UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): October 18, 2025

Olema Pharmaceuticals, Inc.

(Exact name of Registrant as Specified in Its Charter)

Delaware	**001-39712**	**30-0409740**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

780 Brannan Street **San Francisco, California** **(Address of Principal Executive Offices)**	**94103** **(Zip Code)**

Registrant's Telephone Number, Including Area Code: 415 651-3316

N/A
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common Stock, par value $0.0001 per share	OLMA	The Nasdaq Global Select Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

On October 18, 2025, the Company issued a press release announcing new data from its Phase 1b/2 trial of palazestrant in combination with ribociclib in patients with estrogen receptor-positive (ER+), human epidermal growth factor receptor 2-negative (HER2-) advanced or metastatic breast cancer (MBC). A copy of the press release is furnished as Exhibit 99.1 to this Current Report on Form 8-K.

On October 18, 2025, the Company made available on its website a presentation to be shared with investors and others from time to time. A copy of this presentation is being furnished as Exhibit 99.2 to this Current Report on Form 8-K.

The information in Exhibits 99.1 and 99.2 attached hereto is intended to be furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act") or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended (the "Securities Act"), except as expressly set forth by specific reference in such filing.

Item 8.01 Other Events.

Phase 1b/2 Trial of Palazestrant in Combination with Ribociclib

In October 2025, the Company presented updated data from the Phase 1b/2 study of palazestrant in combination with ribociclib in patients with ER+/HER2- advanced or MBC.

As of July 8, 2025, 72 patients were enrolled across the 90 mg and 120 mg palazestrant dose cohorts. 56 patients received 120 mg once-daily palazestrant and 16 patients received 90 mg once-daily palazestrant, all with the approved dose of ribociclib for metastatic breast cancer of 600 mg daily. 45 (63%) patients had prior treatment with CDK4/6i with endocrine therapy for advanced disease. 33% (15/45) of patients who had prior treatment with CDK4/6i in the advanced setting (2/3L) had an *ESR1* mutation at baseline.

In the 90 mg palazestrant dose cohort, with a median follow-up of 10.8 months, mPFS was not reached. In the 120 mg palazestrant dose cohort, with a median follow-up of more than 19 months, mPFS are mature. mPFS was 15.5 months for all patients. mPFS was 12.2 months for those who received prior treatment with CDK4/6i, including 9.2 months for patients with *ESR1* wild-type tumors and 13.8 months for patients with tumors with *ESR1* mutations.

Across 72 patients treated, 90 mg or 120 mg of palazestrant combined with 600 mg of ribociclib daily was well tolerated with no new safety signals or increase in toxicity. Palazestrant and ribociclib did not demonstrate any drug-drug interactions and the overall safety profile was consistent with the established safety profile of ribociclib plus an endocrine therapy. The majority of treatment-emergent adverse events were grade 1 or 2, and the severity and incidence of adverse events were consistent with the expected safety profile of each drug.

These data support the ongoing pivotal Phase 3 OPERA-02 clinical trial of palazestrant in combination with ribociclib in frontline ER+/HER2- MBC.

Forward-Looking Statements

Statements contained in this Current Report on Form 8-K, including the exhibit furnished herewith, regarding matters that are not historical facts are "forward-looking statements" within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act. Words such as "anticipate," "believe," "could," "expect," "goal," "may," "plan," "potential," "seek," "upcoming," "will," and similar expressions (as well as other words or expressions referencing future events, conditions or circumstances) are intended to identify forward-looking statements. These statements include, but are not limited to, the potential beneficial characteristics, safety, tolerability, efficacy, and therapeutic effects of palazestrant in combination with ribociclib in frontline ER+/HER2- advanced or MBC. Because such statements deal with future events and are based on Olema's current expectations, they are subject to various risks and uncertainties, and actual results, performance or achievements of Olema could differ materially from those described in or implied by the statements in this Current Report on Form 8-K, including the exhibits furnished herewith. These forward-looking statements are subject to risks and uncertainties, including, without limitation, those discussed in the section titled "Risk Factors" in Olema's Quarterly Report on Form 10-Q for the quarter ended June 30, 2025, and other filings and reports that Olema makes from time to time with the U.S. Securities and Exchange Commission. Except as required by law, Olema assumes no obligation to update these forward-looking statements, including in the event that actual results differ materially from those anticipated in the forward-looking statements.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	Press Release, dated October 18, 2025, of Olema Pharmaceuticals, Inc.
99.2	Investor Presentation, dated October 18, 2025, of Olema Pharmaceuticals, Inc.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Olema Pharmaceuticals, Inc.

Date: October 20, 2025

By: /s/ Shane Kovacs
Shane Kovacs
Chief Operating and Financial Officer

Exhibit 99.1

Olema Oncology Announces New Data from the Phase 1b/2 Trial of Palazestrant Plus Ribociclib in ER+/HER2- Metastatic Breast Cancer at ESMO 2025

- *Palazestrant in combination with ribociclib demonstrated encouraging activity across all dose cohorts and subgroups*
- *Median PFS was 15.5 months in the 120 mg palazestrant cohort across all patients*
- *In the 120 mg palazestrant cohort among patients with prior CDK4/6i treatment, median PFS was 9.2 months in patients with ESR1 wild-type tumors and 13.8 months in patients with ESR1 mutant tumors*
- *Combination continues to demonstrate favorable tolerability and a safety profile consistent with the known profiles of each drug*
- *Data support the ongoing Phase 3 OPERA-02 trial of palazestrant in combination with ribociclib in frontline advanced or metastatic breast cancer*

SAN FRANCISCO, October 18, 2025 (GlobeNewswire) – Olema Pharmaceuticals, Inc. (“Olema” or “Olema Oncology”, Nasdaq: OLMA), a clinical-stage biopharmaceutical company focused on the discovery, development, and commercialization of targeted therapies for breast cancer and beyond, today announced updated data from the Phase 1b/2 study of palazestrant in combination with ribociclib in patients with estrogen receptor-positive (ER+), human epidermal growth factor receptor 2-negative (HER2-) advanced or metastatic breast cancer. These findings will be presented in a poster session on October 20 at the European Society for Medical Oncology (ESMO) Congress 2025 in Berlin, Germany.

“We are very pleased with these latest data showing compelling progression-free survival and favorable tolerability of palazestrant plus ribociclib, further reinforcing this regimen’s potential as a new standard of care in metastatic breast cancer,” said Sean P. Bohen, M.D., Ph.D., President and Chief Executive Officer of Olema Oncology. “These data showcase the activity of the combination in both *ESR1* mutant and wild-type tumors, an important component for effective frontline treatment, and underscore the importance of complete ER antagonism in the treatment of ER-positive breast cancer. As we work to transform the breast cancer treatment paradigm, we are increasingly confident in palazestrant’s potential to become a best-in-class, backbone endocrine therapy and are excited to now have our second Phase 3 trial, OPERA-02, underway evaluating palazestrant with ribociclib in the frontline setting.”

Key Findings from the Phase 1b/2 Study of Palazestrant in Combination with Ribociclib
As of July 8, 2025, 72 patients were enrolled across the 90 mg and 120 mg palazestrant dose cohorts. 56 patients received 120 mg once-daily palazestrant and 16 patients received 90 mg once-daily palazestrant, all with the approved dose of ribociclib for metastatic breast cancer of 600 mg daily. 45 (63%) patients had prior treatment with cyclin-dependent kinase 4/6 inhibitors (CDK4/6i) with endocrine therapy for advanced disease. 33% (15/45) of patients who had prior treatment with CDK4/6i in the advanced setting (2/3L) had an *ESR1* mutation at baseline.

Efficacy

- In the 90 mg palazestrant dose cohort, with a median follow-up of 10.8 months, median progression-free survival (PFS) was not reached.
- In the 120 mg palazestrant dose cohort, with a median follow-up of more than 19 months, median PFS are mature. Median PFS was 15.5 months for all patients. Median PFS was 12.2 months for those who received prior treatment with CDK4/6i, including 9.2 months for patients with *ESR1* wild-type tumors and 13.8 months for patients with tumors with *ESR1* mutations.

Safety and Pharmacokinetics

- Across 72 patients treated, 90 mg or 120 mg of palazestrant combined with 600 mg of ribociclib daily was well tolerated with no new safety signals or increase in toxicity.
- Palazestrant and ribociclib did not demonstrate any drug-drug interactions and the overall safety profile was consistent with the established safety profile of ribociclib plus an endocrine therapy.
- The majority of treatment-emergent adverse events were grade 1 or 2, and the severity and incidence of adverse events were consistent with the expected safety profile of each drug.

“Despite recent advances in the treatment of ER+/HER2- metastatic breast cancer, there remains a significant need for therapies that can overcome endocrine resistance, particularly following treatment with a CDK4/6 inhibitor,” said Dr. Nancy Lin, Associate Chief of the Division of Breast Oncology, Susan F. Smith Center for Women’s Cancers, at the Dana-Farber Cancer Institute. “I am very encouraged by these new data showing the novel palazestrant-ribociclib combination compares favorably to other endocrine therapy-CDK4/6 inhibitor combinations. With a compelling median PFS in the challenging post-CDK4/6 inhibitor setting, I believe palazestrant has the potential to serve as an important combination agent in the metastatic setting.”

Poster Presentation Details
Title: Palazestrant (OP-1250) plus ribociclib in patients with estrogen receptor-positive, human epidermal growth factor receptor 2-negative (ER+, HER2-) advanced breast cancer (ABC)
Poster Number: 502P
Session: Breast Cancer, Metastatic Session
Date/Time: Monday, October 20, 2025, from 12:00-12:45pm CEST / 6:00-6:45am ET

Additional information can be found on the ESMO 2025 website, including abstracts. A copy of the poster will be made available on the Publications page of Olema’s website in alignment with the ESMO 2025 embargo policy.

About Olema Oncology
Olema Oncology is a clinical-stage biopharmaceutical company committed to transforming the standard of care and improving outcomes for patients living with breast cancer and beyond. Olema is advancing a pipeline of novel therapies by leveraging our deep understanding of endocrine-driven cancers, nuclear receptors, and mechanisms of acquired resistance. Our lead product candidate, palazestrant (OP-1250), is a proprietary, orally available complete estrogen receptor antagonist (CERAN) and a selective estrogen receptor degrader (SERD), currently in two Phase 3 clinical trials. In addition, Olema is developing OP-3136, a potent lysine acetyltransferase 6 (KAT6) inhibitor, now in a Phase 1 clinical study. Olema is headquartered in San Francisco and has operations in Cambridge, Massachusetts. For more information, please visit www.olema.com.

About Palazestrant (OP-1250)
Palazestrant (OP-1250) is a novel, orally available small molecule with dual activity as both a complete estrogen receptor antagonist (CERAN) and selective estrogen receptor degrader (SERD). It is currently being investigated in patients with recurrent, locally advanced or metastatic ER-positive (ER+), human epidermal growth factor receptor 2-negative (HER2-) breast cancer. In clinical studies, palazestrant completely blocks ER-driven transcriptional activity in both wild-type and mutant forms of metastatic ER+ breast cancer and has demonstrated anti-tumor efficacy along with attractive pharmacokinetics and exposure, favorable tolerability, central nervous system penetration, and combinability with cyclin-dependent kinase 4/6 (CDK4/6) inhibitors. Palazestrant has been granted U.S. Food and Drug Administration (FDA) Fast Track designation for the treatment of 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. It is being evaluated as a single agent in the ongoing pivotal Phase 3 clinical trial, OPERA-01 and in combination with ribociclib in the ongoing pivotal Phase 3 clinical trial, OPERA-02. Palazestrant is also being evaluated in multiple Phase 1/2 studies in combination with ribociclib, palbociclib, alpelisib, everolimus, and atirmociclib.

Forward-Looking Statements
Statements contained in this press release regarding matters that are not historical facts are “forward-looking statements” within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. Words such as “anticipate,” “believe,” “could,” “expect,” “goal,” “may,” “plan,” “potential,” “seek,” “upcoming,” “will,” and similar expressions (as well as other words or expressions referencing future events, conditions or circumstances) are intended to identify forward-looking statements. These statements include those related to the potential beneficial characteristics, safety, tolerability, efficacy, and therapeutic effects of palazestrant as a single agent or in combination therapy, the timing for initiation, enrollment, and results of Olema’s existing and planned clinical trials, including OPERA-01 and OPERA-02, the potential of palazestrant to become a standard of care for metastatic breast cancer, Olema’s potential to transform the metastatic breast cancer treatment paradigm, the potential of palazestrant to become a best-in-class, backbone endocrine therapy for metastatic breast cancer, and the potential for palazestrant to serve as an important combination agent in the metastatic setting. Because such statements deal with future events and are based on Olema’s current expectations, they are subject to various risks and uncertainties, and actual results, performance or achievements of Olema could differ materially from those described in or implied by the statements in this press release. These forward-looking statements are subject to risks and uncertainties, including, without limitation, those discussed in the section titled “Risk Factors” in Olema’s Quarterly Report on Form 10-Q for the quarter ended June 30, 2025, and other filings and reports that Olema makes from time to time with the U.S. Securities and Exchange Commission. Except as required by law, Olema assumes no obligation to update these forward-looking statements, including in the event that actual results differ materially from those anticipated in the forward-looking statements.

Media and Investor Relations Contact
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Vice President, Corporate Communications
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Olema ONCOLOGY

Corporate Overview

Advancing medicines for breast cancer and beyond

October 2025

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, though not all forward-looking statements necessarily contain these identifying words. Such forward-looking statements include, without limitation, statements regarding our research and clinical development plans, the scope, progress, results and costs of developing our product candidates or any other future product candidates, strategy, market size and opportunity for palazestrant (OP-1250) and OP-3136 in the U.S. and globally, clinical trial designs, regulatory matters, including the timing and likelihood of success of obtaining drug approvals and timing and likelihood of securing one or more approved indications for palazestrant, the timelines for potential initiation of clinical trials and the result of any such clinical trials of palazestrant 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 for 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 timelines for initiation of potential clinical trials for and the results of any such clinical trials in connection with our KAT6 inhibitor program, including OP-3136, the potential value and impact of our KAT6 inhibitor program, the best-in-class potential for OP-3136, including for breast and other solid tumor cancers, the potential beneficial characteristics, profile, safety, efficacy, tolerability, and therapeutic effects of OP-3136, including potential safety advantages of OP-3136 over alternative products, our opportunity in breast, other solid tumor cancers, and beyond, our ability to impact treatment for endocrine-driven cancers, and future global sales for 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.

Olema is focused on transforming the metastatic breast cancer treatment paradigm

TRANSFORMING THE TREATMENT PARADIGM

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

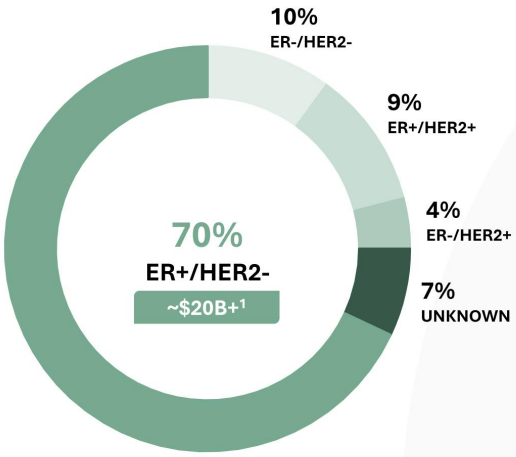
Progressing OP-3136, our potent and potential best-in-class KAT6 inhibitor

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]



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] 2025 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; 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 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]
1L	AI + CDK4/6i	**~6-36+** months
2/3L	ET, ET + CDK4/6i, ET + mTORi, 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; **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 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 drug combining with ribociclib** in 1L MBC

\+

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

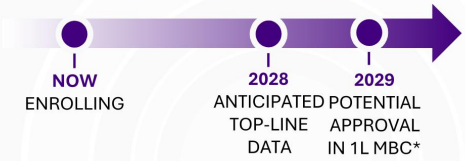
\+

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

=

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

OPERA-02 Breast Cancer Study



[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

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

- **H2 2026** TOP-LINE DATA
- **2027** ANTICIPATED NDA SUBMISSION
- **2027** POTENTIAL APPROVAL AND U.S. LAUNCH*

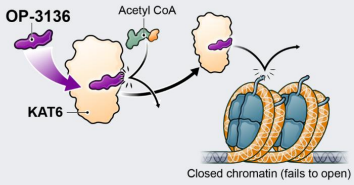
[1] For more details on the data highlighted on this slide, please refer to the oral presentation at this link. Data cutoff date: July 7, 2023. [2] Estimated global market potential. Olema internal data. *Subject to U.S. Food and Drug Administration approval.
2/3L = second/third-line; **±CT** = plus/minus 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

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

- **NOW** — ENROLLING PHASE 1 (Mono and Combo)
- **2026** — ANTICIPATED INITIAL CLINICAL RESULTS
- **~2027** — POTENTIAL ADDITIONAL CLINICAL RESULTS
- **~2028** — POTENTIAL PHASE 3 TRIAL

Olema ONCOLOGY

[1]2024 EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics. Poster #230. [2] Estimated global 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
INITIATING IN Q3 2025

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:

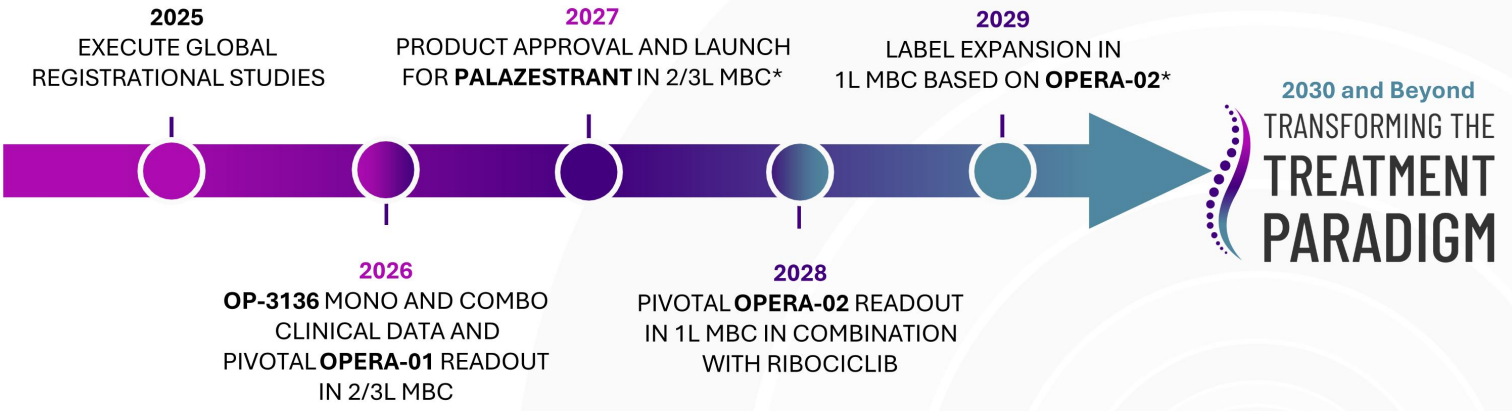
- ER+/HER2- breast cancer
- Castrate-resistant prostate cancer
- Non-small cell lung cancer

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 through 2030 advance us towards our goal of transforming the treatment paradigm for metastatic breast cancer

Corporate Priorities and Anticipated Milestones



*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*

2025 MILESTONES

- Advancing patient enrollment in pivotal Phase 3 OPERA-01 trial of palazestrant monotherapy in 2/3L MBC
- Initiated pivotal Phase 3 OPERA-02 trial of palazestrant + ribociclib in 1L MBC
- Presented mature Phase 1b/2 palazestrant + ribociclib data at ESMO

Olema oncology

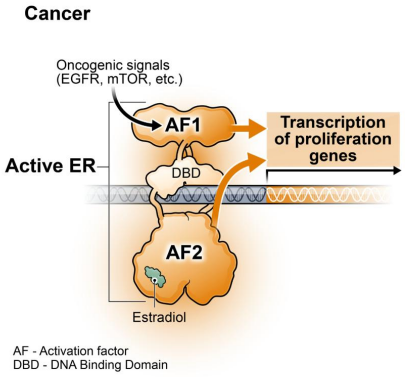
* In patients with ER+/HER2- metastatic breast cancer that has progressed following one or more lines of endocrine therapy with at least one line given in combination with a CDK4/6 inhibitor

1L = frontline; **2/3L** = second /third-line; **ESMO** = European Society for Medical Oncology Congress; **FDA** = U.S. Food and Drug Administration; **MBC** = metastatic breast cancer

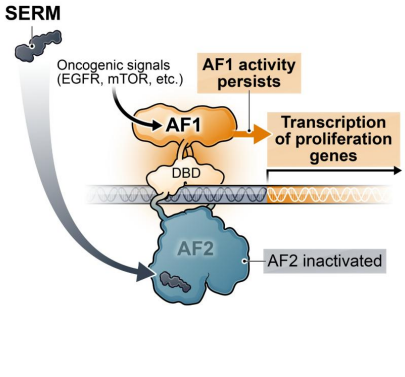
Palazestrant mechanism of action

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

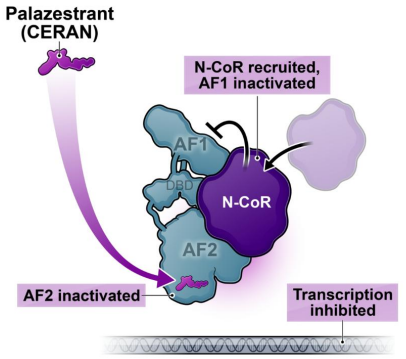
Activated ER **drives cancer cell** growth



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



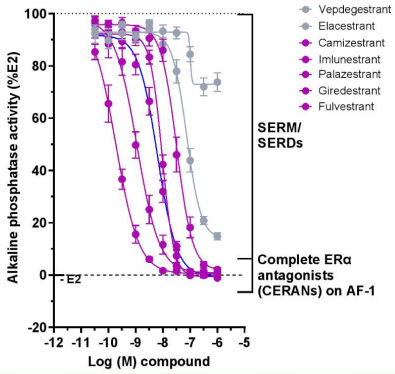
AF = activation factor; **CERAN** = complete estrogen receptor antagonist; **DBD** = DNA binding domain; **EGFR** = epidermal growth factor receptor; **ER** = estrogen receptor; **mTOR** = mammalian target of rapamycin; **N-CoR** = nuclear receptor corepressor; **SERD** = selective estrogen receptor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

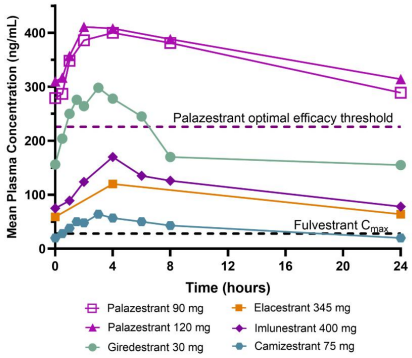
Complete ER antagonism is key to shutting off all ER signaling

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



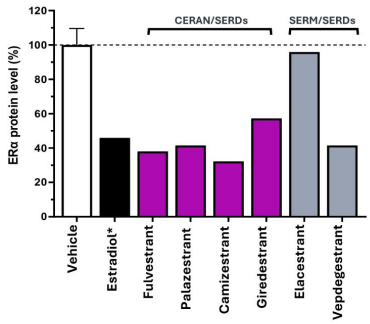
Palazestrant uniquely meets optimal drug-plasma exposure[1]

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

MILESTONES

- **2025:** Pivotal Phase 3 OPERA-02 trial ongoing
- **2025:** Presented mature Phase 1b/2 palazestrant + ribociclib data at ESMO
- **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

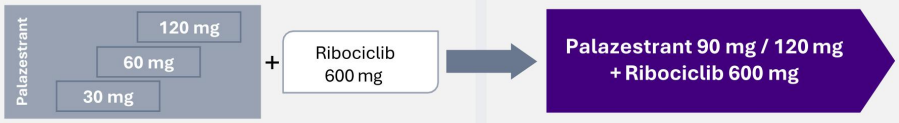
Design: Phase 1b/2 study of palazestrant in combination with ribociclib in ER+/HER2- MBC

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

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) .

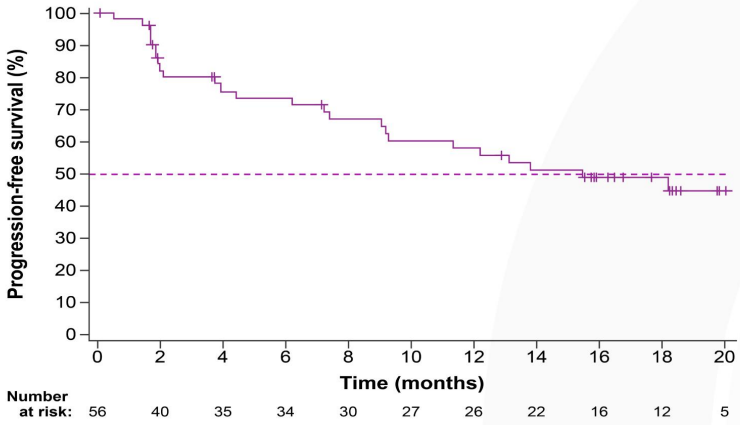
AE = adverse events; **DLTs** = dose-limiting toxicity; **ECG QT** = electrocardiogram QT interval; **ER+** = estrogen receptor positive; **ET** = endocrine therapy; **HER2-** = human epidermal growth factor receptor negative; **LDH** = lactate dehydrogenase; **MBC** = metastatic breast cancer; **NR** = 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

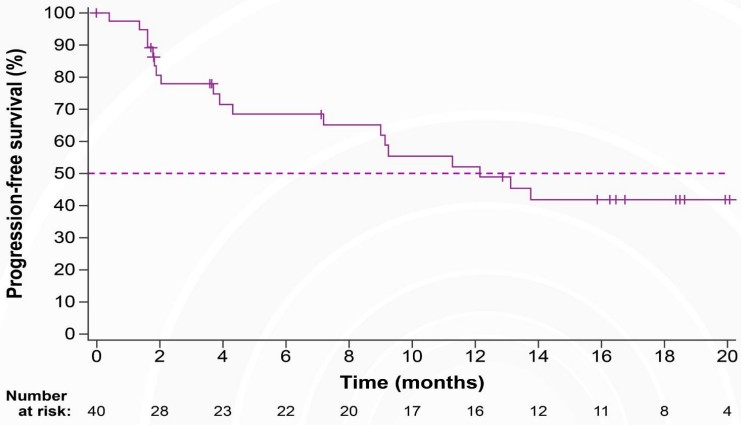
All Patients
120 mg palazestrant + 600 mg ribociclib (n=56)

mPFS: 15.5 months



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

mPFS: 12.2 months



Olema ONCOLOGY

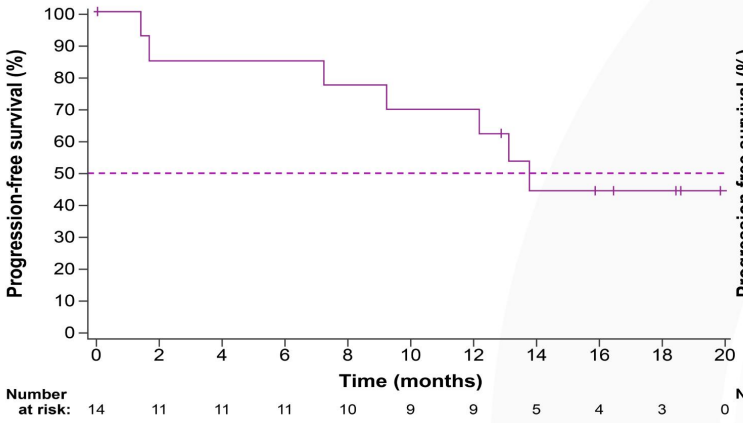
Data cutoff date: July 8, 2025 ; Median follow-up >19 months
CDK4/6i = cyclin-dependent kinase 4/6 inhibitor; **ER+** = estrogen receptor positive; **ET** = endocrine therapy; **HER2-** = human epidermal growth factor receptor negative; **MBC** = metastatic breast cancer; **mPFS** = median progression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

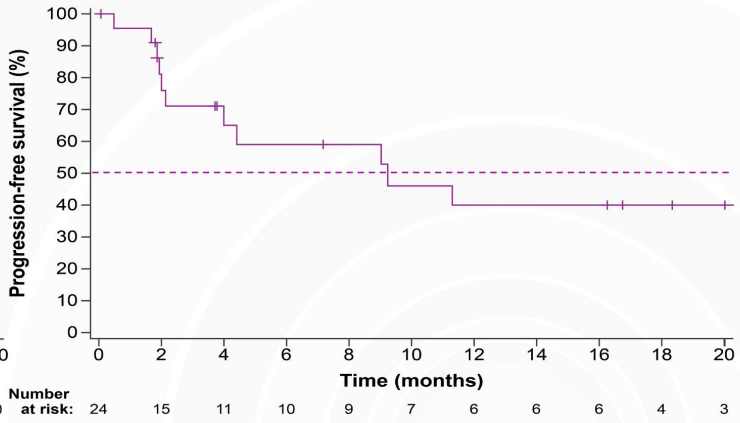
ESR1 Mutant Patients with Prior CDK4/6i
120 mg palazestrant + 600 mg ribociclib (n=14)

mPFS: 13.8 months



ESR1 Wild Type Patients with Prior CDK4/6i
120 mg palazestrant + 600 mg ribociclib (n=24)

mPFS: 9.2 months

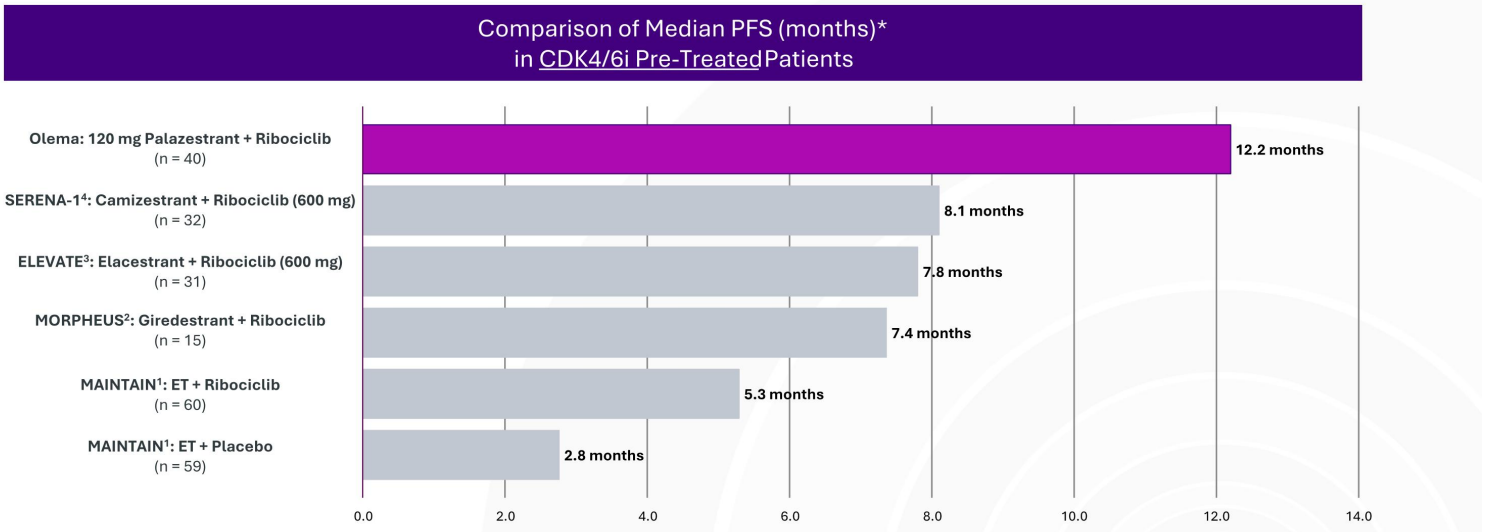


Olema ONCOLOGY

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*



*** 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.**

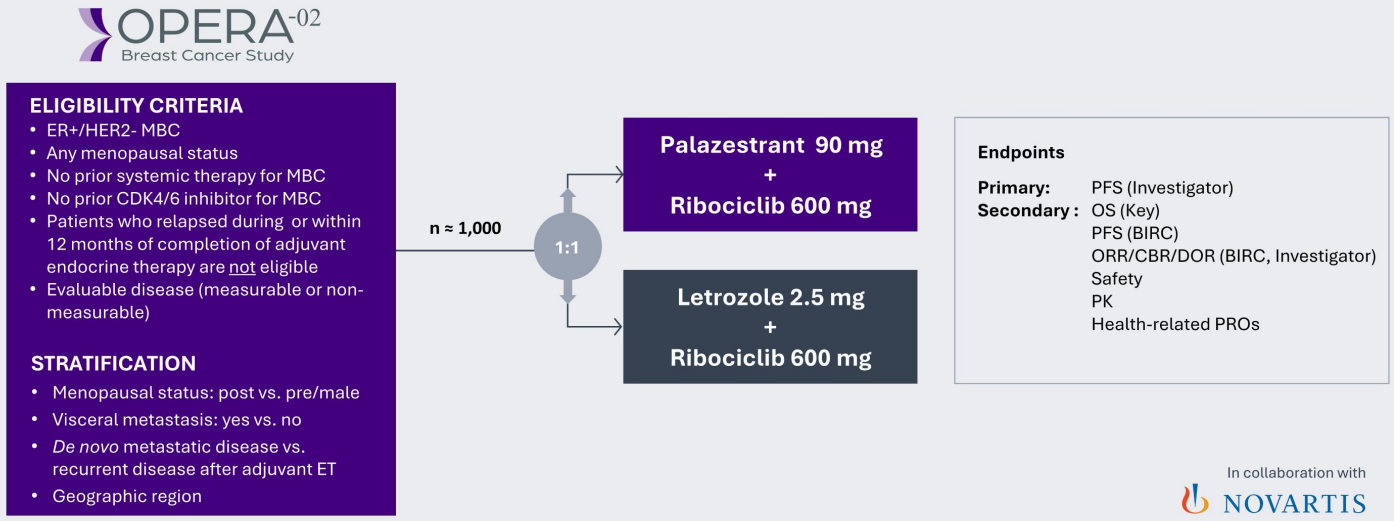
Data cutoff date: July 8, 2025.

[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



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 T790M 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.**

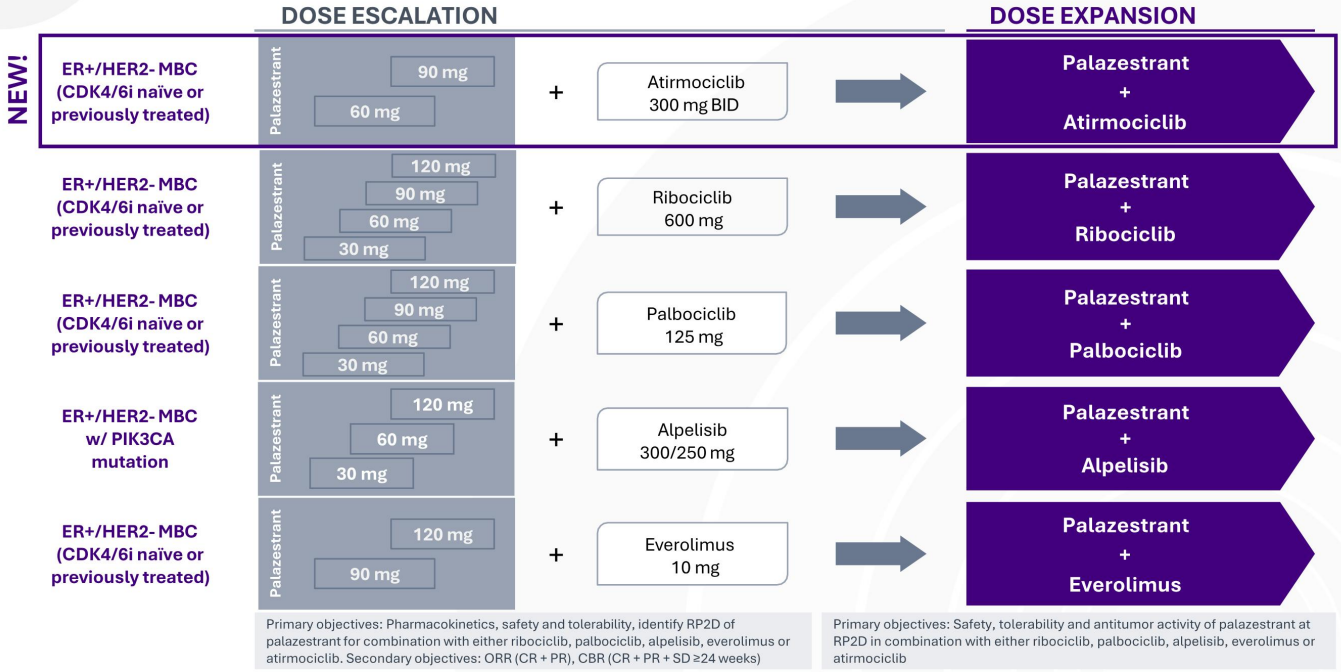
[1] Soria, J-C, Ohe, Y, Vansteenkiste, J. et al. Osimertinib in untreated EGFR-mutated advanced non-small-cell lung cancer. New Engl J Med 2018: 378:113-125.

[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), initiating 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

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

MILESTONES

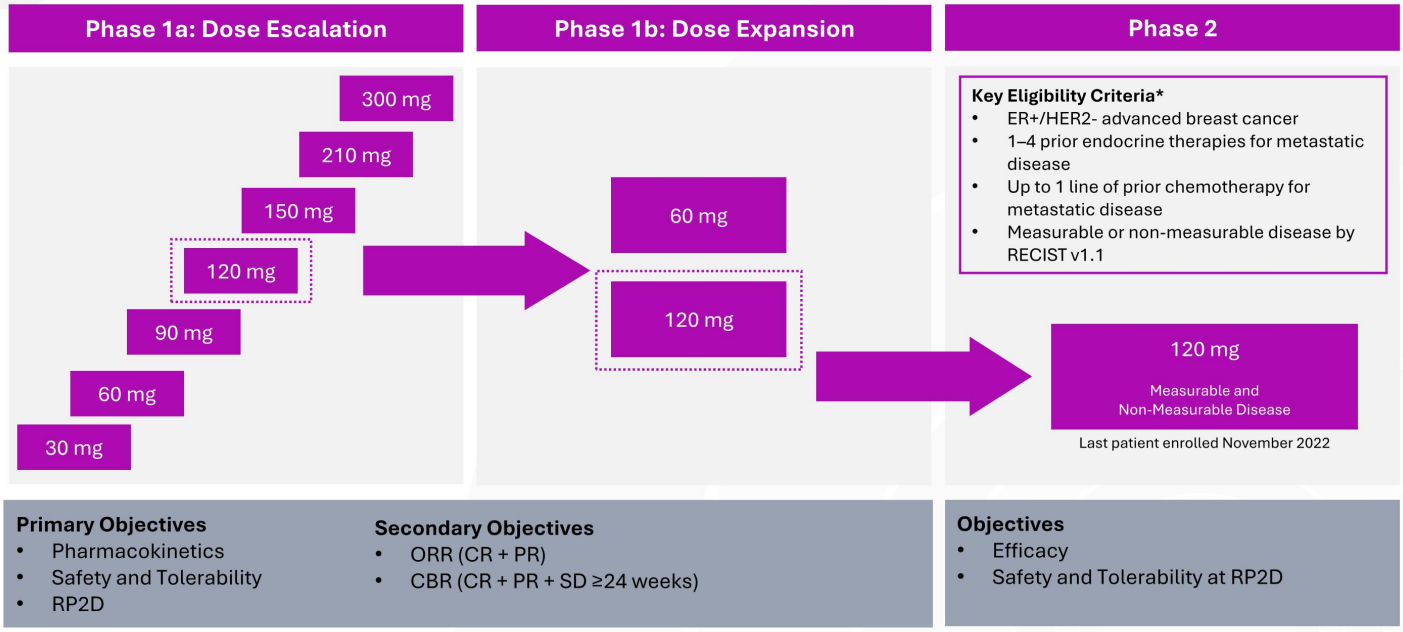
- **2025:** Pivotal Phase 3 OPERA-01 trial ongoing
- **2026:** Announce top-line results from OPERA-01 in H2
- **2027:** Anticipated submission of New Drug Application for potential approval of palazestrant as a monotherapy in 2/3L ER+/HER2-MBC and prepare for commercial launch
- **2027:** Potential FDA approval and U.S. commercial launch of palazestrant

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



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

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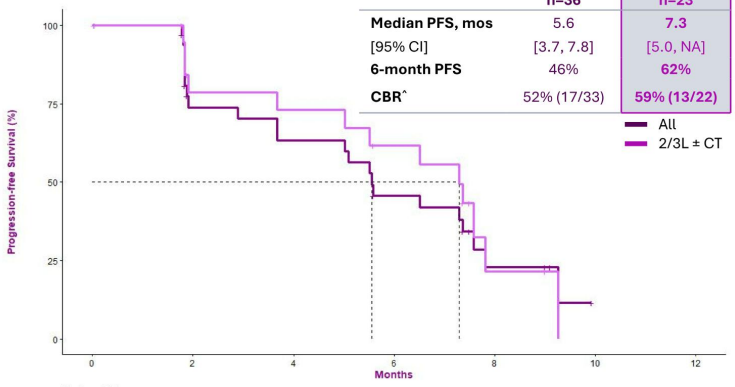
Data cutoff date: July 7, 2023. Data shown are n or n (%).
AE = adverse events; **AST** = aspartate aminotransferase; **TEAEs** = treatment-emergent adverse events

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)**

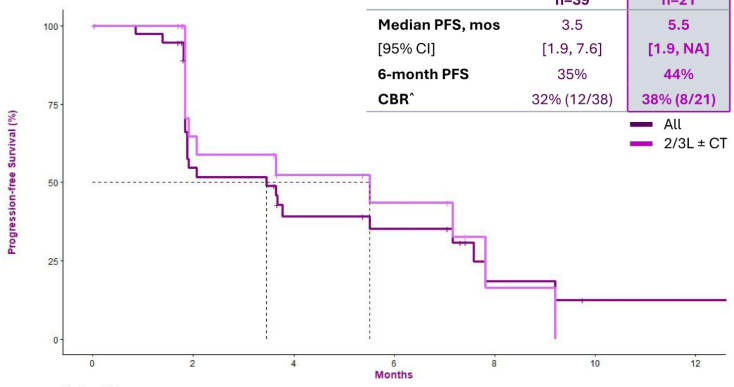


Number at Risk

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.**

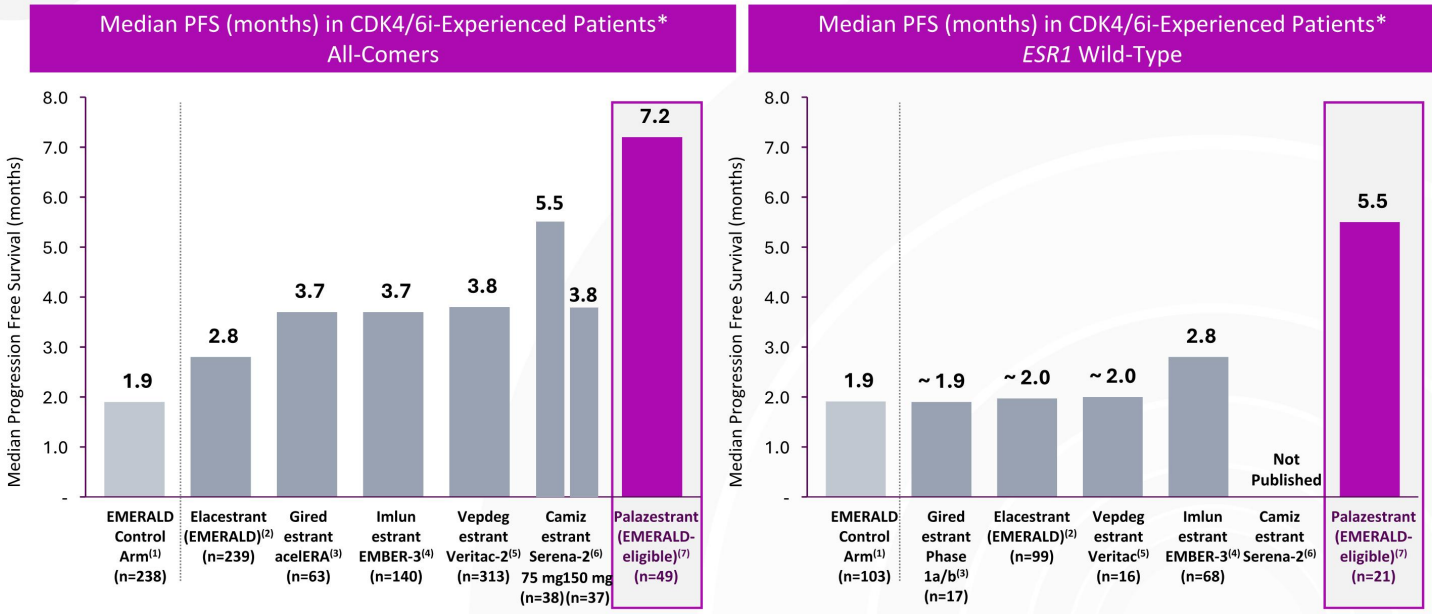
[1] Palazestrant Phase 2 dataset at 120 mg with ESR1 mutations detected at baseline. [2] Palazestrant Phase 2 dataset at 120 mg with ESR1 mutations not detected at baseline.

` 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

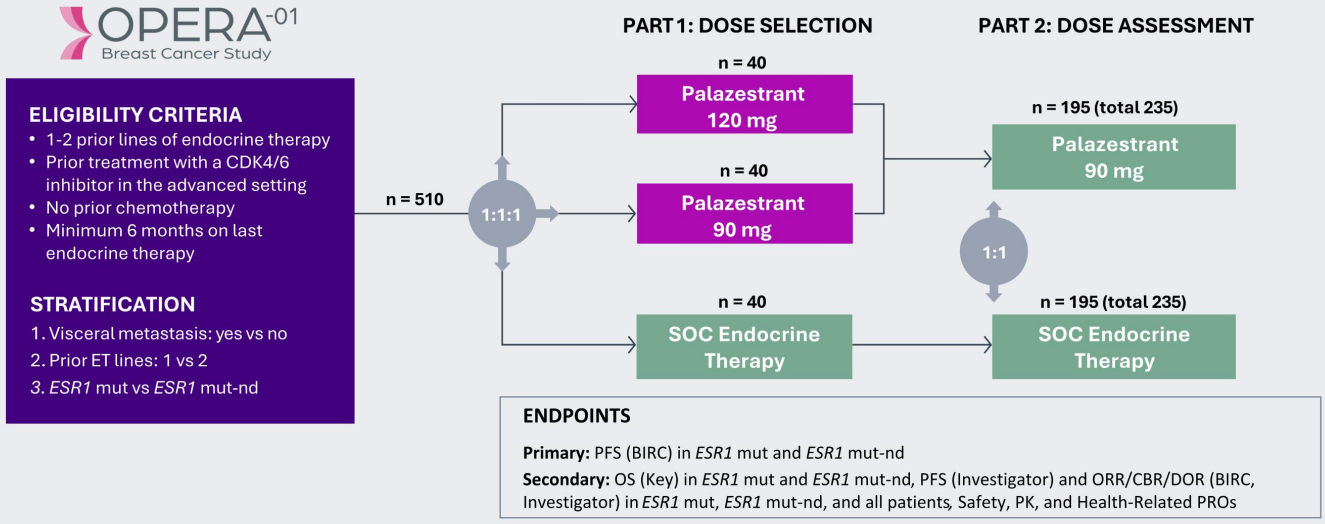


*** NOTE: This analysis is the aggregation of results across independent studies. There are risks inherent in conducting cross-trial comparisons. Refer to further disclaimers on slide 2.**

[1] SABCS 2021 EMERALD data. Median PFS in control arm. Note: ORR of 4.4% (8/182). [2] SABCS 2021 EMERALD data. Median PFS in elacestrant 400 mg dose. Note: ORR of 4.5% (8/179). [3] JCO acelERA data. Median PFS on CDK4/6i experienced patients. [4] SABCS 2024 EMBER data. Median PFS in CDK4/6i-experienced patients. [5] ASCO 2025 Veritac-2 data. Median PFS at 200 mg dose across all patients. [6] SABCS 2022 Serena-2 data. Median PFS in CDK4/6i-experienced patients at 75 mg (5.5 months) and 150 mg (3.8 months). Represents <2 prior lines of ET-only +/- CT. Note: Serena-1 data at 75 mg dose had 2 PRs out of 22 patients; both were CDK4/6i naive. [7] mPFS at 120 mg dose in Emerald-eligible patient population from palazestrant Phase 2 dataset (2/3L +/-CT) with ESR1 mutations detected at baseline.

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

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



Trial initiated in 4Q 2023. Top-line results expected in H2 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 2027

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

Commercial launch planning beginning 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

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

- **2026:** Anticipated initial monotherapy and combination data from the Phase 1 study

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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*

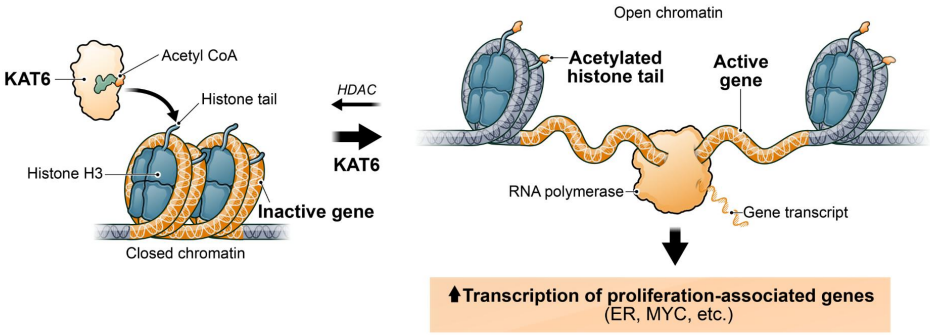
An exciting new and validated target** for the treatment of ER+/HER2- metastatic breast cancer

- 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 2025 Annual Meeting
- IND cleared by FDA and Phase 1 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

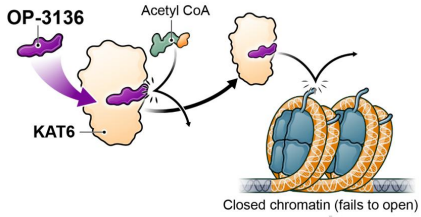
OP-3136 mechanism of action

KAT6 acetylates chromatin enabling transcription and proliferation



⬆**Transcription of proliferation-associated genes** (ER, MYC, etc.)

OP-3136 prevents transcription

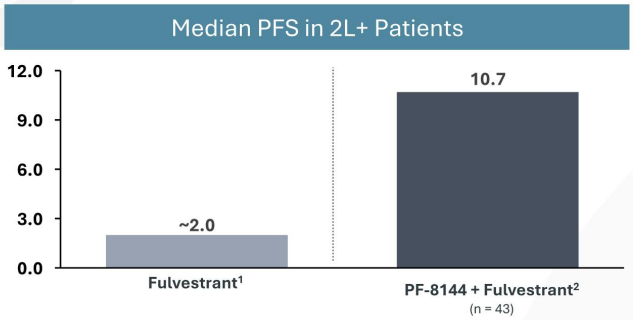


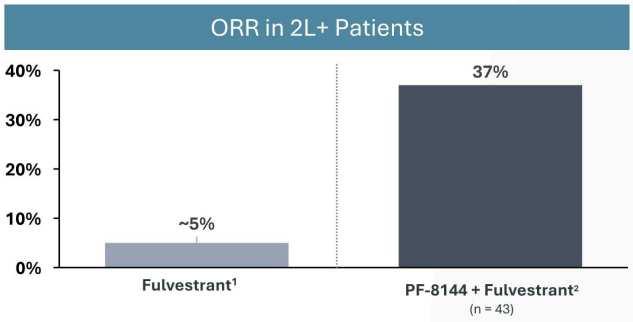
KAT6 inhibition by **OP-3136 stops acetylation** of histones and **blocks transcription of proliferation-associated genes** (ER, MYC, etc.)

- 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*





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

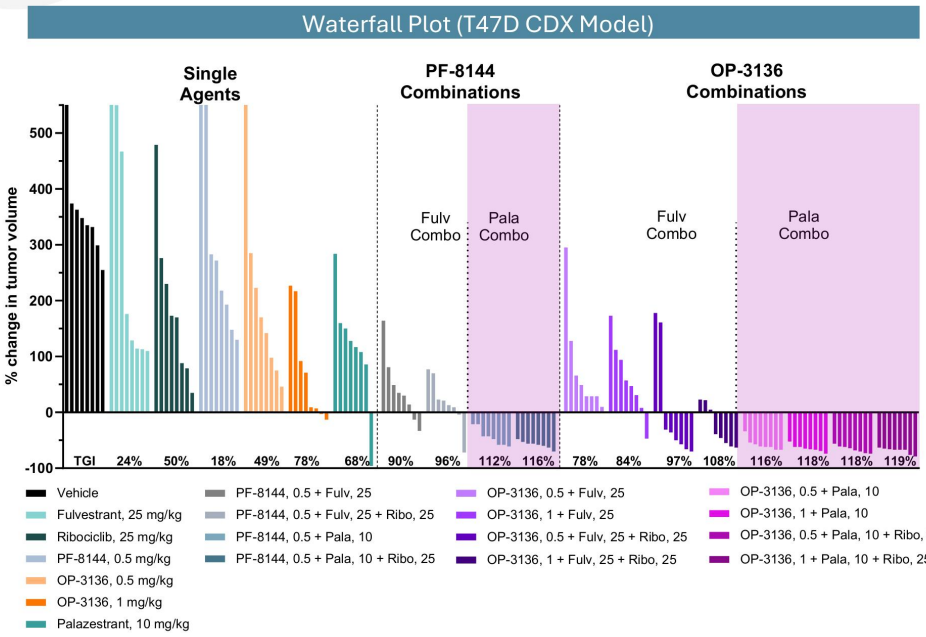
- OP-3136 showed >500-fold selectivity over other essential KAT family members: KAT5 and KAT8
- OP-3136 had higher selectivity over KAT5 and KAT8
  - May confer safety advantage
  - PF-8144 5 mg QD steady state exposure is ~3000-4000 nM, above IC50 for KAT5 and KAT8

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

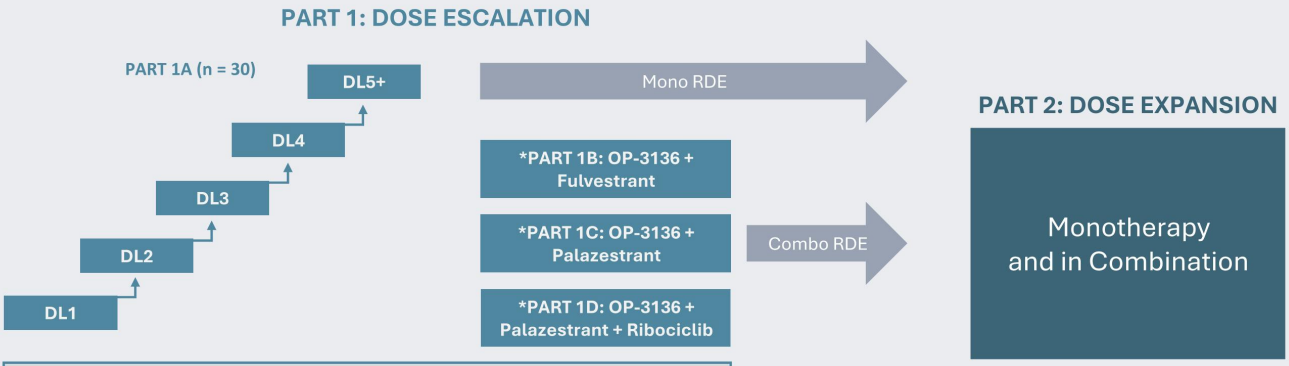


- Palazestrant in combination with either OP-3136 or PF-8144 resulted in strong tumor regression relative to fulvestrant combinations
- OP-3136 and palazestrant combinations showed significantly improved anti-tumor efficacy compared to PF-8144 in combination with fulvestrant
- All OP-3136 combinations 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

IND cleared by FDA and Phase 1 study is recruiting patients



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

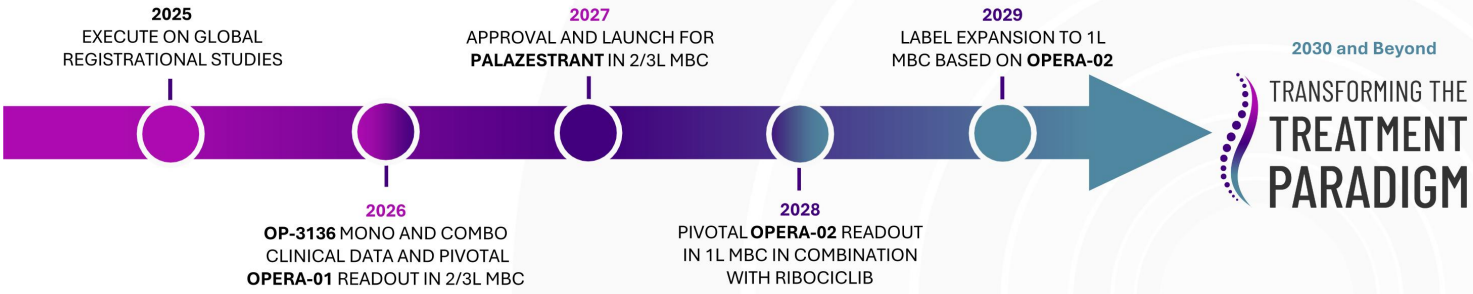
Palazestrant

- Highly differentiated with activity in *ESR1* mutant and wild-type tumors
- OPERA-01 Phase 3 trial on track for top-line data in H2 2026
- OPERA-02 Phase 3 trial in combination with ribociclib now enrolling patients
- Mature palazestrant + ribociclib efficacy data presented at ESMO 2025
- 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 now enrolling patients
- Initial data expected in 2026

Corporate Priorities and Anticipated Milestones



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

Thank You

— Advancing medicines for breast cancer and beyond

Olema ONCOLOGY