Olema ONCOLOGY

Corporate Overview

# Advancing medicines for breast cancer and beyond

April 2026

# Forward-looking statements and legal disclaimer

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 “aim,” “anticipate,” “aspire,” “believe,” “estimate,” “expect,” “goal,” “intend,” “may,” “milestone,” “plan,” “potential,” “priority,” “project,” “will,” and similar expressions are intended to identify forward-looking statements, although 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, our capital and other financial results, our strategy, market size and opportunity for palazestrant (OP-1250) and OP-3136 in the U.S. and globally, clinical trial designs, regulatory matters, including the timing and likelihood of obtaining drug approvals and timing and likelihood of securing one or more approved indications for palazestrant, the timelines for the potential initiation of clinical trials and the result of any such clinical trials of palazestrant or OP-3136 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 pivotal Phase 3 clinical trial of palazestrant in combination with ribociclib, the timelines for patient enrollment and presenting data from our clinical trials, and the timing of any potential commercial launch and related preparatory work, including but not limited to establishing manufacturing supply and distribution for commercial use, anticipated field force of representatives in the U.S., the timing and likelihood of generating stockholder value, 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 and overall survival rate under palazestrant in combination trials, the potential of palazestrant to become a therapeutic leader and a best-in-class treatment option for metastatic breast cancer and a backbone therapy for women living with breast cancer and beyond, the combinability of palazestrant with other drugs, the potential value and impact of our KAT6 inhibitor program, the best-in-class potential for OP-3136 as a monotherapy or in combination trials, including for breast and other solid tumor cancers, the potential beneficial characteristics, profile, safety, efficacy, tolerability, and therapeutic effects of OP-3136, including potential safety advantages of OP-3136 over alternative products, the combinability of OP-3136 with other drugs including palazestrant, our opportunity in breast, other solid tumor cancers, and beyond, our ability to impact treatment for endocrine-driven cancers, and the future growth potential of ribociclib. 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.

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# Olema is focused on transforming the metastatic breast cancer treatment paradigm


Advancing palazestrant with blockbuster potential in 2/3L MBC as a monotherapy and in 1L MBC in combination with ribociclib

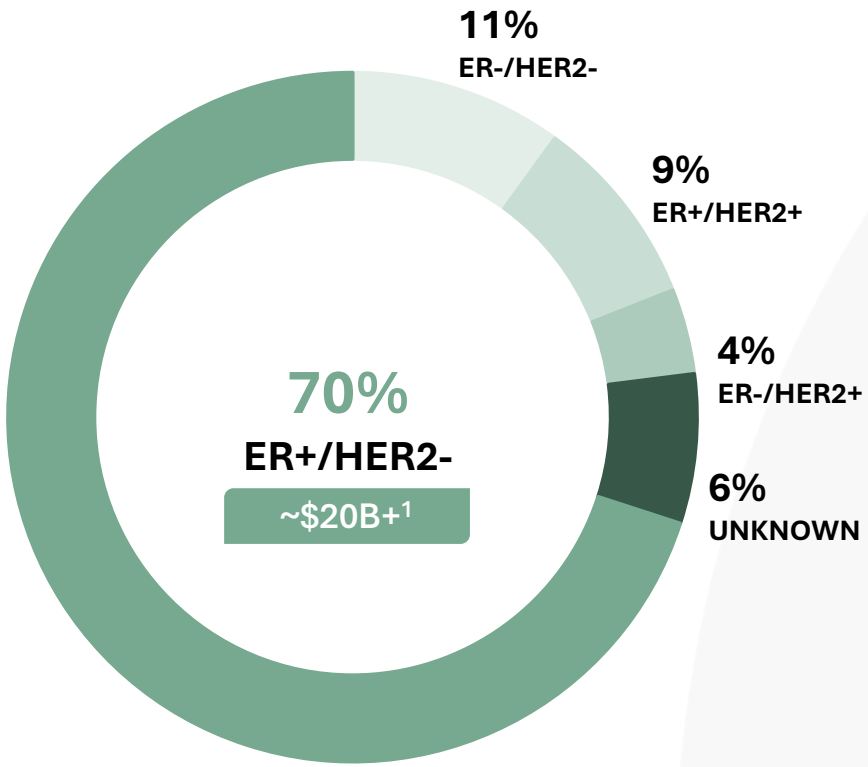
Progressing OP-3136, our potent and potential best-in-class KAT6 inhibitor

**1L** = frontline; **2/3L** = second/third-line; **KAT6** = lysine acetyltransferase 6; **MBC** = metastatic breast cancer

# The ER+/HER2- global metastatic breast cancer market presents a $20B+ opportunity[1]

TRANSFORMING THE TREATMENT PARADIGM

## The majority of all breast cancers are ER+/HER2-[2]




## Adjuvant ER+/ HER2- MBC

- Patients[3]: ~200K+
- Duration of Therapy[4]: Up to 5 years
- Global Market Potential[5]: $20B+

## 1L ER+/ HER2- MBC

OPERA-02 Breast Cancer Study

- Patients[3]: ~100K+
- Duration of Therapy[4]: ~6-36+ months
- Global Market Potential[5]: $10B+

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

OPERA-01 Breast Cancer Study

- Patients[3]: ~150K+
- Duration of Therapy[4]: ~2-12+ months
- Global Market Potential[5]: $5B+

## OP-3136

**Phase 1 study in ER+/HER2- MBC currently enrolling**

- Anti-Tumor Activity in Multiple Tumor Types
- Synergizes with Palazestrant
- Global Market Potential[5]: $5B+

[1] 2026 opportunity estimates for global endocrine therapy market. Olema internal data. [2]National Breast Cancer Foundation, World Health Organization; American Cancer Society. Facts and Figures 2024-2025; SEER database. [3] 2025 global incidence projection estimates. Olema internal data, Informa ER+/HER2- BC Prevalence Based Market Forecast. [4] Olema internal data, based on clinical trial data and package inserts. [5] Estimated global breast cancer market potential, Olema internal data.
**ER** = estrogen receptor; **HER2** = human epidermal growth factor receptor 2; **MBC** = metastatic breast cancer ; **+** = positive; **-** = negative

# Palazestrant has the potential to become a best-in-class, backbone endocrine therapy for metastatic breast cancer

TRANSFORMING THE TREATMENT PARADIGM

| Line | Current Standard of Care | Duration of Therapy[1] |
|---|---|---|
| Low Risk Adjuvant | Tamoxifen | Up to **5 years** |
| Moderate to High-Risk Adjuvant | AI +/- CDK4/6i | Up to **5 years** |
| 1L | AI + CDK4/6i | **~6-36+** months |
| 2L/3L | ET, ET + CDK4/6i, ET + mTOR, or AKTi or PI3Ki | **~2-12+** months |
| 3L+ | Chemotherapy or ADC (Enhertu, Trodelvy) | **~2-12+** months |

**Palazestrant has the right properties to succeed**

- Complete ER antagonism
- Activity in *ESR1* wild-type and mutant tumors
- Well-tolerated and combinable at full doses
- Optimal PK profile with oral administration

**Designed to help patients feel better, longer**

[1]Olema internal data, based on clinical trial data and package inserts.

**1L** = frontline; **2/3L** = second/third-line; **3L+** = more than three lines of therapy; **ADC =** antibody-drug conjugate; **AI =** aromatase inhibitor; **AKTi** = serine/threonine protein kinase 1; **CDK4/6i** = cyclin-dependent kinase 4/6 inhibitor; **CNS** = central nervous system; **ER** = estrogen receptor; **ESR1** = estrogen receptor 1 gene; **ET** = endocrine therapy; **HER2** = human epidermal growth factor receptor 2; **mTORi** = mammalian target of rapamycin inhibitor; **PI3Ki** = phosphatidylinositol 3-kinase inhibitor; **PK** = pharmacokinetic

# Palazestrant monotherapy in 2/3L ER+/HER2- MBC offers our first opportunity for market entry in 2027

TRANSFORMING THE TREATMENT PARADIGM

**Palazestrant has the potential to become the best-in-class single agent endocrine therapy and improve upon current standard of care**

### Differentiated Efficacy Profile

Median PFS[1] of:

- 7+ months in 2/3L ±CT *ESR1* mutant
- 5+ months in 2/3L ±CT *ESR1* wild-type

### Promising Safety

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

### Favorable Pharmacokinetics

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

**Palazestrant's approval in *ESR1* mutant and wild-type tumors in the 2/3L ER+/HER2- MBC setting would be paradigm-shifting**

**Pharmacokinetic properties** poised to succeed where others have failed

+

High PoS in ***ESR1* mutant** with additional benefit in ***ESR1* wild-type**

+

Initial **opportunity for market entry** and use by oncologists

=

Potential **$5B+** global market opportunity[2]

OPERA-01 Breast Cancer Study

**FALL 2026** TOP-LINE DATA

**2027** ANTICIPATED NDA SUBMISSION

**2027** POTENTIAL APPROVAL AND U.S. LAUNCH*

[1] For more details on the data highlighted on this slide, please refer to the oral presentation at this link. Data cutoff date: July 7, 2023. [2] Estimated global market potential. Olema internal data. *Subject to U.S. Food and Drug Administration approval.
**2/3L** = second/third-line; **±CT** = plus/minus chemotherapy; **AEs** = adverse events; **ER+** = estrogen receptor positive; **ESR1** = estrogen receptor 1 gene; **HER2-** = human epidermal growth factor receptor 2 negative; **MBC** = metastatic breast cancer; **NDA** = new drug application; **PFS** = progression free survival; **PoS** = probability of success

# Palazestrant in combination with ribociclib has the potential to become the new standard of care in 1L ER+/HER2- MBC

TRANSFORMING THE TREATMENT PARADIGM

## Emerging resistance mutations, AEs, and suboptimal drug exposure limit the utility of currently approved therapies in 1L MBC

### Combination Partner of Choice

Ribociclib is quickly becoming the CDK4/6i of choice for MBC[1]

- OPERA-02 Phase 3 trial combines palazestrant with ribociclib in 1L MBC

### Differentiated Efficacy Profile

In the 120 mg dose cohort, median PFS in patients previously treated with a CDK4/6i + ET:

- 13.8 months in 2L+ *ESR1* mutant [2]
- 9.2 months in 2L+ *ESR1* wild-type [2]

### Promising Safety

- Palazestrant + ribociclib safety profile is consistent with the established label of ribociclib + ET[3]
- No dose modifications required

## By targeting the right patients, with the right properties, with the right combo partner, palazestrant has the potential to succeed in 1L MBC

Palazestrant is the **only investigational CERAN combining with ribociclib** in endocrine-sensitive 1L MBC

+

Activity in ***ESR1* wild-type and mutant** tumors

+

Potential for significant improvement in **PFS and OS**

=

Potential **$10B+** global market opportunity[4]

OPERA-02 Breast Cancer Study

**NOW** ENROLLING

**2028** ANTICIPATED TOP-LINE DATA

**2029** POTENTIAL APPROVAL IN 1L MBC*

[1] Novartis full year earnings reports, 2018-2024. [2]ESMO 2025 Poster. Data cutoff date: July 8, 2025. [3]**This analysis is based on 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: February 18, 2025. Median follow-up of 15 months. [4]Estimated global market potential. Olema internal data. *Subject to U.S. Food and Drug Administration approval.
**1L** = frontline; **2L** = second-line; **AEs** = adverse events; **CDK4/6i** = cyclin-dependent kinase 4/6 inhibitor; **ER+** = estrogen receptor positive; **ESR1** = estrogen receptor 1 gene; **ET** = endocrine therapy; **HER2-** = human epidermal growth factor receptor 2 negative; **MBC** = metastatic breast cancer ; **OS** = overall survival; **PFS** = progression free survival

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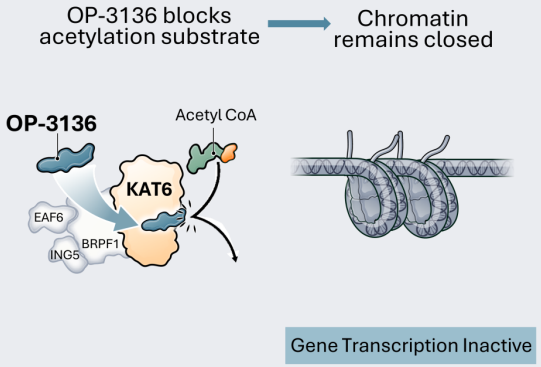
# OP-3136 has the potential to generate further value and meaningfully impact the MBC treatment landscape

TRANSFORMING THE TREATMENT PARADIGM

## KAT6 is an exciting new target in breast cancer

### OP-3136 Prevents Transcription




### Promising Preclinical Data in Breast Cancer

- Synergistic activity with palazestrant and superiority to KAT6 inhibitors + fulvestrant[1]
- Well tolerated, with no significant changes in body weight

### Promising Preclinical Data in Other Solid Tumors

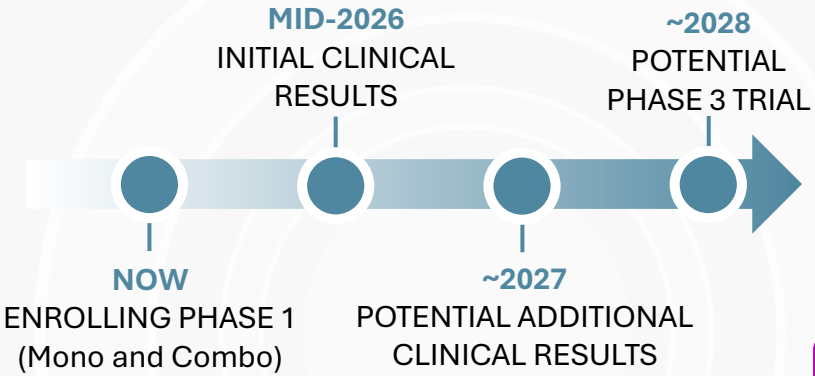
Potent anti-proliferative activity independent of KAT6 amplification or over expression across tumor models:

- Ovarian
- Non-small cell lung
- Prostate

## OP-3136 has the right characteristics to become a combination agent of choice across mutations in MBC

Potent and selective against **KAT6A/B** + Selective over **KAT5/8** with fewer off target effects + **Synergistic with palazestrant** in preclinical models = Potential **$5B+** global market opportunity[2]

### OP-3136 PROGRAM




[1]2024 EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics. Poster #230. [2] Estimated global metastatic breast cancer market potential, Olema internal data.

**KAT6** = lysine acetyltransferase 6; **MBC** = metastatic breast cancer

# We are rapidly advancing our pipeline of novel therapies through the clinic

TRANSFORMING THE TREATMENT PARADIGM

## Palazestrant: CERAN/SERD

ER+/HER2- metastatic breast cancer

OPERA-01 Breast Cancer Study

**Ongoing pivotal Phase 3 trial** evaluating palazestrant as a monotherapy in 2/3L MBC

**POTENTIAL GLOBAL MARKET OPPORTUNITY*** **$5B+**

OPERA-02 Breast Cancer Study

IN COLLABORATION WITH NOVARTIS

**Ongoing pivotal Phase 3 trial** evaluating palazestrant combination with ribociclib in 1L MBC

**POTENTIAL GLOBAL MARKET OPPORTUNITY*** **$10B+**

## OP-3136: KAT6 Inhibitor

Breast cancer and other solid tumors

**Ongoing Phase 1 study** evaluating OP-3136 monotherapy and combination in advanced or metastatic:

- ER+/HER2- breast cancer
- Castrate-resistant prostate cancer
- Non-small cell lung cancer

**POTENTIAL GLOBAL MARKET OPPORTUNITY*** **$5B+**

*Internal Olema estimates.

**1L** = frontline; **2/3L** = second/third-line; **CERAN =** complete estrogen receptor antagonist; **ER+** = estrogen receptor positive; **HER2-** = human epidermal growth factor receptor 2 negative; **KAT6** = lysine acetyltransferase 6; **MBC** = metastatic breast cancer; **SERD** = selective estrogen receptor degrader

# Value-generating catalysts advance us towards our goal of transforming the treatment paradigm for metastatic breast cancer

## Corporate Priorities and Anticipated Milestones

**2025**
WELL-CAPITALIZED WITH ~**$505M** IN CASH[1]

**MID-2026**
**OP-3136** MONO CLINICAL DATA

**FALL 2026**
PIVOTAL **OPERA-01** READOUT IN 2/3L MBC

**2027**
PRODUCT APPROVAL AND LAUNCH FOR **PALAZESTRANT** IN 2/3L MBC*

**2028**
PIVOTAL **OPERA-02** READOUT IN 1L MBC IN COMBINATION WITH RIBOCICLIB

**2029 and Beyond**
TRANSFORMING THE TREATMENT PARADIGM

*1 Cash position as of December 31, 2025, includes the Company's cash, cash equivalents, and marketable securities.*
*Subject to U.S. Food and Drug Administration approval.
**1L** = frontline; **2/3L** = second/third-line; **KAT6** = lysine acetyltransferase 6; **MBC** = metastatic breast cancer

# Palazestrant

## AT A GLANCE

- **Mechanism of Action**
  Complete estrogen receptor antagonist (CERAN) and selective estrogen receptor degrader (SERD)
- **Stage of Development**
  Monotherapy: Phase 3
  In Combination: Phase 3; multiple studies in Phase 1/2
- **Special Designations**
  FDA Fast Track*

## 2026 MILESTONES

- Advance patient enrollment in pivotal Phase 3 OPERA-01 trial of palazestrant monotherapy in 2/3L MBC
- Advance patient enrollment in pivotal Phase 3 OPERA-02 trial of palazestrant + ribociclib in 1L MBC
- Announce top-line data from pivotal Phase 3 OPERA-01 trial

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* In patients with ER+/HER2- metastatic breast cancer that has progressed following one or more lines of endocrine therapy with at least one line given in combination with a CDK4/6 inhibitor
**1L** = frontline; **2/3L** = second /third-line; **ESMO** = European Society for Medical Oncology Congress; **FDA** = U.S. Food and Drug Administration; **MBC** = metastatic breast cancer

# Palazestrant mechanism of action

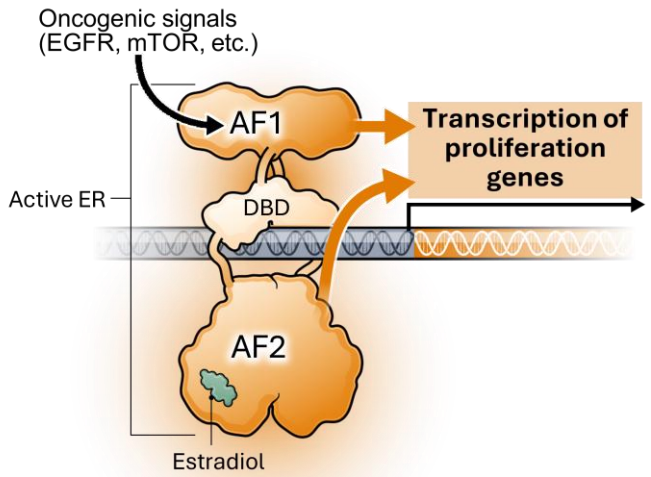
Palazestrant is a differentiated oral CERAN/SERD targeting the growth and proliferation mechanism driving ER+ breast cancer

Activated ER
**drives cancer cell** growth

SERM/SERDs
**partially** inactivate ER
(AF2 only)

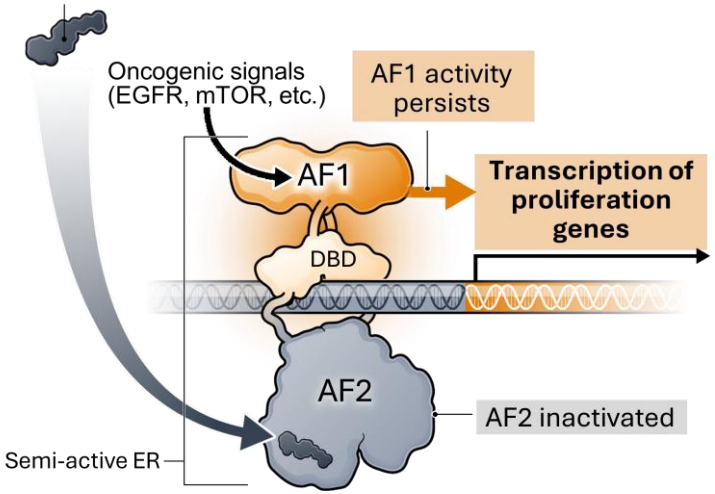
Palazestrant, a CERAN/SERD,
not only degrades but also
**completely inactivates** ER
(AF1 and AF2) by recruiting N-CoR

**Cancer**

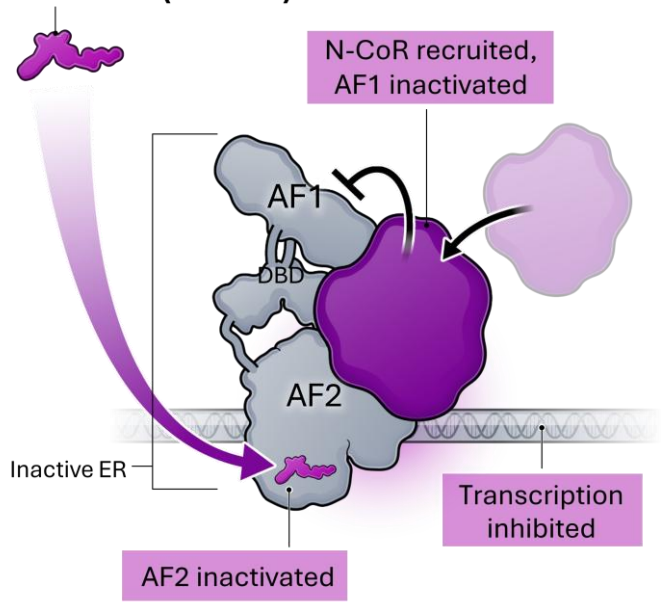



AF - Activation factor
DBD - DNA Binding Domain

**SERM/SERD**




**Palazestrant (CERAN)**



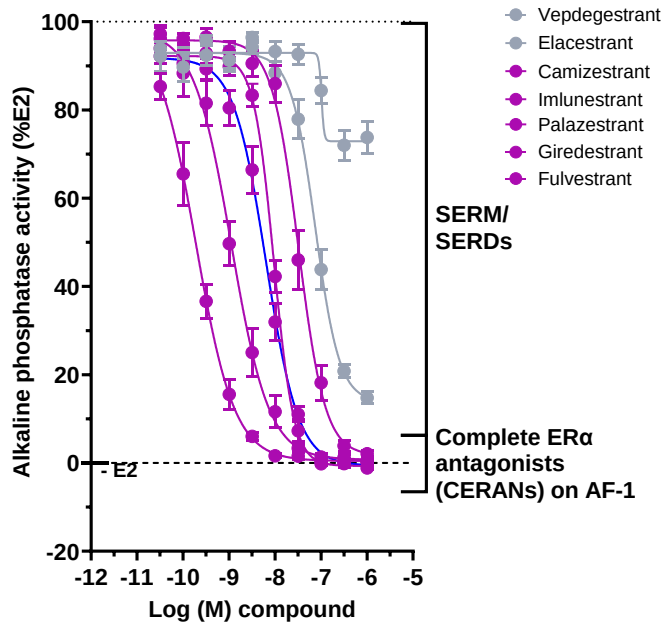

**AF** = activation factor; **CERAN** = complete estrogen receptor antagonist; **DBD** = DNA binding domain; **EGFR** = epidermal growth factor receptor; **ER** = estrogen receptor; **mTOR** = mammalian target of rapamycin; **N-CoR** = nuclear receptor corepressor; **SERD** = selective estrogen receptor degrader; **SERM** = selective estrogen receptor modulator; **+** = positive

# Palazestrant has the right properties to become a best-in-class agent

## Palazestrant completely inactivates the ER and delivers superior therapeutic exposure

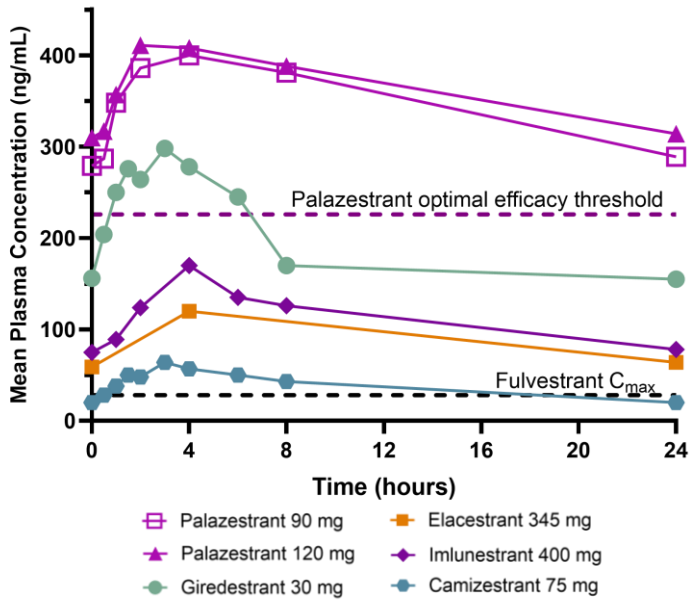
### Complete ER antagonism is key to shutting off all ER signaling

Inactivating the ER (AF1):
Antagonist Mode (Estrogen Present)



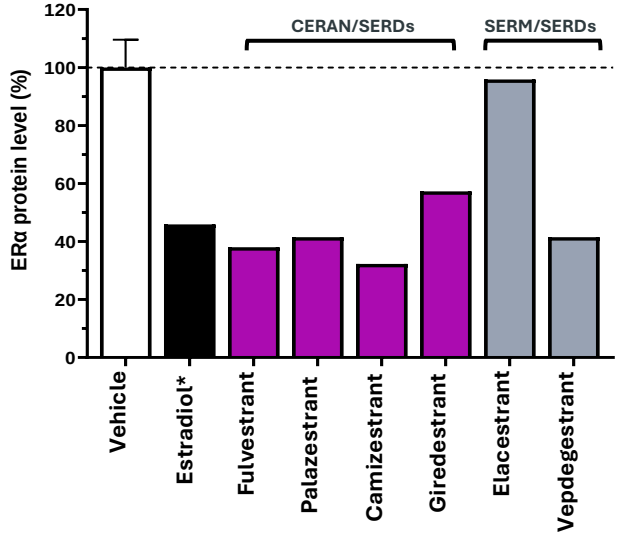

### Palazestrant uniquely meets optimal drug-plasma exposure[1]

Clinical Drug-Plasma
Steady-State Exposure*




### Palazestrant is a potent ER degrader

MCF-7 BC Cell Line:
ER+/HER2- (*ESR1*$^{WT}$)




**Palazestrant has the potential to demonstrate activity in *ESR1* wild-type and mutant tumors and become backbone ER therapy given complete ER antagonism and optimal drug-plasma exposure**

*** NOTE: This analysis incorporates publicly-available third-party data that we have not independently verified. Results and outcomes presented should be interpreted with caution. Refer to further disclaimers on slide 2.**

[1] Optimal drug-plasma exposure is calculated based on Olema's internal calculation.

**AF** = activation factor; **CERAN** = complete estrogen receptor antagonist; **CNS** = central nervous system; **DBD** = DNA binding domain; **EGFR** = epidermal growth factor receptor; **ER** = estrogen receptor; **SERD** = selective estrogen receptor degrader; **SERM** = selective estrogen receptor modulator; **+** = positive

# *Palazestrant as a monotherapy in 2/3L ER+/HER2- metastatic breast cancer*

## MILESTONES

- **2026:** Pivotal Phase 3 OPERA-01 trial ongoing
- **2026:** Announce top-line results from OPERA-01 in the Fall
- **2027:** Anticipated submission of New Drug Application for potential approval of palazestrant as a monotherapy in 2/3L ER+/HER2-MBC and prepare for commercial launch
- **2027:** Potential FDA approval and U.S. commercial launch of palazestrant

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**2/3L** = second/third-line; **ER+** = estrogen receptor positive; **HER2-** = human epidermal growth factor receptor 2 negative; **FDA** = U.S. Food and Drug Administration; **MBC** = metastatic breast cancer

# Design: Phase 1/2 study of palazestrant as a monotherapy

## In patients with advanced or metastatic ER+/HER2- breast cancer

### Phase 1a: Dose Escalation

300 mg
210 mg
150 mg
120 mg
90 mg
60 mg
30 mg

### Phase 1b: Dose Expansion

60 mg
120 mg

### Phase 2

**Key Eligibility Criteria***
- ER+/HER2- advanced breast cancer
- 1–4 prior endocrine therapies for metastatic disease
- Up to 1 line of prior chemotherapy for metastatic disease
- Measurable or non-measurable disease by RECIST v1.1

120 mg

Measurable and
Non-Measurable Disease

Last patient enrolled November 2022

**Primary Objectives**
- Pharmacokinetics
- Safety and Tolerability
- RP2D

**Secondary Objectives**
- ORR (CR + PR)
- CBR (CR + PR + SD ≥24 weeks)

**Objectives**
- Efficacy
- Safety and Tolerability at RP2D

* Phase 1a dose escalation allowed patients with at least 1 prior line of endocrine therapy and up to 2 prior lines of chemotherapy for metastatic disease.

**CBR =** clinical benefit rate; **CR =** complete response; **ER+ =** estrogen receptor-positive; **HER2 =** human epidermal growth factor receptor 2; **ORR =** overall response rate; **PR =** partial response; **RECIST** = Response Evaluation Criteria in Solid Tumours; **RP2D =** recommended phase 2 dose; **SD =** stable disease

# Safety: Phase 1/2 study of palazestrant as a monotherapy

## Palazestrant is well-tolerated, with most TEAEs Grade 1/2

| TEAEs in ≥15% of patients | Palazestrant 120 mg (n = 83) | | | | |
|---|---|---|---|---|---|
| | Grade 1 | Grade 2 | Grade 3 | Grade 4 | All (%) |
| Nausea | 47 | 4 | 3 | 0 | 54 (65%) |
| Vomiting | 19 | 2 | 4 | 0 | 25 (30%) |
| Fatigue | 13 | 6 | 3 | 0 | 22 (27%) |
| Neutropenia | 6 | 6 | 3 | 6 | 21 (25%) |
| Headache | 16 | 1 | 0 | 0 | 17 (20%) |
| Constipation | 13 | 2 | 0 | 0 | 15 (18%) |
| AST increased | 10 | 2 | 1 | 0 | 13 (16%) |

- **Most AEs were low grade (grade 1/2)**
- Grade 4 neutropenia events were observed in 6 patients, occurring approximately 4–6 weeks into therapy
  - 3 patients had a dose interruption followed by recovery and dose reduction (2 patients to 90 mg and 1 patient to 60 mg) without any recurrence of neutropenia
  - 3 patients had dose discontinuation followed by recovery
- In OPERA-01 pivotal Phase 3 trial, patients are receiving tablet formulation instead of the capsules utilized in current dataset
  - Expected to reduce rate and grade of nausea and vomiting

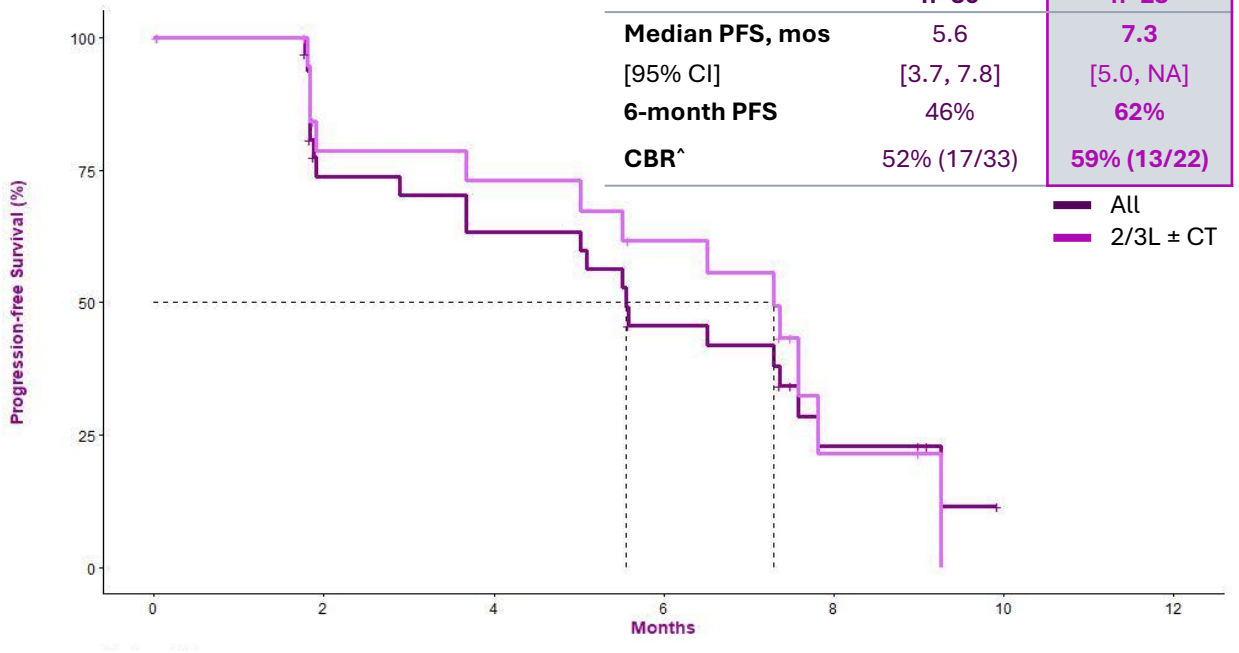
**Data cutoff date: July 7, 2023.** Data shown are n or n (%).
**AE** = adverse events; **AST** = aspartate aminotransferase; **TEAEs** = treatment-emergent adverse events

# Efficacy: Compelling Phase 1/2 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[1]

| | All *ESR1* mut n=36 | 2/3L ±CT n=23 |
|---|---|---|
| **Median PFS, mos** | 5.6 | **7.3** |
| [95% CI] | [3.7, 7.8] | [5.0, NA] |
| **6-month PFS** | 46% | **62%** |
| **CBR^** | 52% (17/33) | **59% (13/22)** |

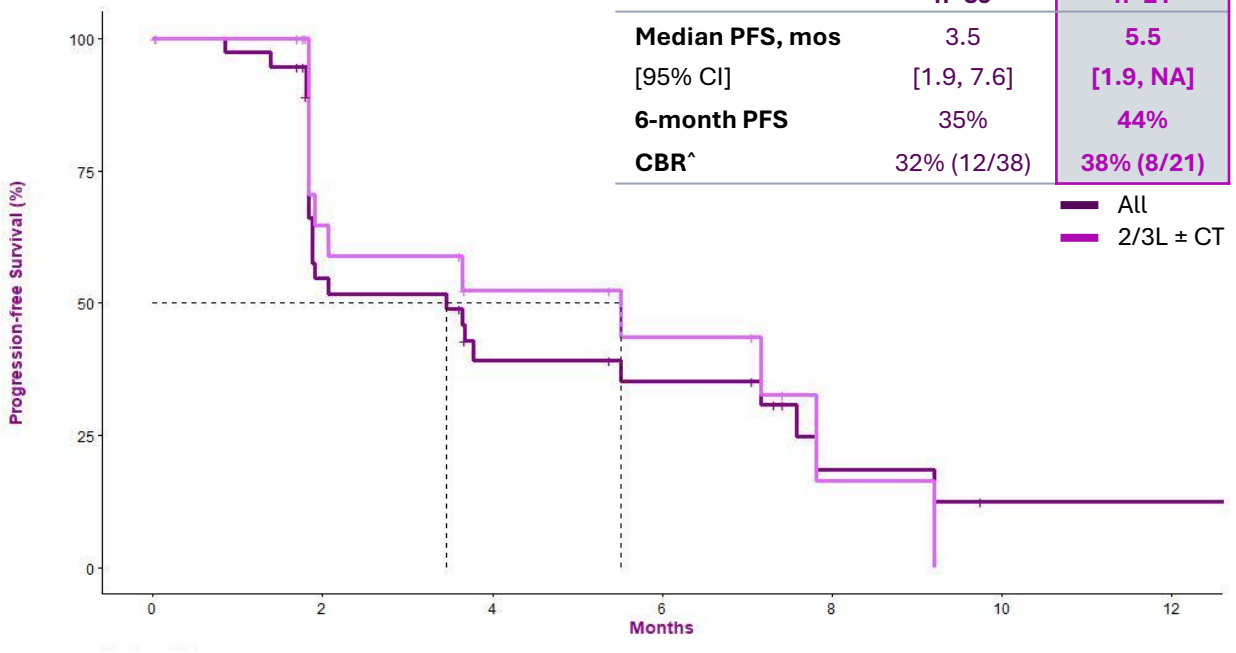



**Number at Risk**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| All | 36 | 21 | 18 | 12 | 4 | 0 | 0 |
| 2/3L ±CT | 23 | 14 | 13 | 10 | 2 | 0 | 0 |

### Patients with *ESR1* Wild-Type[2]

| | All *ESR1* WT n=39 | 2/3L ±CT n=21 |
|---|---|---|
| **Median PFS, mos** | 3.5 | **5.5** |
| [95% CI] | [1.9, 7.6] | **[1.9, NA]** |
| **6-month PFS** | 35% | **44%** |
| **CBR^** | 32% (12/38) | **38% (8/21)** |




**Number at Risk**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| All | 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.**

[1] Palazestrant Phase 2 dataset at 120 mg with ESR1 mutations detected at baseline. [2] Palazestrant Phase 2 dataset at 120 mg with ESR1 mutations not detected at baseline.

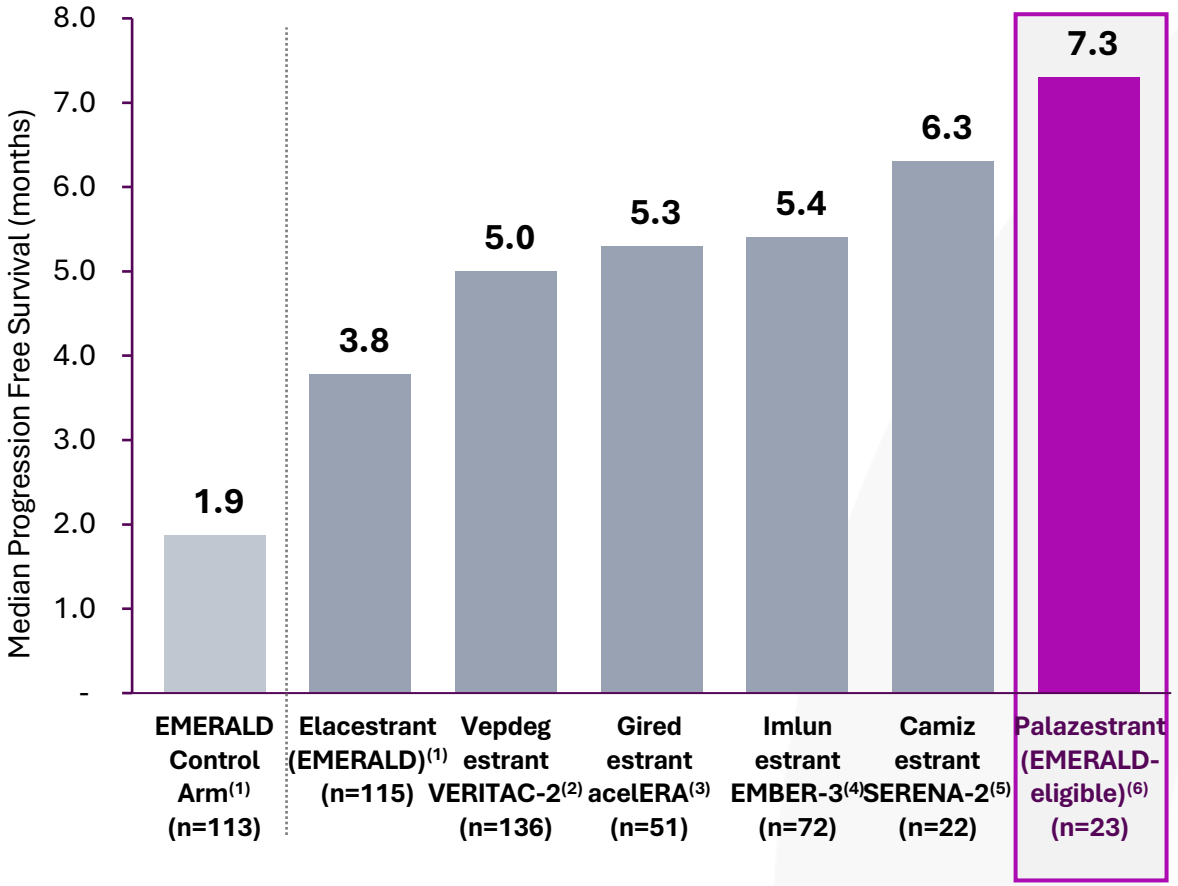
^ Clinical Benefit Rate (CBR) is defined as the proportion of subjects who remained on OP-1250 treatment through at least 24 weeks with a confirmed CR or PR, or stable disease. The CBR analysis includes patients who received at least one evaluable post-baseline radiographic assessment. Data cut-off as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

**± 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

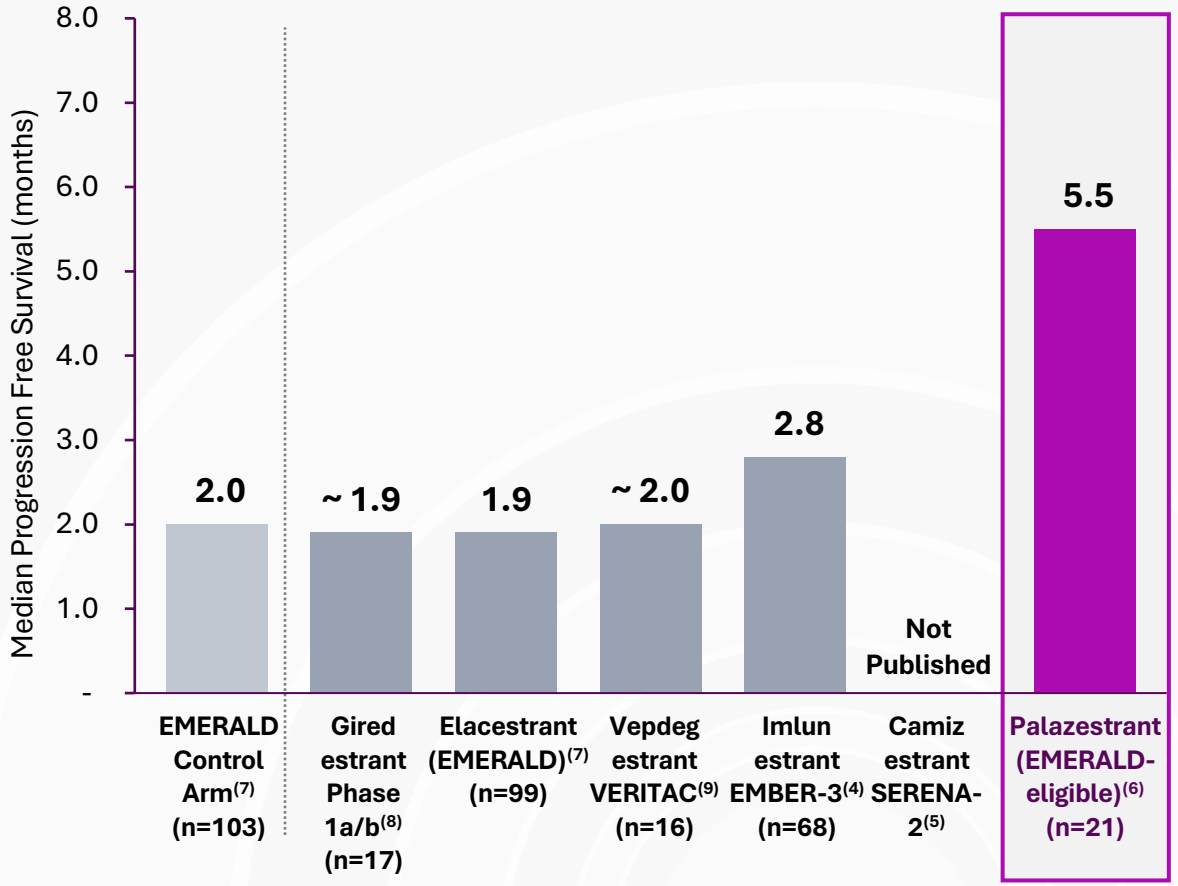
# Palazestrant in the competitive landscape: best-in-class potential*

## Palazestrant is the only CERAN/SERD with potential for approval in both *ESR1* mutant and wild-type

### Median PFS (months) in *ESR1* Mutant Patients*




### Median PFS (months) in *ESR1* Wild-Type CDK4/6i-Experienced Patients*




*** 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.**

[1] SABCS 2021 EMERALD data . [2] NEJM 2025 VERITAC-2 data. [3] JCO acelERA data. Median PFS in ESR1m patients at 30 mg. [4] ESMO Breast 2025 EMBER-3 data. Median PFS in ESR1m CDK4/6i pre-treated patients. [5] SABCS 2022 Serena-2 data. Median PFS in ESR1m patients at 75 mg. [6] mPFS at 120 mg dose in Emerald-eligible patient population from palazestrant Phase 2 dataset (2/3L +/-CT) with ESR1 mutations detected at baseline. [7] ASCO 2023 EMERALD data. Median PFS in ESR1m non-detected with ≥6 months prior CDK4/6i. [8] ASCO 2021 Phase 1/2 data. mPFS in 30 mg cohort with prior CDK4/6i and no ESR1m. [9] SABCS 2023 VERITAC data. Median PFS at 200 mg dose across ESR1 wild-type patients.

**CDK4/6i** = cyclin-dependent kinase 4/6 inhibitor; **CERAN =** complete estrogen receptor antagonist; **ESR1 =** estrogen receptor 1 gene; **PFS** = progression free survival; **SERD** = selective estrogen receptor degrader

Olema ONCOLOGY

# OPERA-01 Phase 3 monotherapy trial designed to show superior efficacy in ESR1 mutant and ESR1 wild-type tumors

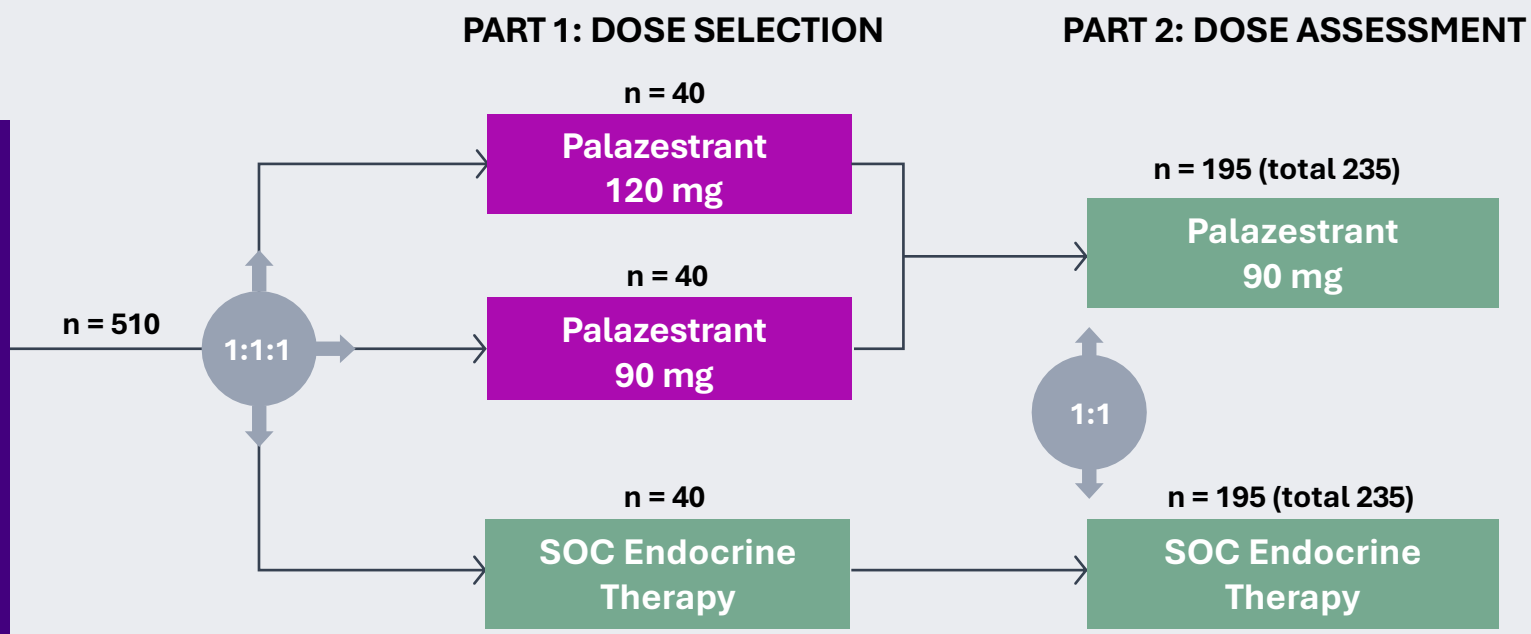
OPERA-01 Breast Cancer Study

**ELIGIBILITY 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




**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

*Trial initiated in 4Q 2023. Top-line results expected in Fall 2026.*

For more details on this trial, please visit www.opera01study.com.

**BIRC** = blinded independent review committee; **CBR** = clinical benefit rate; **CDK4/6i** = cyclin dependent kinase 4/6 inhibitor; **DOR** = duration of response; **ESR1** = estrogen receptor 1 gene; **ET** = endocrine therapy; **mut** = mutation; **mut-nd** = mutation not detected; **ORR** = objective response rate; **OS** = overall survival; **PFS** = progression free survival; **PK** = pharmacokinetics; **PROs** = patient reported outcomes; **SOC** = standard of care

# Planning for commercial launch of palazestrant as a monotherapy in 2/3L ER+/HER2- MBC anticipated in late 2027

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

Commercial launch planning began in 2025

Early commercial leadership build expected to begin 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

*Olema internal estimate of US market.

**2/3L** = second/third-line; **ER+** = estrogen receptor positive; **HER2-** = human epidermal growth factor receptor 2 negative; **MBC** = metastatic breast cancer

# *Palazestrant in combination with ribociclib in 1L ER+/HER2- metastatic breast cancer*

## MILESTONES

- **2026:** Pivotal Phase 3 OPERA-02 trial ongoing
- **2028:** Anticipated announcement of top-line results from OPERA-02
- **2029:** Potential FDA approval and U.S. launch of palazestrant + ribociclib in 1L MBC

Olema ONCOLOGY

**1L** = frontline; **ER+** = estrogen receptor positive; **ESMO** = European Society for Medical Oncology Congress; **HER2-** = human epidermal growth factor receptor 2 negative; **FDA** = U.S. Food and Drug Administration; **MBC** = metastatic breast cancer

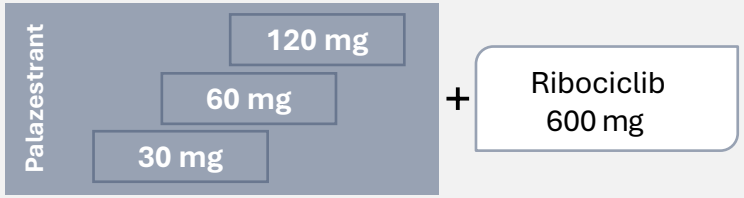
# Design: Phase 1b/2 study of palazestrant in combination with ribociclib in ER+/HER2- MBC

**ER+/HER2- advanced or metastatic breast cancer (CDK4/6i-naïve or previously treated)**

### Key eligibility criteria

- Women or men with ER+/HER2– advanced or metastatic breast cancer
- Up to 2 prior endocrine therapies ± a CDK4/6i for locally advanced or metastatic disease; up to 1 prior line of chemotherapy for advanced or metastatic breast cancer was allowed
- Evaluable disease (measurable by RECIST v1.1 or bone only)
- No contraindication to ribociclib

## Part 1: Dose Escalation




**Primary endpoints:** DLTs, MTD and/or RP2D of palazestrant when administered in combination with ribociclib, incidence and severity of adverse events, PK

**Secondary endpoints:** ORR (CR + PR), CBR (CR + PR + SD ≥ 24 weeks), DOR

## Part 2: Dose Expansion

**Palazestrant 90 mg / 120 mg + Ribociclib 600 mg**

**Primary endpoints:** incidence and severity of adverse events, PK

**Secondary endpoints:** ORR (CR + PR), CBR (CR + PR + SD ≥ 24 weeks), DOR, time to progression, PFS

**CDK4/6i =** cyclin-dependent kinase 4/6 inhibitor; **CBR** = clinical benefit rate; **CR** = complete response; **DLT** = dose-limiting toxicity; **DOR** = duration of response; **ER+** = estrogen receptor positive; **HER2-** = human epidermal growth factor receptor negative; **MBC** = metastatic breast cancer; **MTD** = maximum tolerated dose; **ORR** = objective response rate; **PFS** = progression free survival; **PK =** pharmacokinetics; **PR** = partial response; **QTcF** = QT corrected for heart rate using Fridericia's formula; **RECIST** = response evaluation criteria in solid tumors; **RP2D** = recommended Phase 2 dose; **SD** = stable disease

# Demographics: Phase 1b/2 study of palazestrant in combination with ribociclib in ER+/HER2- MBC

| Patient Characteristics | 90 mg (N=16) | 120 mg (N=56) | Total (N=72) |
|---|---|---|---|
| **Median age (years)** | 60 | 61 | 61 |
| Range | 25-76 | 28-85 | 25–85 |
| **Female sex** | 16 (100%) | 56 (100%) | 72 (100%) |
| **Premenopausal** | 4 (25%) | 8 (14%) | 12 (17%) |
| **ECOG performance status, n (%)** | | | |
| 0 | 10 (63%) | 34 (61%) | 44 (61%) |
| 1 | 6 (38%) | 22 (39%) | 28 (39%) |
| **Measurable disease at baseline, n (%)** | 12 (75%) | 37 (66%) | 49 (68%) |
| **Visceral disease, n (%)** | 6 (38%) | 33 (59%) | 39 (54%) |
| **Prior lines of therapy in advanced setting, n (%)** | | | |
| 0 | 10 (63%) | 14 (25%) | 24 (33%) |
| 1 | 5 (31%) | 26 (46%) | 31 (43%) |
| 2 | 1 (6%) | 12 (21%) | 13 (18%) |
| 3 | 0 | 4 (7%) | 4 (6%) |
| **Prior lines of endocrine therapy in advanced setting, n (%)** | | | |
| 0 | 10 (63%) | 14 (25%) | 24 (33%) |
| 1 | 6 (38%) | 32 (57%) | 38 (53%) |
| 2 | 0 | 10 (18%) | 10 (14%) |
| **Types of prior therapy in advanced setting, n (%)** | | | |
| CDK4/6 inhibitor | 5 (31%) | 40 (71%) | 45 (63%) |
| Aromatase inhibitor (AI) | 5 (31%) | 27 (48%) | 32 (44%) |
| Fulvestrant | 1 (6%) | 22 (39%) | 23 (32%) |
| Chemotherapy | 1 (6%) | 10 (18%) | 11 (15%) |
| ***ESR1* mutations at baseline (ctDNA), n/N (%)** | 1/15 (7%) | 14/54 (26%) | 15/69[a] evaluated (22%) |

- N=72; N=56 at 120 mg; N=16 at 90 mg
- 54% with visceral disease
- 68% with measurable disease
- 67% received prior endocrine therapy in advanced setting
- **63% received prior CDK4/6i + ET**
  - 36 (50%) patients received 1 prior line of CDK4/6i
    - Palbociclib, n=23; abemaciclib n=8 ribociclib, n=5
  - 9 patients (13%) received 2 prior lines of CDK4/6i
    - Palbociclib → abemaciclib, n=2
    - Palbociclib → palbociclib, n=2
    - Palbociclib → ribociclib, n=3
    - Ribociclib → ribociclib, n=1
    - Abemaciclib → palbociclib, n=1
- **22% with *ESR1* mutation**
  - 33% with *ESR1* mutation in 2L+

**Data cutoff date: July 8, 2025.**

[a] ESR1 mutations in ctDNA at baseline were determined centrally using SafeSEQ Breast Cancer Panel (Sysmex Inostics, Baltimore, MD). Three samples were not evaluable.

**CDK4/6i =** cyclin-dependent kinase 4/6 inhibitor; **ctDNA** = circulating tumor DNA; **ECOG =** Eastern Cooperative Oncology Group; **ESR1** = estrogen receptor 1 gene; **ET** = endocrine therapy

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

## Phase 1b/2 study of palazestrant in combination with ribociclib in ER+/HER2- MBC

| TEAEs in ≥25% of patients | Palazestrant 120 mg + Ribociclib (n = 56) | | | Palazestrant 90 mg + Ribociclib (n = 16) | | | MONALEESA-2* Letrozole + Ribociclib† (n = 334) | | |
|---|---|---|---|---|---|---|---|---|---|
| | All grades‡ | Grade 3 | Grade 4 | All grades‡ | Grade 3 | Grade 4 | All grades | Grade 3 | Grade 4 |
| Neutropenia§ | 47 (84%) | 28 (50%) | 5 (9%) | 13 (81%) | 9 (56%) | 2 (16%) | 93%‖ | 49% | 11% |
| Nausea | 41 (73%) | 2 (4%) | 0% | 11 (69%) | 1 (6%) | 0% | 52% | 2% | 0% |
| Fatigue | 30 (54%) | 3 (5%) | 0% | 9 (50%) | 0% | 0% | 37% | 2% | <1% |
| WBC decrease | 24 (43%) | 9 (16%) | 1 (2%) | 6 (38%) | 4 (25%) | 0% | 93%‖ | 31% | 3% |
| Diarrhea | 24 (43%) | 2 (4%) | 0% | 4 (25%) | 0% | 0% | 35% | 1% | 0% |
| Anemia | 22 (39%) | 2 (4%) | 0% | 5 (31%) | 0% | 0% | 57%‖ | 2% | 0% |
| Vomiting | 21 (38%) | 1 (2%) | 0% | 4 (25%) | 0% | 0% | 29% | 4% | 0% |
| ECG QT prolonged | 16 (29%) | 4 (5%) | 0% | 4 (25%) | 1 (6%) | 0% | 43%¶ | 8%¶ | NR |
| Lymphocyte count decreased | 16 (29%) | 3 (5%) | 1 (2%) | 3 (19%) | 0% | 0% | 51%‖ | 12% | 2% |
| AST Increased | 15 (27%) | 2 (4%) | 0% | 3 (19%) | 0% | 0% | 44%‖ | 6% | 1% |
| Constipation | 15 (27%) | 0% | 0% | 3 (19%) | 0% | 0% | 25% | 1% | 0% |

*** 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.**

†Adverse reactions reported in ≥10% of patients who received ribociclib plus letrozole in the MONALEESA-2 trial.(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) .

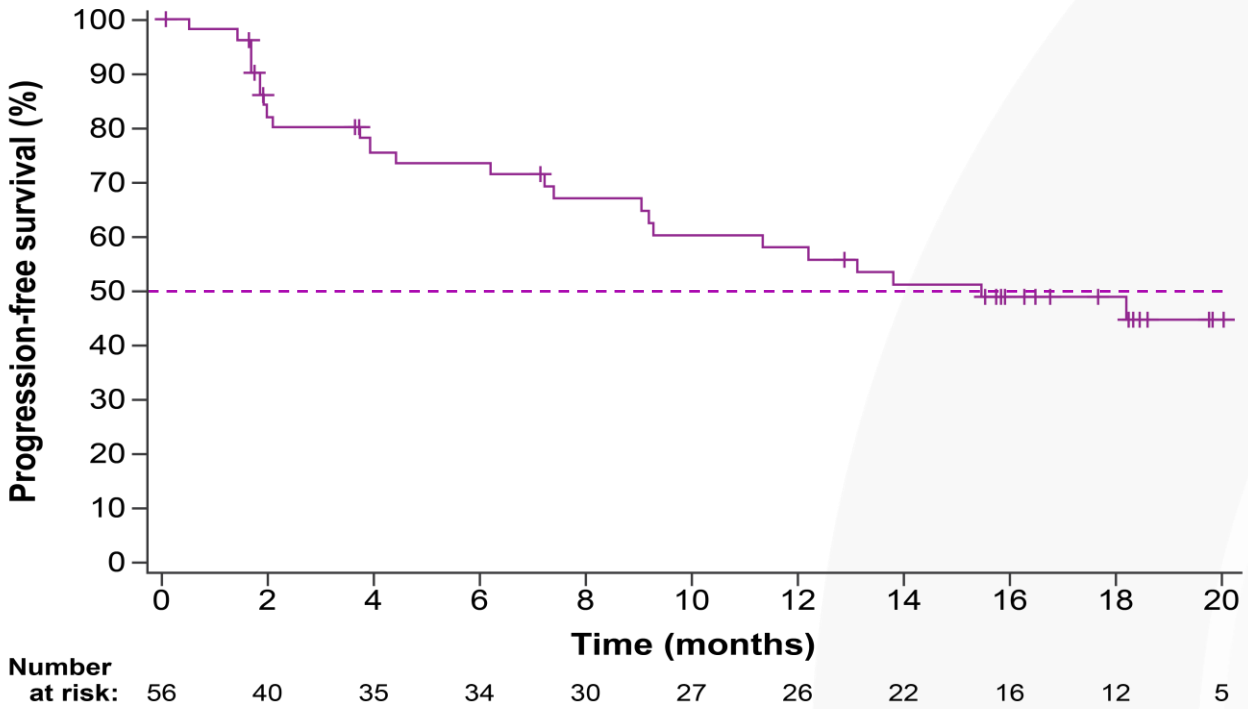
**AE** = adverse events; **DLTs** = dose-limiting toxicity; **ECG QT** = electrocardiogram QT interval; **ER+** = estrogen receptor positive; **ET** = endocrine therapy; **HER2- =** human epidermal growth factor receptor negative; **LDH** = lactate dehydrogenase; **MBC** = metastatic breast cancer; **NR** = not reported; **TEAEs** = treatment-emergent adverse events; **WBC** = white blood cell **Data cutoff date: July 8, 2025.** Data shown are n or n (%).

# Median PFS of 15.5 months for all 120 mg patients

## Phase 1b/2 study of palazestrant in combination with ribociclib in ER+/HER2- MBC

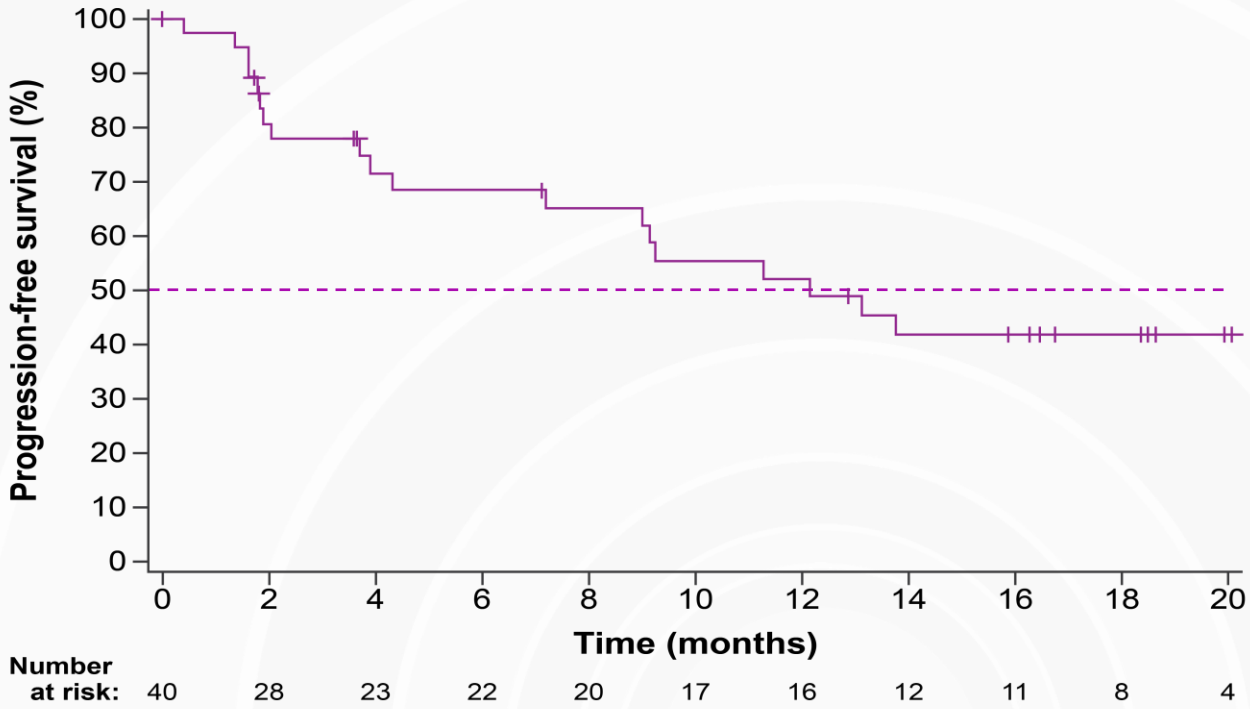
**All Patients**
120 mg palazestrant + 600 mg ribociclib (n=56)

**mPFS: 15.5 months**




**Patients with Prior CDK4/6i + ET**
120 mg palazestrant + 600 mg ribociclib (n=40)

**mPFS: 12.2 months**




**Data cutoff date: July 8, 2025 ; Median follow-up >19 months**
**CDK4/6i =** cyclin-dependent kinase 4/6 inhibitor; **ER+** = estrogen receptor positive; **ET** = endocrine therapy; **HER2-** = human epidermal growth factor receptor negative; **MBC** = metastatic breast cancer; **mPFS** = median progression free survival; **PFS** = progression free survival

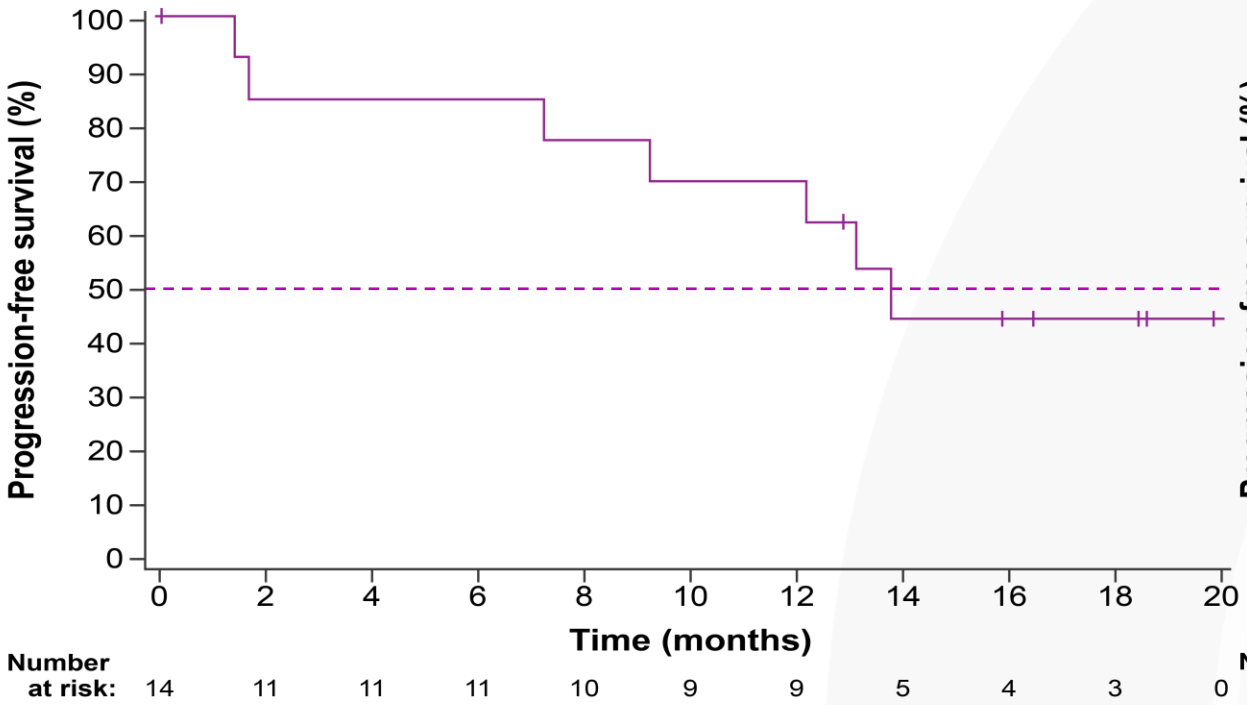
# Demonstrated activity in both ESR1 mutant and wild-type 2L+ patients

## Phase 1b/2 study of palazestrant in combination with ribociclib in ER+/HER2- MBC

### ESR1 Mutant Patients with Prior CDK4/6i

120 mg palazestrant + 600 mg ribociclib (n=14)

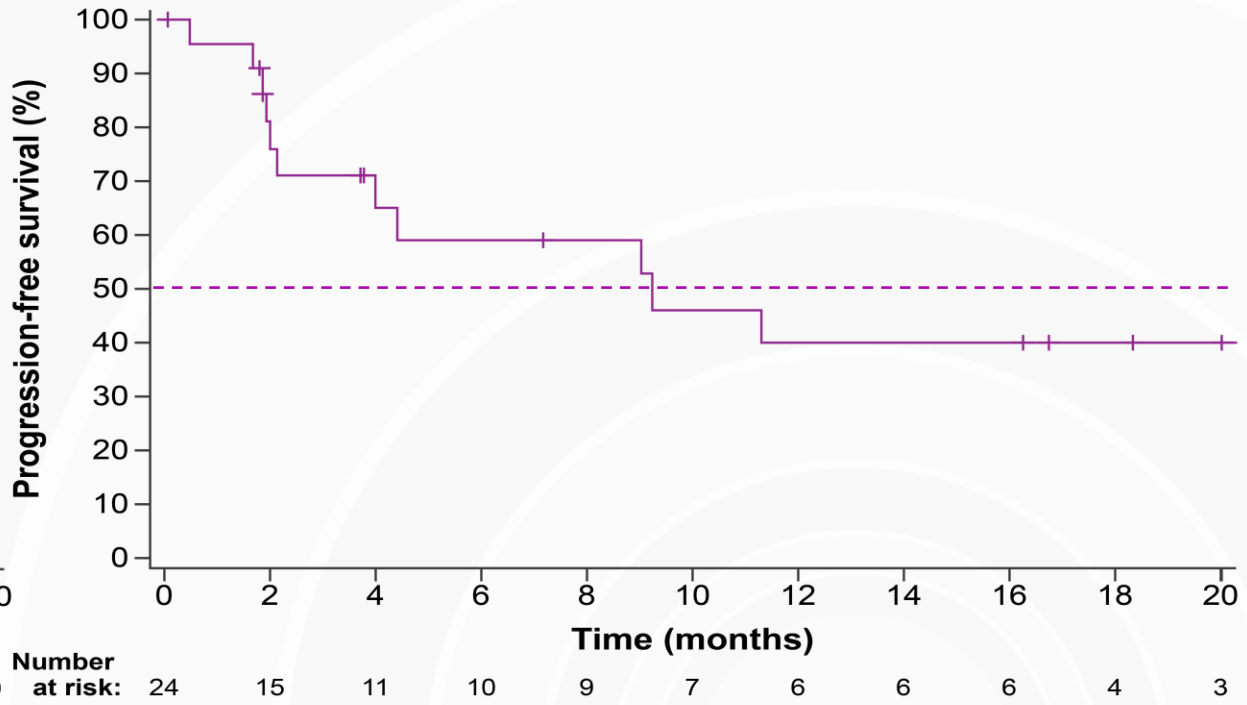
**mPFS: 13.8 months**




### ESR1 Wild Type Patients with Prior CDK4/6i

120 mg palazestrant + 600 mg ribociclib (n=24)

**mPFS: 9.2 months**



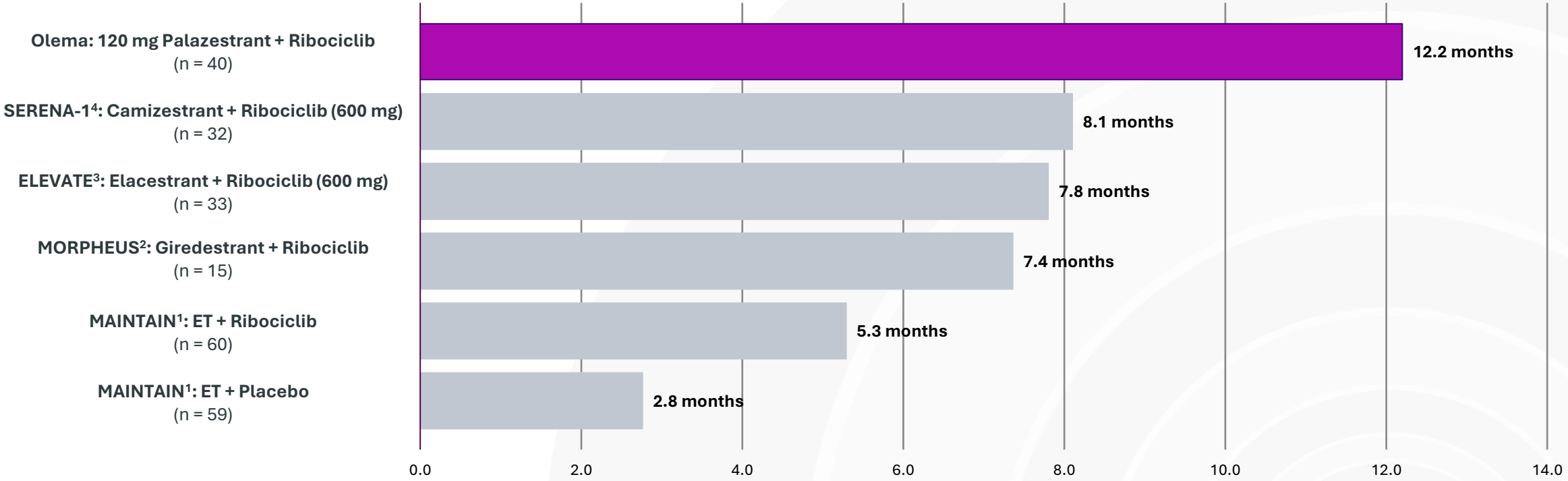

**Data cutoff date: July 8, 2025; Median follow-up >19 months**

**CDK4/6i** = cyclin-dependent kinase 4/6 inhibitor; **ER+** = estrogen receptor positive; **HER2-** = human epidermal growth factor receptor negative; **MBC** = metastatic breast cancer; **mPFS** = median progression free survival; **PFS** = progression free survival

# Pala + Ribo shows promising activity in 2L+ patients with prior CDK4/6i

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

### Comparison of 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: July 8, 2025.**

[1] ASCO 2022 MAINTAIN data. [2] ASCO 2023 MORPHEUS data. [3] ASCO 2025 ELEVATE data. [4] SABCS 2024 SERENA-1 data Parts K-L, ribociclib 600 mg dose arm.

**2L+** = second-line plus; **CDK4/6i =** cyclin-dependent kinase 4/6 inhibitor; **ET =** endocrine therapy; **PFS** = progression free survival

# Design: OPERA-02 Phase 3 pivotal trial of palazestrant in combination with ribociclib in 1L ER+/HER2- MBC

Ongoing ~1,000-patient trial vs. standard of care

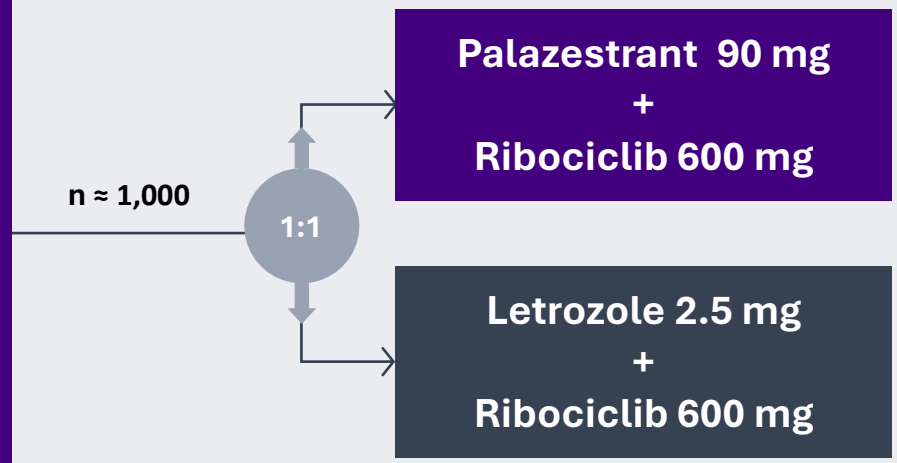
OPERA-02 Breast Cancer Study

**ELIGIBILITY CRITERIA**

- ER+/HER2- MBC
- Any menopausal status
- No prior systemic therapy for MBC
- No prior CDK4/6 inhibitor for MBC
- Patients who relapsed during or within 12 months of completion of adjuvant endocrine therapy are not eligible
- Evaluable disease (measurable or non-measurable)

**STRATIFICATION**

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




**Endpoints**

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

In collaboration with NOVARTIS

**1L** = frontline; **BIRC** = blinded independent review committee; **CDK4/6i** = cyclin-dependent kinase 4/6 inhibitor; **CBR** = clinical benefit rate; **DOR** = duration of response; **ER+** = estrogen receptor positive; **ET** = endocrine therapy; **HER2-** = human epidermal growth factor receptor 2 negative; **MBC** = metastatic breast cancer; **ORR** = objective response rate; **OS** = overall survival; **PFS** = progression free survival; **PK** = pharmacokinetics; **PROs** = patient reported outcomes

# Case study: TAGRISSO's® path to approval and label expansion by suppressing resistance mutations*

FLAURA trial demonstrated that suppressing the most common resistance mechanism was a proven clinical development strategy

*Comparable EGFR mutation rates after 1L TKI to ESR1 mutation rates after 1L CDK4/6i + AI = ~40 – 50%*

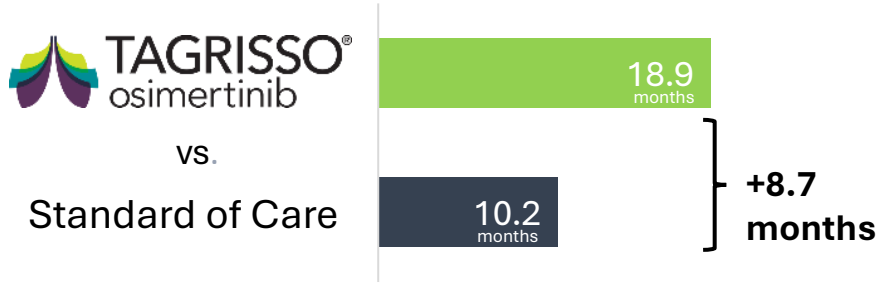
**TAGRISSO's first approval came in 2015 in 2L+ EGFR T790M mutant NSCLC on the basis of the Phase 2 AURA study**

**mPFS AURA Study[1]***


**Significant mPFS improvement in 1L resulting in movement up the treatment paradigm**

**TAGRISSO's label expanded in 2018 into 1L EGFR mutant NSCLC on the basis of the Phase 3 FLAURA trial**

**mPFS FLAURA Trial[2]***




By suppressing the most common resistance mutation (*ESR1*), OPERA-02 is designed to demonstrate greater PFS vs standard of care in 1L endocrine sensitive MBC patients, just as TAGRISSO did for EGFR T790M mutations

*** NOTE: This analysis incorporates publicly-available third-party data that we have not independently verified. Results and outcomes presented should be interpreted with caution. Refer to further disclaimers on slide 2.**

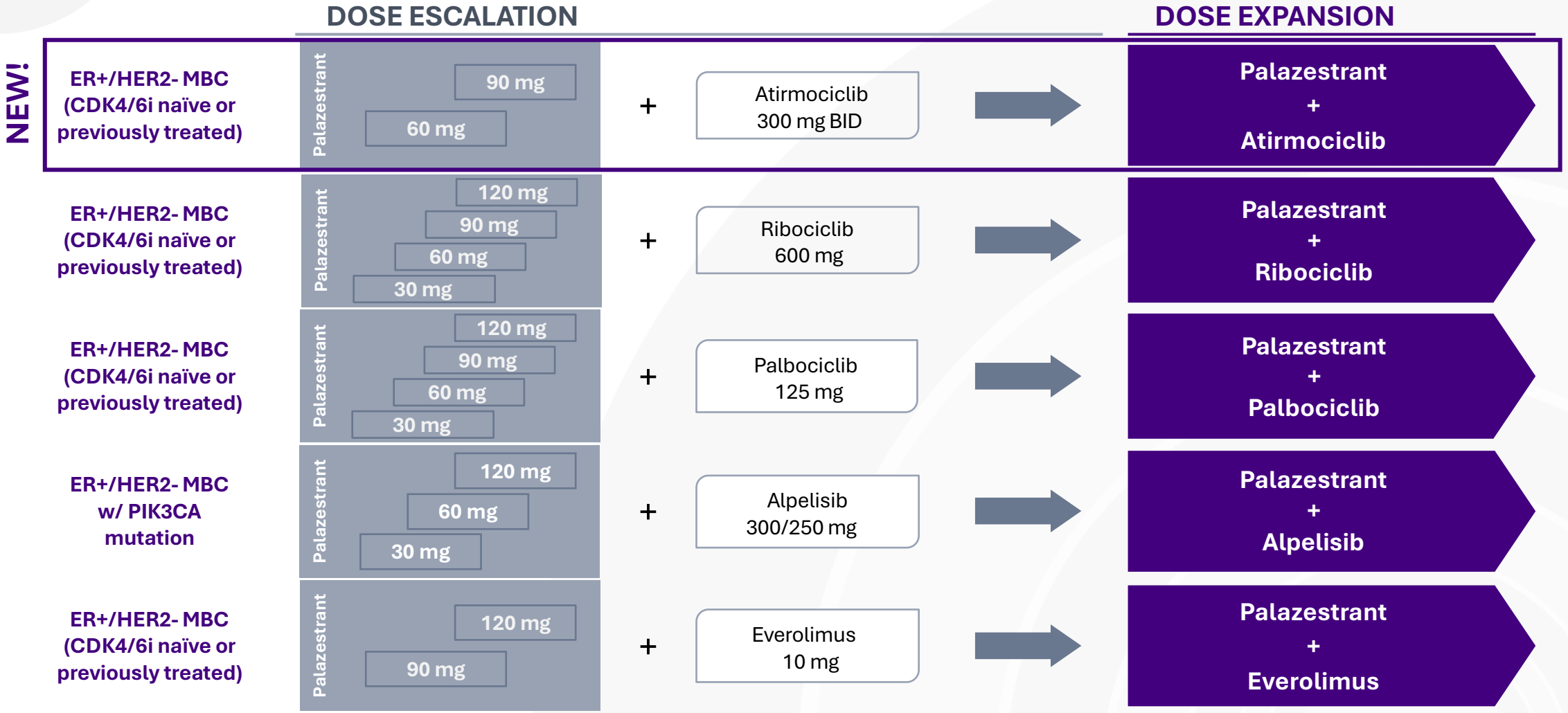
[1] Soria, J-C, Ohe, Y, Vansteenkiste, J. et al. Osimertinib in untreated EGFR-mutated advanced non-small-cell lung cancer. New Engl J Med 2018: 378:113-125.

[2] Osimertinib FDA package insert, Ramalingam, S. et al. Overall Survival with Osimertinib in Untreated, EGFR-Mutated Advanced NSCLC. N Engl J Med 2020;382:41-50.

**1L** = frontline; **2L** = second-line; **AI** = aromatase inhibitor; **CDK46i** = cyclin-dependent kinase 4/6 inhibitor; **EGFR** = epidermal growth factor receptor; **ESR1** = estrogen receptor 1 gene; **mPFS** = median progression free survival; **NSCLC** = non-small cell lung cancer; **T790M** = Thr790Met; **TKI** = tyrosine kinase inhibitor

# Palazestrant demonstrates combinability with other targeted agents

## Combination with Pfizer's selective CDK4 inhibitor, atirmociclib (PF-07220060), initiated in H2 2025




***BID** = twice daily; **CDK4i** = cyclin dependent kinase 4 inhibitor; **CDK4/6i** = cyclin dependent kinase 4/6 inhibitor; **CBR** = clinical benefit rate; **CR** = complete response; **ER+** = estrogen receptor positive; **HER2-** = human epidermal growth factor receptor 2 negative; **MBC** = metastatic breast cancer; **ORR** = objective response rate; **PIK3CA** = phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha; **PR** = partial response; **RP2D** = recommended Phase 2 dose; **SD** = stable disease*

# OP-3136

## AT A GLANCE

- **Mechanism of Action**
  KAT6A/B inhibitor
- **Stage of Development**
  Phase 1
- **Initial Development Indication**
  2/3L ER+/HER2- MBC

## MILESTONES

- **Mid-2026:** Initial monotherapy data from the Phase 1 study

Olema ONCOLOGY

**2/3L** = second/third-line; **ER+** = estrogen receptor positive; **KAT6** = lysine acetyltransferase 6; **HER2-** = human epidermal growth factor receptor 2 negative; **MBC** = metastatic breast cancer

# OP-3136: Olema's KAT6 inhibitor*

An exciting new and validated target** for the treatment of ER+/HER2- metastatic breast cancer

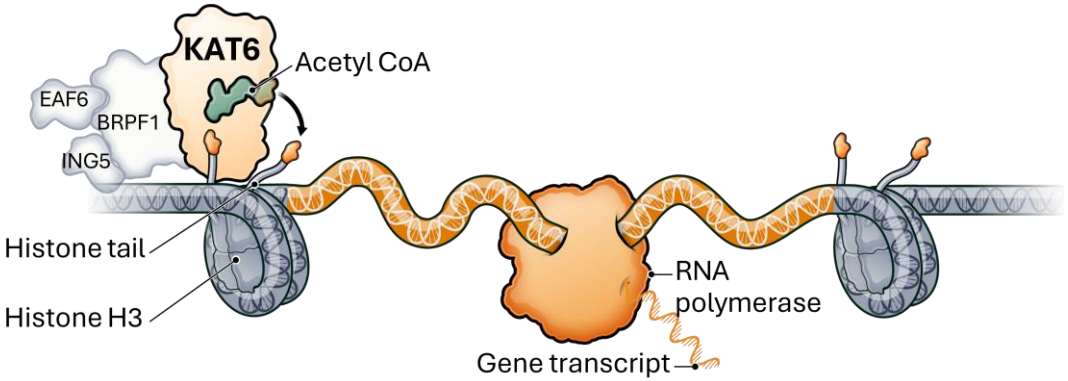
- Potent and selective against KAT6A/B
- Orally bioavailable with high levels of free drug exposure
- OP-3136 synergizes with palazestrant and CDK4/6 inhibitors in preclinical models
- New preclinical data presented at AACR 2026 Annual Meeting; first clinical data to be presented at ASCO 2026
- Phase 1/2 monotherapy and combination clinical trial is ongoing

*Discovered in collaboration with Aurigene. **Mukohara T, et al. Inhibition of lysine acetyltransferase KAT6 in ER+ HER2- metastatic breast cancer: a phase 1 trial. Nat Med (2024).
**AACR** = American Association for Cancer Research; **CDK4/6 =** cyclin-dependent kinase 4/6; **ER+** = estrogen receptor positive; **FDA** = U.S. Food and Drug Administration; **HER2-** = human epidermal growth factor receptor 2 negative; **IND** = investigational new drug application; **KAT6** = lysine acetyltransferase 6

# OP-3136 mechanism of action

KAT6 acetylates chromatin,
enabling transcription and proliferation

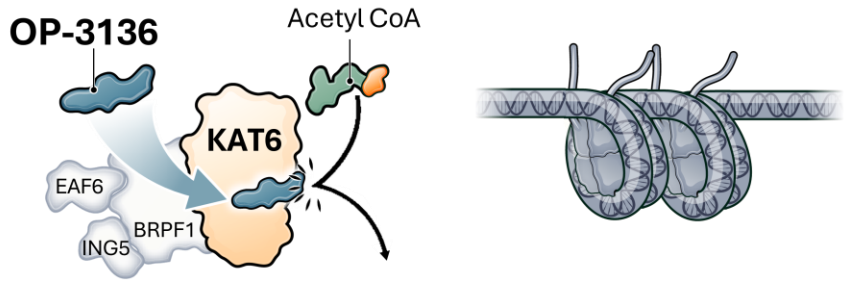
KAT6 acetylates histone tails → Chromatin opens




Gene Transcription Active

OP-136 inhibits KAT6, stopping acetylation of histones and preventing transcription of proliferation-associated genes

OP-3136 blocks acetylation substrate → Chromatin remains closed



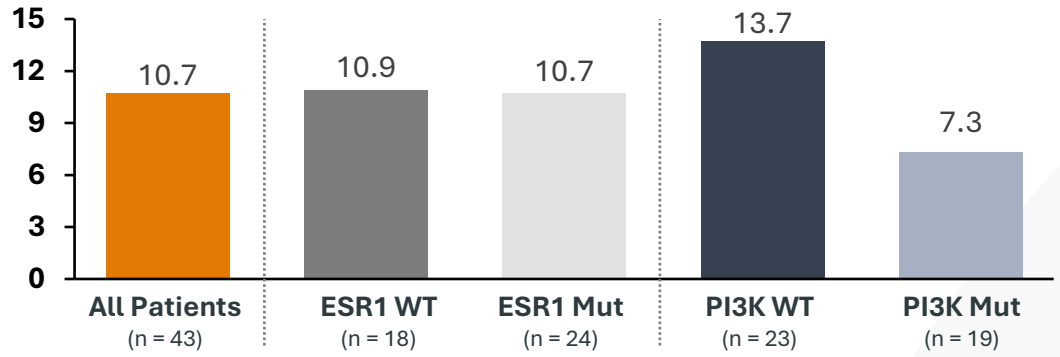

Gene Transcription Inactive

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

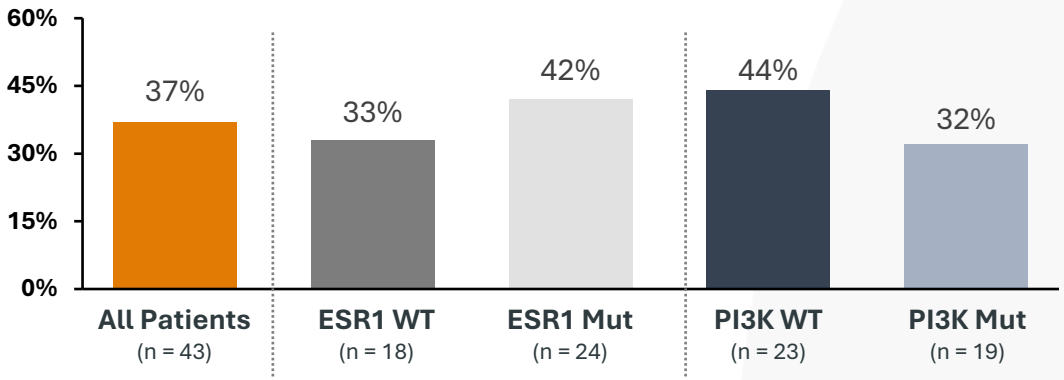
[1] Sommerhalder D, et al. First-in-human phase 1 dose escalation study of the KAT6 inhibitor PF-07248144 in patients with advanced solid tumors. JCO. 2023. 41(16)1054-1054.
[2] Yu L, et, al. Identification of MYST3 as a novel epigenetic activator of ERα frequently amplified in breast cancer. Oncogene. 2017 May 18;36(20):2910-2918.
[3] 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; **CoA** = coenzyme A; **ER =** estrogen receptor; **KAT6 =** lysine acetyltransferase 6; **MYC** = myelocytomatosis oncogene**; +** = positive

# KAT6 validated as an active new target in metastatic breast cancer*

## PF-8144 Median PFS with ET[1]




## PF-8144 Overall Response Rate (ORR) with ET[1]




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.**

[1] SABCS 2021 EMERALD data. Median PFS in control arm. ORR of 4.4% (8/182) [2] Mukohara T, et al. SABCS 2024: PF-07248144, a First-in-Class KAT6 Inhibitor, in Patients With HR+ HER2- Metastatic Breast Cancer: Updated Results From Phase 1 Dose Expansion Study.

**2L**= second-line; **ERS1** = estrogen receptor 1 gene; **ESR1** = estrogen receptor 1; **ET** = endocrine therapy; **KAT6** = lysine acetyltransferase 6; **ORR** = overall response rate; **PFS** = progression free survival; **PI3K** = phosphatidylinositol 3-kinase **PTEN** = phosphatase and tensin homolog

# OP-3136 preclinical data demonstrated specificity for KAT6A/B

## OP-3136 is potent and selective against KAT6A/B

| Biochemical Potency and Selectivity | | |
|---|---|---|
| **$IC_{50}$ (nM)** | **OP-3136** | **PF-8144** |
| **KAT6A** | 9 | 7 |
| **KAT6B** | 1 | 1 |
| **KAT7** | 108 | 88 |
| **KAT5** | **6792** | **1288** |
| **KAT8** | **4490** | **1372** |

- OP-3136 showed >500-fold selectivity over other essential KAT family members: KAT5 and KAT8
- OP-3136 had higher selectivity over KAT5 and KAT8
  - May confer safety advantage
  - PF-8144 5 mg QD steady state exposure is ~3000-4000 nM, above IC50 for KAT5 and KAT8

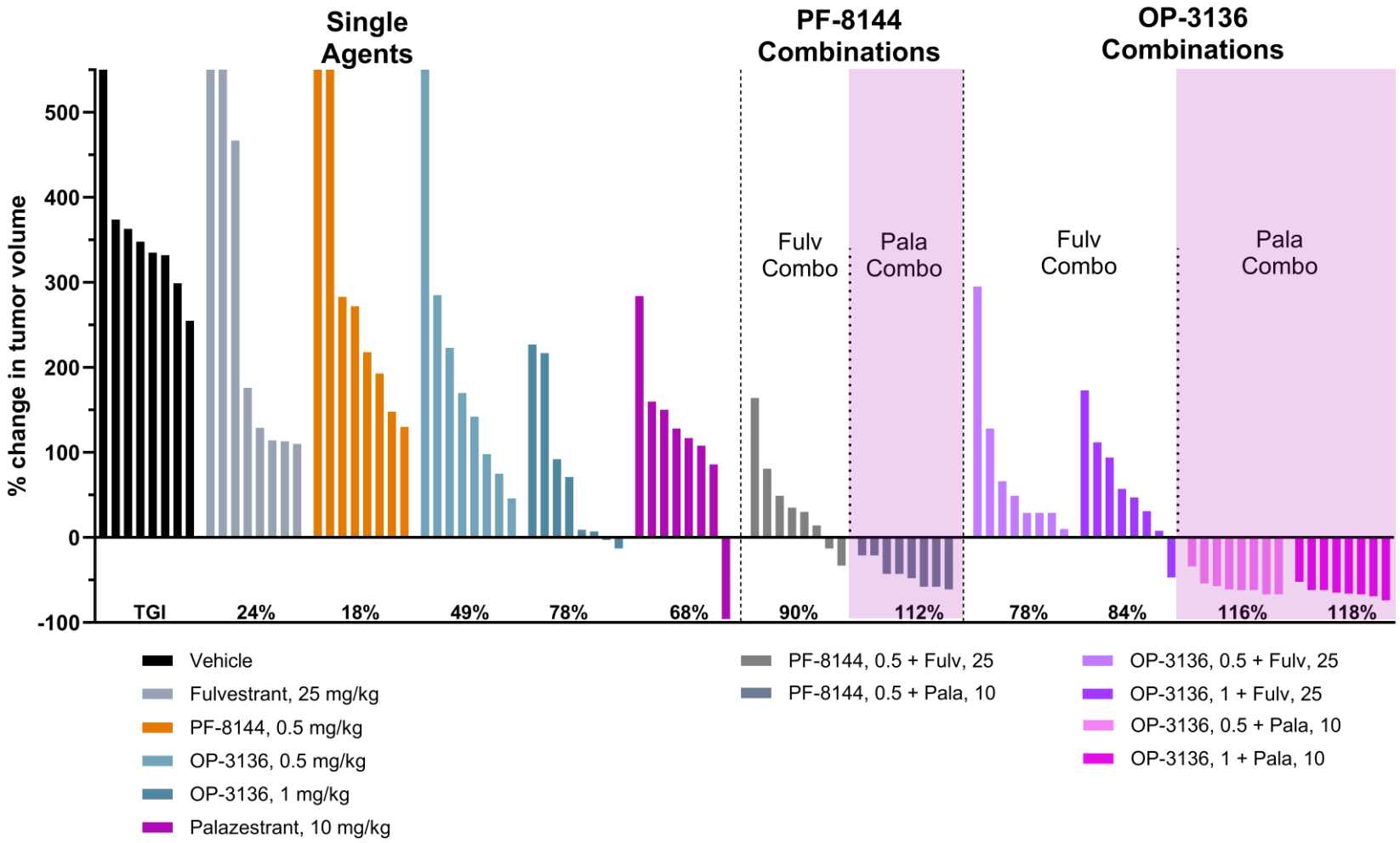
Note: Olema KAT6 inhibitors discovered in collaboration with Aurigene

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

**CDK4/6i =** cyclin dependent kinase 4/6 inhibitor; **KAT =** lysine acetyltransferase

# OP-3136 demonstrated synergistic activity in combination with palazestrant in preclinical breast cancer models

## Waterfall Plot (T47D CDX Model)



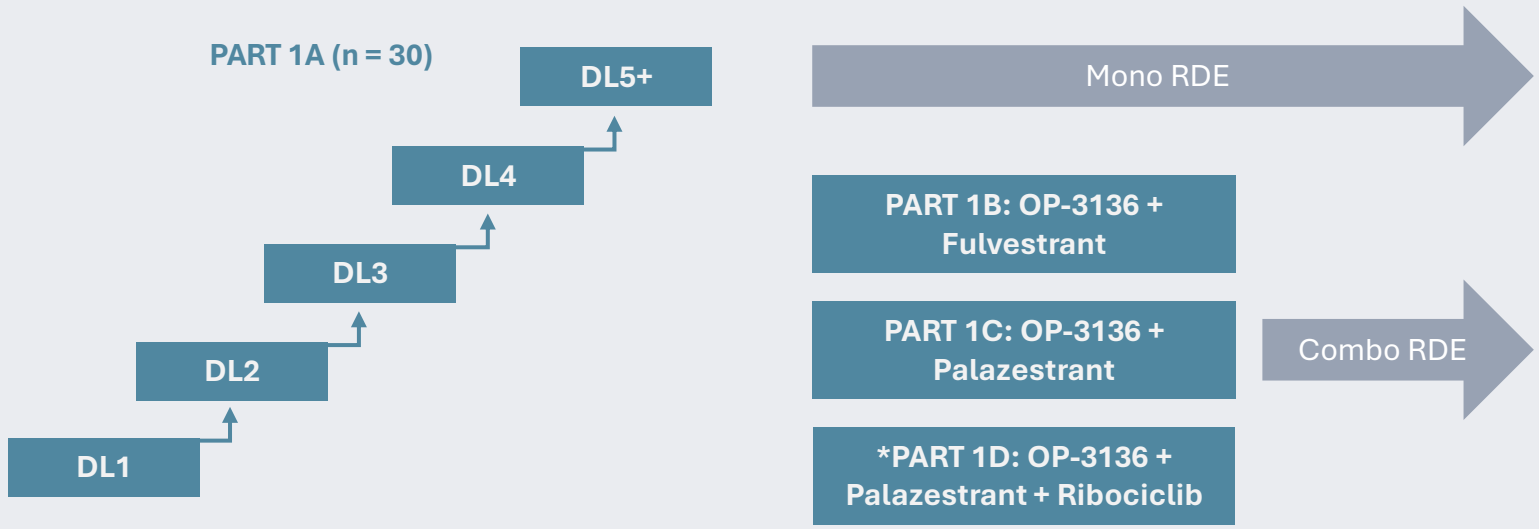

- Palazestrant in combination with either OP-3136 or PF-8144 resulted in strong tumor regression relative to fulvestrant combinations
- OP-3136 and palazestrant combinations showed significantly improved anti-tumor efficacy compared to PF-8144 in combination with fulvestrant
- All OP-3136 combinations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

Source: 2024 EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics. Poster #230. T47D model (ER+, HER2-, KAT6A overexpressing, ESR1 wild-type, PIK3CA H1047R cell line).
**Fulv** = fulvestrant; **Pala** = Palazestrant; **Ribo** = ribociclib

# OP-3136 Phase 1 study design

## Enrollment ongoing in monotherapy as well as palazestrant and fulvestrant combination arms

### PART 1: DOSE ESCALATION




### PART 2: DOSE EXPANSION

Monotherapy and in Combination

**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; **Combo** = combination; **CR** = complete response; **DL** = dose level; **DOR** = duration of response; **ER+** = estrogen receptor positive; **ET** = endocrine therapy; FDA = U.S. Food and Drug Administration; **HER2-** = human epidermal growth factor receptor 2 negative; **IND** = investigational new drug application; **MCRPC** = metastatic castrate resistant prostate cancer; **MBC** = metastatic breast cancer; **Mono** = monotherapy; **MNSCLC** = metastatic non-small cell lung cancer; **ORR** = objective response rate; **PK** = pharmacokinetics; **PR** = partial response; **RDE** = recommended dose for expansion; **SD** = stable disease; **SOC** = standard of care

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

## Focused on transforming the metastatic breast cancer treatment paradigm and the potential to generate significant shareholder value by 2030

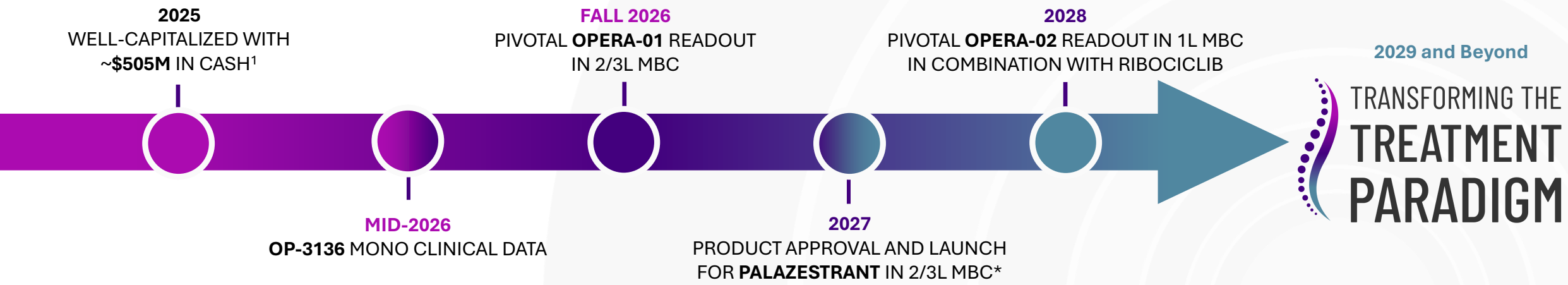
### Palazestrant

- Highly differentiated with activity in *ESR1* mutant and wild-type tumors
- OPERA-01 Phase 3 trial on track for top-line data in Fall 2026
- OPERA-02 Phase 3 trial in combination with ribociclib enrolling patients
- Potential U.S. approval and launch in 2027 and label expansion in 2029

### OP-3136

- Exciting new target in breast cancer
- Synergizes with palazestrant and CDK4/6 inhibitors in preclinical models
- Phase 1 study enrolling patients
- Initial clinical data to be presented at ASCO 2026

### Corporate Priorities and Anticipated Milestones




*1 Cash position as of December 31, 2025, includes the Company's cash, cash equivalents, and marketable securities.* *Subject to U.S. Food and Drug Administration approval.

**1L** = frontline; **2/3L** = second/third-line; **CDK4/6** = cyclin dependent kinase 4/6; **ESMO** = European Society for Medical Oncology Congress; **ESR1** = estrogen receptor 1 gene; **IND** = investigational new drug application; **MBC** = metastatic breast cancer

# Advancing medicines for breast cancer and beyond

Olema ONCOLOGY