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

October 18, 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, Oct. 18, 2025 (GLOBE NEWSWIRE) -- 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.

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