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

December 10, 2024

- *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 a 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, Dec. 10, 2024 (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 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% (13/16) 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. 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.

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 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 progression-free survival, the initiation and timing of clinical trials, and Olema's potential to transform the endocrine therapy standard of care treatments for patients living with ER+/HER2- metastatic breast cancer. 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