Olema Oncology Announces OP-1250 Continues to Demonstrate Attractive Combinability with CDK4/6 Inhibitor Palbociclib in Phase 1b/2 Study

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- *OP-1250 in combination with palbociclib was well-tolerated in patients with ER+/HER2- metastatic breast cancer, with no dose-limiting toxicities, and no observed drug-drug interaction*
- *Overall tolerability profile of the combination is consistent with the FDA-approved label of palbociclib plus an endocrine agent*
- *Tumor responses have been observed in patients previously treated with CDK4/6 inhibitors*

SAN FRANCISCO, May 11, 2023 (GLOBE NEWSWIRE) -- Olema Pharmaceuticals, Inc. ("Olema", "Olema Oncology", or the "Company", Nasdaq: OLMA) today announced interim results from an ongoing Phase 1b/2 clinical study of OP-1250, the Company's complete estrogen receptor (ER) antagonist (CERAN) and selective ER degrader (SERD), in combination with palbociclib, a CDK4/6 inhibitor, for the treatment of ER+/HER2- metastatic breast cancer. These results, as of March 8, 2023, were presented today in a poster session at the 2023 ESMO Breast Cancer Annual Congress in Berlin, Germany.

The poster, titled "A Phase 1b/2 Study of OP-1250, an Oral Complete Estrogen Receptor Antagonist (CERAN) and Selective ER Degrader (SERD) with Palbociclib in Patients with Advanced or Metastatic HR+/HER2- Breast Cancer", highlighted that:

- Across 29 patients, the combination of up to 120 mg of OP-1250 with 125 mg of palbociclib is safe and well-tolerated with no drug-drug interaction (DDI), no induced metabolism of palbociclib, and exposure of both palbociclib and OP-1250 in combination with each other was consistent with the observed monotherapy exposure levels.
- No dose-related increases in the incidence, severity, or timing of adverse events were observed, and neutropenia events observed were consistent with the expected profile of palbociclib plus endocrine therapy.
- Tumor responses and prolonged disease stabilization were observed in this group of patients, including in those previously exposed to palbociclib and other CDK4/6 inhibitors.

"We are very pleased with our emerging combination clinical results of OP-1250 with palbociclib," said Sean P. Bohen, M.D., Ph.D., President and Chief Executive Officer of Olema Oncology. "The findings presented today support the potential for OP-1250 to become a best-in-class endocrine therapy in the first-line treatment of ER+/HER2- metastatic breast cancer. OP-1250, in combination with palbociclib, did not display the drug-drug interactions or increased toxicity that have been observed with some novel endocrine therapies."

Interim Phase 1b/2 Clinical Results

Enrollment

As of the data cut-off of March 8, 2023, 29 patients with recurrent, locally advanced or metastatic ER+/HER2- breast cancer were treated. In the dose-escalation part, 12 patients were enrolled across four cohorts: three patients per cohort dosed at 30, 60, 90, and 120 mg in combination with palbociclib 125 mg. In the dose-expansion part (ongoing), patients received 120 mg OP-1250 plus palbociclib 125 mg. Seventeen patients had been enrolled in the dose expansion at the time of data cut-off, with a total planned enrollment of approximately 45 patients. The majority of patients (27 or 93%) were 2/3 line, with 25 (86%) patients having received prior endocrine therapy for advanced disease, 20 (69%) patients having received prior CDK4/6 inhibitors including prior palbociclib, and six (21%) patients having received chemotherapy in the advanced setting. Of 18 patients whose circulating tumor DNA (ctDNA) was assessed as of the data cut-off, 44% had activating mutations in ESR1 at baseline.

Pharmacokinetics

OP-1250 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 ER for the full dosing interval. There was no observed DDI between palbociclib and OP-1250 in the dose range of 30 mg to 120 mg. Palbociclib did not affect OP-1250 drug exposures compared to monotherapy dosing, and OP-1250 had no effect on palbociclib 125 mg drug exposures when compared to published concentrations for single-agent palbociclib.

Safety and Tolerability

Treatment with OP-1250 up to the Recommended Phase 2 Dose (RP2D) of 120 mg was safe and well tolerated with no dose-limiting toxicities. The

majority of treatment-emergent adverse events (TEAEs) were Grade 1 or 2, and there were no dose-related increases in incidence or severity of TEAEs. OP-1250 was not dose-reduced in any patients, and no patients discontinued treatment with OP-1250 due to an adverse event, including neutropenia. Neutropenia events observed were consistent with the expected profile of palbociclib plus an endocrine therapy. Neutropenia was reversible in all patients and the timing was consistent with palbociclib-related neutropenia.

Efficacy

In a maturing dataset, anti-tumor activity and prolonged disease stabilization was demonstrated in patients previously treated with CDK4/6 inhibitors, including palbociclib. Partial responses were observed in five patients (one confirmed, four unconfirmed as of data cut-off) with a clinical benefit rate to date of 42% (5/12 CBR-eligible patients). Fifty-nine percent of patients remain on treatment as of the data cut-off date with additional enrollment ongoing.

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

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, 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. OP-1250 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.

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, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. 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 OP-1250, the development of OP-1250, OP-1250's combinability with other drugs, and the potential of OP-1250 to become a best-in-class endocrine therapy in the first-line treatment of ER+/HER2- metastatic breast cancer or significantly improve endocrine therapy 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 Annual Report on Form 10-Q for the quarter ended March 31, 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 or to update the reasons if actual results differ materially from those anticipated in the forward-looking statements.

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