



Olema Oncology Announces First Clinical Data on OP-1250 in Advanced ER+ / HER2- Breast Cancer

November 30, 2021

- *Successful completion of dose-escalation stage of ongoing Phase 1/2 clinical study; OP-1250 demonstrated highly attractive pharmacokinetics, favorable tolerability, and clear efficacy signals*
- *Robust anti-tumor activity, including three partial responses (two confirmed and one unconfirmed) and up to 100% target lesion reduction, observed in a heavily pretreated patient population*
- *Overall Response Rate of 17% and Clinical Benefit Rate of 46% in recommended Phase 2 dose range; Efficacy data continues to mature with 32% of patients still on study*
- *Rapidly advancing clinical development program with dose expansion ongoing; Phase 2 monotherapy and first CDK4/6 inhibitor combination studies to initiate in Q1 2022*
- *Company to host investor conference call today at 8:30 a.m. ET*

SAN FRANCISCO, Nov. 30, 2021 (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 women's cancers, today announced the first clinical data from the Phase 1 dose-escalation portion of the ongoing Phase 1/2 clinical trial of OP-1250, a complete estrogen receptor (ER) antagonist (CERAN) and a selective ER degrader (SERD) in development for the treatment of metastatic breast cancer and other women's cancers. Data as of October 1, 2021, is scheduled to be presented in a poster presentation at the San Antonio Breast Cancer Symposium (SABCS), taking place December 7-10, 2021. Updated data as of November 1, 2021, are detailed below.

These initial data provide strong proof-of-concept for OP-1250 as a once-daily oral monotherapy in women with recurrent, locally advanced or metastatic ER+ / HER2- breast cancer and demonstrate OP-1250's potential to become a best-in-class endocrine therapy. In the trial, OP-1250 showed highly attractive pharmacokinetics supporting once-daily dosing, favorable tolerability, and clear evidence of anti-tumor activity. Three partial responses (2 confirmed, 1 unconfirmed) and robust target lesion reduction up to 100% were observed in a heavily pretreated patient population. In the recommended Phase 2 dose (RP2D) range of 60-120 mg OP-1250 once daily, the overall response rate (ORR) was 17% and the clinical benefit rate (CBR) was 46%.

"We successfully delivered on our objectives for the dose-escalation stage of our ongoing Phase 1/2 trial of OP-1250, with the desired pharmacokinetics, favorable tolerability, and early but clear efficacy signals. We are particularly encouraged by the responses observed in patients who had received multiple prior lines of therapy and harbored ESR1 activating mutations, demonstrating that OP-1250 is an active drug and achieved sufficient exposure levels to block the ER-mediated cancer cell growth and proliferation signal," said Sean P. Bohlen, M.D., Ph.D., President and Chief Executive Officer of Olema Oncology. "These data give us confidence to rapidly advance our development program in both monotherapy and combination settings, as we work to further position OP-1250 as a differentiated, potential best-in-class CERAN that we believe could become the backbone endocrine therapy of choice for ER+ breast cancer."

"These promising interim data suggest OP-1250 may provide meaningful benefit to patients with advanced or metastatic breast cancer, and who may have limited treatment options remaining," said Pamela M. Klein, M.D., Chief Medical Officer. "Having accomplished our intended goals with the completed Phase 1 dose escalation, we are currently enrolling patients in dose expansion at two dose levels and expect to initiate Phase 2 monotherapy and the first combination study with a CDK4/6 inhibitor in the first quarter of 2022. As we accelerate enrollment in the coming months, we look forward to gaining additional insights into OP-1250's potentially differentiated and best-in-class profile."

Interim Results from Phase 1a Dose Escalation of OP-1250 as a Monotherapy

Pharmacokinetics (PK), safety, tolerability, and anti-tumor activity of once-daily OP-1250 monotherapy were evaluated in the open-label, dose-escalation portion of the ongoing Phase 1/2 clinical trial (NCT04505826). As of November 1, 2021, a total of 41 patients with recurrent, locally advanced or metastatic ER+ / HER2- breast cancer were enrolled across 7 dose cohorts (30 mg, 60 mg, 90 mg, 120 mg, 150 mg, 210 mg, and 300 mg once-daily).

This was a difficult-to-treat, heavily pretreated population: 95% of patients were previously treated with a cyclin-dependent kinase (CDK) 4/6 inhibitor (9 patients, or 22%, received 2 or more prior CDK4/6 inhibitor regimens), 68% of patients received prior fulvestrant, and 42% received prior chemotherapy in the advanced setting. Overall, patients received a median of 3 prior lines of anti-cancer therapy and 2 prior lines of endocrine therapy in advanced settings. Of 39 patients whose circulating tumor DNA (ctDNA) was assessed, ESR1 mutations were detected in 49% at baseline.

PK

Pharmacokinetic analyses demonstrated dose-proportional increases in OP-1250 exposures across all evaluated doses, high oral bioavailability and steady-state plasma levels with minimal peak-to-trough variability. At doses 60 mg and above, OP-1250 achieved exposures exceeding the predicted

thresholds for maximal anti-tumor efficacy based on preclinical models.

Tolerability

OP-1250 was generally well tolerated, and no dose-limiting toxicities were reported at any of the seven dose levels studied. A maximum tolerated dose was not reached. The majority of reported adverse events were grade 1 or 2 at all dose levels, and the most common treatment-related adverse events as assessed by study investigator were nausea (49%), fatigue (34%), vomiting (22%) and headache (17%). No clinically significant bradycardia, ocular toxicities or diarrhea occurred. A RP2D range of 60 to 120 mg was identified for further evaluation based on pharmacokinetics, favorable tolerability, and initial evidence of anti-tumor efficacy.

Efficacy

Three partial responses were observed among 24 efficacy-evaluable patients, including 2 confirmed partial responses and 1 unconfirmed partial response in a patient with robust target lesion reduction of 100%, but whose response remained unconfirmed due to progressive disease with a new lesion appearing at a follow-up visit. All 3 responses occurred in patients with ESR1 mutations and who had previously received CDK4/6 and aromatase inhibitors, and fulvestrant. Four response-eligible patients had target lesion reductions of greater than 30%.

Patients were considered efficacy-evaluable for ORR if they had RECIST-measurable disease at baseline and at least one post-baseline tumor assessment or discontinued treatment prior to their first post-baseline assessment, and for CBR if they were enrolled at least 24 weeks prior to the data cut-off date. Across all doses, the ORR was 8% (2/24) and the CBR was 29% (7/24). For the dose levels within the RP2D range, the ORR was 17% (2/12) and the CBR was 46% (6/13).

As of the data cut-off date, 32% of patients (13/41) remained on treatment with efficacy data continuing to mature, including both patients with confirmed partial responses.

Anticipated Milestones

Based on these promising data, Olema is rapidly advancing OP-1250's clinical development program with a number of anticipated program milestones. Phase 1b dose expansion is ongoing at two dose levels (60 mg and 120 mg daily) and is expected to enroll 15 patients in each cohort. Findings from this stage will help inform selection of the RP2D.

Phase 2 efficacy evaluation is expected to initiate in Q1 2022 with approximately 80 patients enrolled across three cohorts: patients with measurable disease (n=50), patients with non-measurable disease (n=15), and patients with CNS metastasis (n=15). The first Phase 1b combination study with a CDK4/6 inhibitor is expected to initiate in Q1 2022, with additional combination studies with CDK4/6 and PIK3CA inhibitors planned in 2022. A pivotal study for OP-1250 in the metastatic setting is expected to initiate in 2023.

Conference Call and Webcast Details

Olema will host a conference call and webcast presentation for analysts and investors on Tuesday, November 30, 2021, at 8:30 a.m. ET (5:30 a.m. PT) to review the Phase 1 clinical data for OP-1250. The webcast player and accompanying slides may be accessed on the Investors section of Olema's website at www.olema.com. The conference call may be accessed by dialing +1 (833) 303-1210 for U.S. callers and +1 (918) 922-6526 for international callers and providing the passcode 7627078. A replay of the webcast will be available approximately two hours after the completion of the event and may be accessed by visiting Olema's website.

About Breast Cancer

Breast cancer is the second-most common cancer worldwide, with nearly two million new diagnoses per year. In the U.S., breast cancer represents approximately 30% of all new diagnoses of women's cancer. In 2021, the American Cancer Society estimates there will be approximately 281,550 new cases of invasive breast cancer diagnosed in women, and more than 43,600 women will die from breast cancer in the U.S. The estrogen receptor plays an important role in the development, progression, and treatment of hormone-dependent breast cancer. Approximately 75% of all breast cancers are ER+, and approximately 65% are ER+, HER2-.

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 an orally available small molecule with combined activity as both a complete estrogen receptor (ER) antagonist (CERAN) and a selective ER degrader (SERD). It is currently being evaluated as a single agent in an ongoing Phase 1/2 clinical trial in patients with recurrent, locally advanced or metastatic ER-positive (ER+), human epidermal growth factor receptor 2-negative (HER2-) breast cancer. 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 and Section 21E of the Securities Exchange Act of 1934. Words such as "anticipate," "expect," "intend," "will," "may," "goal," "estimate," "potential", "suggest", "promising" 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, the timelines for clinical trials of OP-1250 as a monotherapy and in combination trials, and the number of patients in the United States who suffer from 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, the risk that Olema's ongoing or future clinical studies in humans may show that OP-1250 is not a tolerable and effective treatment for breast cancer and other risks and uncertainties affecting Olema, as well as those discussed in the section titled "Risk Factors" in Olema's Quarterly Report on Form 10-Q for the quarter ended September 30, 2021, filed on November 10, 2021 and future filings and reports that Olema makes from time to time with the United States 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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