Olema Oncology Announces Complete ER Antagonist OP-1250 Continues to Demonstrate Robust Activity in Phase 1/2 Clinical Trial

October 26, 2022

- *OP-1250 continues to demonstrate favorable tolerability, high drug exposure, and strong anti-tumor activity in preliminary Phase 1/2 study results presented at the 34th EORTC-NCI-AACR Symposium*
- *Initial clinical data for OP-1250 in combination with CDK 4/6 inhibitor palbociclib expected in the fourth quarter of 2022*
- *Pivotal monotherapy Phase 3 study planned for initiation mid-2023*
- *Company to host investor conference call today at 8:00 a.m. ET*

SAN FRANCISCO, Oct. 26, 2022 (GLOBE NEWSWIRE) -- Olema Pharmaceuticals, Inc. ("Olema" or "Olema Oncology" or the "Company", Nasdaq: OLMA) today announced preliminary clinical results from a Phase 1/2 clinical study of OP-1250, the Company's complete estrogen receptor (ER) antagonist (CERAN) and selective ER degrader (SERD) in development for the treatment of metastatic breast cancer. These results, as of September 2, 2022, were presented at a poster session of the 34th EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics (ENA 2022) in Barcelona, Spain. The poster, titled "Preliminary Phase 1/2 results from OP-1250-001, a study of OP-1250, an oral CERAN/SERD, in patients with advanced and/or metastatic estrogen receptor (ER)-positive, HER2-negative breast cancer (NCT04505826)", highlighted that:

- Across 68 patients at 60 mg and 120 mg once daily oral dosing, OP-1250 was well tolerated with attractive pharmacokinetics (PK) and drug exposure levels approximately 20 times that of fulvestrant at the 120 mg dose.
- OP-1250 demonstrated strong anti-tumor activity and durable benefit with 41% of patients seeing reductions in target tumor lesions, and 6 partial responses (4 confirmed and 2 unconfirmed) out of 57 efficacy-evaluable patients.

Dr. Erika Hamilton, Director of Breast Cancer and Gynecologic Cancer Research for Sarah Cannon Research Institute at Tennessee Oncology, lead author of the presentation, said, "The data generated to date and the emerging profile of OP-1250 are promising. The reductions in target lesions, including confirmed partial responses with good durability for patients that remain endocrine sensitive, is impressive considering the extensive prior treatment that these patients have seen. The data provide strong support that OP-1250 has the potential to provide meaningful benefit to patients with advanced or metastatic breast cancer. I look forward to seeing additional results from ongoing monotherapy and combination studies and the initiation of pivotal trials."

"The results we presented today from our monotherapy dose expansion study provide further validation of our belief in OP-1250's potential to become the endocrine therapy of choice for ER+ breast cancer. OP-1250 has a compelling profile for a CERAN/SERD as it is well-tolerated, achieves high drug exposure, and has demonstrated encouraging efficacy across both wild-type and ESR1 mutant tumors," said Sean P. Bohen, M.D., Ph.D., President and Chief Executive Officer of Olema Oncology. "We have now treated over 125 patients with OP-1250, and we are grateful to the patients, their families, and the investigators for their dedication and enthusiasm for our clinical trials. Our mission is to transform the breast cancer treatment landscape and to develop therapies that offer the potential to improve outcomes for women living with cancer. We believe in the potential of OP-1250, and we look forward to initiating our first pivotal Phase 3 trial mid-next year."

Preliminary Phase 1/2 Clinical Results

Enrollment

As of the data cut-off of September 2, 2022, 68 patients with recurrent, locally advanced or metastatic ER+/HER2- breast cancer were treated across two doses of 60 mg and 120 mg orally once per day. This group was heavily pretreated with 69% having received 2 or more prior lines of therapy and 32% having received prior chemotherapy. Almost all patients (96%) received prior treatment with a cyclin-dependent kinase 4/6 (CDK4/6) inhibitor, and 65% received prior treatment with fulvestrant. Of 46 patients whose circulating tumor DNA (ctDNA) was assessed, 59% had activating mutations in ESR1 at baseline.

Pharmacokinetics

OP-1250 demonstrated favorable pharmacokinetics characterized by high oral bioavailability and dose proportional exposure. With an approximately 8-day half-life, OP-1250 exhibited the desired low peak-to-trough variability in a 24-hour period at steady state, supporting once daily dosing with complete inhibition of the ER for the full dosing interval. A recommended Phase 2 dose (RP2D) of 120 mg once per day orally was selected based on overall PK, tolerability and efficacy. Dosing at the RP2D yielded drug exposure that exceeded targeted efficacy thresholds based on pre-clinical models.

Safety and Tolerability

Treatment with OP-1250 was well tolerated at both the 60 mg and 120 mg dose levels with no dose-limiting toxicities. The most common treatment-related adverse events (TRAEs) that occurred in at least 15% of subjects as assessed by the treating physician were nausea (42%), fatigue (25%) and vomiting (15%). Of the 68 patients treated, one patient experienced Grade 3 neutropenia concurrent with progressive disease, and three patients experienced Grade 4 neutropenia at the 120 mg dose. Of these cases, one patient had dosing interrupted for one week, restarted therapy at 60 mg and subsequently had a confirmed response with no further incidence of neutropenia. The two other patients discontinued treatment with recovery of their neutrophil counts. These events have occurred at a low rate and are manageable and reversible.

Efficacy

Six partial responses across the two doses have been observed to date among 57 efficacy-evaluable patients (per response evaluation criteria in solid tumors (RECIST) measurable lesions and at least one on-treatment tumor assessment), including four confirmed partial responses and two unconfirmed partial responses awaiting confirmation at a follow-up scan. Strong anti-tumor activity was observed with 41% of patients demonstrating reduction in target lesions and evidence of activity in both wild-type and mutant estrogen receptors across both doses. Given the advanced and heavily pretreated nature of the patients, many are expected to be endocrine resistant. Efficacy data continues to mature.

Anticipated Milestones

- Present preliminary Phase 1b dose escalation study data in combination with CDK4/6 inhibitor, palbociclib, in late 2022.
- Continue Phase 1b combination studies with CDK4/6 inhibitor, ribociclib, and phosphoinositide 3-kinase inhibitor, alpelisib.
- Present additional monotherapy and combination therapy data in 2023.
- Initiate pivotal Phase 3 monotherapy study in the second/third-line setting in mid-2023.

Company Investor Webcast and Conference Call

Olema will host a webcast and conference call for analysts and investors to review data presented at ENA 2022 today, Wednesday, October 26, 2022, at 8:00 a.m. ET (5:00 a.m. PT). Lead study author, Dr. Erika Hamilton, Director of Breast Cancer and Gynecologic Cancer Research for Sarah Cannon Research Institute at Tennessee Oncology, will join Olema management for the call. Please register for the conference call at this link or by visiting the Investors & Media section of Olema's website at olema.com.

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 1/2 clinical trial, and in combination with CDK 4/6 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. 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" 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 timelines for clinical trials of OP-1250 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 Quarterly Report on Form 10-Q for the year quarter June 30, 2022, filed on August 9, 2022, 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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