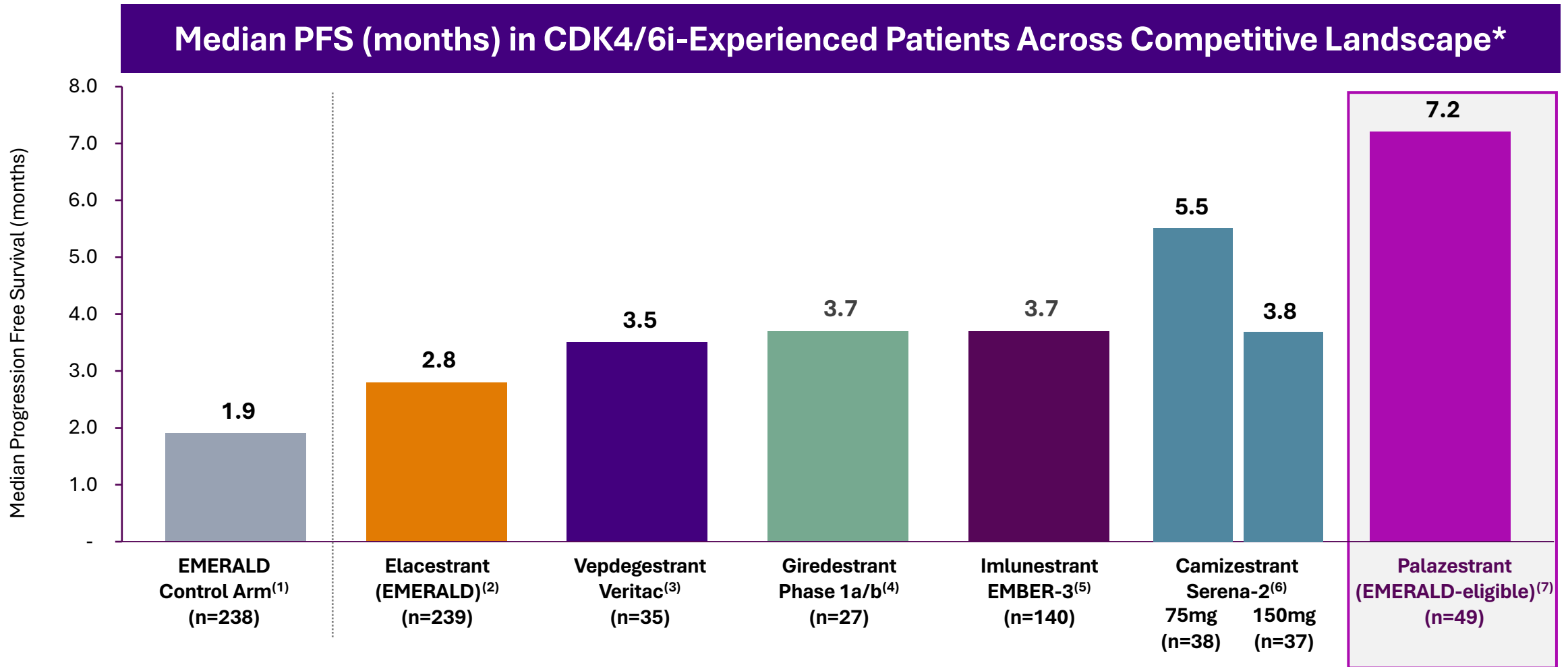
<sup>1</sup> Palazestrant Phase 2 dataset with *ESR1* mutations detected at baseline. <sup>2</sup> Palazestrant Phase 2 dataset with *ESR1* mutations *not* detected at baseline.

<sup>^</sup> Clinical Benefit Rate (CBR) is defined as the proportion of subjects who remained on OP-1250 treatment through at least 24 weeks with a confirmed CR or PR, or stable disease. The CBR analysis includes patients who received at least one evaluable post-baseline radiographic assessment. Data cut-off as of July 7, 2023.

2/3L = second/third line; ± CT = plus/minus chemotherapy; CBR = clinical benefit rate; CI = confidence interval; *ESR1* = estrogen receptor 1 gene; mos= months; mPFS = median progression-free survival; mut = mutation; NA = not applicable; WT= wild-type

# Palazestrant in the competitive landscape: best-in-class potential

Median progression-free survival across CDK4/6i-experienced patient populations\*



\*NOTE: This analysis is the aggregation of results across independent studies. There are risks inherent in conducting cross-trial comparisons. Refer to further disclaimers on slide 2.

<sup>1</sup> SABCS 2021 EMERALD data. Median PFS in control arm. Note: ORR of 4.4% (8/182). <sup>2</sup> SABCS 2021 EMERALD data. Median PFS in elacestrant 400 mg dose. Note: ORR of 4.5% (8/179). <sup>3</sup> SABCS 2023 Veritac data. Median PFS at 200 mg dose across all patients. Note: One cPR at 200 mg dose. <sup>4</sup> ASCO 2021 Phase 1a/b giredestrant results. Median PFS estimated based on subset of giredestrant patients at 30 mg dose with CDK4/6i experience (27 of 41). Note: Six cPRs at 30 mg were all in CDK4/6i-naïve patients. <sup>5</sup> SABCS 2024 EMBER data. Median PFS in CDK4/6i-experienced patients. <sup>6</sup> SABCS 2022 Serena-2 data. Median PFS in CDK4/6i-experienced patients at 75 mg (5.5 months) and 150 mg (3.8 months). Represents <2 prior lines of ET-only +/- CT. Note: Serena-1 data at 75 mg dose had 2 PRs out of 22 patients; both were CDK4/6i naïve. <sup>7</sup> Emerald-eligible patient population from palazestrant Phase 2 dataset (2/3L +/-CT) with ESR1 mutations detected at baseline.

CDK4/6i = cyclin-dependent kinase 4/6 inhibitor; PFS = progression-free survival

# — OPERA-01 Phase 3 monotherapy trial designed to show superior efficacy in *ESR1* mutant and/or *ESR1* wild-type patients

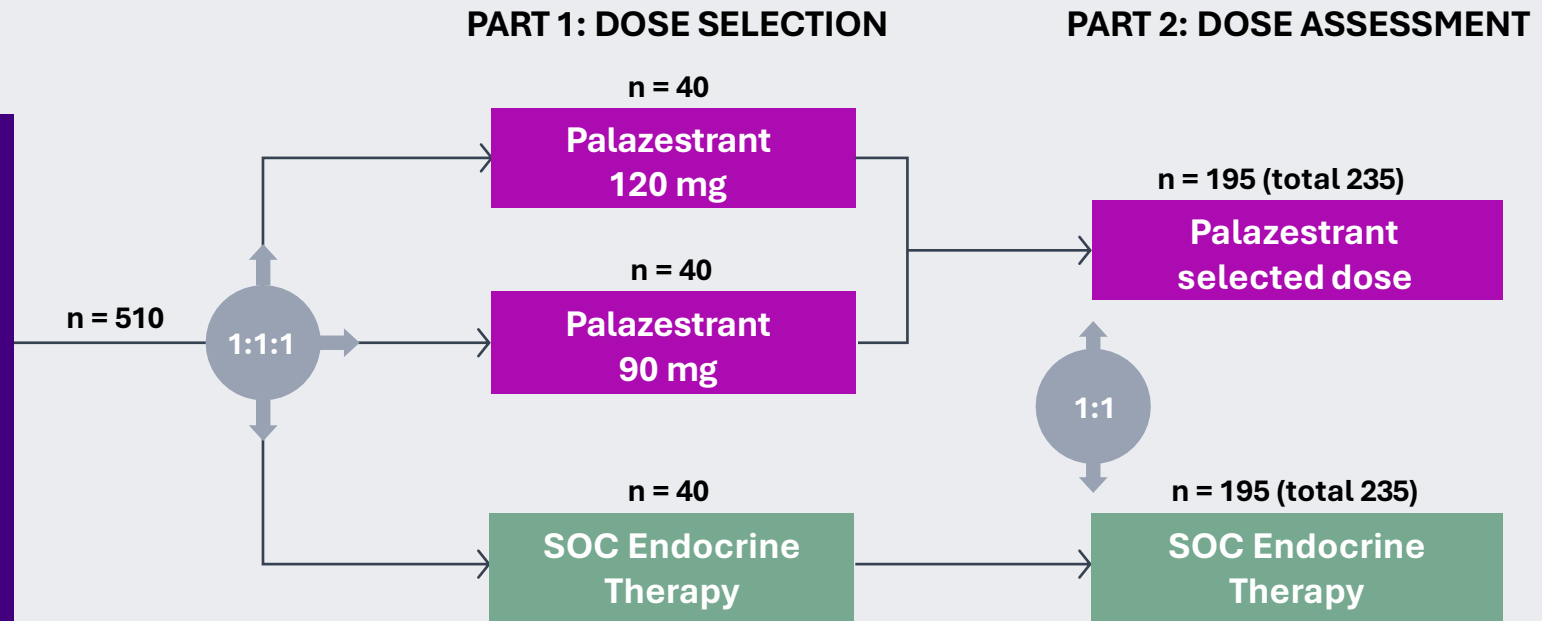


## INCLUSION CRITERIA

- 1-2 prior lines of endocrine therapy
- Prior treatment with a CDK4/6 inhibitor in the advanced setting
- No prior chemotherapy
- Minimum 6 months on last endocrine therapy

## STRATIFICATION

1. Visceral metastasis: yes vs no
2. Prior ET lines: 1 vs 2
3. *ESR1* mut vs *ESR1* mut-nd



## STUDY ENDPOINTS

**Primary:** PFS (BIRC) in *ESR1* mut and *ESR1* mut-nd

**Secondary:** OS (key) in *ESR1* mut and *ESR1* mut-nd, PFS (Investigator) and ORR/CBR/DOR (BIRC, Investigator) in *ESR1* mut, *ESR1* mut-nd, and all patients, Safety, PK, and Health-Related PROs

Study initiated in 4Q 2023. Results expected in 2026.

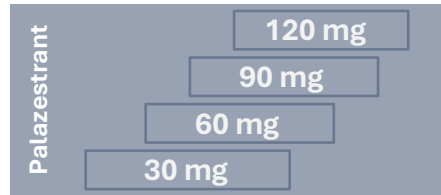


# Palazestrant demonstrates combinability with other targeted agents in frontline and later lines of therapy

## DOSE ESCALATION

## DOSE EXPANSION

ER+/HER2- MBC  
(CDK4/6i naïve or previously treated)



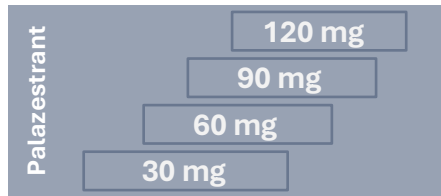
+

Ribociclib  
600 mg



Palazestrant  
+  
Ribociclib

ER+/HER2- MBC  
(CDK4/6i naïve or previously treated)



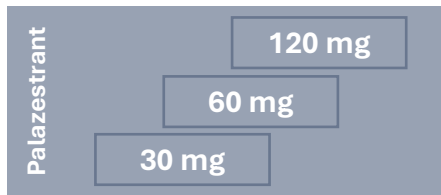
+

Palbociclib  
125 mg



Palazestrant  
+  
Palbociclib

ER+/HER2- MBC  
w/ PIK3CA  
mutation



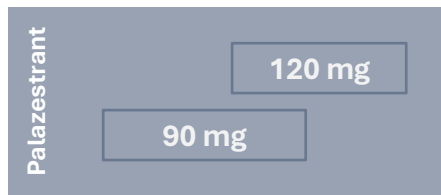
+

Alpelisib  
300/250 mg



Palazestrant  
+  
Alpelisib

ER+/HER2- MBC  
(CDK4/6i naïve or previously treated)



+

Everolimus  
10 mg



Palazestrant  
+  
Everolimus

Primary objectives: Pharmacokinetics, safety and tolerability, identify RP2D of palazestrant for combination with either ribociclib, palbociclib, alpelisib or everolimus.  
Secondary objectives: ORR (CR + PR), CBR (CR + PR + SD ≥24 weeks)

Primary objectives: Safety, tolerability and antitumor activity of palazestrant at RP2D in combination with either ribociclib, palbociclib, alpelisib or everolimus

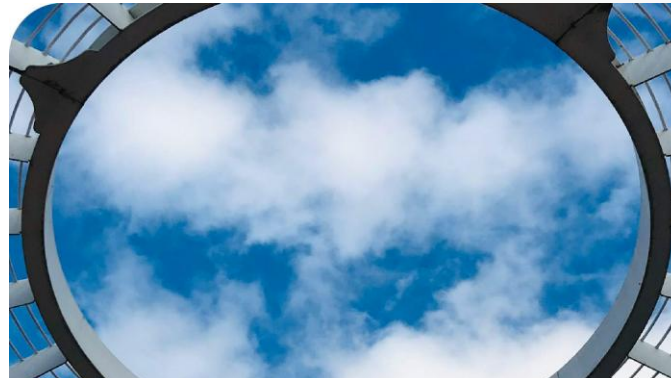
# — Palazestrant + ribociclib Phase 2 data supports planned Phase 3 trial

Palazestrant + ribociclib combination demonstrated promising clinical activity, a safety profile consistent with ribociclib + ET, and favorable tolerability



## Differentiated Efficacy Profile

- Six-month PFS rate of:
  - 73% in all patients
  - 68% in patients with prior CDK4/6i
  - 81% in *ESR1*-mutant patients
  - 70% in *ESR1* wild-type patients



## Favorable Pharmacokinetics

- No drug-drug interaction; palazestrant did not affect ribociclib drug exposure
- All patients received the combination with the full and approved dose of 600mg of ribociclib



## Summary Safety

- Overall safety profile was consistent with the established safety profile of ribociclib 600 mg + AI

# — Well tolerated with no DLTs; safety profile consistent with ribociclib + ET

## Treatment-emergent AEs

TEAEs in ≥25% of patients	Palazestrant + Ribociclib**			MONALEESA-2* Letrozole + Ribociclib†		
	All grades‡	(n = 62) Grade 3	Grade 4	All grades	(n = 334) Grade 3	Grade 4
Neutropenia§	51 (82%)	28 (45%)	6 (10%)	93%	49%	11%
Nausea	49 (79%)	2 (3%)	0%	52%	2%	0%
Fatigue	37 (60%)	2 (3%)	0%	37%	2%	<1%
Diarrhea	31 (50%)	2 (3%)	0%	35%	1%	0%
Anemia	27 (44%)	1 (2%)	0%	57%	2%	0%
WBC decrease	26 (42%)	10 (16%)	1 (2%)	93%	31%	3%
Constipation	24 (39%)	0%	0%	25%	1%	0%
Creatinine increased	20 (32%)	0%	0%	20%	1%	0%
Vomiting	20 (32%)	1 (2%)	0%	29%	4%	0%
ECG QT prolonged	19 (31%)	3 (5%)	0%	43%¶	8%¶	NR
Arthralgia	18 (29%)	0%	0%	27%	1%	NR
Lymphocyte count decreased	16 (26%)	5 (8%)	1 (2%)	51%	12%	2%
Cough	16 (26%)	0%	0%	20%	0%	0%
LDH increased	16 (26%)	0%	0%	NR	NR	NR

- No patients discontinued only palazestrant due to a treatment-emergent AE; 4 patients discontinued both treatments due to a TEAE; 2 patients discontinued ribociclib but stayed on palazestrant
- 30 (48%) patients still on treatment at the data cut-off
- Overall safety and tolerability profile consistent with ribociclib + endocrine therapy
- No DLTs were observed during dose escalation and the maximum tolerated dose was not reached

Data cutoff date: November 11, 2024. Data shown are n or n (%).

\*NOTE: This analysis is the aggregation of results across independent studies. There are risks inherent in conducting cross-trial comparisons and results should be interpreted with caution. Refer to further disclaimers on slide 2.

\*\*Includes 3 patients at each of 30 mg and 60 mg palazestrant and 56 patients at 120 mg palazestrant in combination with 600 mg ribociclib. †Adverse reactions reported in ≥10% of patients who received ribociclib plus letrozole in the MONALEESA-2 study. (KISQALI (ribociclib).

Prescribing information. Novartis; 2022; Hortobagyi, 2016) ‡Two subjects experienced Grade 5 AEs, heart failure and depressed level of consciousness not related to study drugs but disease progression. §Combined term includes neutropenia, decreased neutrophil count and febrile

neutropenia. ¶These values were taken from MONALEESA-2 lab abnormalities data; source: KISQALI (ribociclib). Prescribing information. Novartis; 2022. \*Ribociclib + fulvestrant in MONALEESA-3 per the Ribociclib Approval Package (NUMBER:209092Orig1s001, June 2018); ribociclib

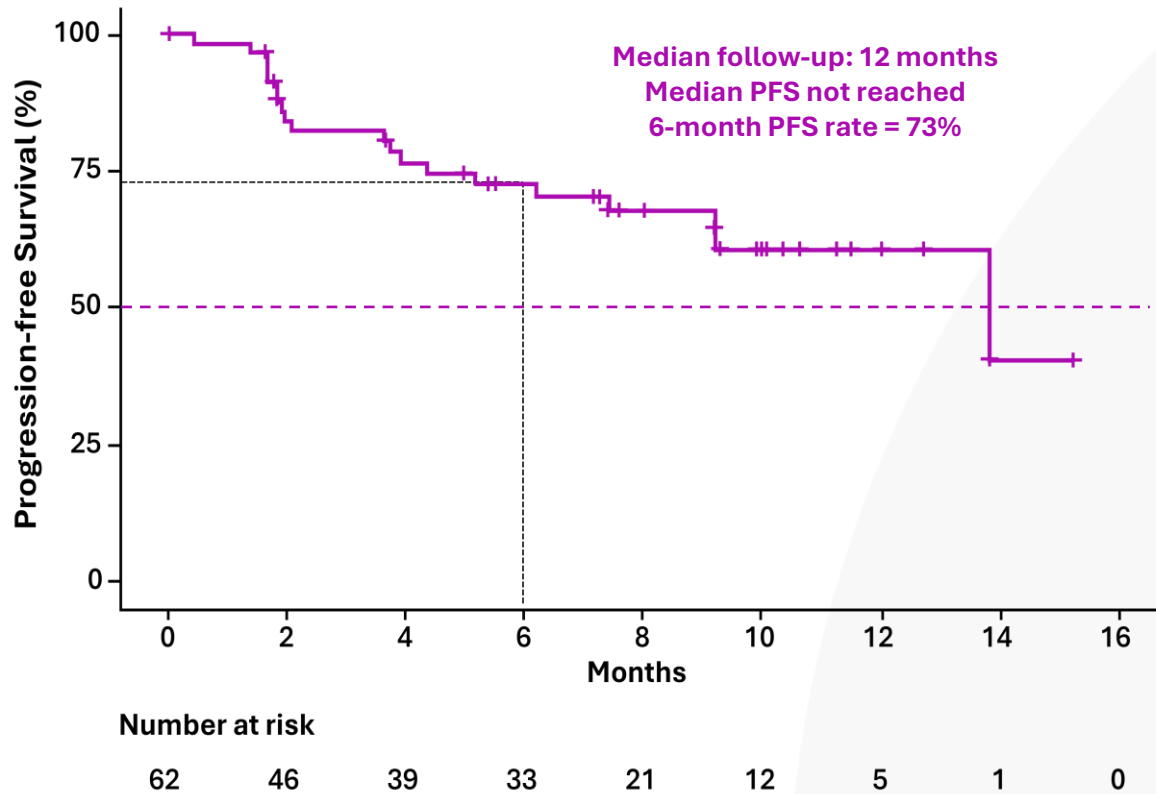
+ non-steroidal aromatase inhibitors in MONALEESA-7: all grade QTcF prolongation was 46.5% (Grade 2, 5.3%; Grade 3, 9%). Aggregate analysis (n=1054 patients).

AE = adverse event; DLTs = dose-limiting toxicity; ET = endocrine therapy; NR = not reported; TEAEs = treatment-emergent adverse events; WBC = white blood cell

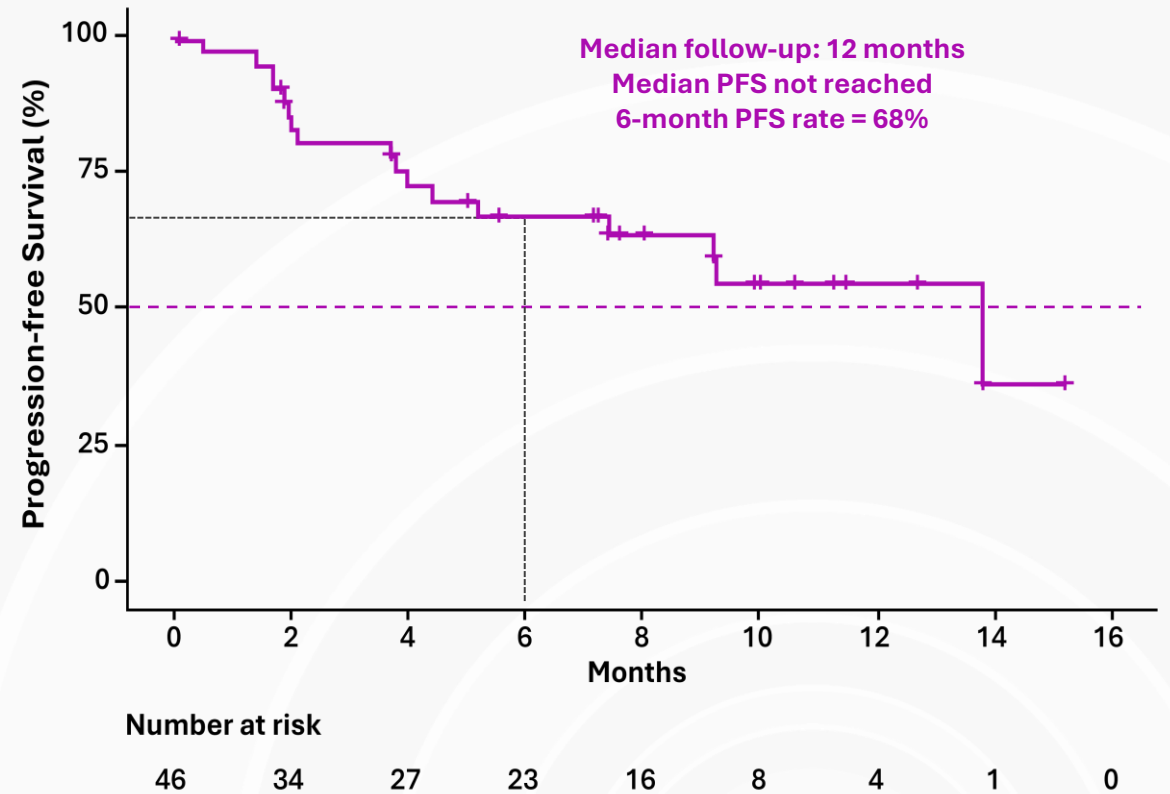
# — Six-month PFS rate of 73% in all patients, 68% in those with prior CDK4/6i

Median follow-up of 12 months; median PFS not yet reached; 48% of patients remain on study

**All patients (N=62)**

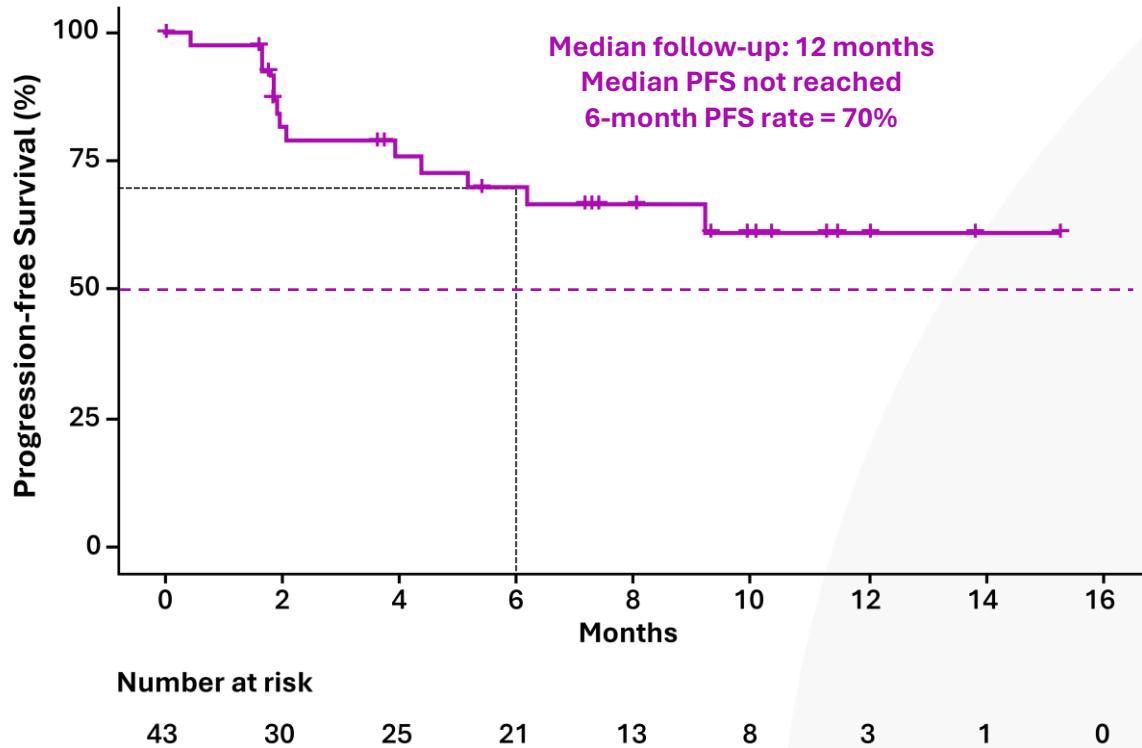


**Patients with prior CDK4/6i plus ET (N=46)**

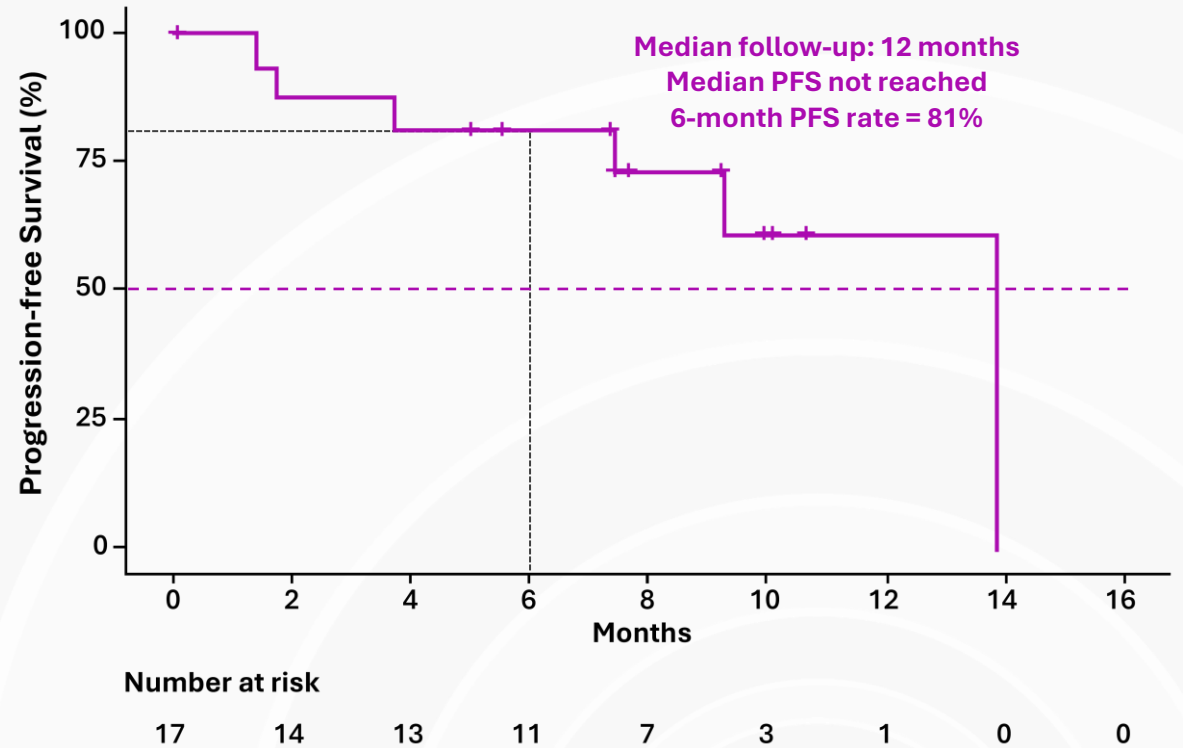


— Six-month PFS rate of 81% in *ESR1*-mutant patients, 70% in *ESR1* wild-type  
 Median follow-up of 12 months; median PFS not reached; sustained efficacy regardless of *ESR1* status

*ESR1* wild-type (n=43)



*ESR1*-mutant (n=17)

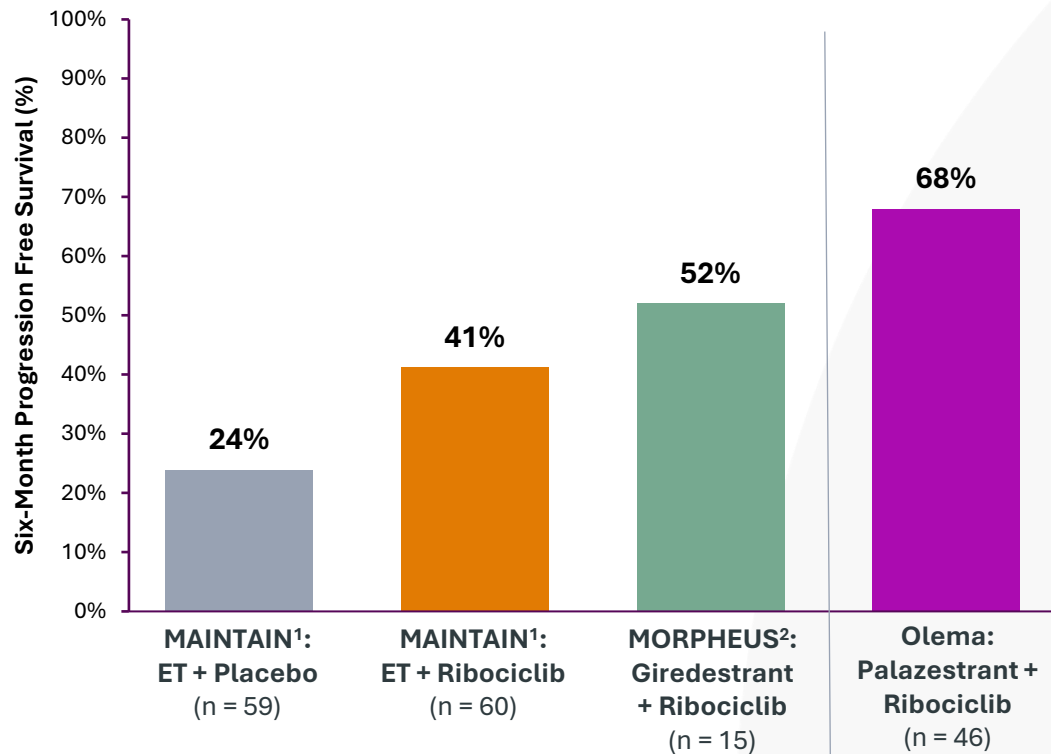


# — Efficacy comparison in 2/3L patients vs. competitive landscape

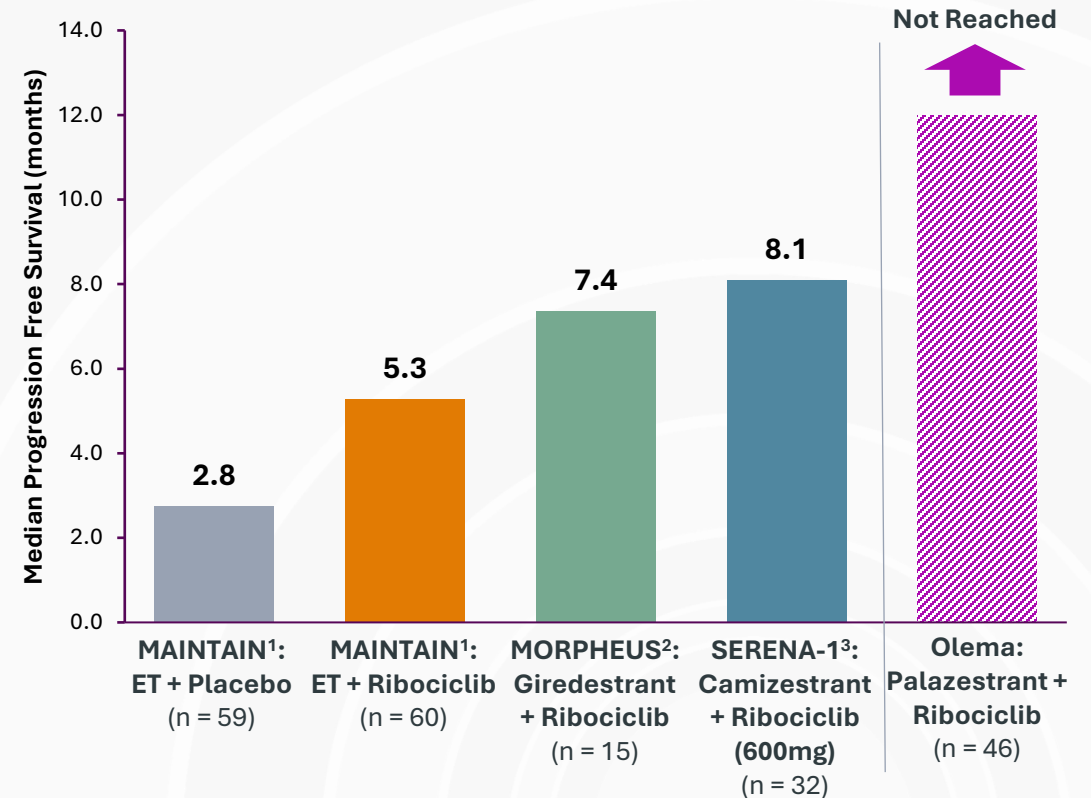
MAINTAIN study of ribociclib plus ET after CDK4/6i progression serves as best clinical benchmark\*

## Interim efficacy signals for palazestrant in combination with ribociclib

**Six-Month PFS Rate\*  
in CDK4/6i pre-treated patients**



**Median PFS (months)\*  
in CDK4/6i pre-treated patients**



\* NOTE: This analysis is the aggregation of results across independent studies. There are risks inherent in conducting cross-trial comparisons and results should be interpreted with caution. Refer to further disclaimers on slide 2.  
Data cutoff date: November 11, 2024.

<sup>1</sup> ASCO 2022 MAINTAIN data; <sup>2</sup> ASCO 2023 MORPHEUS data; <sup>3</sup> SABCS 2024 SERENA-1 data Parts K-L, ribociclib 600mg dose arm  
CDK4/6i = cyclin-dependent kinase 4/6 inhibitor; ESR1-mut = ESR1-mutant; ESR1-wt = ESR1 wild-type; ET = endocrine therapy; PFS = progression-free survival

# – Proposed OPERA-02 1L Phase 3 pivotal trial in combination with ribociclib

~1,000-patient trial vs. standard of care; initiation expected in 2025



## INCLUSION CRITERIA

- ER+/HER2- MBC
- Any menopausal status
- No prior systemic therapy for MBC
- No prior CDK4/6 inhibitor for MBC
- Evaluable disease (measurable or non-measurable)
- Patients who relapsed within 2 years of adjuvant endocrine therapy are not eligible

## STRATIFICATION

- Menopausal status: post vs. pre/male
- Visceral metastasis: yes vs. no
- *De novo* metastatic disease vs. recurrent disease after adjuvant ET

n ≈ 1,000

1:1

Palazestrant +  
ribociclib

Letrozole +  
ribociclib

## Study Endpoints

**Primary:** PFS (BIRC)

**Secondary:** OS (key)  
PFS (Investigator)  
ORR/CBR/DOR (BIRC, Investigator)  
Safety  
PK  
Health-related PROs




In collaboration with



# — Building momentum for palazestrant as a potential backbone therapy

Registration-directed pivotal Phase 3 clinical trials underway and planned

## Key factors driving palazestrant momentum

-  • Complete inhibition of key ER+ receptors
-  • Mono and combo potential
-  • Experience in 400+ patients and counting

## OPERA<sup>-01</sup> Breast Cancer Study

- 510-patient 2/3L Phase 3 monotherapy trial vs. standard of care
- Currently enrolling
- Visit [opera01study.com](https://opera01study.com) for more information

## OPERA<sup>-02</sup> Breast Cancer Study

- ~1,000-patient 1L Phase 3 combination trial with ribociclib vs. standard of care
- Planned initiation in mid-2025



# — Planning for palazestrant U.S. commercial launch in 2027

Initial launch anticipated in 2/3L setting with potential 1L launch following positive OPERA-02 trial



Annual U.S. incidence estimated at **~40K\*** patients



Commercial launch planning beginning in 2025



Early commercial leadership build in 2026



Establishing manufacturing supply and distribution for commercial use



Anticipated targeted field force of **~75–100 reps** to cover U.S. breast oncologists



U.S. market potential of **\$3-5B\*** in 2/3L setting



Potential Best-in-Class KAT6 Inhibitor

# — OP-3136

“Building on our earlier studies that showed compelling single agent activity for OP-3136, this new data demonstrates the potential for OP-3136 in combination with palazestrant, with strong tumor growth inhibition and regression relative to combinations with fulvestrant. Taken together, these data reinforce our belief in the potential of OP-3136 as an exciting new therapy for breast and other cancers.”

– David C. Myles, Ph.D.  
Chief Discovery and Non-Clinical Development Officer  
Olema Oncology

## — OP-3136: Olema's KAT6 inhibitor\*

An exciting new and validated target<sup>^</sup> for the treatment of ER+/HER2- metastatic breast cancer

Highly potent and selective against KAT6A/B

Orally bioavailable with high levels of free drug exposure

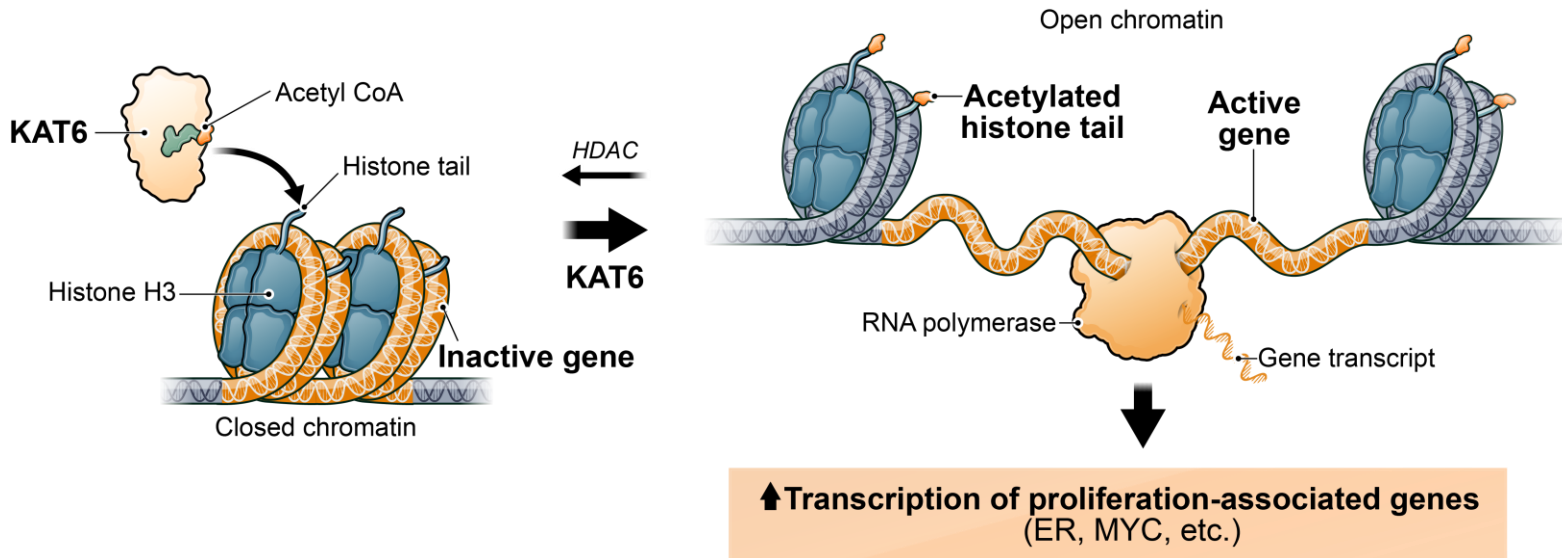
OP-3136 synergizes with palazestrant and CDK4/6 inhibitors in preclinical models

New data presented at the ENA meeting in October 2024

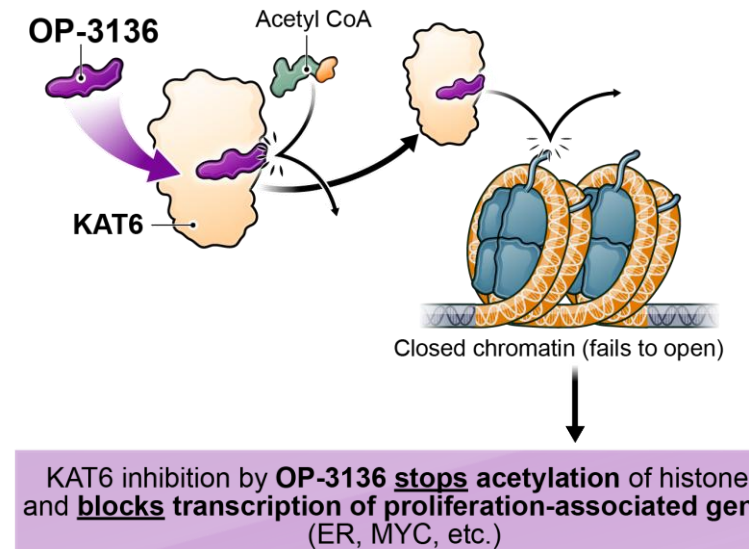
IND cleared by FDA and Phase 1 clinical trial is recruiting patients

# – OP-3136 mechanism of action

## KAT6 acetylates chromatin enabling transcription and proliferation



## OP-3136 prevents transcription



- KAT6 is a clinically validated target<sup>1</sup> and overexpression correlated with worse clinical outcomes in ER+ breast cancer<sup>2</sup>
- KAT6 inhibition downregulates genes involved in **estrogen receptor signaling** and other signaling pathways<sup>3</sup>
- Inhibition regulated gene expression through blockade of acetylation of histones

<sup>1</sup> Sommerhalder D, et al. First-in-human phase 1 dose escalation study of the KAT6 inhibitor PF-07248144 in patients with advanced solid tumors. JCO. 2023. 41(16)1054-1054.

<sup>2</sup> Yu L, et al. Identification of MYST3 as a novel epigenetic activator of ERα frequently amplified in breast cancer. Oncogene. 2017 May 18;36(20):2910-2918.

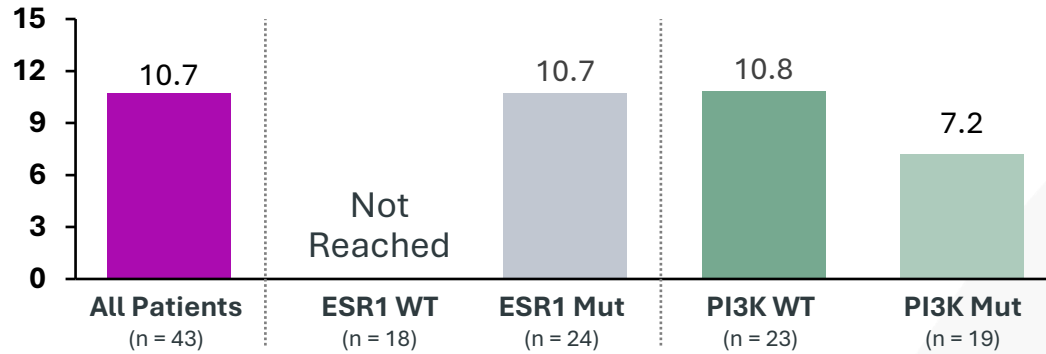
<sup>3</sup> Sharma S, et al. Discovery of a highly potent, selective, orally bioavailable inhibitor of KAT6A/B histone acetyltransferases with efficacy against KAT6A-high ER+ breast cancer. Cell Chemical Biology. 30, 1–20.

Note: Olema KAT6 inhibitors discovered in collaboration with Aurigene.

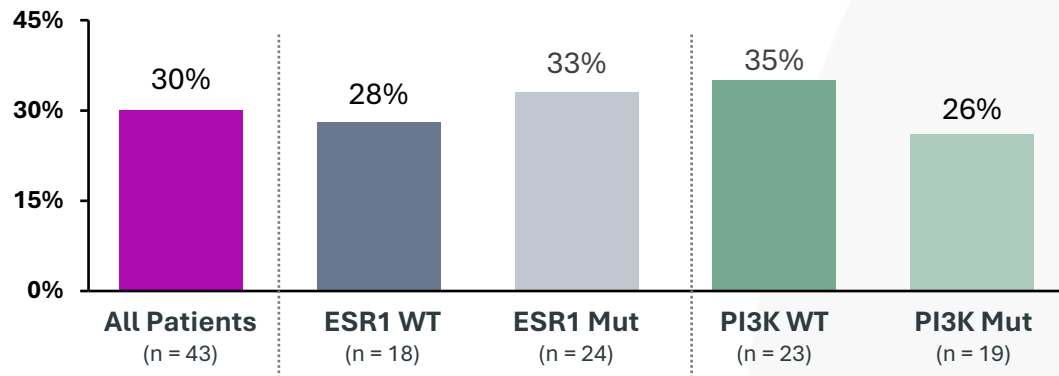
AR = androgen receptor; ER = estrogen receptor; ER+ = estrogen receptor positive; KAT6i = lysine acetyltransferase 6 inhibitor

# — KAT6i validated as an active new target in metastatic breast cancer\*

## PF-8144 Median PFS with ET<sup>1</sup>



## PF-8144 Overall Response Rate (ORR) with ET<sup>1</sup>



First-in-human clinical proof of concept for KAT6 inhibitor from Pfizer has important implications:

- **Validates KAT6 as an active new target for the treatment of metastatic breast cancer**
  - Activity demonstrated regardless of mutation status (*ESR1* and PI3K/AKT/PTEN)
- **Demonstrates promising avenue to have a significant impact on future standard of care**
  - Combination of KAT6 inhibitor + ET demonstrated synergistic activity, consistent with preclinical observations
- **Highlights opportunity for potential best-in-class KAT6 inhibitor OP-3136 in combination with potential best-in-class CERAN palazestrant**

\* NOTE: Incorporates publicly-available third-party data that we have not independently verified. These results should be interpreted with caution. Such third-party data has been pulled by us from publicly-available sources for supplemental informational purposes, only. Refer to further disclaimers on slide 2.

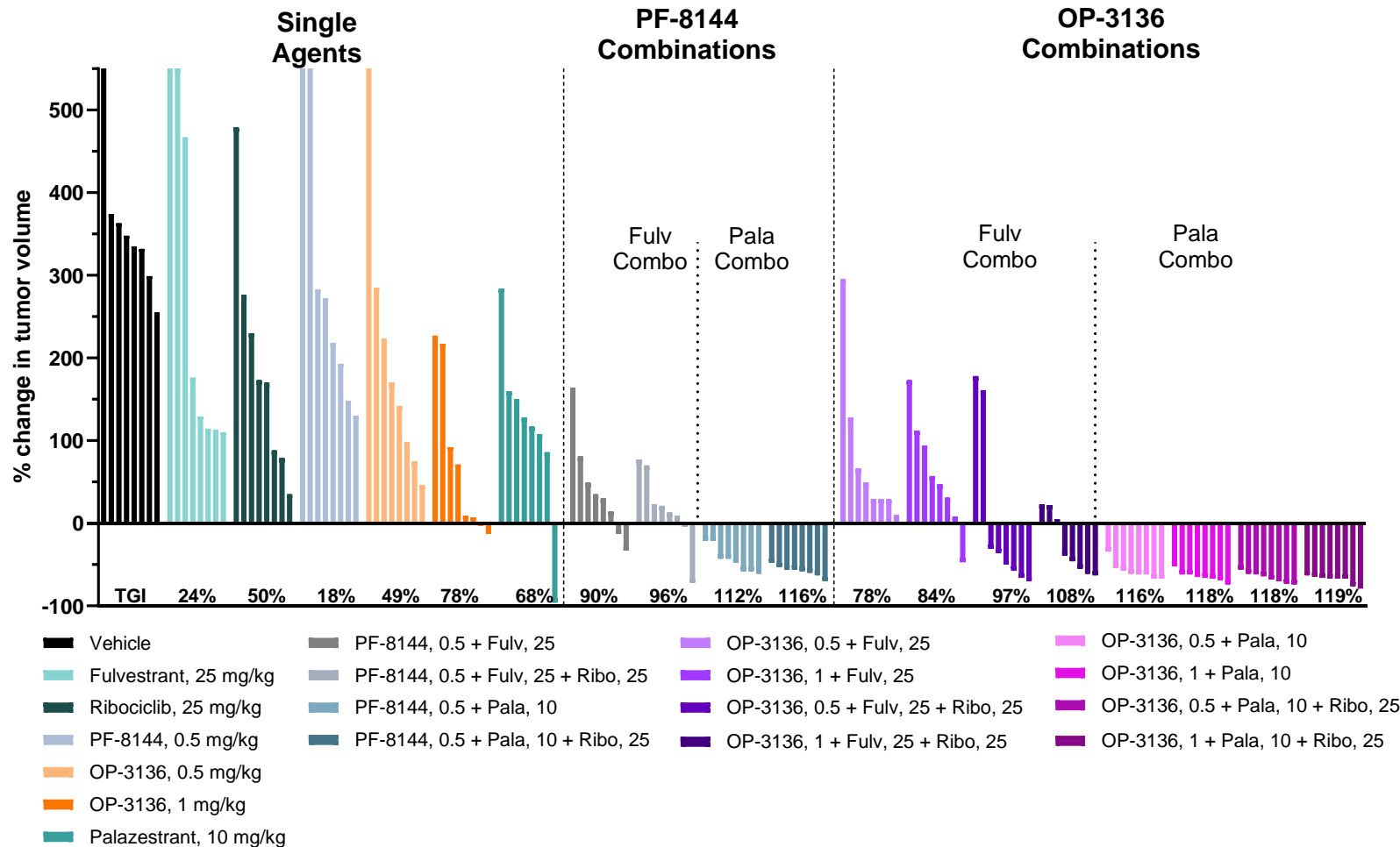
<sup>1</sup> Mukohara T, et al. Inhibition of lysine acetyltransferase KAT6 in ER+/HER2- metastatic breast cancer: a phase 1 trial. *Nat Med* (2024).

CERAN = complete estrogen receptor antagonist; ERS1 = estrogen receptor 1 gene; ERS1 Mut = estrogen receptor 1 mutant; ESR1 WT = estrogen receptor 1 wild-type; ET = endocrine therapy; KAT6i = lysine acetyltransferase 6 inhibitor; PI3K Mut = phosphatidylinositol 3-kinase mutant; PI3K WT = phosphatidylinositol 3-kinase wild-type; PFS = progression-free survival

# OP-3136 demonstrates synergistic activity in combination with palazestrant

OP-3136 + palazestrant combinations appear superior to OP-3136+fulvestrant combinations

Waterfall Plot (T47D CDX model)

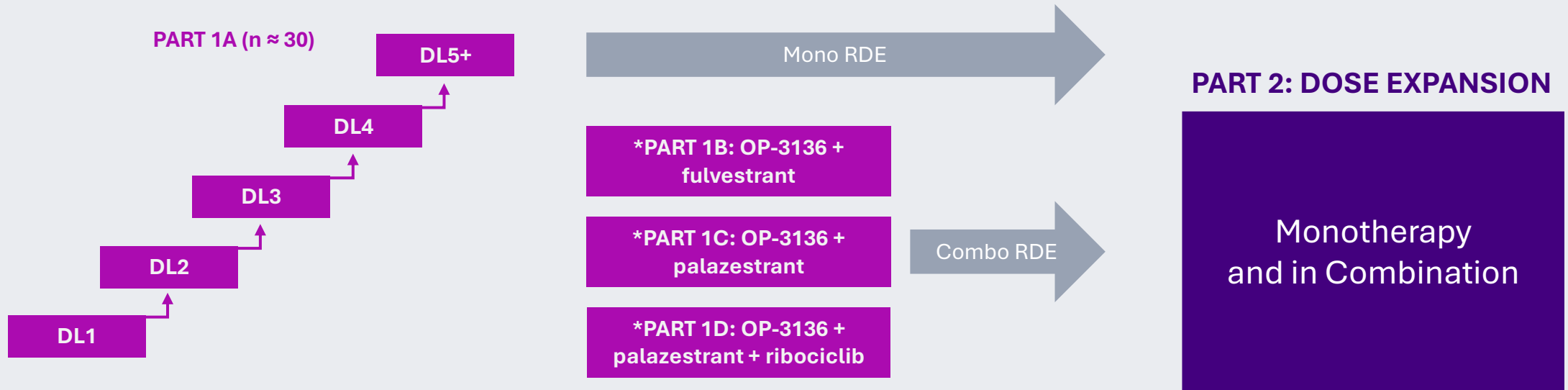


- Palazestrant in combination with either OP-3136 or PF-8144 resulted in strong tumor regression relative to fulvestrant combinations
- OP-3136 and palazestrant combinations showed significantly improved anti-tumor efficacy compared to PF-8144 in combination with fulvestrant
- All OP-3136 combinations were well tolerated, with no significant changes in body weight and no mortality

# — OP-3136 Phase 1 study design

IND cleared by FDA and Phase 1 clinical trial is recruiting patients

## PART 1: DOSE ESCALATION



**Primary objectives:** Safety and tolerability, RDE (monotherapy + combination)  
**Secondary objectives:** PK, ORR (CR + PR), CBR (CR + PR + SD ≥24 weeks), DOR

### KEY ELIGIBILITY CRITERIA

- ER+/HER2- mBC (or mCRPC or mNSCLC for PART 1A)
- Post-SOC (PART 1A)
- At least 1 prior line with CDK4/6i + ET (PART 1B/1C/1D)

References: 1. Mukohara T, et al. Inhibition of lysine acetyltransferase KAT6 in ER+ HER2- metastatic breast cancer: a phase 1 trial. Nat Med (2024).

\* Cohort to be added in the protocol amendment.

CBR = clinical benefit rate; CDK4/6i = cyclin dependent kinase 4/6 inhibitor; CR = complete response; DL = dose level; DOR = duration of response; ER+ = estrogen receptor positive; ET = endocrine therapy; mut = mutation; HER2- = mCRPC = metastatic castrate resistant prostate cancer; MBC = metastatic breast cancer; mNSCLC = metastatic non-small cell lung cancer; ORR = objective response rate; PK = pharmacokinetics; PR = partial response; RDE = recommended dose for expansion; SD = stable disease



Why Olema?

— A Compelling  
Late-Stage  
Opportunity in  
Breast Cancer  
and Beyond



# — Olema: a compelling late-stage opportunity in breast cancer and beyond

Changing the treatment paradigm for endocrine-driven cancers

1. Palazestrant anchors Olema's breast cancer program as a potential backbone therapy for metastatic breast cancer
  - Highly differentiated as first oral CERAN/SERD endocrine agent
  - Ongoing 2/3L OPERA-01 Phase 3 trial on track for top-line data in 2026
  - Planned 1L OPERA-02 Phase 3 trial in combination with ribociclib enabled; initiation expected in 2025
  - Mature Phase 1b/2 palazestrant + ribociclib efficacy data to be presented at major medical meeting in 2025
  - Go-to-market strategy for potential U.S. launch in 2027
2. OP-3136 expands pipeline with novel and validated KAT6 target
  - IND cleared by FDA; Phase 1 clinical trial recruiting patients
3. Well-capitalized with \$434.1M<sup>1</sup>



# Thank You

— Advancing medicines for  
breast cancer and beyond

