Olema Oncology Announces Positive Phase 2 Monotherapy Clinical Study Results for Palazestrant

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- *Across all 86 heavily pretreated patients, the median PFS was 4.6 months with a CBR of 40%; in patients with ESR1 mutations at baseline, the median PFS was 5.6 months with a CBR of 52%*
- *In an analysis of 49 second- and third-line patients, the median PFS was 7.2 months with a CBR of 48%; the median PFS was 7.3 months with a CBR of 59% in patients with ESR1 mutations*
- *Results support continued development of palazestrant in the OPERA-01 monotherapy Phase 3 pivotal trial*
- *Olema will host an investor conference call at 8:00 a.m. ET on Monday, October 23, 2023*

SAN FRANCISCO, Oct. 22, 2023 (GLOBE NEWSWIRE) -- Olema Pharmaceuticals, Inc. ("Olema", "Olema Oncology", or the "Company", Nasdaq: OLMA), a clinical-stage biopharmaceutical company focused on the discovery, development and commercialization of targeted therapies for women's cancers, today announced results from a Phase 2 clinical study of palazestrant (OP-1250), the Company's complete estrogen receptor (ER) antagonist (CERAN) and selective ER degrader (SERD), for the treatment of metastatic ER+/HER2- breast cancer. These results were presented in an oral presentation at the European Society for Medical Oncology (ESMO) Congress 2023 in Madrid, Spain, on October 22, 2023.

The presentation, titled "Results from the phase 1/2 study of OP-1250, an oral complete estrogen receptor (ER) antagonist (CERAN) and selective ER degrader (SERD) in patients (pts) with advanced or metastatic ER-positive, HER2-negative breast cancer", highlighted that:

- Across 86 heavily pretreated patients, where 42% of patients were 4th line or later at study entry, 120 mg once-daily, monotherapy palazestrant was well tolerated and achieved a median progression-free survival (PFS) of 4.6 months and clinical benefit rate (CBR) of 40%, and a median PFS of 5.6 months and CBR of 52% in patients with ESR1 mutations at baseline.
- In a subset analysis of 49 second- or third-line patients with or without prior chemotherapy (the EMERALD trial eligibility criteria), the median PFS was 7.2 months and CBR was 48% across all patients, and the median PFS was 7.3 months and CBR was 59% ESR1-mutant patients.

"These Phase 2 monotherapy study results demonstrate that palazestrant (OP-1250) has the potential to become a best-in-class endocrine therapy and improve upon current standard of care treatments for women living with metastatic breast cancer. In addition to being well-tolerated, palazestrant has demonstrated compelling progression-free survival as monotherapy in a heavily pretreated patient population," said Sean P. Bohen, M.D., Ph.D., President and Chief Executive Officer of Olema Oncology. "Going forward, we are in the process of initiating OPERA-01, our first pivotal Phase 3 clinical trial testing palazestrant as monotherapy in second- and third-line metastatic breast cancer."

Phase 2 Clinical Study Results

Enrollment

As of the data cut-off of July 7, 2023, 86 patients with recurrent, locally advanced or metastatic ER+/HER2- breast cancer were treated at the Recommended Phase 2 Dose (RP2D) of 120 mg. The group was heavily pretreated with 42% of patients being fourth-line or later at study entry, 65% of patients having received two or more prior lines of endocrine therapy for metastatic disease, and 31% having received prior chemotherapy. Almost all patients (97%) received prior treatment with a cyclin-dependent kinase 4/6 (CDK4/6) inhibitor, and 66% received prior treatment with fulvestrant. Of 75 patients whose circulating tumor DNA (ctDNA) was assessed, 48% had activating mutations in ESR1 at baseline.

Pharmacokinetics

Palazestrant demonstrated favorable pharmacokinetics characterized by high oral bioavailability, dose proportional exposure and a long half-life of eight days, with steady-state plasma levels showing minimal peak-to-trough variability, enabling consistent inhibition of the ER for the full dosing interval.

Safety and Tolerability

Treatment with palazestrant at the RP2D of 120 mg was well tolerated with no dose-limiting toxicities, and the maximum tolerated dose (MTD) was not reached. The majority of treatment-emergent adverse events (TEAEs) were Grade 1 or 2. Of the 86 patients treated, events of Grade 4 neutropenia were observed in six patients, occurring approximately 4–6 weeks into therapy. Of these patients, three had a dose interruption with recovery and subsequent dose reduction (two continued at 90 mg and one continued at 60 mg) without any recurrence, and three had dose discontinuation followed by recovery. All six patients had prior exposure to CDK4/6 inhibitors.

Efficacy

Across all 86 patients, the median PFS was 4.6 months and the CBR was 40% with a 6-month PFS rate of 38%. In patients with an ESR1 mutation, the median PFS was 5.6 months and the CBR was 52% with a 6-month PFS rate of 46%. In ESR1 wild-type patients, the median PFS was 3.5 months and the CBR was 32% with a 6-month PFS rate of 35%.

In a subset analysis of 49 patients that received palazestrant as a second- or third-line therapy with or without prior chemotherapy (the EMERALD trial eligibility criteria), the median PFS was 7.2 months and the CBR was 48% across all patients with a 6-month PFS rate of 54%. In patients with an ESR1 mutation, the median PFS was 7.3 months and CBR was 59% with a 6-month PFS rate of 62%. In ESR1 wild-type patients the median PFS was 5.5 months and the CBR was 38% with a 6-month PFS rate of 44%.

Anti-tumor activity was observed in this heavily pretreated population, with 40% of patients demonstrating reduction in target lesions and evidence of activity in both ESR1 wild-type and ESR1-mutant patients. Given the advanced and heavily pretreated nature of the patients, many of these patients are expected to be resistant to monotherapy endocrine treatment.

Company Investor Webcast and Conference Call

Olema will host a webcast and conference call for analysts and investors to review data presented at ESMO 2023 on Monday, October 23, 2023, at 8:00 a.m. ET (5:00 a.m. PT). 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 in Boston, MA, will join Olema management for the call. Please register for the webcast by visiting the Investors & Media section of Olema's website at olema.com.

A copy of the oral presentation is available on Olema's website under the Science section of the Olema website.

About Olema Oncology
Olema Oncology is a clinical-stage biopharmaceutical company focused on the discovery, development and commercialization of targeted therapies for women's cancers. Olema's lead product candidate, palazestrant (OP-1250), is a proprietary, orally-available small molecule with dual activity as both a complete estrogen receptor (ER) antagonist (CERAN) and a selective ER degrader (SERD). It is currently being evaluated both as a single agent in an ongoing Phase 2 clinical trial, and in combination with CDK4/6 inhibitors (palbociclib and ribociclib) and a PI3Ka inhibitor (alpelisib), in patients with recurrent, locally advanced or metastatic ER-positive (ER+), human epidermal growth factor receptor 2-negative (HER2-) breast cancer. Palazestrant has been granted 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. Olema is headquartered in San Francisco and has operations in Cambridge, Massachusetts. For more information, please visit us at www.olema.com, or follow us on Twitter and LinkedIn.

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," "expect," "will," "may," "goal," "potential" 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, the development of palazestrant, the initiation and timing of clinical trials, palazestrant's combinability with other drugs, and the potential of palazestrant to become a best-in-class endocrine therapy in the treatment of ER+/HER2- metastatic breast cancer or improve upon the standard of care treatments for women 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 June 30, 2023, 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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