

Olema ONCOLOGY

Corporate Overview

Advancing medicines for breast cancer and beyond

November 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, the timing of any potential commercial launch and related preparatory work, including but not limited to establishing manufacturing, supply, and distribution for commercial use or the 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 or OP-3136, each 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 or OP-3136 with other drugs, including with each other, 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, prostate, and other solid tumor cancers, as well as the potential for OP-3136 to become a combination agent of choice across mutations in metastatic breast cancer, our opportunity in breast, prostate, 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.

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.

Olema is focused on transforming the metastatic breast cancer treatment paradigm



TRANSFORMING THE TREATMENT PARADIGM

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

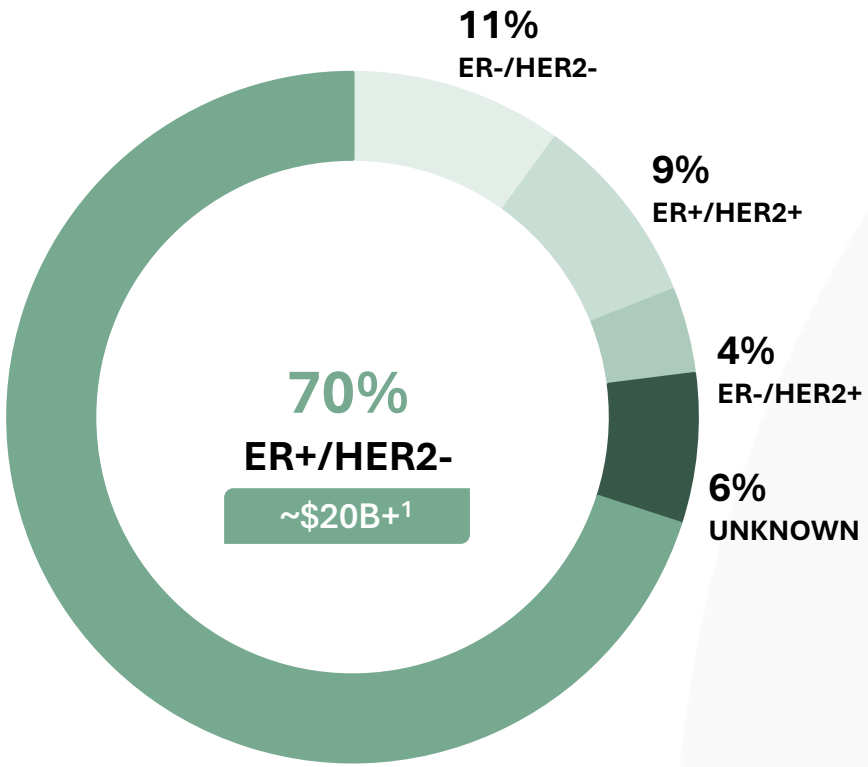
Progressing OP-3136, our potent and potential best-in-class KAT6 inhibitor

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 1b/2 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

Olema ONCOLOGY

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	**~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; **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; **+** = plus

Palazestrant monotherapy in 2/3L ER+/HER2- MBC offers our first opportunity for market entry in 2028

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
- ~15-day 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

- **Q1 2027** TOP-LINE DATA
- **2027** ANTICIPATED NDA SUBMISSION
- **2028** 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

Olema ONCOLOGY

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

[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

Olema ONCOLOGY

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 and initial results from the Phase 1 clinical study of OP-3136 are encouraging

Promising Anti-Tumor Activity[1]

- Preliminary monotherapy efficacy observed; tumor shrinkage in 2/3 of response-evaluable patients
- Confirmed, durable responses in patients with MBC and MCRPC

Manageable Safety[1]

- Well-tolerated monotherapy with no DLTs across evaluated dose levels up to 45mg
- Most TRAEs were grade 1-2; no grade 4-5 TRAEs

Favorable Pharmacokinetics[1]

- Predictable, dose-proportional plasma exposure across all monotherapy doses tested
- Steady-state concentrations exceeded efficacy targets based on preclinical models at 6mg and above

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

Potent and selective against **KAT6A/B** and selective over **KAT5/8** with fewer off target effects

+

Synergistic with palazestrant in preclinical ER+/HER2- breast cancer models [2, 3]

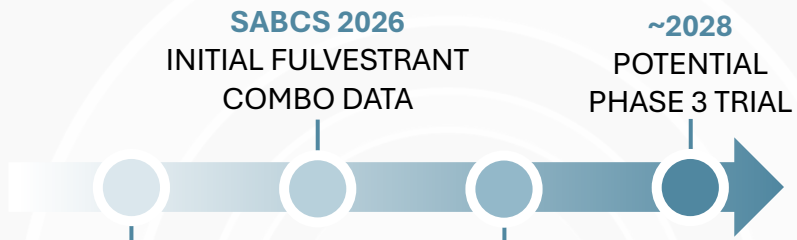
+

Encouraging Phase 1 data in patients with MBC[1]

=

Potential **$5B+** global market opportunity[4]

OP-3136 PROGRAM



[1]2026 ASCO Annual Meeting. Poster #225. [2]2026 AACR Annual Meeting. Poster #2950. [3]2024 EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics. Poster #230. [4] Estimated global metastatic breast cancer market potential, Olema internal data.

combo = combination; **DLT** = dose limiting toxicity; **ER+** = estrogen receptor positive; **HER2-** = human epidermal growth factor receptor 2 negative; **KAT6** = lysine acetyltransferase 6; **MBC** = metastatic breast cancer; **MCRPC** = metastatic castration resistant prostate cancer; **mono** = monotherapy; **TRAEs** = treatment-related adverse events

Olema ONCOLOGY

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 1b/2 study evaluating OP-3136 monotherapy and combination in advanced or metastatic:

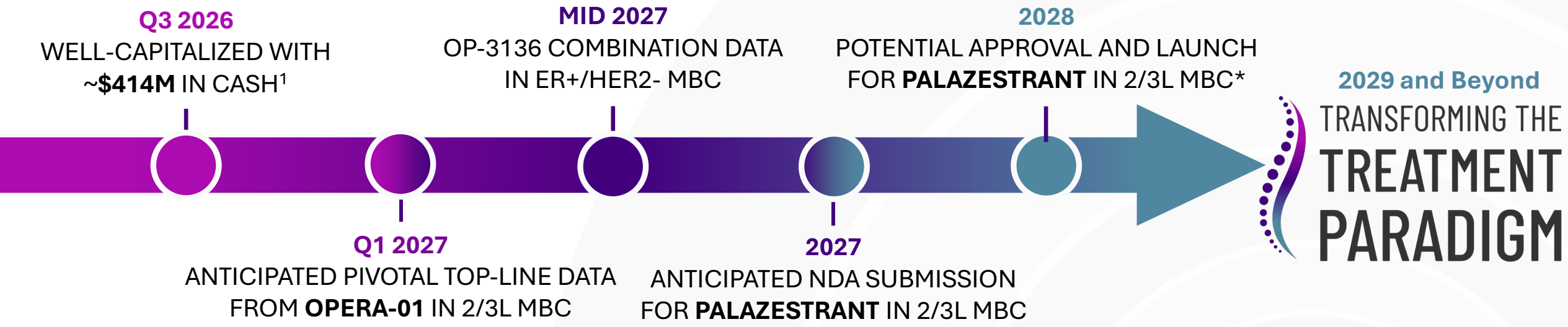
- ER+/HER2- breast cancer[1]
- Castration-resistant prostate cancer[2]
- Non-small cell lung cancer

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

*Internal Olema estimates. [1]In combination with fulvestrant and palazestrant. [2]In combination with darolutamide.
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



[1]*Cash position as of September 30, 2026, 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; **ER+** = estrogen receptor positive; **HER2-** = human epidermal growth factor receptor 2 negative; **MBC** = metastatic breast cancer; **NDA** = New Drug Application

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*

MILESTONES

- Completed patient enrollment in pivotal Phase 3 OPERA-01 trial of palazestrant monotherapy in 2/3L MBC
- Announce top-line data from pivotal Phase 3 OPERA-01 trial in Q1 2027
- Advance patient enrollment in pivotal Phase 3 OPERA-02 trial of palazestrant + ribociclib in 1L MBC

Olema ONCOLOGY

* 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; **FDA** = U.S. Food and Drug Administration; **MBC** = metastatic breast cancer

Palazestrant mechanism of action

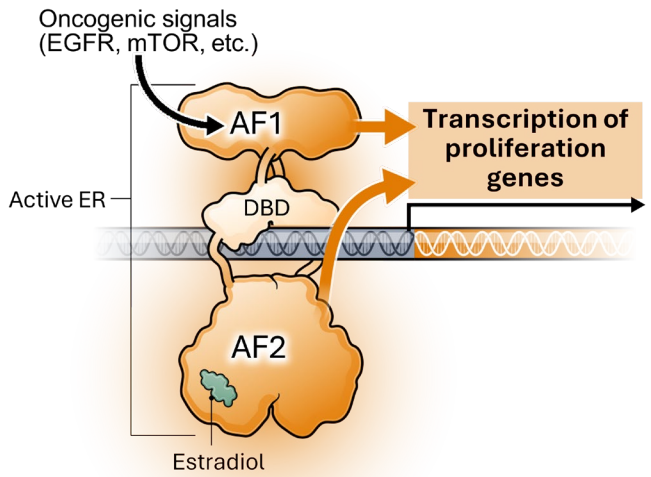
Palazestrant is a differentiated oral CERAN/SERD targeting the growth and proliferation mechanism driving ER+ breast cancer

Activated ER
drives cancer cell growth

SERM/SERDs
partially inactivate ER
(AF2 only)

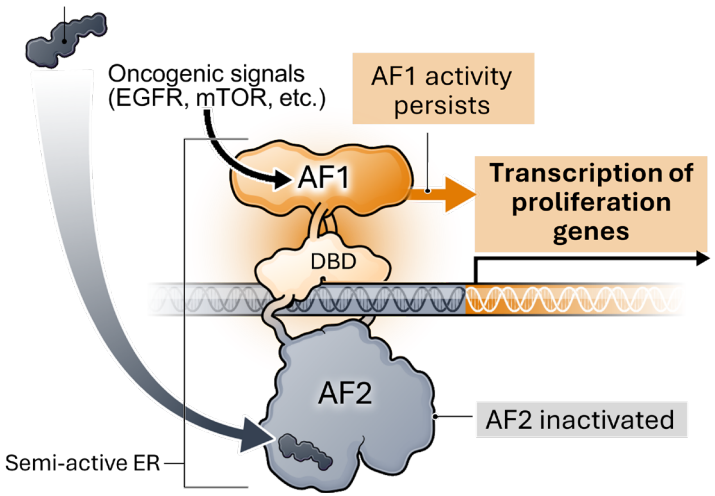
Palazestrant, a CERAN/SERD,
not only degrades but also
completely inactivates ER
(AF1 and AF2) by recruiting N-CoR[1]

Cancer

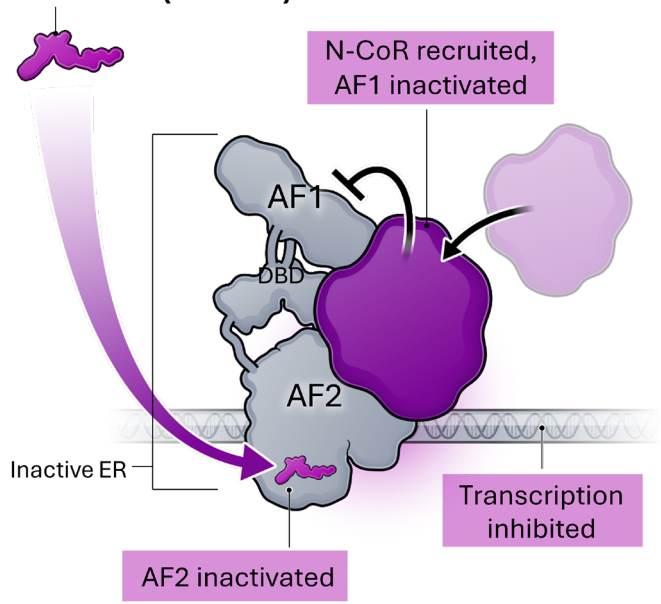


AF - Activation factor
DBD - DNA Binding Domain

SERM/SERD



Palazestrant (CERAN)



[1]2026 AACR Annual Meeting. Poster #2950.

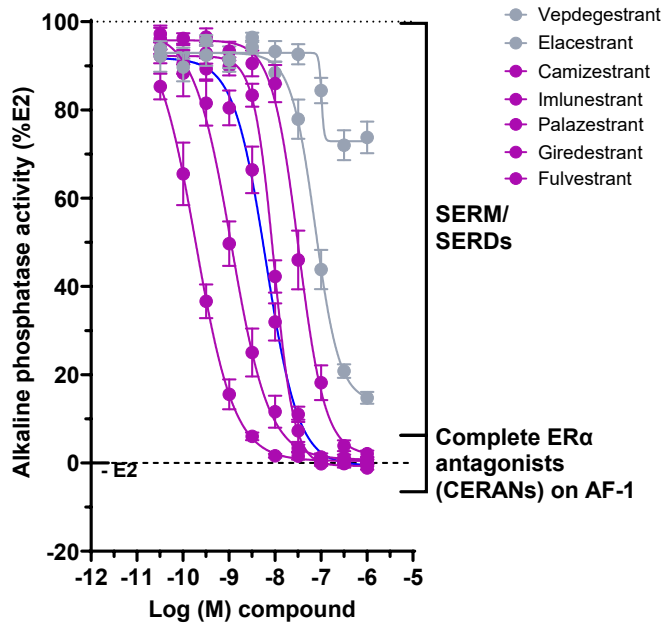
AF = activation factor; **CERAN** = complete estrogen receptor antagonist; **DBD** = DNA binding domain; **EGFR** = epidermal growth factor receptor; **ER** = estrogen receptor; **mTOR** = mammalian target of rapamycin; **N-CoR** = nuclear receptor corepressor; **SERD** = selective estrogen receptor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

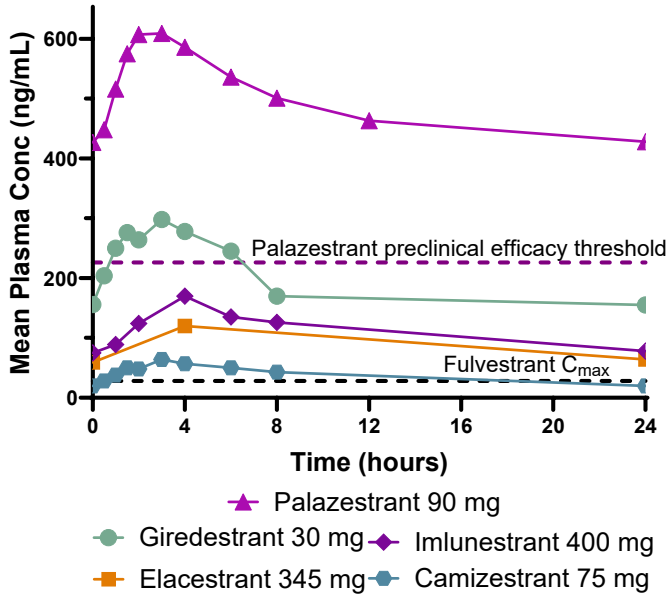
Complete ER antagonism is key to shutting off all ER signaling

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



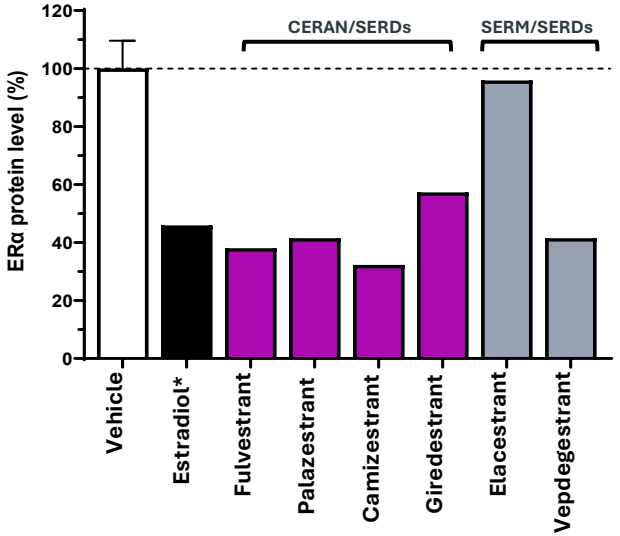
Palazestrant uniquely meets optimal drug-plasma exposure[1]

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; **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

- **2027:** Announce top-line results from OPERA-01 in Q1
- **2027:** Anticipated submission of New Drug Application for potential approval of palazestrant as a monotherapy in 2/3L ER+/HER2-MBC and preparations for commercial launch
- **2028:** Potential FDA approval and U.S. commercial launch of palazestrant

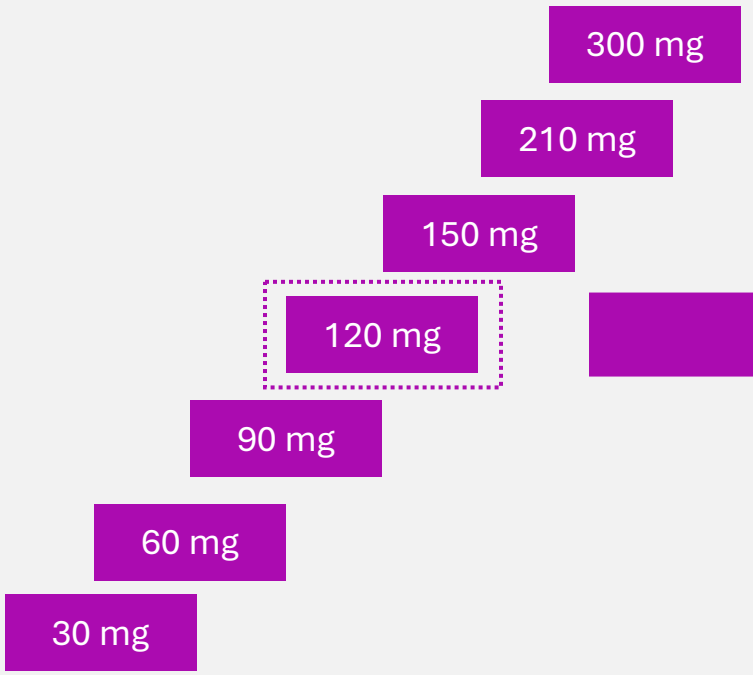
Olema ONCOLOGY

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



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 was 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

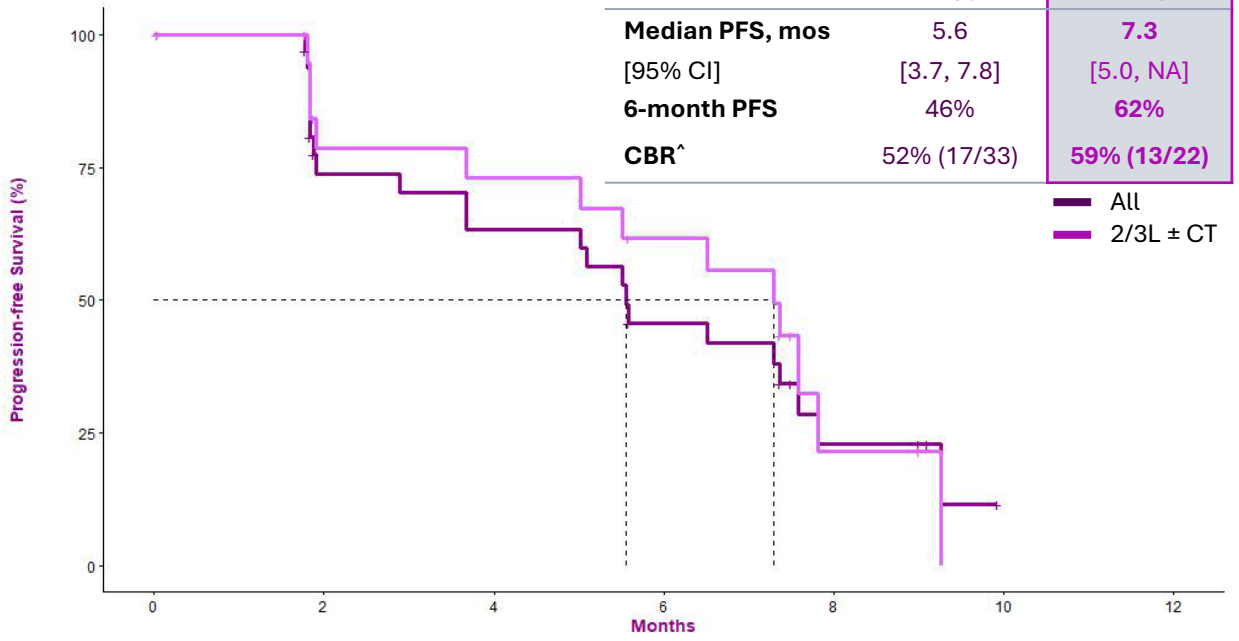
Data cutoff date: July 7, 2023. Data shown are n or n (%).
AE = adverse events; **AST** = aspartate aminotransferase; **TEAEs** = treatment-emergent adverse events

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)**

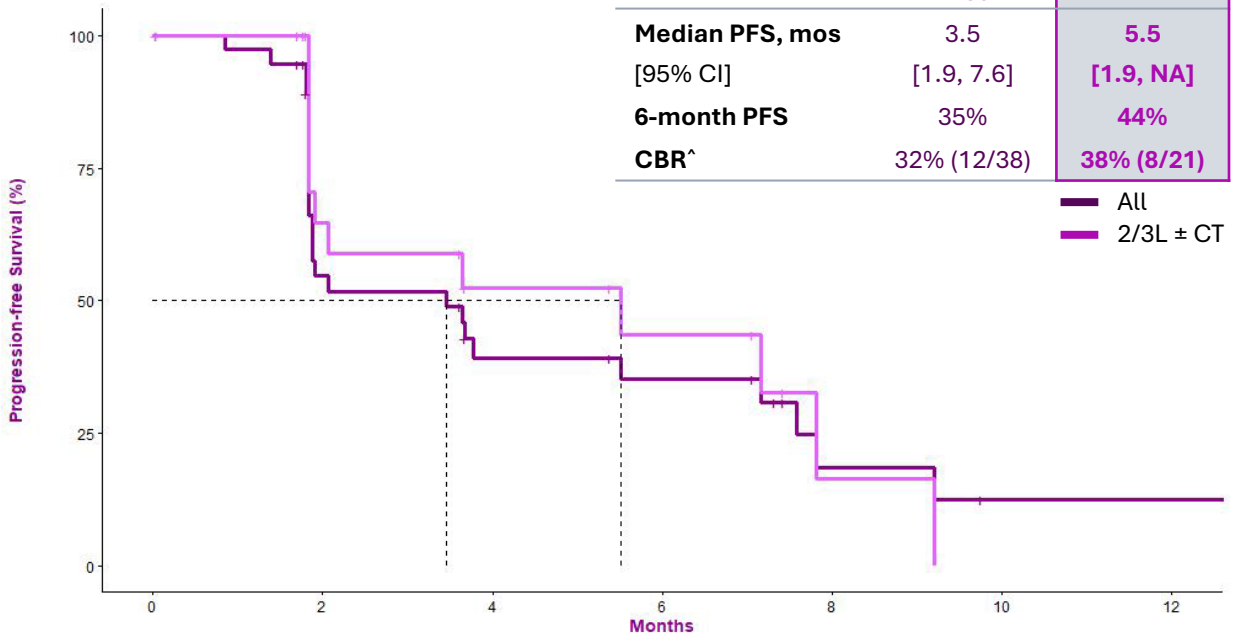


Number at Risk

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.

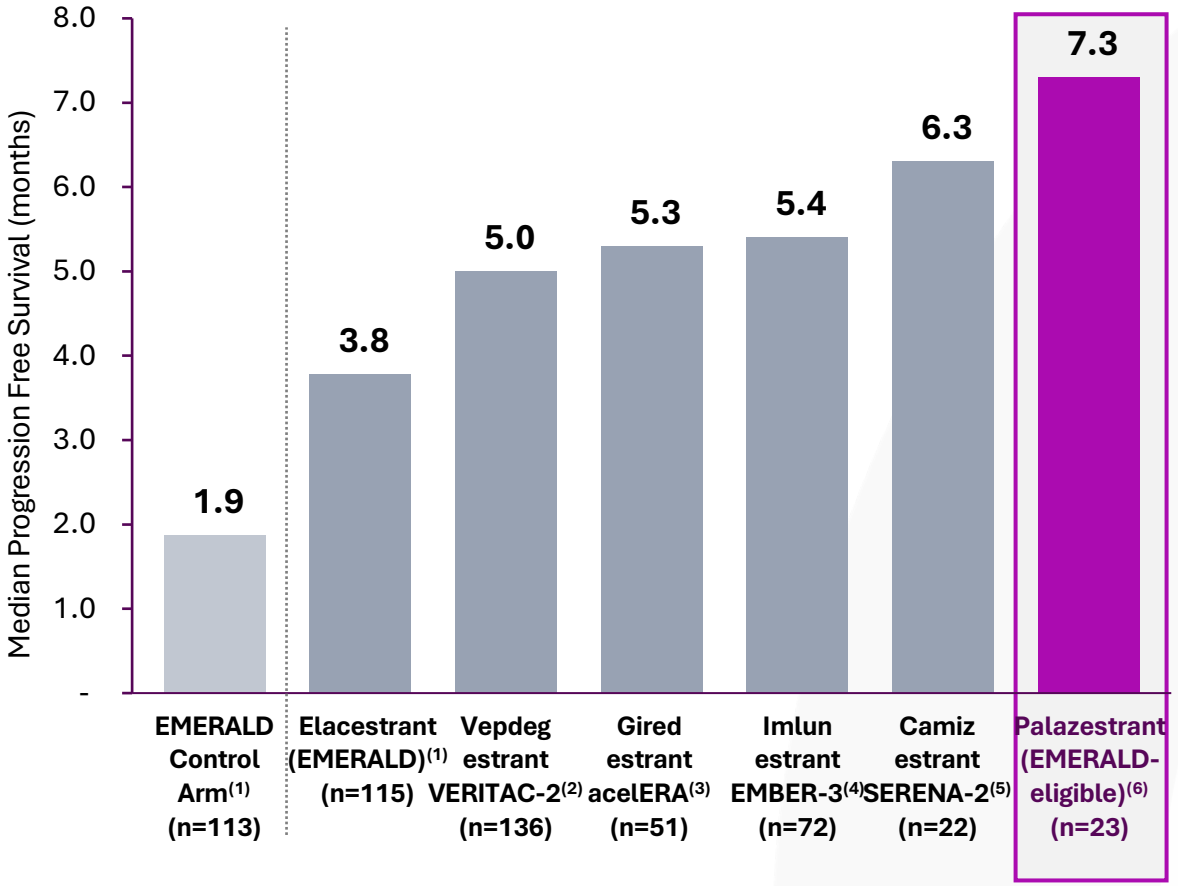
± CT = plus/minus chemotherapy; **CBR =** clinical benefit rate; **CI =** confidence interval; **ESR1 =** estrogen receptor 1 gene; **mos=** months; **mPFS =** median progression free survival; **mut =** mutation; **NA =** not applicable; **WT=** wild-type

Olema ONCOLOGY

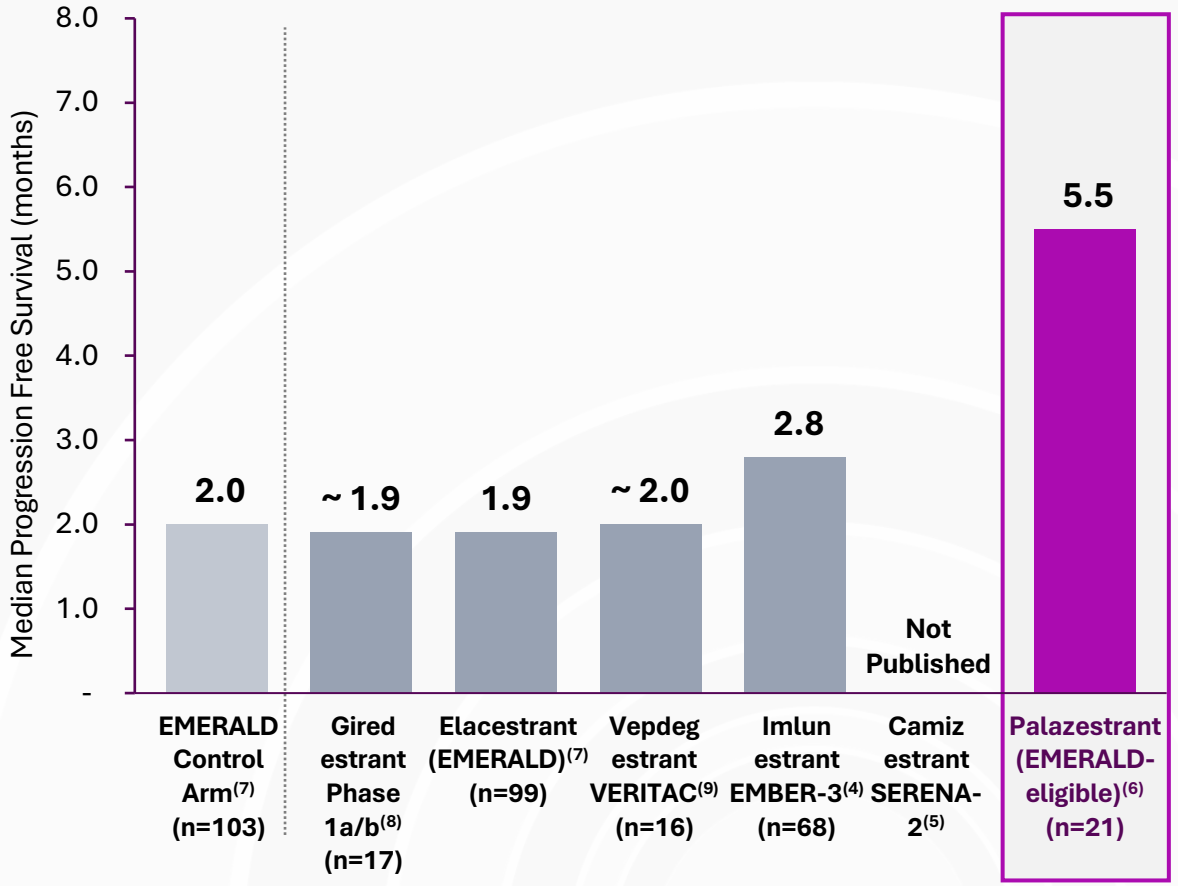
Palazestrant in the competitive landscape: best-in-class potential*

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

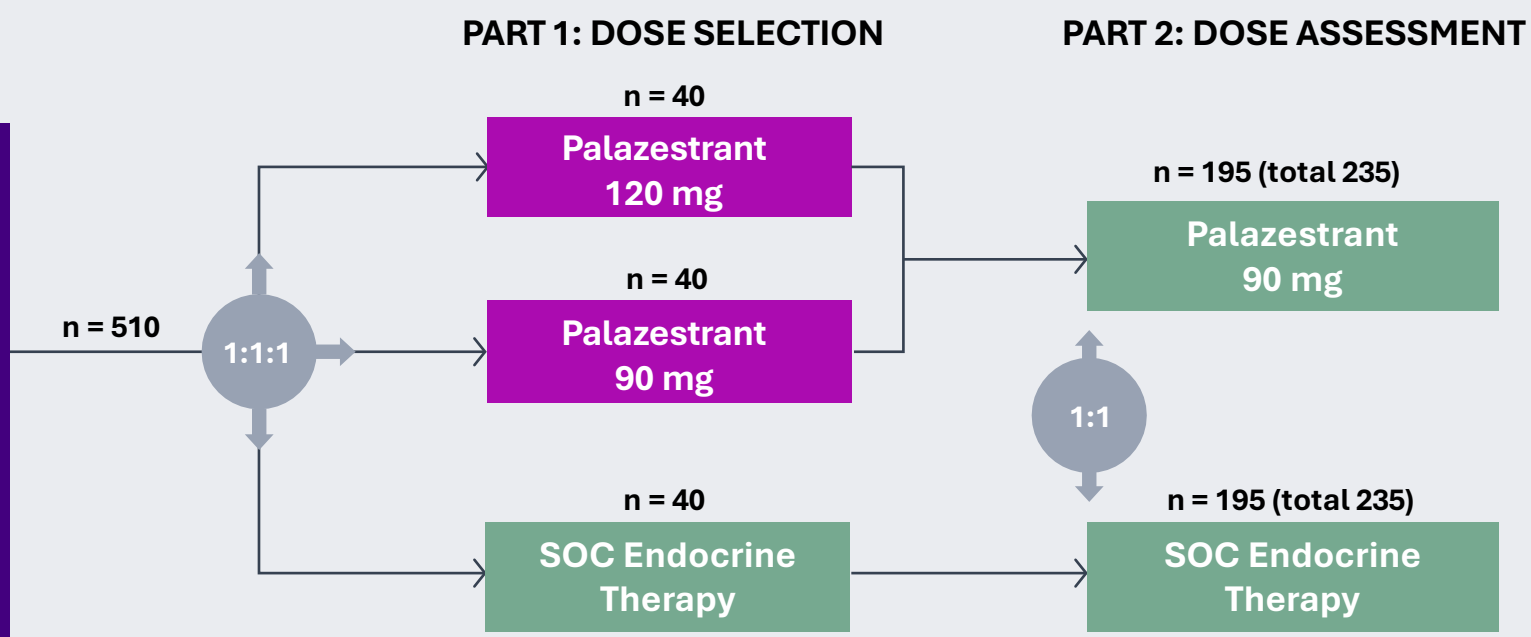
OPERA-01 Breast Cancer Study

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 Q1 2027.

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 2028



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

1L = frontline; **ER+** = estrogen receptor positive; **ESMO** = European Society for Medical Oncology Congress; **HER2-** = human epidermal growth factor receptor 2 negative;

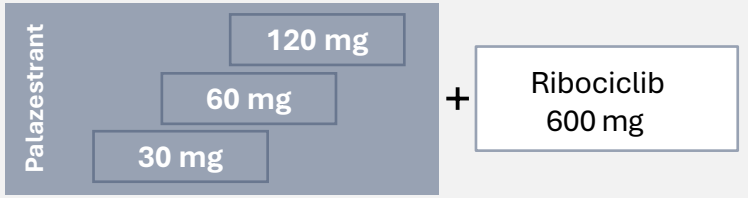
Design: Phase 1b/2 study of palazestrant in combination with ribociclib in ER+/HER2- MBC

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	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.

AI = aromatase inhibitor; **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.**

Data cutoff date: July 8, 2025. Data shown are n or n (%).

†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) .

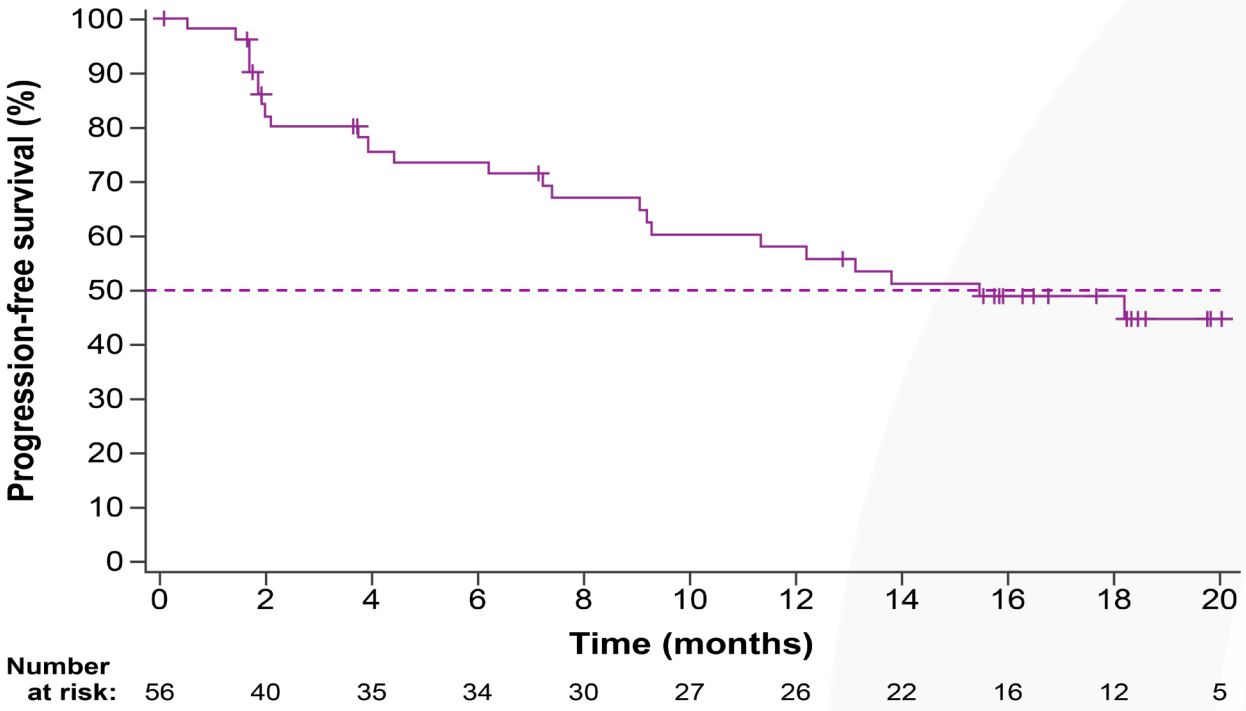
AE = adverse events; **DLTs** = dose-limiting toxicity; **ECG QT** = electrocardiogram QT interval; **ER+** = estrogen receptor positive; **ET** = endocrine therapy; **HER2- =** human epidermal growth factor receptor negative; **MBC** = metastatic breast cancer; **NR** = not reported; **TEAEs** = treatment-emergent adverse events; **WBC** = white blood cell

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

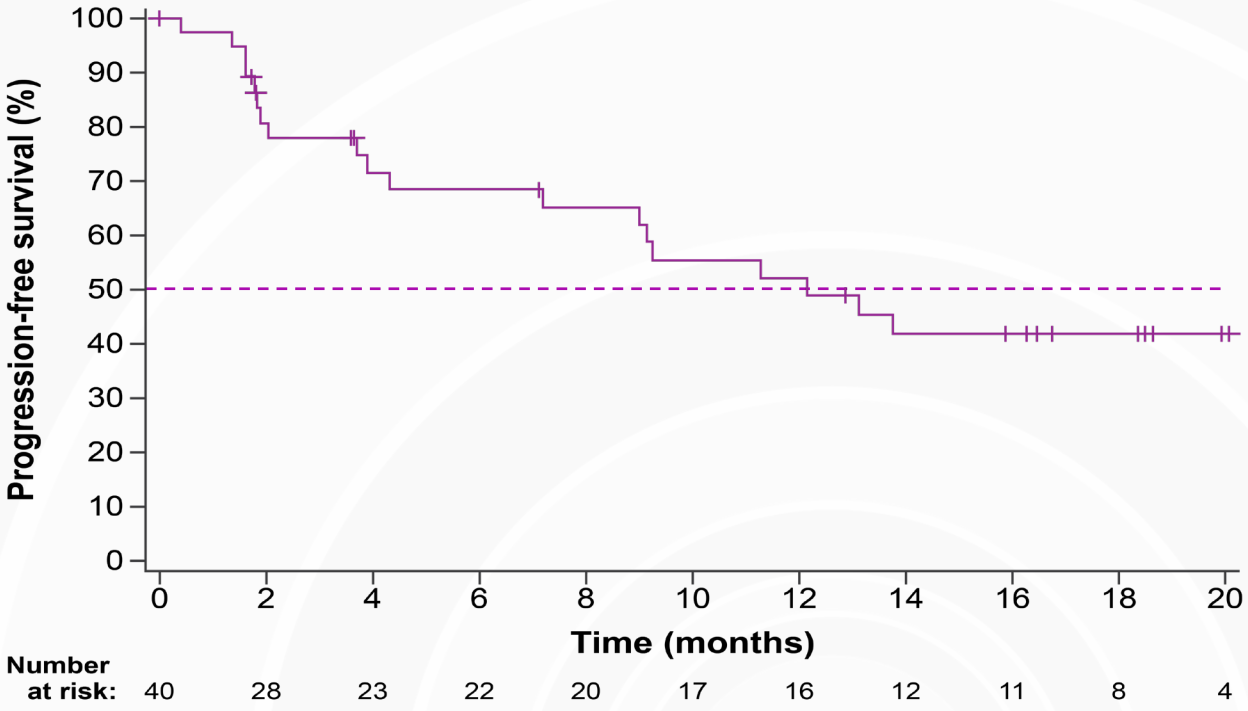
All Patients
120 mg palazestrant + 600 mg ribociclib (n=56)

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

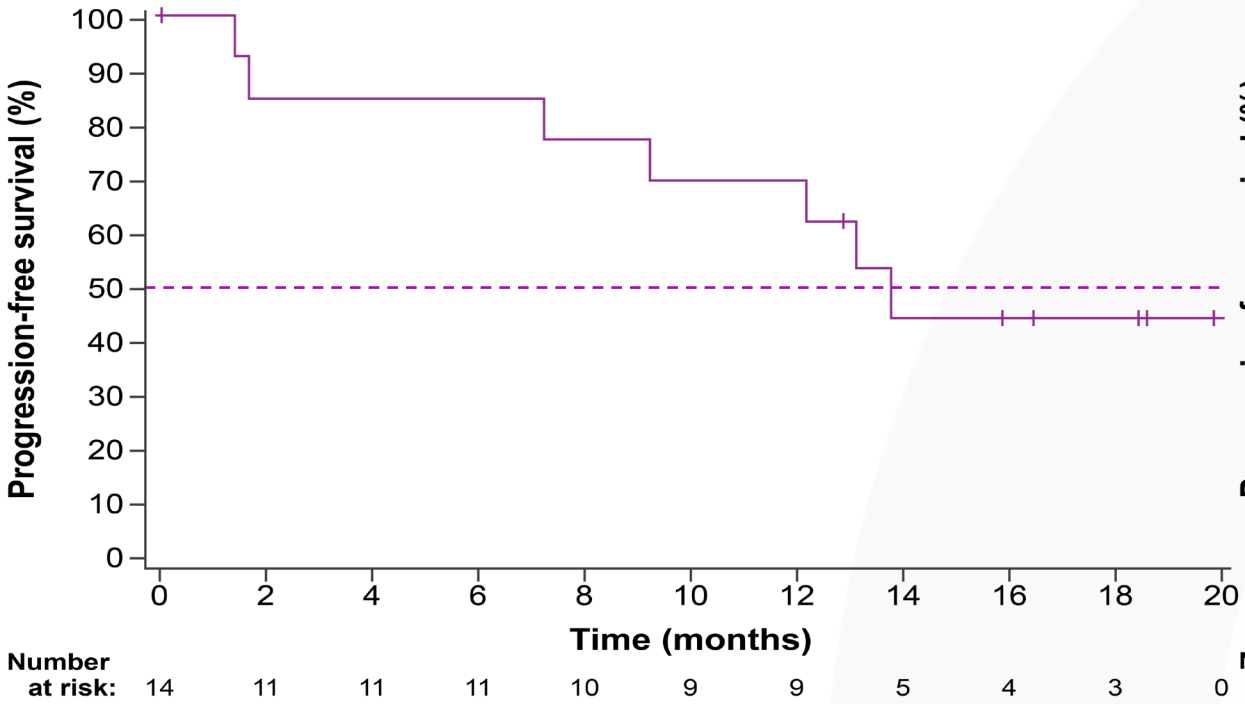
Demonstrated activity in both *ESR1* mutant and wild-type 2L+ patients

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)

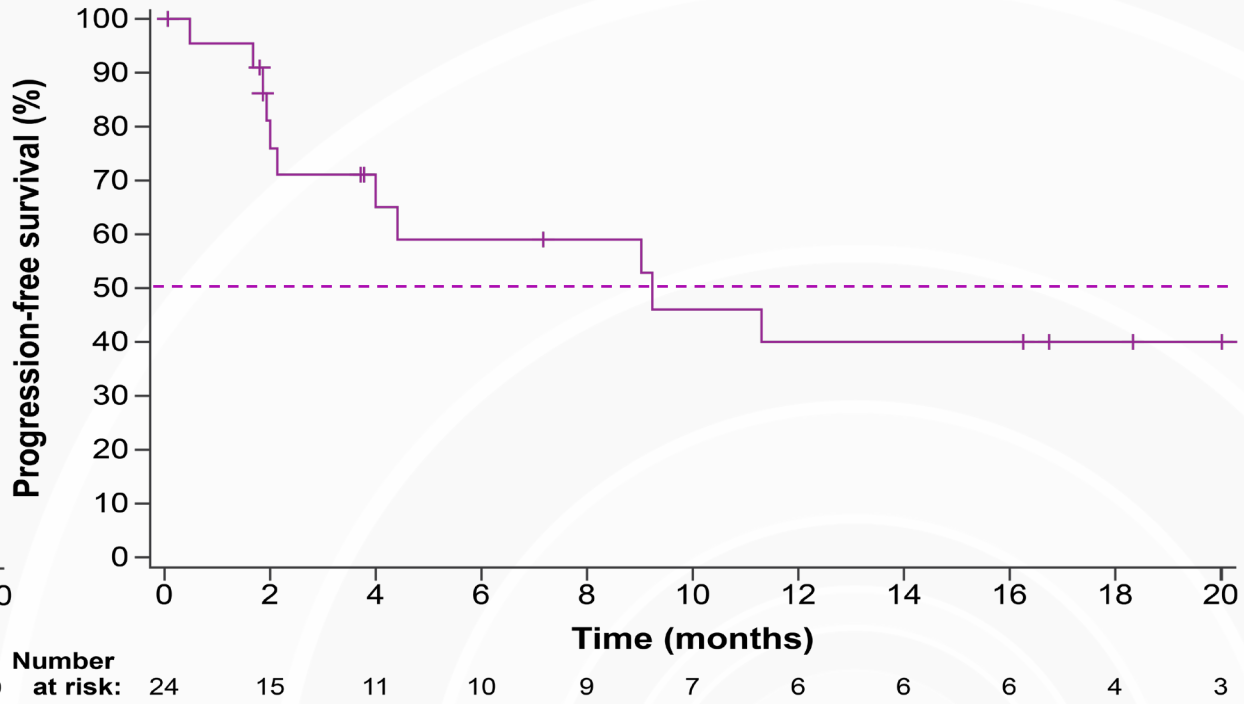
mPFS: 13.8 months



ESR1 Wild-Type Patients with Prior CDK4/6i

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

mPFS: 9.2 months



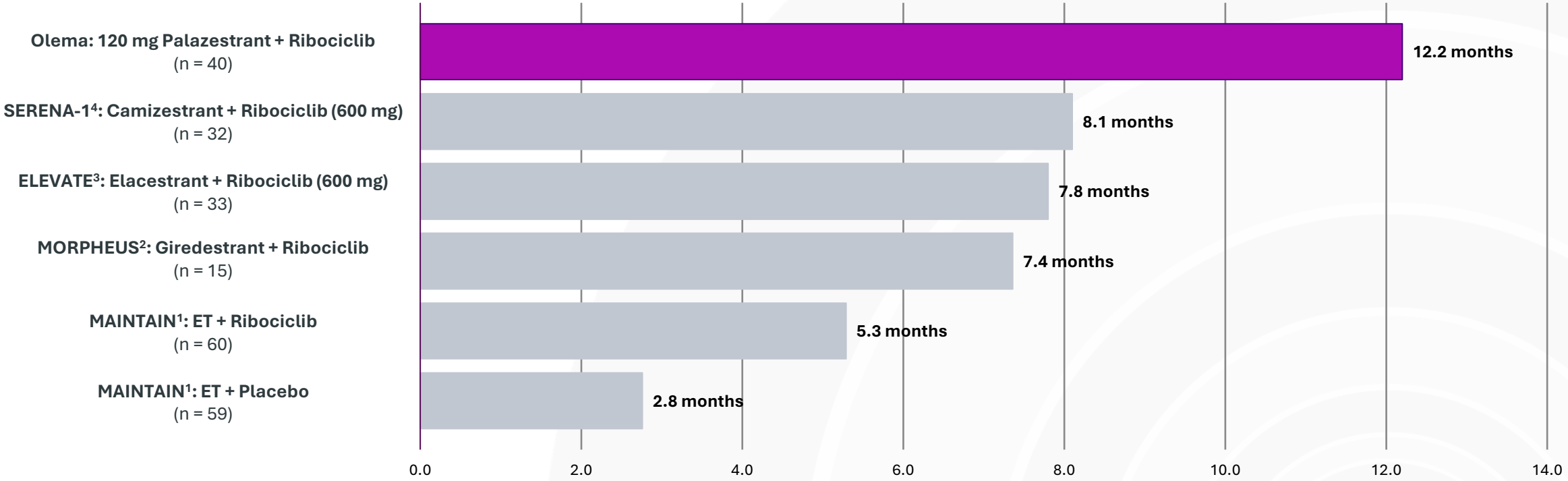
Data cutoff date: July 8, 2025; Median follow-up >19 months

2L = second line; **CDK4/6i =** cyclin-dependent kinase 4/6 inhibitor; **ER+** = estrogen receptor positive; **ESR1** = estrogen receptor 1 gene; **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

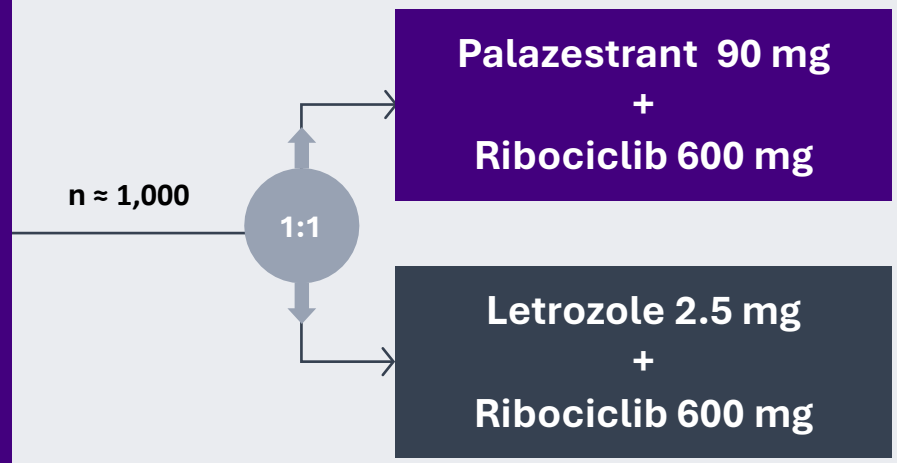
OPERA-02 Breast Cancer Study

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)

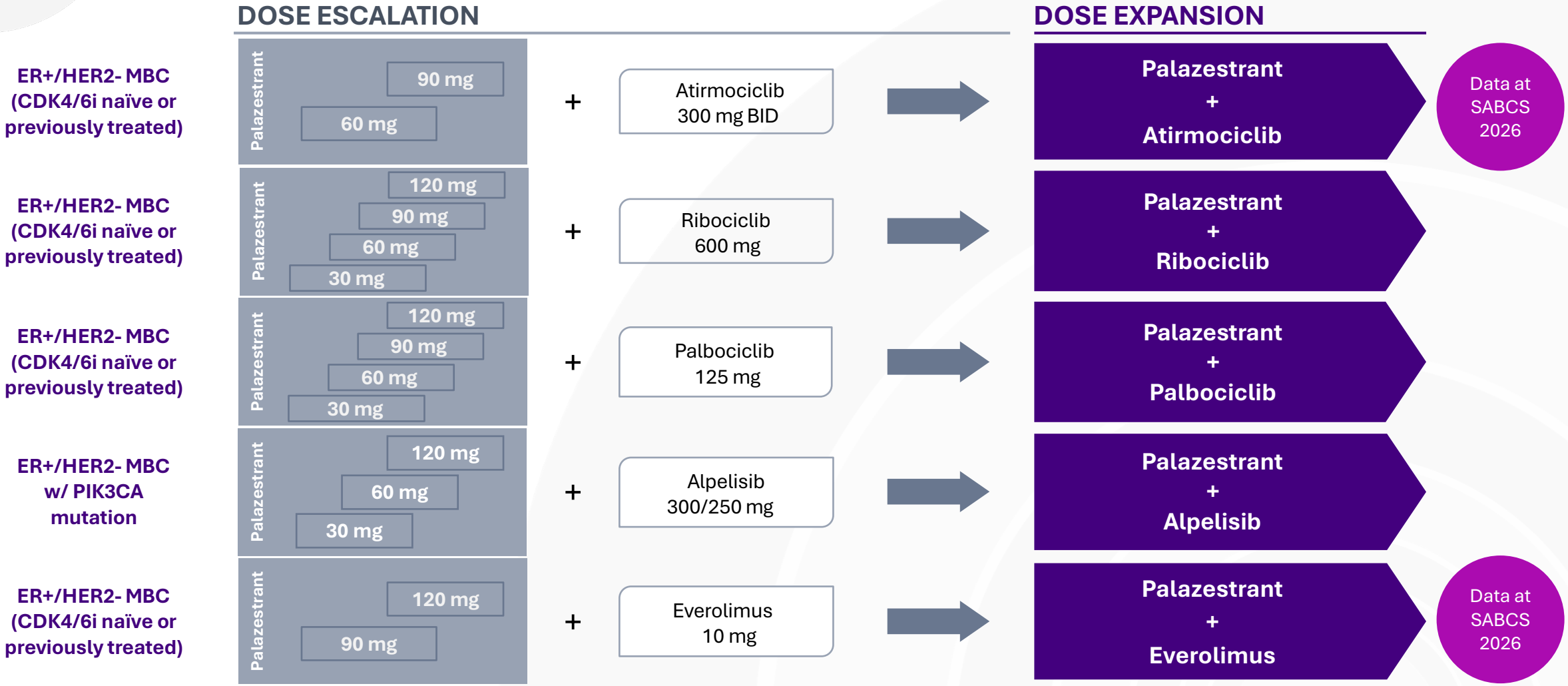
Secondary : OS (Key)
PFS (BIRC)
ORR/CBR/DOR (BIRC, Investigator)
Safety
PK
Health-related PROs

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

Palazestrant demonstrates combinability with other targeted agents

Working to establish palazestrant as the potential combination agent of choice in breast cancer



***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 1b/2
- **Initial Development Indication**
  2/3L ER+/HER2- MBC

MILESTONES

- **May 2026**: Announced CTCSA with Bayer to combine OP-3136 with darolutamide in MCRPC; combo to initiate in Q4 2026
- **ASCO 2026**: Presented initial monotherapy data from the Phase 1 clinical study
- **SABCS 2026**: Initial fulvestrant combination data in ER+/HER2- MBC
- **Mid-2027**: Additional combination data in ER+/HER2- MBC

Olema ONCOLOGY

2/3L = second/third-line; **CTCSA** = clinical trial collaboration and supply agreement; **ER+** = estrogen receptor positive; **KAT6** = lysine acetyltransferase 6; **HER2-** = human epidermal growth factor receptor 2 negative; **MBC** = metastatic breast cancer; **MCRPC** = metastatic castration resistant prostate cancer

OP-3136: Olema's KAT6 inhibitor*

An exciting new and validated target** for the treatment of ER+/HER2- MBC and beyond

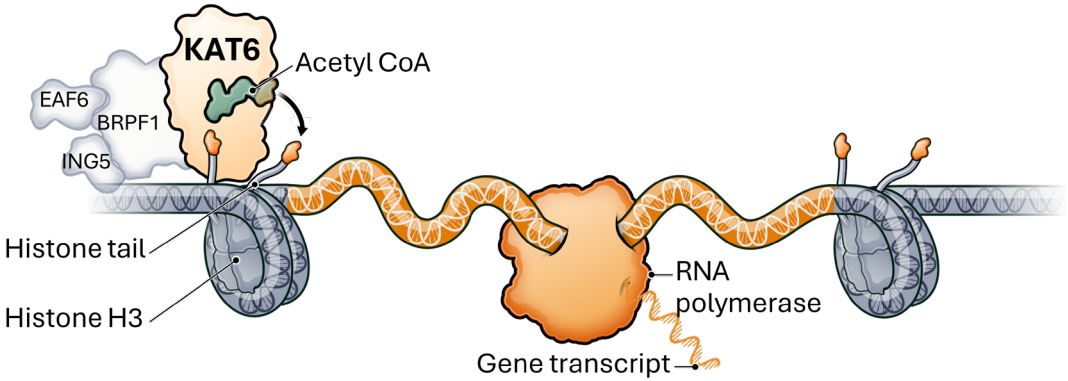
- Potent and selective against KAT6A/B; orally bioavailable with high levels of free drug exposure
- OP-3136 synergizes with palazestrant and CDK4/6 inhibitors in preclinical models[1, 2]
- Initial monotherapy data demonstrated acceptable tolerability and preliminary anti-tumor activity across advanced solid tumor types[3]
- Announced first clinical collaboration for OP-3136 in May 2026 to combine with Bayer's darolutamide in MCRPC
- Initial fulvestrant combination data to be presented at SABCS 2026; additional combination data expected in mid-2027; darolutamide combination expected to initiate in Q4 2026

*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). [1]2026 AACR Annual Meeting. Poster #2949. [2]2024 EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics. Poster #230. [3]2026 ASCO Annual Meeting. Poster #225. **CDK4/6 =** cyclin-dependent kinase 4/6; **ER+** = estrogen receptor positive; **HER2-** = human epidermal growth factor receptor 2 negative; **KAT6** = lysine acetyltransferase 6; **MBC** = metastatic breast cancer; **MCRPC** = metastatic castration-resistant prostate cancer

OP-3136 mechanism of action

KAT6 acetylates chromatin, enabling transcription and proliferation

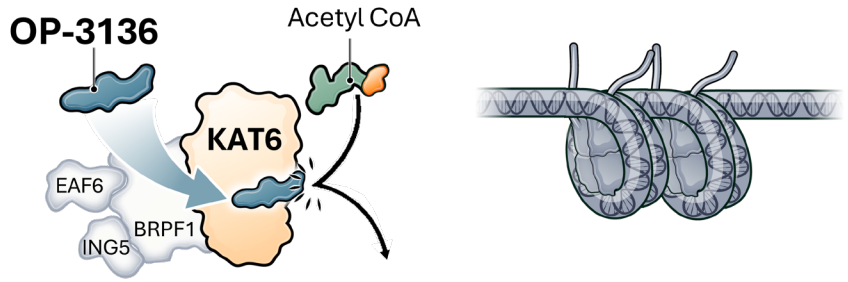
KAT6 acetylates histone tails → Chromatin opens



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



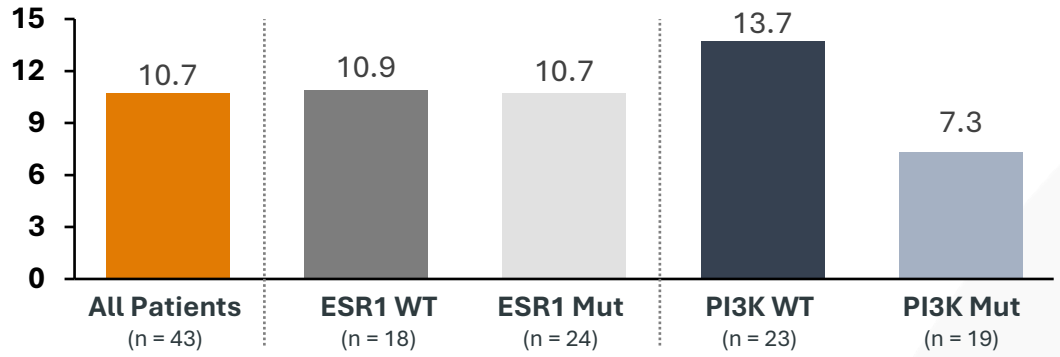
Gene Transcription Inactive

- 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

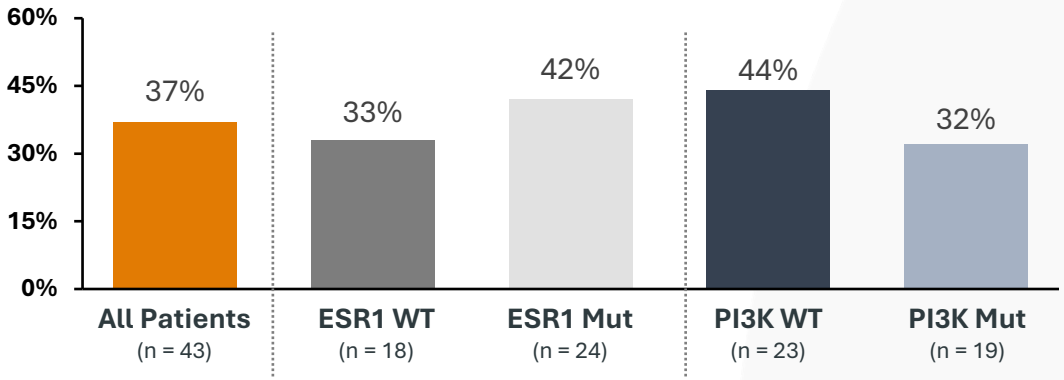
[1] Sommerhalder D, et al. First-in-human phase 1 dose escalation study of the KAT6 inhibitor PF-07248144 in patients with advanced solid tumors. JCO. 2023. 41(16)1054-1054.
[2] Yu L, et, al. Identification of MYST3 as a novel epigenetic activator of ERα frequently amplified in breast cancer. Oncogene. 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.
CoA = coenzyme A; **ER =** estrogen receptor; **KAT6 =** lysine acetyltransferase 6; **+** = 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] 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; **CERAN** = complete estrogen receptor antagonist; **ERS1** = estrogen receptor 1 gene; **ESR1** = estrogen receptor 1; **ET** = endocrine therapy; **KAT6** = lysine acetyltransferase 6; **Mut** = mutant; **ORR** = overall response rate; **PFS** = progression free survival; **PI3K** = phosphatidylinositol 3-kinase **PTEN** = phosphatase and tensin homolog; **WT** = wild-type

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

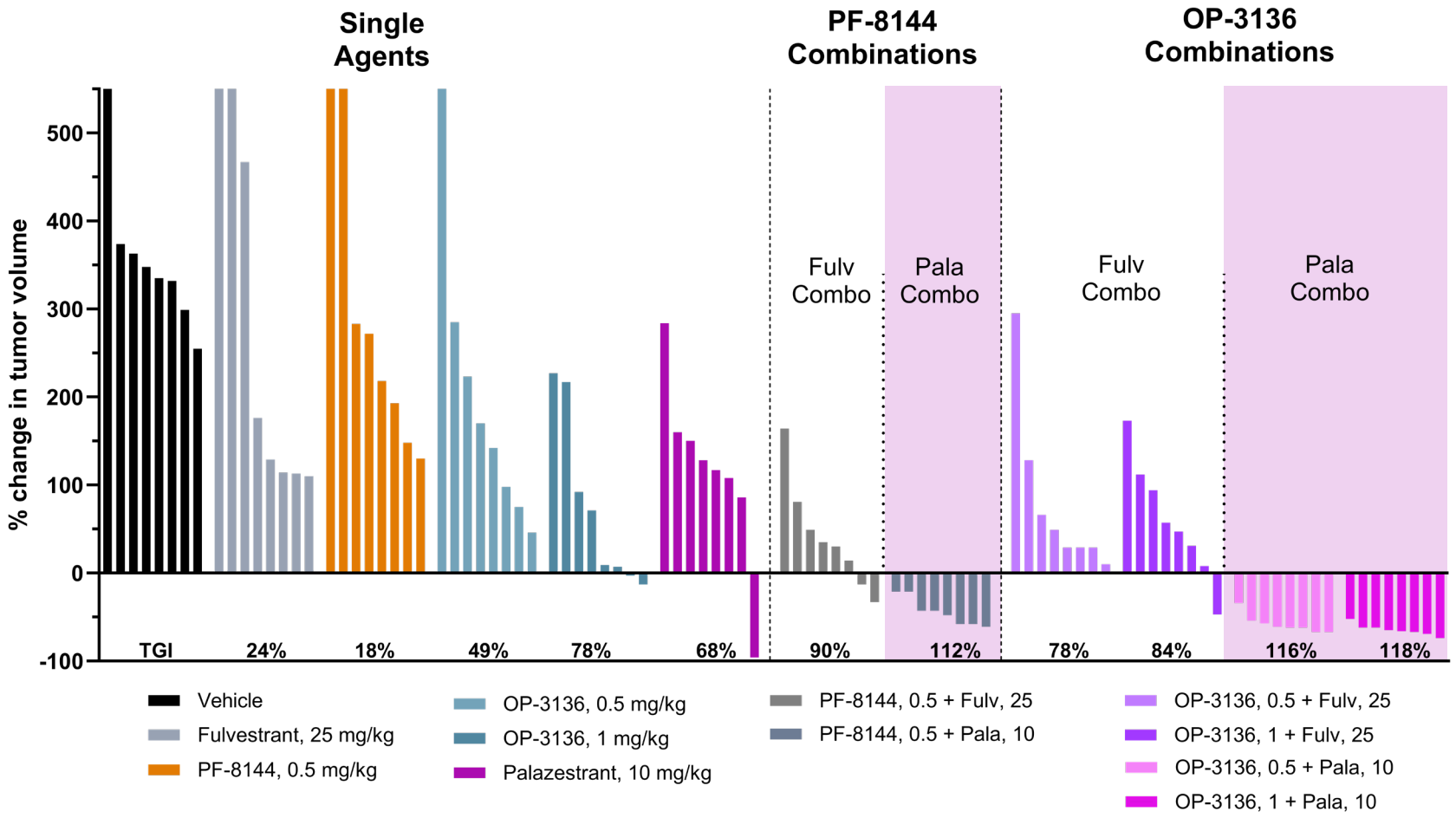
Note: Olema KAT6 inhibitors discovered in collaboration with Aurigene

[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[1]

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

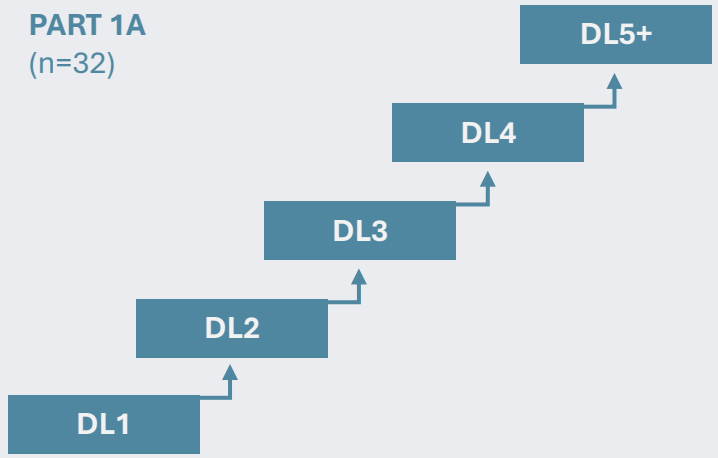
[1]2024 EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics. Poster #230. T47D model (ER+, HER2-, KAT6A overexpressing, ESR1 wild-type, PIK3CA H1047R cell line).
Fulv = fulvestrant; **Pala** = Palazestrant; **Ribo** = ribociclib

OP-3136 Phase 1b/2 study design

Enrollment in palazestrant and fulvestrant combination arms ongoing; darolutamide combination expected to initiate in Q4 2026

PART 1: DOSE ESCALATION

PART 1A
(n=32)



Mono RDE

PART 1B
OP-3136 + Fulvestrant
MBC

PART 1C
OP-3136 + Palazestrant
MBC

NEW!

PART 1D
OP-3136 + Darolutamide[1]
MCRPC

Combo RDE

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)

[1]CTCSA with Bayer announced May 2026; combination arm to initiate in H2 2026

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; **HER2-** = human epidermal growth factor receptor 2 negative; **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

OP-3136 monotherapy was well tolerated with no DLTs observed across evaluated dose levels up to 45 mg daily[1]

Preliminary safety from Part 1A of the Phase 1 study of OP-3136 in multiple solid tumor types

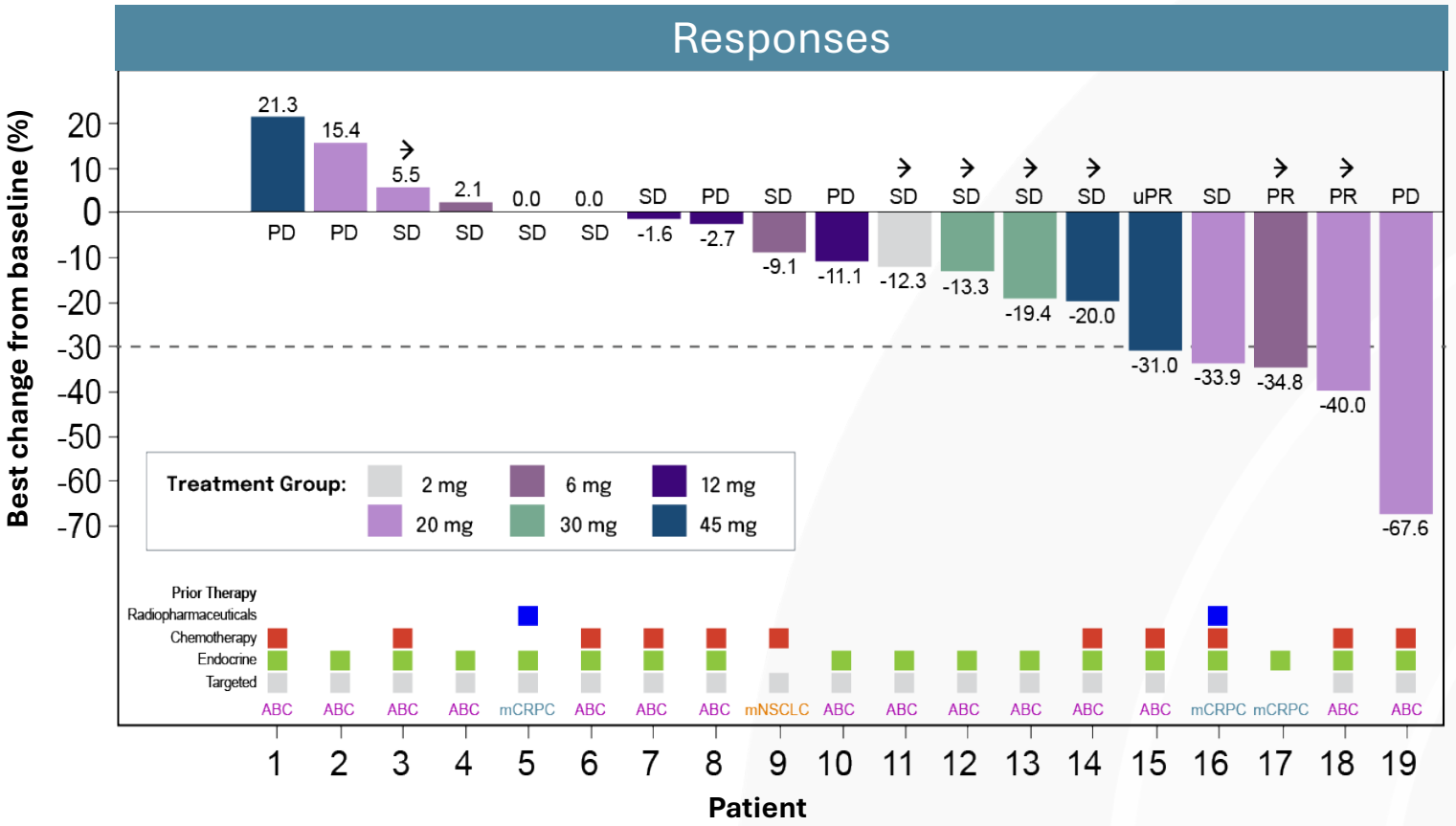
TRAE	Any Grade, n (%)	Grade 3, n (%)
Any TRAE	31 (97%)	11‡ (34%)
Dysgeusia*	26 (81%)	N/A
Anemia	12 (38%)	2 (6%)
Fatigue	12 (38%)	1 (3%)
Neutropenia†	11 (34%)	9 (28%)
Nausea	8 (25%)	0
Platelet count decreased	6 (19%)	0
ALT increased	4 (12.5%)	0
Back pain	4 (12.5%)	0

- Most TRAEs were grade 1 or 2; no grade 4 or 5 TRAEs were observed
- TRAEs were manageable with few dose modifications; no treatment discontinuations occurred due to TRAEs
- The most common TRAEs were dysgeusia (81% any grade; 56% grade 1, 25% grade 2), anemia (38% any grade; 6% grade 3), and neutropenia (34% any grade; 28% grade 3)

Data cutoff: March 2, 2026 [1]2026 ASCO Annual Meeting. Poster #225. *Includes preferred terms 'Dysgeusia' and 'Taste Disorder.' †Includes preferred terms 'Neutropenia' and 'Neutrophil count decreased. ‡Grade 3 TRAEs included anemia (1 patient each at 6 mg and 30 mg); neutropenia† (1 at 6 mg, 4 at 12 mg, 1 at 20 mg, 1 at 30 mg, and 2 at 45 mg); thrombocytopenia (1 at 30 mg); leukopenia (1 at 30 mg); fatigue (1 at 12 mg); syncope (1 at 12 mg).
ALT = alanine aminotransferase; **DLT** = dose limiting toxicity; **N/A =** not applicable; **TRAE =** treatment-related adverse event

OP-3136 monotherapy demonstrated tumor shrinkage in over 2/3 of patients across dose levels in various advanced solid tumor types[1]

Durable responses and evidence of on-target engagement reinforce best-in-class potential



- Among 19 response-evaluable patients across dose levels and tumor types, tumor shrinkage was observed in 13 patients
  - PRs were observed in 3 patients with measurable disease, with 2 confirmed PRs and 1 unconfirmed PR
- The longest duration of treatment is 62 weeks
  - 11 patients remain on treatment, including 9 with MBC and 2 with MCRPC
- Across all doses tested, OP-3136 demonstrated rapid, sustained, and significant reduction in levels of acetylation of lysine 23 of histone H3, a direct target of KAT6, consistent with on-target KAT6 inhibition

Data cutoff: March 2, 2026 [1]2026 ASCO Annual Meeting. Poster #225. **ABC** = advanced breast cancer; **MBC** = metastatic breast cancer; **MCRPC** = metastatic castration resistant prostate cancer; **MNSCLC** = metastatic non-small cell lung cancer; **PD** = progressive disease; **PR** = partial response; **uPR** = unconfirmed partial response; **SD** = stable disease

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

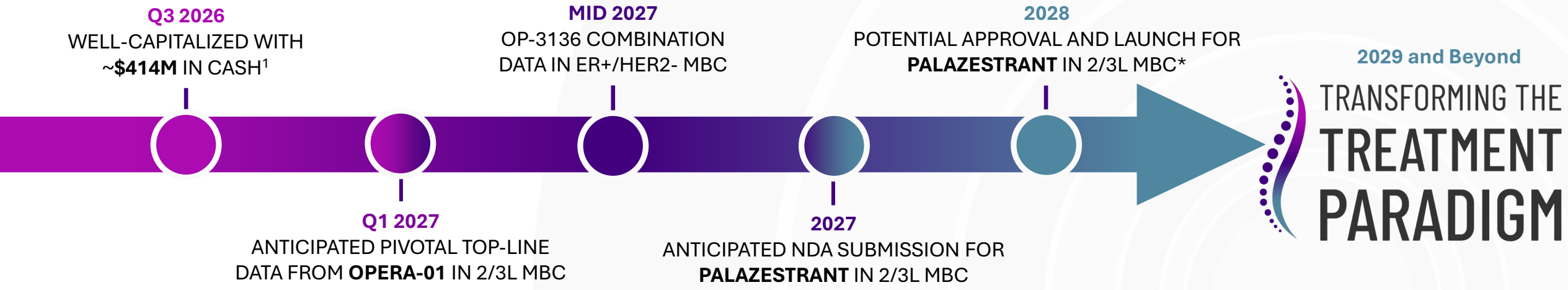
Palazestrant

- Highly differentiated with activity in *ESR1* mutant and wild-type tumors
- Combinable at full doses with other targeted agents
- OPERA-01 Phase 3 trial top-line data expected in Q1 2027
- OPERA-02 Phase 3 trial in combination with ribociclib enrolling patients
- First potential U.S. approval and launch in 2028

OP-3136

- Exciting new target in breast cancer
- Synergizes with palazestrant and CDK4/6 inhibitors in preclinical models
- Expansion opportunity in prostate cancer
- Encouraging initial clinical data presented at ASCO 2026; fulvestrant combination data to be presented at SABCS with additional combination data expected in mid-2027

Corporate Priorities and Anticipated Milestones



[1]*Cash position as of September 30, 2026, 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; **ESR1** = estrogen receptor 1 gene; **MBC** = metastatic breast cancer; **NDA** = New Drug Application

Advancing medicines for breast cancer and beyond

Olema ONCOLOGY