# 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): December 09, 2024**

# 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**<br>**San Francisco, California** | | **94103** |
| **(Address of Principal Executive Offices)** | | **(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 December 9, 2024, Olema Pharmaceuticals, Inc. (the "Company") announced that the U.S. Food and Drug Administration ("FDA") has cleared its Investigational New Drug ("IND") application for OP-3136, a novel small molecule that potently and selectively inhibits KAT6, a validated epigenetic target that is dysregulated in breast and other cancers. A copy of the press release issued in connection with the announcement is being furnished as Exhibit 99.1 to this Current Report on Form 8-K.

On December 10, 2024, the Company announced updated clinical results from its ongoing Phase 1b/2 study of palazestrant in combination with CDK4/6 inhibitor ("CDK4/6i"), ribociclib in patients with estrogen receptor-positive, human epidermal growth factor receptor 2-negative ("ER+/HER2-") advanced or metastatic breast cancer. A copy of the press release issued in connection with the announcement is being furnished as Exhibit 99.2 to this Current Report on Form 8-K.

On December 10, 2024, 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 99.3 to this Current Report on Form 8-K.

The information in Exhibits 99.1, 99.2, and 99.3 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 or the Exchange Act, except as expressly set forth by specific reference in such filing.

**Item 8.01 Other Events.**

**FDA Clearance of Investigational New Drug Application for OP-3136**

On December 9, 2024, the Company announced that the FDA has cleared its IND application for OP-3136.

The Company expects to initiate the Phase 1 clinical trial in early 2025.

**Interim Results from the Phase 1b/2 Study of Palazestrant in Combination with Ribociclib**

On December 10, 2024, the Company announced updated clinical results from its ongoing Phase 1b/2 study of palazestrant in combination with CDK4/6 inhibitor, ribociclib in patients with ER+/HER2- advanced or metastatic breast cancer. Results as of a data cutoff date of September 25, 2024 will be presented at the San Antonio Breast Cancer Symposium ("SABCS") being held December 10-13, 2024. Updated results as of a data cutoff date of November 11, 2024 are detailed below.

*Enrollment*
62 patients with advanced or metastatic ER+/HER2- breast cancer were treated with palazestrant (n=56 at the recommended Phase 2 dose of 120 mg once daily continuously) plus ribociclib (600 mg once daily, three weeks on treatment followed by one week off treatment).

- The majority of participants (48 (77%)) were patients who were second-line, third-line or later in treatment; 48 (77%) patients received prior endocrine therapy for metastatic breast cancer, 46 (74%) patients received prior treatment of endocrine therapy with CDK4/6i, 12 (19%) received two prior lines of treatment with CDK4/6i), and 11 (18%) patients received chemotherapy for metastatic breast cancer.
- 36 (58%) patients had visceral disease; 42 (68%) patients had measurable disease at baseline. Of 60 patients whose circulating tumor DNA was assessed, 28% had activating mutations in *ESR1* at baseline.

*Efficacy*
Palazestrant combined with ribociclib showed promising clinical activity including tumor responses, prolonged disease stabilization, and progression-free survival ("PFS") in patients with *ESR1*wild-type and *ESR1* activating mutations at baseline and in those previously treated with one or two lines of CDK4/6i. Efficacy data continue to mature; 30 (48%) patients remained on treatment as of the November 11, 2024 data cutoff date, and the longest duration on treatment was approximately 18 months (79 weeks) and was ongoing as of the data cutoff date of November 11, 2024.

- With a median follow-up of 12 months, the median PFS was not reached as of the data cutoff date. Across all patients, the 6-month PFS rate was 73%. In those who received prior treatment with a CDK4/6i plus an endocrine therapy, the 6-month PFS rate was 68%. The 6-month PFS rate in *ESR1*mutant patients was 81% and in *ESR1* wild-type patients it was 70%.
- In those who were clinical benefit rate (CBR)[1]-eligible, the CBR was 76% (37/49) in all patients, 81% (13/16) in patients with *ESR1*mutations, and 74% (23/31) in *ESR1*wild-type patients. In patients with prior CDK4/6i treatment, the CBR was 71% (25/35), 81% (12/16) in patients with *ESR1* mutations, and 65% (11/17) in*ESR1* wild-type patients.

- As of the data cutoff date, there were 11 responses (two confirmed complete responses, eight confirmed partial responses, and one unconfirmed partial response. Among 37 response-evaluable patients with measurable disease, the ORR was 27% (10/37). 60% of the 37 had a reduction in target lesion size.

[1] CBR is the proportion of patients who remained on treatment through at least 24 weeks with a confirmed complete response or partial response, or stable disease.

*Safety and Tolerability*
Across 62 treated patients, the combination of up to 120 mg of palazestrant with the approved dose for metastatic disease of 600 mg of ribociclib daily was well tolerated with no new safety signals or increase in toxicity. The overall safety profile was consistent with the established safety profile of ribociclib 600 mg plus an endocrine therapy.

- Treatment with palazestrant up to 120 mg combined with ribociclib (600 mg) was well tolerated with no dose-limiting toxicities.
- 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 ribociclib plus endocrine therapy.

*Pharmacokinetics*
Palazestrant did not affect ribociclib drug exposure when compared with published exposure data for single-agent ribociclib. Steady-state trough values showed no clinically significant difference between the combination and single-agent palazestrant.

*Conclusions*
Findings from this study support the advancement of palazestrant in combination with ribociclib into clinical development for the first-line treatment of ER+/HER2- advanced or metastatic breast cancer.

**Forward Looking Statements**

Statements contained in this Current Report on Form 8-K, including the exhibits furnished herewith, 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," "will," "may," "goal," "may," "potential," "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 forward-looking statements include, without limitation, statements regarding the advancement of OP-3136 into clinical development, including timelines for initiation and enrollment for potential clinical studies, the combinability of OP-3136 with other drugs and potential beneficial characteristics, including but not limited to safety, tolerability, activity, efficacy and therapeutic effects of OP-3136 as a monotherapy and in combination with other drugs, potential beneficial characteristics, safety, tolerability, efficacy, and therapeutic effects of palazestrant, and the development of palazestrant, in each case, including in combination with other drugs, the potential of palazestrant to work in combination with ribociclib to suppress tumor growth or extend PFS, palazestrant in combination with ribociclib advancing into clinical development for the first-line treatment of ER+/HER2- advanced or metastatic breast cancer, the timing and likelihood of initiating clinical trials, and the timing of generating and announcing trial results, the timing and content of potential New Drug Application submissions, and commercial launch of product candidates, including the timing thereof. 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 September 30, 2024, 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 set forth in the forward-looking statements.

**Item 9.01 Financial Statements and Exhibits.**

(d) Exhibits

| Exhibit No. | Description |
|---|---|
| 99.1 | Press Release, dated December 9, 2024, of Olema Pharmaceuticals, Inc. |
| 99.2 | Press Release, dated December 10, 2024, of Olema Pharmaceuticals, Inc. |
| 99.3 | Investor Presentation, dated December 10, 2024, of Olema Pharmaceuticals, Inc. |

| Exhibit No. | Description |
| --- | --- |
| 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: December 10, 2024

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

**EXHIBIT 99.1**

# Olema Oncology Announces FDA Clearance of Investigational New Drug Application for OP-3136, a Potent KAT6 Inhibitor

- *Phase 1 clinical trial for OP-3136 to initiate in early 2025*

SAN FRANCISCO, CA - (GLOBE NEWSWIRE) - December 9, 2024 - 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 that the U.S. Food and Drug Administration (FDA) has cleared its Investigational New Drug (IND) application for OP-3136, a novel small molecule that potently and selectively inhibits KAT6, a validated epigenetic target that is dysregulated in breast and other cancers.

"We are very pleased to have received notification from the FDA that OP-3136 may proceed into the clinic,” said David C. Myles, Ph.D., Chief Discovery and Non-Clinical Development Officer of Olema Oncology. “The compelling activity demonstrated by OP-3136 in preclinical models both as a single agent and in combination with palazestrant has generated strong investigator interest in OP-3136. We expect to initiate the Phase 1 clinical trial early next year and are excited by OP-3136’s potential in breast cancer and beyond.”

**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 (ER) antagonist (CERAN) and a selective ER degrader (SERD), currently in a Phase 3 clinical trial called OPERA-01. In addition, Olema is developing a potent KAT6 inhibitor (OP-3136). Olema is headquartered in San Francisco and has operations in Cambridge, Massachusetts. For more information, please visit us at www.olema.com.

**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,” “potential,” “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 advancement of OP-3136 into clinical development, including timelines for initiation and enrollment, the combinability of OP-3136 with other drugs and potential beneficial characteristics of OP-3136 as a monotherapy and in combination with other drugs. 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 September 30, 2024, 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**
Courtney O’Konek
Vice President, Corporate Communications
Olema Oncology
media@olema.com

**EXHIBIT 99.2**

# Olema Oncology Presents Updated Clinical Results for Palazestrant in Combination with Ribociclib at the San Antonio Breast Cancer Symposium

- *Palazestrant, in combination with ribociclib, demonstrated promising clinical activity, a safety profile consistent with ribociclib and endocrine therapy, and favorable tolerability in patients with ER+/HER2- advanced or metastatic breast cancer*
- *With median follow-up of 12 months, median progression-free survival (PFS) has not been reached*
- *6-month PFS rate was 73% in all patients, 81% in patients with ESR1 mutations, 70% in ESR1 wild-type patients, and 68% in patients with prior CDK4/6 inhibitor treatment; data continue to mature*
- *Conference call today at 8:00 a.m. ET*

**SAN FRANCISCO - December 10, 2024 - (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 clinical results from the ongoing Phase 1b/2 study of palazestrant in combination with CDK4/6 inhibitor, ribociclib, in patients with estrogen receptor-positive, human epidermal growth factor receptor 2-negative (ER+/HER2-) advanced or metastatic breast cancer. Results as of September 25, 2024, will be presented in a poster session at the San Antonio Breast Cancer Symposium (SABCS 2024) being held December 10-13 at the Henry B. Gonzalez Convention Center in San Antonio, Texas. Updated results as of November 11, 2024, are detailed below.

“We believe these data, while still maturing, are compelling and highly differentiated, with robust clinical activity shown across both *ESR1* wild-type and mutant patient populations after prior treatment with a CDK4/6 inhibitor in combination with endocrine therapy. Mutations in the *ESR1* gene are one of the most common resistance mechanisms arising during current front-line standard of care treatment, leading to progression. Palazestrant has demonstrated its potential to work in combination with ribociclib by completely blocking estrogen receptor signaling and suppressing tumor growth to extend progression-free survival after prior progression on the current standard of care, regardless of *ESR1* status,” said Sean P. Bohen, M.D., Ph.D., President and Chief Executive Officer of Olema Oncology. “These data provide the foundation to initiate OPERA-02, our planned pivotal Phase 3 trial of palazestrant in combination with ribociclib in front-line metastatic breast cancer next year. We look forward to sharing mature data from this combination in 2025 and continuing the development of palazestrant as we work to advance our goal of creating innovative therapies to improve the lives of breast cancer patients.”

**Interim Results from the Phase 1b/2 Study of Palazestrant in Combination with Ribociclib**

*Enrollment*

62 patients with advanced or metastatic ER+/HER2- breast cancer were treated with palazestrant (n=56 at the recommended Phase 2 dose (RP2D) of 120 mg once daily) plus ribociclib (600 mg once daily; three weeks on treatment followed by one week off treatment).

- The majority of participants (48 (77%)) were 2/3+ line patients; 48 (77%) patients received prior endocrine therapy for metastatic breast cancer, 46 (74%) patients received prior treatment of endocrine therapy with CDK4/6 inhibitors (CDK4/6i), 12 (19%) received two prior lines of treatment with CDK4/6i), and 11 (18%) patients received chemotherapy for metastatic breast cancer.
- 36 (58%) patients had visceral disease; 42 (68%) patients had measurable disease at baseline. Of 60 patients whose circulating tumor DNA (ctDNA) was assessed, 28% had activating mutations in *ESR1* at baseline.

*Efficacy*

Palazestrant combined with ribociclib showed promising clinical activity including tumor responses, prolonged disease stabilization, and progression-free survival in patients with *ESR1* wild-type and *ESR1* activating mutations at baseline and in those previously treated with one or two lines of CDK4/6i. Efficacy data continue to mature; 30 (48%) patients remain on treatment, and the longest duration on treatment is approximately 18 months (79 weeks) and was ongoing as of the data cutoff date of November 11, 2024.

- With a median follow-up of 12 months, the median PFS was not reached as of the data cutoff date. Across all patients, the 6-month PFS rate was 73%. In those who received prior treatment with a CDK4/6i plus an endocrine therapy, the 6-month PFS rate was 68%. The 6-month PFS rate in *ESR1* mutant patients was 81% and in *ESR1* wild-type patients it was 70%.
- In those who were clinical benefit rate (CBR)[1]-eligible, the CBR was 76% (37/49) in all patients, 81% (13/16) in patients with *ESR1* mutations, and 74% (23/31) in *ESR1* wild-type patients. In patients with prior CDK4/6i treatment, the CBR was 71% (25/35), 81% (12/16) in patients with *ESR1* mutations, and 65% (11/17) in *ESR1* wild-type patients.
- As of the data cutoff date, there were 11 responses (two confirmed complete responses, eight confirmed partial responses, and one unconfirmed partial response. Among 37 response-evaluable patients with measurable disease, the ORR was 27% (10/37). 60% of the 37 had a reduction in target lesion size.

*Safety and Tolerability*

Across 62 treated patients, the combination of up to 120 mg of palazestrant with the approved dose for metastatic disease of 600 mg of ribociclib daily was well tolerated with no new safety signals or increase in toxicity. The overall safety profile was consistent with the established safety profile of ribociclib 600 mg plus an endocrine therapy.

- Treatment with palazestrant up to 120 mg combined with ribociclib (600 mg) was well tolerated with no dose-limiting toxicities.
- The majority of treatment-emergent adverse events (TEAEs) were Grade 1 or 2, and the severity and incidence of adverse events were consistent with the expected safety profile of ribociclib plus endocrine therapy.

*Pharmacokinetics*

Palazestrant did not affect ribociclib drug exposure when compared with published exposure data for single-agent ribociclib. Steady-state trough values showed no clinically significant difference between the combination and single-agent palazestrant.

*Conclusions*
Findings from this study support the advancement of palazestrant in combination with ribociclib into clinical development for the first-line treatment of ER+/HER2- advanced or metastatic breast cancer.

“Palazestrant is not an endocrine therapy where you need to wait six months to see a patient derive benefit. We have seen impressive responses quickly and a significant reduction of disease burden. The patients I have seen feel much better than they have on other treatments available in the armamentarium today,” said Virginia Borges, M.D., Professor, Medicine-Medical Oncology at the University of Colorado, and Principal Investigator for the palazestrant plus ribociclib combination study. “The findings presented at SABCS show that the combination of palazestrant and ribociclib is well-tolerated with meaningful preliminary efficacy that I believe has the potential to outperform the current standard of care and change how metastatic breast cancer is treated. I look forward to the continued development of palazestrant.”

A copy of the poster presented at SABCS reflecting a September 25, 2024 data cutoff date will be made available on the Publications page of Olema’s website in alignment with the Symposium’s embargo policy.

*[1]CBR is the proportion of patients who remained on treatment through at least 24 weeks with a confirmed complete response or partial response, or stable disease.*

**Conference Call Information**
Olema will hold a conference call to discuss these results today with the investment community at 8:00 a.m. ET (7:00 a.m. CT). Register to join the webcast by visiting the Events and Presentations page on the Investors section of Olema’s website.

**About Palazestrant (OP-1250)**
Palazestrant (OP-1250) is a novel, orally available small molecule with dual activity as both a complete estrogen receptor (ER) antagonist (CERAN) and selective ER 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 preclinical studies, palazestrant completely blocks ER-driven transcriptional activity in both *ESR1* wild-type and mutant forms of breast cancer cell. In Olema’s ongoing clinical trials for advanced or metastatic ER+/HER2- breast cancer, palazestrant has demonstrated anti-tumor activity along with attractive pharmacokinetics and exposure, favorable tolerability, and combinability with 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 both as a single agent in an ongoing Phase 3 clinical trial, OPERA-01, and in Phase 1/2 combination studies with CDK4/6 inhibitors (palbociclib and ribociclib), a PI3Ka inhibitor (alpelisib), and an mTOR inhibitor (everolimus). For more information on OPERA-01, please visit www.opera01study.com.

**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 (ER) antagonist (CERAN) and a selective ER degrader (SERD), currently in a Phase 3 clinical trial called OPERA-01. In addition, Olema is developing a

potent KAT6 inhibitor (OP-3136). Olema is headquartered in San Francisco and has operations in Cambridge, Massachusetts. For more information, please visit us at www.olema.com.

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**Media and Investor Relations Contact**
Courtney O’Konek
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Olema Oncology
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EXHIBIT 99.3

SABCS 2024

# Palazestrant in Combination with Ribociclib Clinical Update

December 10, 2024

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

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

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

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

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

### Molecular Advantage

Expertise in endocrine-driven cancers with mechanistically superior scientific approach that fully inactivates estrogen receptors

### Lead Asset – Palazestrant

OP-1250, a promising potential backbone therapy for ER+/HER2- breast cancer in late-stage clinical development, forms basis of breast cancer program

### OP-3136 Expands Pipeline

Exciting new and potent KAT6 inhibitor with potential to significantly impact breast cancer treatment; IND cleared by FDA and initiation of Phase 1 clinical trial anticipated early 2025

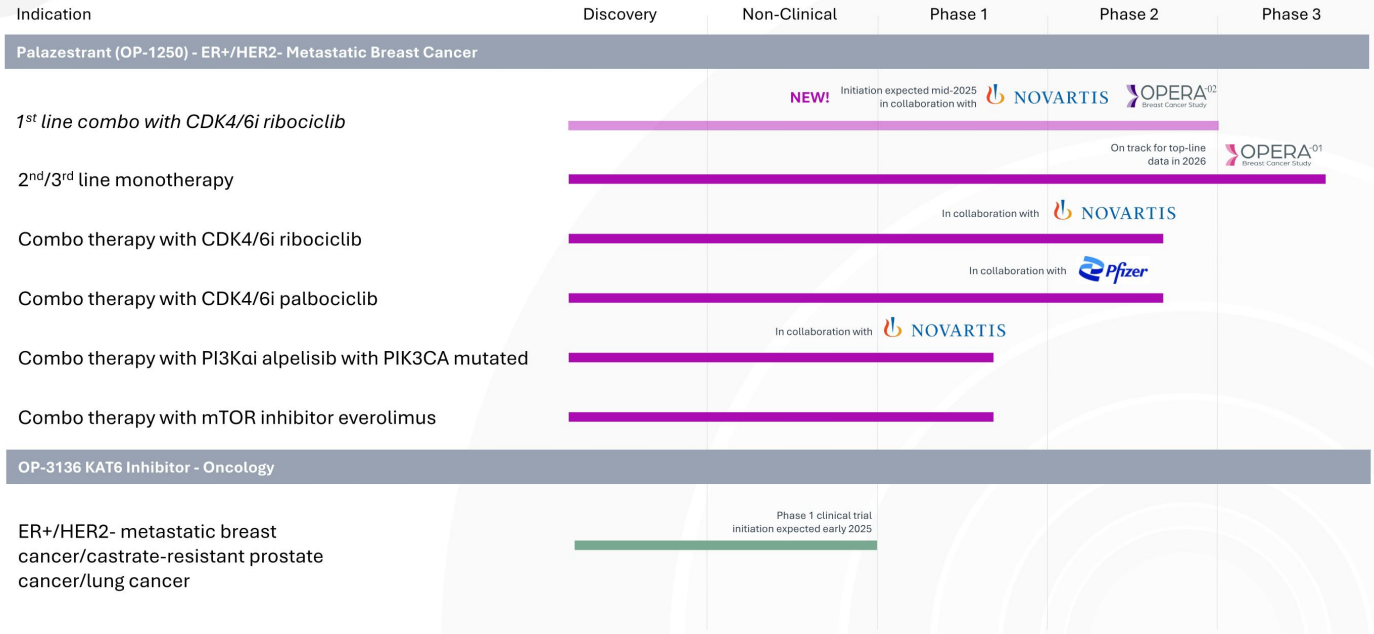
### Proven Leadership

Management and Board with deep expertise developing and commercializing oncology medicines

Olema Oncology

# Rapidly advancing clinical pipeline

## Palazestrant second/third-line and first-line clinical trials in metastatic breast cancer




**KAT6** = lysine acetyltransferase 6; **ER** = estrogen receptor; **HER2** = human epidermal growth factor receptor 2; **CDK4/6i** = cyclin-dependent kinase 4/6 inhibitor; **PI3Kαi** = phosphatidylinositol 3-kinase alpha inhibitor; **mTORi** = mammalian target of rapamycin inhibitor; **PI3Kαi** = phosphoinositide-3 kinase alpha-specific inhibitors; **PI3KCA** = phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha

“A Phase 1b/2 study of palazestrant (OP-1250) in combination with ribociclib, in patients with estrogen receptor-positive, human epidermal growth factor receptor 2-negative (ER+/HER2-), advanced or metastatic breast cancer”

*SABCS 2024 Poster #P2-09-16*

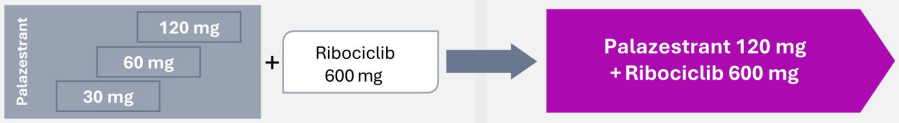
# Phase 1b/2 combination study design

**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)
- Screening QTcF <450 ms, resting heart rate 50-90 beats/min

## 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; **ctDNA** = circulating tumor DNA; **DLT** = dose-limiting toxicity; **DOR** = duration of response; **MTD** = maximum tolerated dose; **ORR** = objective response rate; **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

| Patient Characteristics | Total (N=62) |
|---|---|
| **Median age (years)** | 61 |
| Range | 28–85 |
| **Female sex** | 62 (100%) |
| **Premenopausal** | 9 (15%) |
| **ECOG performance status, n (%)** | |
| 0 | 38 (61%) |
| 1 | 24 (39%) |
| **Measurable disease at baseline, n (%)** | 42 (68%) |
| **Visceral disease, n (%)** | 36 (58%) |
| **Prior lines of therapy in advanced setting, n (%)** | |
| 0 | 14 (23%) |
| 1 | 29 (47%) |
| 2 | 14 (23%) |
| 3 | 5 (8%) |
| **Prior lines of endocrine therapy in advanced setting, n (%)** | |
| 0 | 14 (23%) |
| 1 | 35 (56%) |
| 2 | 13 (21%) |
| **Types of prior therapy in advanced setting, n (%)** | |
| CDK4/6 inhibitor | 46 (74%) |
| Aromatase inhibitor (AI) | 33 (53%) |
| Fulvestrant | 25 (40%) |
| Chemotherapy | 11 (18%) |
| ***ESR1* mutations at baseline (ctDNA), n/N (%)** | 17/60[a] evaluated (28%) |

- N=62; N=56 at 120 mg
- 58% with visceral disease
- 68% with measurable disease
- 77% received prior endocrine therapy in advanced setting
- **74% received prior CDK4/6i + ET**
  - 34 (55%) patients received 1 prior line of CDK4/6i
    - Palbociclib, n=23; abemaciclib n=7 ribociclib, n=4
  - 12 patients (19%) received 2 prior lines of CDK4/6i
    - Palbociclib → abemaciclib, n=3
    - Palbociclib → palbociclib, n=3
    - Palbociclib → ribociclib, n=3
    - Ribociclib → ribociclib, n=1
    - Abemaciclib → palbociclib, n=1
    - Palbociclib → experimental CDK4/6i, n=1
- **28% with *ESR1* mutation**

**Data cutoff date: November 11, 2024.**

[a] *ESR1* mutations in ctDNA at baseline were determined centrally using SafeSEQ Breast Cancer Panel (Sysmex Inostics, Baltimore, MD). Two 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

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

## Treatment-emergent AEs

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

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

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

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

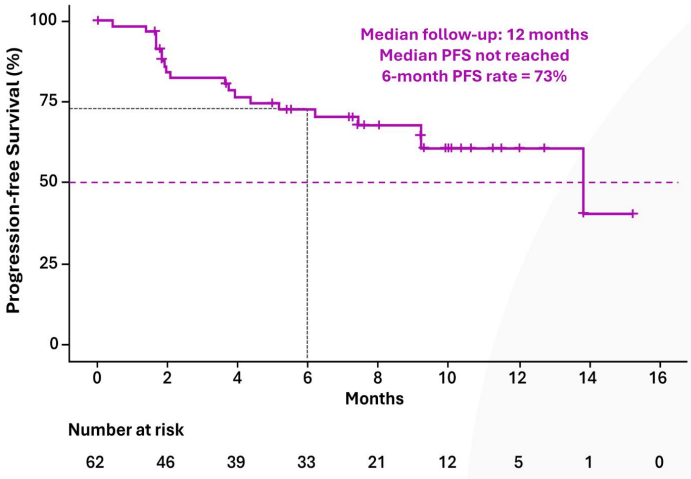
**Includes 3 patients at each of 30 mg and 60 mg palazestrant and 56 patients at 120 mg palazestrant in combination with 600 mg ribociclib. †Adverse reactions reported in ≥10% of patients who received ribociclib plus letrozole in the MONALEESA-2 study.(KISQALI (ribociclib). Prescribing information. Novartis; 2022; Hortobagyi, 2016) ‡Two subjects experienced Grade 5 AEs, heart failure and depressed level of consciousness not related to study drugs but disease progression. §Combined term includes neutropenia, decreased neutrophil count and febrile neutropenia. ¶These values were taken from MONALEESA-2 lab abnormalities data; source: KISQALI (ribociclib). Prescribing information. Novartis; 2022. ¶Ribociclib + fulvestrant in MONALEESA-3 per the Ribociclib Approval Package (NUMBER:209092Orig1s001, June 2018); ribociclib + non-steroidal aromatase inhibitors in MONALEESA-7: all grade QTcF prolongation was 46.5% (Grade 2, 5.3%; Grade 3, 9%). Aggregate analysis (n=1054 patients) .

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

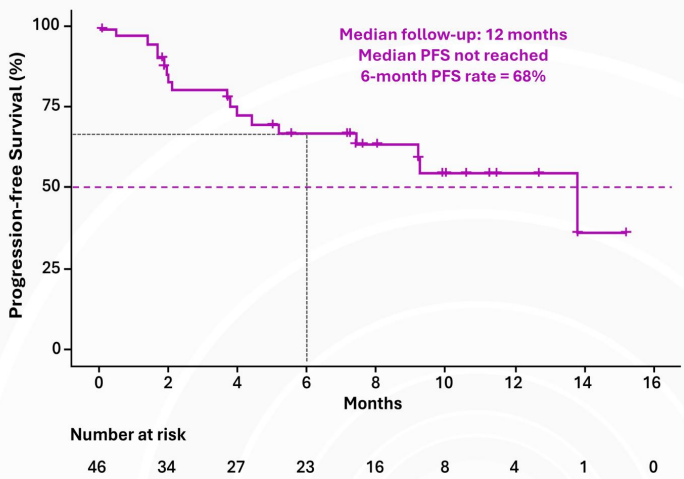
# Six-month PFS rate of 73% in all patients, 68% in those with prior CDK4/6i

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

## All patients (N=62)




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




**Data cutoff date: November 11, 2024**

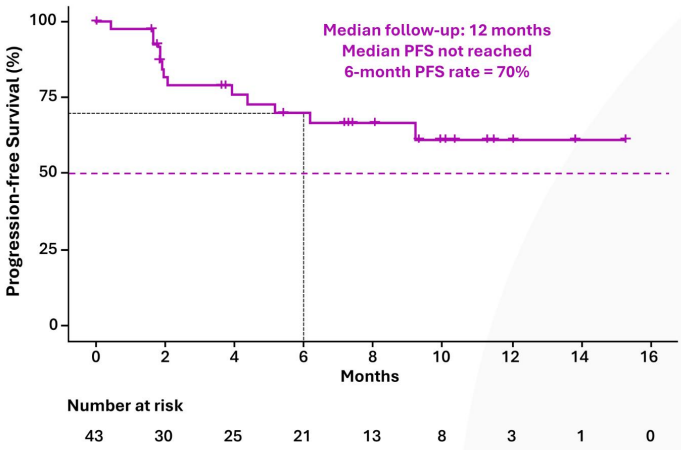
* Follow up was calculated from first dose date to data cutoff date regardless of disease progression status.

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

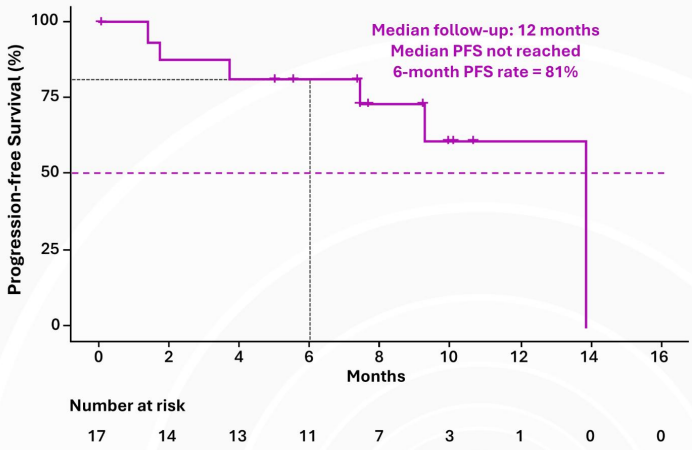
# Six-month PFS rate of 81% in *ESR1*-mutant patients, 70% in *ESR1* wild-type

Median follow-up of 12 months; median PFS not yet reached; sustained efficacy regardless of *ESR1* status

***ESR1* wild-type (n=43)**




***ESR1*-mutant (n=17)**




**Data cutoff date: November 11, 2024**

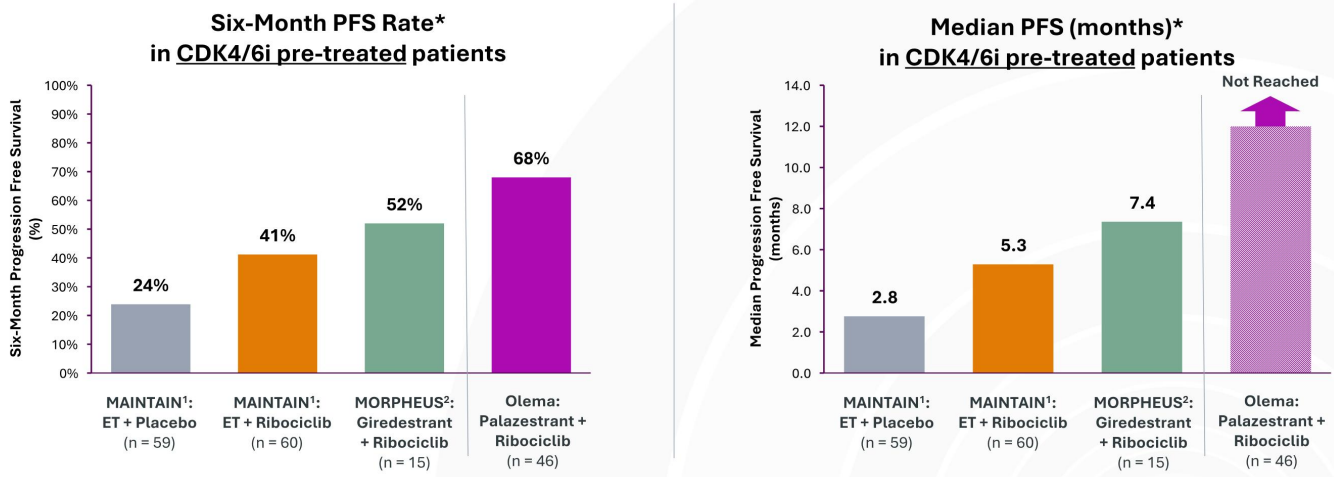
* Follow up was calculated from first dose date to data cutoff date regardless of disease progression status.

**ESR1** = estrogen receptor 1 gene; **PFS** = progression-free survival

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

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

**Interim efficacy signals for palazestrant in combination with ribociclib**

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**Data cutoff date: November 11, 2024.**

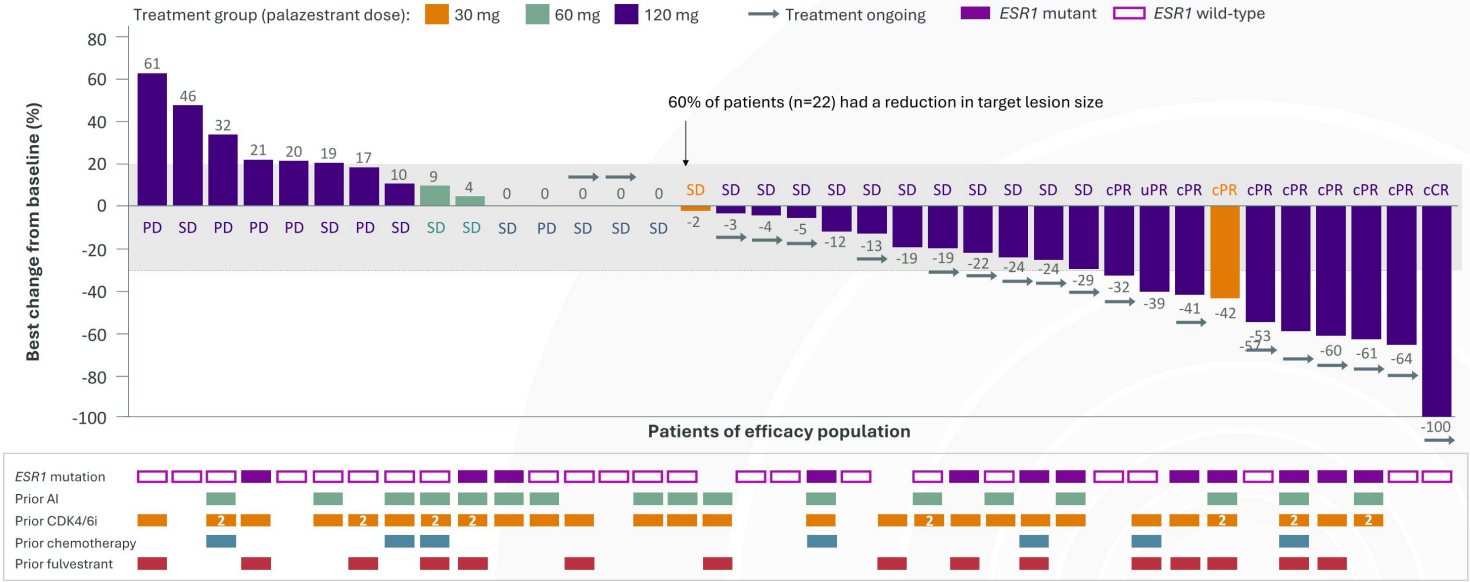
**CDK4/6i =** cyclin-dependent kinase 4/6 inhibitor; ***ESR1*-mut** = *ESR1*-mutant; ***ESR1*-wt** = *ESR1* wild-type; **ET =** endocrine therapy

[1] ASCO 2022 MAINTAIN data; [2] ASCO 2023 MORPHEUS data

# Compelling anti-tumor activity in both wild-type and *ESR1* mutant tumors

60% of patients showed tumor reduction

## Best percent change from baseline in target lesions and best overall response




**Data cutoff date: November 11, 2024.**
**Waterfall plot n=37. 2** = 2 prior CDK4/6 inhibitors in metastatic setting.
**SD** = stable disease; **PD** = progressive disease; **AI** = aromatase inhibitor; **PR** = partial response; **cPR** = confirmed PR; **uPR** = unconfirmed PR; **uCR** = unconfirmed complete response; **cCR** = confirmed complete response; **CDK4/6i** = cyclin-dependent kinase 4/6 inhibitor; ***ESR1*** = estrogen receptor 1 gene

# Highly encouraging preliminary efficacy from the combined agents, including in patients with prior CDK4/6i treatment

## Efficacy

- **Median follow-up of 12 months with mPFS not yet reached**
- 6-month progression-free survival rate was:
  - 73% across all patients
  - 68% in patients with prior CDK4/6i exposure
  - 70% in patients with ESR1-wt disease
  - 81% in those with ESR1-mut disease
- 11 responses to date (2 confirmed CRs*, 8 confirmed PRs, and 1 unconfirmed PR)
- 27% (10/37) ORR among response-evaluable patients with measurable disease
- Clinical benefit rate (CBR)^:
  - 76% in all patients (37/49 CBR-eligible)
  - 81% in ESR1-mut (13/16 CBR-eligible)
  - 74% in ESR1-wt (23/31 CBR-eligible)
- CBR in patients who received prior CDK4/6i:
  - 71% in all patients (25/35 CBR-eligible)
  - 81% in ESR1-mut (13/16 CBR-eligible)
  - 65% in ESR1-wt (11/17 CBR-eligible)
- Longest duration of treatment 79 weeks and ongoing
- Efficacy data are maturing; 30 (48%) patients remain on treatment

## Safety and Tolerability

- Palazestrant (120 mg) in combination with full dose ribociclib was well tolerated
- Safety was consistent with combinations of ribociclib (600 mg) with endocrine therapy

## Pharmacokinetics

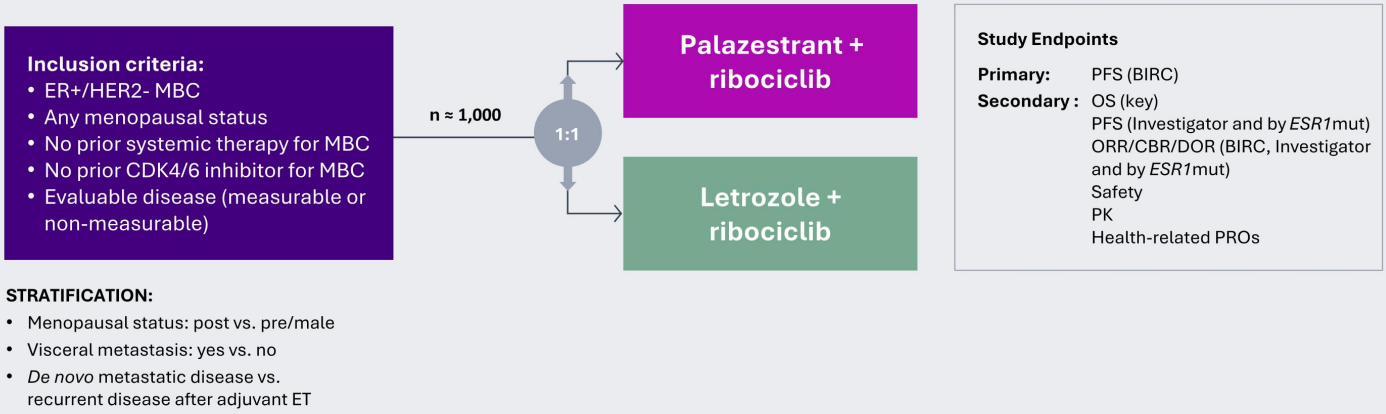
- No clinically meaningful drug-drug interaction

*1 cCR in patient with non-measurable but evaluable disease. ^ CBR is the proportion of patients who remained on treatment through at least 24 weeks with a confirmed complete response or partial response, or stable disease.
Abbreviations: **CDK4/6i** = cyclin-dependent kinase 4/6 inhibitor; ***ESR1*** = estrogen receptor 1 gene; **PR** = partial response; **CR** = complete response.

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

~1,000-patient trial vs. standard of care in preparation for 2025 initiation; in collaboration with Novartis

OPERA-02
Breast Cancer Study




**STRATIFICATION:**

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

**CDK4/6i** = cyclin-dependent kinase 4/6 inhibitor; **CBR** = clinical benefit rate; **DOR** = duration of response; **ER+** = estrogen receptor positive; **HER2-** = human epidermal growth factor receptor 2 negative; **MBC** = metastatic breast cancer; **ORR** = objective response rate; **OS** = overall survival; **PFS** = progression free survival; ***ESR1*mut** = *ESR1*-mutant; **ET** = endocrine therapy

# Preparing to initiate OPERA-02 in 2025

New clinical trial collaboration and supply agreement with Novartis combined with $250M private placement enables execution of Olema operating plan

- Novartis agreement enables pivotal Phase 3 OPERA-02 clinical trial of palazestrant in combination with ribociclib in frontline ER+/HER2- advanced or metastatic breast cancer
- Ribociclib drug supply expected to be sufficient to conduct the planned OPERA-02 trial; valued at ~$275M
- Olema responsible for the day-to-day operational activities for OPERA-02
- Olema retains global commercial rights to palazestrant
- All clinical data from OPERA-02 will be jointly owned; each party retains rights to its background IP

- $250M equity private placement strengthens Olema's balance sheet
- Participation by new and existing high-quality institutional and accredited investors
- Pro forma cash and cash equivalents expected to fund research and development activities including the execution of OPERA-01, OPERA-02, OP-3136 Phase 1/2, and for working capital and general corporate purposes

# Significant opportunity for palazestrant across the spectrum of care

Estimated >$20B ER+/HER2- global metastatic breast cancer market[1]

| | | |
|---|---|---|
| 2L/3L+ ER+/HER2- MBC OPERA-01 Breast Cancer Study | Patients[2] | ~150K |
| | Duration of Therapy[3] | ~2-12+ months |
| | Global Market Potential[4] | $5B+ |
| 1L ER+/HER2- MBC OPERA-02 Breast Cancer Study | Patients[2] | ~115K |
| | Duration of Therapy[3] | ~6-36+ months |
| | Global Market Potential[4] | $10B+ |

[1] 2025 opportunity estimates for total endocrine therapy market (US and Europe). Olema internal data.
[2] 2025 incidence projection estimates. Olema internal data, Informa ER+/HER2- BC Prevalence Based Market Forecast.
[3] Olema internal data.
[4] Olema internal data.

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

## Changing the treatment paradigm for endocrine-driven cancers

1. Palazestrant anchors Olema's breast cancer program as a potential backbone therapy for metastatic breast cancer
   - Highly differentiated as first oral CERAN/SERD endocrine agent
   - Ongoing 2/3L OPERA-01 Phase 3 trial on track for top-line data in 2026
   - Planned 1L OPERA-02 Phase 3 trial in combination with ribociclib enabled; initiation expected in 2025
   - Go-to-market strategy for potential U.S. launch in 2027
2. OP-3136 expands pipeline with novel and validated KAT6 target
   - IND cleared by FDA; first patient expected to enroll in Phase 1 clinical trial by early 2025
3. Well-capitalized with ~$452M of pro forma cash and cash equivalents as of September 30, 2024[1]

[1] *Pro forma position includes the Company's cash, cash equivalents, and marketable securities as of September 30, 2024, plus net proceeds of approximately $237.5 million from equity private placement which closed on December 4, 2024.*

# Thank You

— Advancing medicines for breast cancer and beyond

Olema ONCOLOGY