Olema Oncology Announces Publication of Data Highlighting Palazestrant's Ability to Inhibit Wild-Type and Mutant ER+ Breast Cancer Both as Monotherapy and in Combination with CDK4/6 Inhibitors

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- *Data published in* Molecular Cancer Therapeutics *describes the scientific background underlying the design, discovery and optimization of palazestrant (OP-1250)*
- *Pre-clinical results demonstrate that palazestrant, as both a CERAN and a SERD, has a highly differentiated mechanism of action as a potential therapy for advanced ER+/HER2- breast cancer*

SAN FRANCISCO, March 06, 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 women's cancers, today announced that *Molecular Cancer Therapeutics*, an American Association for Cancer Research journal, has selected as a featured article a data publication that describes the distinct properties of palazestrant (OP-1250). The paper, titled "Palazestrant (OP-1250), a Complete Estrogen Receptor Antagonist, Inhibits Wild-type and Mutant ER-positive Breast Cancer Models as Monotherapy and in Combination", describes the scientific background underlying the design, discovery and optimization of palazestrant.

"The research described in this paper reviews the deliberate design and processes used in discovering and optimizing palazestrant as a molecule purpose-built to address a crucial unmet need in the treatment of women's cancers, and we are delighted that *Molecular Cancer Therapeutics* has featured our work," said David C. Myles, Ph.D., Olema's Chief Discovery and Non-Clinical Development Officer. "What's even more exciting is to see how faithfully the pre-clinical research predicted the behavior of palazestrant now that it is in late-stage clinical development. We saw the potential then, as told in the paper, and we believe that every day brings us closer to having a real impact transforming the treatment paradigm for women with cancer."

As part of the discovery and optimization process, palazestrant was assessed across an extensive series of biochemical, cell culture, and *in vivo* assays comparing it with other antiestrogens and compounds that are either approved for use by the FDA or are currently in clinical development, including aromatase inhibitors, selective ER modulators (SERMs), traditional SERDs, and proteolysis-targeting chimeras (PROTACs). As a CERAN, palazestrant has a distinct mechanism of action (MOA), and though it actively degrades the ER, the paper shows that degradation alone is not a reliable mechanism to drive the efficacy of an endocrine agent. In mouse xenograft models, palazestrant demonstrated excellent pharmacokinetics, was well tolerated, showed synergy with CDK4/6 inhibitors, and was highly effective at reducing tumor growth in both wild-type and ESR1-mutant ER+ breast cancer. In addition, in an ESR1-mutant intercranial xenograft model, palazestrant inhibited tumor growth and improved survival of animals with CNS metastases, even after stopping drug treatment.

The paper can be accessed in the latest print edition of *Molecular Cancer Therapeutics* or online at https://aacrjournals.org/mct/article/doi/10.1158/1535-7163.MCT-23-0351/731746/Palazestrant-OP-1250-a-Complete-Estrogen-Receptor.

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 clinical studies, palazestrant completely blocks ER-driven transcriptional activity in both wild-type and mutant forms of metastatic ER+ breast cancer and has demonstrated anti-tumor efficacy along with attractive pharmacokinetics and exposure, favorable tolerability, CNS penetration, 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 currently being evaluated both as a single agent in an ongoing Phase 3 clinical trial, OPERA-01, and in Phase 2 combination studies with CDK4/6 inhibitors (palbociclib and ribociclib) and a PI3Ka inhibitor (alpelisib). For more information, 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 women living with cancer. Olema is advancing a pipeline of novel therapies by leveraging our deep understanding of endocrine-driven cancers, nuclear receptors, and mechanisms of acquired resistance. In addition to our lead product candidate, palazestrant (OP-1250), a proprietary, orally-available complete estrogen receptor (ER) antagonist (CERAN) and a selective ER degrader (SERD), Olema is developing a potent KAT6 inhibitor. 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,” “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 Olema’s preclinical program, including the potential beneficial characteristics of palazestrant (OP-1250), both as a monotherapy and in combination with CDK4/6 inhibitors, palazestrant’s potential to address to address an unmet need in the treatment of women’s cancers, and palazestrant’s ability to transform the treatment paradigm for women with 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, 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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