Olema Oncology Announces Preclinical Data for Palazestrant and OP-3136 at the 2026 AACR Annual Meeting

April 17, 2026

- *Palazestrant's mechanism of action confirmed; full recruitment of corepressor protein NCoR1 enables complete antagonism of the estrogen receptor*
- *OP-3136, in combination with palazestrant, exhibits synergistic anti-tumor activity in ER+/HER2- breast cancer models driven by suppression of cell-cycle and estrogen receptor-driven oncogenic signaling*
- *Palazestrant is currently being evaluated in two Phase 3 clinical trials; OP-3136 is enrolling patients in the ongoing Phase 1 study*

SAN FRANCISCO, April 17, 2026 (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 new preclinical data for palazestrant, a complete estrogen receptor antagonist (CERAN) and selective estrogen receptor degrader (SERD), alone and in combination with OP-3136, a novel small molecule that potently and selectively inhibits acetyltransferase 6 (KAT6) inhibitor. The data will be presented in two poster presentations at the American Association for Cancer Research (AACR) Annual Meeting taking place April 17-22 in San Diego, California.

"We are very excited to share, for the first time ever, data that confirm the mechanism by which palazestrant completely blocks estrogen receptor transcription and signaling by recruiting the corepressor protein NCoR1," said David C. Myles, Ph.D., Chief Scientific Officer of Olema Oncology. "Further, the synergistic anti-tumor activity of OP-3136 combined with palazestrant in preclinical models highlights the role that both complete ER antagonism and KAT6 inhibition play in addressing acquired resistance associated with metastatic disease. We are pleased to continue to explore the potential of this combination in our ongoing Phase 1 study of OP-3136 and look forward to announcing top-line data from our Phase 3 OPERA-01 trial of palazestrant monotherapy, which is anticipated this fall."

Poster Presentation Details
Title: Palazestrant directly recruits the corepressor protein NCoR1 *in vitro* leading to complete antagonism of estrogen receptor alpha
Poster/Abstract: 2950
Session: Experimental and Molecular Therapeutics: Cellular Responses to Anticancer Drugs
Date/Time: April 20, 2026, from 2:00pm-5:00pm PT / 5:00pm-8:00pm ET

Key findings:

- Palazestrant completely blocks estrogen-driven transcription and demonstrates robust anti-tumor activity *in vitro*.
- In a split-luciferase assay, palazestrant was shown to fully recruit the corepressor, NCoR1, enabling complete estrogen receptor (ER) antagonism.
- In both *ESR1* wild-type and mutant models, palazestrant more potently suppressed ER-regulated and cell-cycle genes, including PGR and GREB1, than selective estrogen receptor modulators (SERMs), delivering complete inhibition of tumor cell proliferation without partial agonist effects.

These findings position palazestrant as a differentiated endocrine therapy designed to achieve deeper, more consistent ER pathway suppression in estrogen receptor-positive, human epidermal growth factor receptor 2-negative (ER+/HER2-) breast cancer.

Title: Palazestrant, a CERAN, in combination with OP-3136, a KAT6 inhibitor, synergistically downregulates cell proliferation and metastasis related gene signatures
Poster/Abstract: 2949
Session: Experimental and Molecular Therapeutics: Cellular Responses to Anticancer Drugs
Date/Time: April 20, 2026, from 2:00pm-5:00pm PT / 5:00pm-8:00pm ET

Key findings:

- Combining OP-3136 with palazestrant drives synergistic anti-tumor activity in *in vivo* ER+/HER2- breast cancer models, which is mediated by suppression of cell-cycle and estrogen receptor-driven oncogenic signaling processes.
- The combination of OP-3136 plus palazestrant downregulates genes associated with MYC, E2F, and G2M more effectively than either agent alone or OP-3136 in combination with fulvestrant.

- Combining OP-3136 with palazestrant or fulvestrant suppresses expression of genes associated with MTORC1 signaling, indicating that targeting KAT6 and ER-alpha can suppress mechanisms of acquired resistance.

These findings provide a strong biological rationale for advancing palazestrant in combination with OP-3136 for the treatment of ER+ metastatic breast cancer.

Copies of these posters will be available on the Publications page of Olema's website in alignment with the AACR embargo. Additional information, including abstracts, is available on the AACR Annual Meeting website.

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.

About OP-3136
OP-3136 is a novel, orally available small molecule that potently and selectively inhibits lysine acetyltransferase 6 (KAT6), an epigenetic target that is dysregulated in breast and other cancers. In preclinical studies, OP-3136 has demonstrated significant anti-proliferative activity in ER+ breast cancer models and is combinable and synergistic with endocrine therapies including palazestrant and cyclin-dependent kinase 4/6 (CDK4/6) inhibitors. The Investigational New Drug (IND) application for OP-3136 was cleared by the U.S. Food and Drug Administration (FDA) in December 2024 and patients are currently enrolling in the Phase 1 clinical study.

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," "intend," "may," "on track," "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 potential differentiated profile of palazestrant as an endocrine therapy, including its ability to achieve deeper and more consistent ER pathway suppression in ER+/HER2- breast cancer; the potential beneficial characteristics, including but not limited to safety, tolerability, activity, efficacy and therapeutic effects of palazestrant or OP-3136; the potential beneficial effects of combining palazestrant with OP-3136 or with other drugs, including in the metastatic setting; the potential for such data to support further clinical development of palazestrant or OP-3136, alone or in combination; and the timelines for enrollment for current clinical studies and for the receipt and presentation of results of clinical trials of palazestrant and OP-3136 each as a monotherapy and in combination trials. 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 Annual Report on Form 10-K for the year ended December 31, 2025, and future 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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