UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): May 11, 2023

Olema Pharmaceuticals, Inc.

(Exact name of registrant as specified in its charter)

Delaware	001-39712	30-0409740
(State or other jurisdiction of incorporation)	(Commission File Number)	(I.R.S. Employer Identification No.)
512 2nd Street, 4th Floor San Francisco, California (Address of principal executive offices)		94107 (Zip Code)

(415) 651-3316
(Registrant's Telephone Number, Including Area Code)

Not Applicable
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instructions A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c)) Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.0001 par value per share	OLMA	The Nasdaq Global Select Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 8.01 Other Events.

On May 11, 2023, Olema Pharmaceuticals, Inc. (the "Company") 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.

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.

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.

A copy of the press release issued in connection with the announcement is being furnished as Exhibit 99.1 to this Current Report on Form 8-K. Additionally, a copy of the Company’s presentation to be shared with investors and others from time to time in connection with today’s announcement is being furnished as Exhibit 99.2 to this Current Report on Form 8-K.

The information in Exhibits 99.1 and 99.2 attached hereto is intended to be furnished and shall not be deemed “filed” for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the “Exchange Act”) or otherwise subject to the liabilities of that section, nor shall it be deemed

incorporated by reference in any filing under the Securities Act of 1933, as amended or the Exchange Act, except as expressly set forth by specific reference in such filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	Press Release, dated May 11, 2023, of Olema Pharmaceuticals, Inc.
99.2	Corporate Presentation of Olema Pharmaceuticals, Inc., dated May 11, 2023.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

OLEMA PHARMACEUTICALS, INC.

Dated: May 11, 2023

By: /s/ Shane Kovacs
Shane Kovacs
Chief Operating and Financial Officer

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

- *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 – 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.

# # #

IR Contact:
Shane Kovacs, Chief Operating and Financial Officer
ir@olema.com

Media Contact:
Ignacio Guerrero-Ros, Ph.D., Russo Partners
ignacio.guerrero-ros@russopartnersllc.com


Olema
ONCOLOGY
Aspiring to Improve the Lives of Women with Breast Cancer
May 2023

Forward-Looking Statements

This presentation contains forward-looking statements made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Statements in presentation that are not statements of historical fact are forward-looking statements. Such forward-looking statements include, without limitation, statements regarding research and clinical development plans, the scope, progress, results and costs of developing our product candidate or any other future product candidates, expected manufactu capabilities, strategy, regulatory matters, including the timing and likelihood of success of obtaining drug approvals, the timelines for potential clinical study results and clinical tr of OP-1250 as a monotherapy and in combination trials, the potential beneficial characteristics, safety, tolerability, efficacy and therapeutic effects of OP-1250, the developmen OP-1250, the potential of OP-1250 to become a best-in-class treatment option for ER+/HER2- metastatic breast cancer, the endocrine therapy of choice, and a transforma therapy for women living with breast cancer, the combinability of OP-1250 with other drugs, market size and opportunity, our ability to complete certain milestones, our financial condition, cash position and sufficiency of our financial resources. Words such as “believe,” “anticipate,” “plan,” “expect,” “intend,” “will,” “may,” “goal,” “proje “estimate,” “potential” and similar expressions are intended to identify forward-looking statements, though not all forward-looking statements necessarily contain these identify words. These forward-looking statements are based on the beliefs of the Company’s management as well as assumptions made by and information currently available to Company. Such statements reflect the current views of the Company with respect to future events and are subject to known and unknown risks, including business, regulat economic and competitive risks, uncertainties, contingencies and assumptions about the Company, including, without limitation, risks inherent in developing products technologies, future results from the Company’s ongoing and planned clinical trials, the Company’s ability to obtain adequate financing to fund its planned clinical trials and ot expenses, trends in the industry, the legal and regulatory framework for the industry and future expenditures, and other risks and uncertainties affecting Olema, including th described under the caption "Risk Factors" and elsewhere in Olema’s Quarterly Report on Form 10-Q, Annual Report on Form 10-K, and future filings and reports of Olema with Securities and Exchange Commission. In light of these risks and uncertainties, the events or circumstances referred to in the forward-looking statements may not occur. The ac results may vary from the anticipated results and the variations may be material. These forward-looking statements should not be taken as forecasts or promises nor should they taken as implying any indication, assurance or guarantee that the assumptions on which such forward-looking statements have been made are correct or exhaustive or, in the cas the assumptions, fully stated in this presentation. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date presentation is given.

This presentation discusses product candidates that are under clinical study and which have not yet been approved for marketing by the U.S. Food and Drug Administration. representation is made as to the safety or effectiveness of these product candidates for the use for which such product candidates are being studied.

Olema ONCOLOGY

Leading the Next Generation of Oral CERAN/SERDs for the Treatment of ER+/HER- Metastatic Breast Cancer (MBC)

OP-1250, Potential Best-in-Class CERAN/SERD for ER+/HER2- MBC

- Completely shuts down estrogen receptor signaling pathways in women with ER+/HER2- MBC
- Internally-discovered, wholly-owned IP with no royalty burden

Clinical Validation as a Monotherapy and in Combo w/ CDK4/6i

- Over 190 patients treated to date with OP-1250
- Highly encouraging Phase 1/2 clinical results in both monotherapy and combination studies

Initiating 1st Pivotal Phase 3 monotherapy trial in 2H 23

- FDA Fast Track designation in 2L+ ER+/HER2- MBC
- Combination studies ongoing with Ibrance®, Kisqali® and Piqray®

Multi-Billion Dollar Commercial Market Opportunity

- 2L/3L+ MBC, represents **$3-5B** commercial opportunity
- 1L MBC in combination with CDK4/6i, represents **$5-10B** commercial opportunity

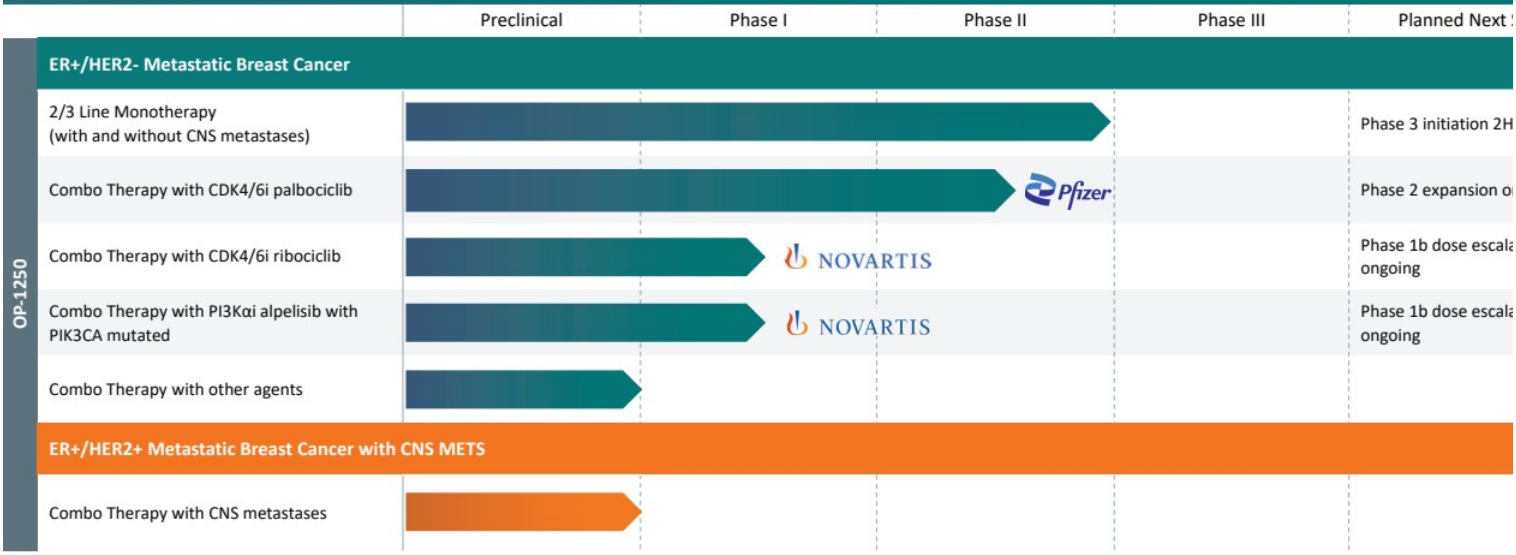
Strong cash position of $186.0M(1) to support clinical development and operations into 2025

(1) As of March 31, 2022.

Olema ONCOLOGY

Rapidly Advancing OP-1250 into Pivotal Trials Beginning in 2023

Evaluating OP-1250 across a range of ER cohorts in monotherapy and combination trials



MBC = metastatic breast cancer; PI3Kα = phosphatidylinositol 3-kinase alpha; CDK4/6i = CDK4/6 inhibitor
(1) Patient population may be studied as additional cohort(s) of current Phase 1/2 clinical trial or may be studied in a separate clinical trial.

Olema ONCOLOGY

Breast Cancer is the Second Most Common Diagnosed Cancer Worldwide

Estimated $22B market for endocrine therapies (ET) and targeted agents for ER+ breast cancer

In 2022, approximately

288K

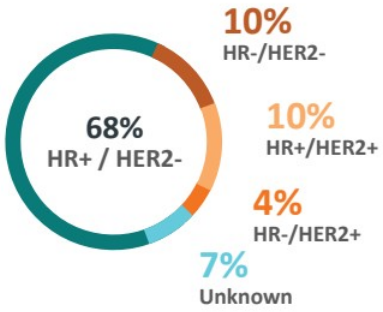
Women in the U.S. were diagnosed with breast cancer

43,250

Women in the U.S. expected to have succumbed to metastatic breast cancer

Majority of All Breast Cancers

express Estrogen Receptor (ER+)



Current Endocrine Therapy Options

SERMs, AIs, SERDs

Limitations include:

- Incomplete ER antagonism
- Sub-optimal PK profile
- Limited CNS penetration
- Tolerability issues

Better ER-targeting agents are needed

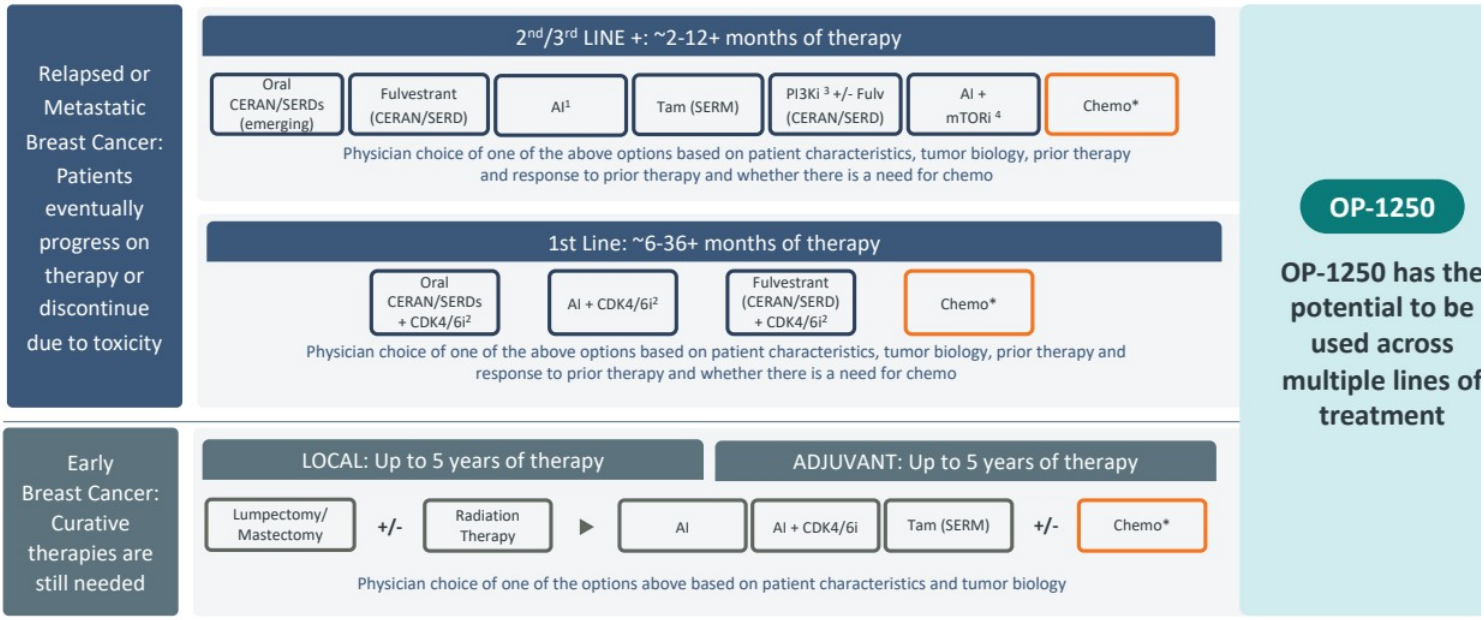
References: World Health Organization; American Cancer Society. Facts and Figures 2022; SEER database

Olema

Endocrine Therapy Remains the Backbone of ER+ Breast Cancer Treatment

OP-1250 has the potential to improve upon existing treatments to become the best-in-class ET

Illustrative Examples of ER+/HER2- Breast Cancer Treatment Options



* Indications for Chemo include impending visceral crisis, endocrine resistance or other need for rapid debulking

Sources: American Cancer Society; UptoDate.com; Sammons et al. *Target Oncol.* (2019); industry knowledge

Tam: tamoxifen; Fulv: fulvestrant

(1) anastrozole, letrozole, exemestane; (2) abemaciclib, palbociclib, ribociclib; (3) copanlisib; (4) sirolimus, everolimus, temsirolimus

Olema ONCOLOGY

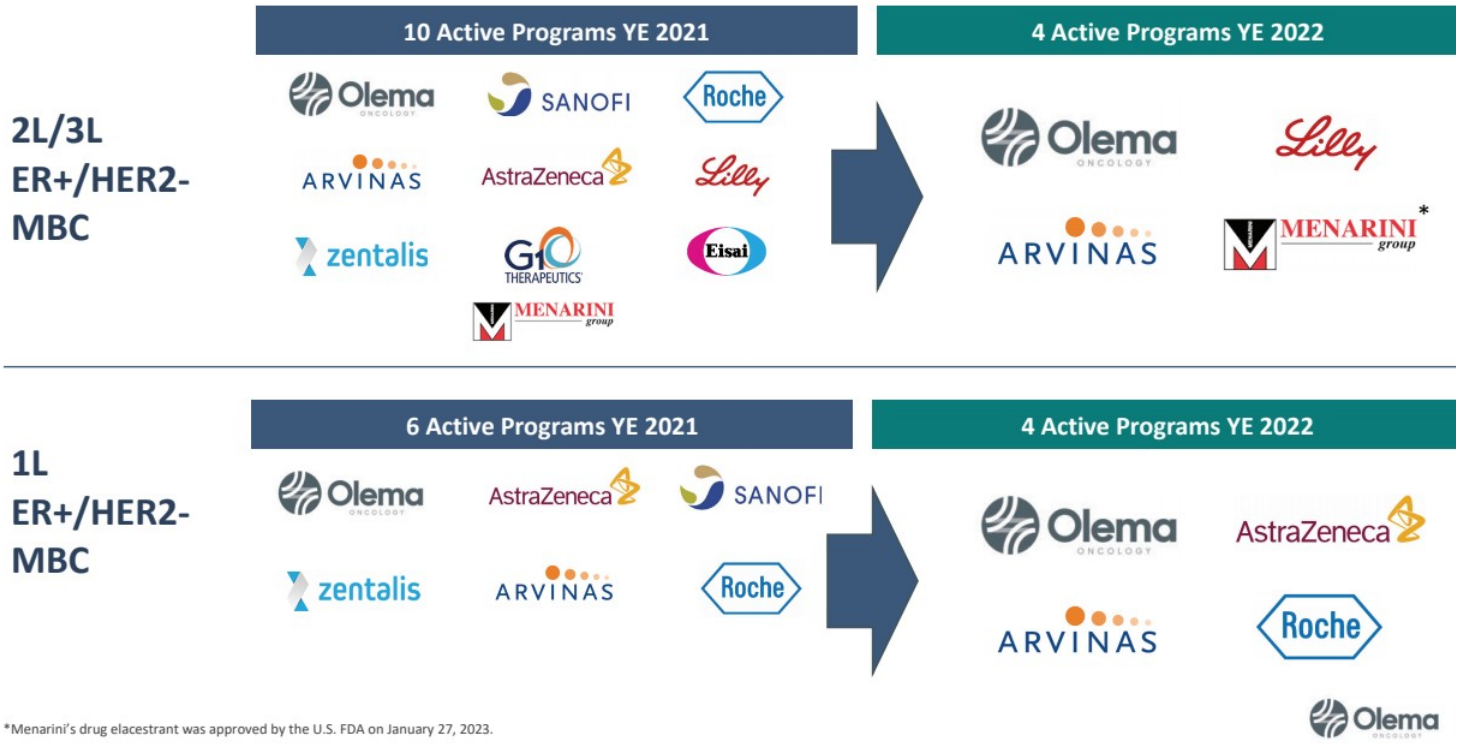
Segments of Therapy in ER+/HER2- Breast Cancer

First Pivotal Trial will target 2L/3L therapy, followed by trials in 1L therapy setting

	ER+/HER2-[1]				ER+/HER2+[2]
LINE OF THERAPY	2L/3L+	1L	High-Risk Adjuvant	Early Breast Cancer	HER2+ w/ CNS Mets
PATIENTS	~150K	~115K	~75K	~285K+	~10K
DURATION OF THERAPY[3]	~2-12+ months	~6-36+ months	Up to 5 years	Up to 5 years	~12 months
MARKET POTENTIAL[4]	~$3-5B	$5-10B+	~$3-5B	$10B+	~$500M

[1]2025 incidence projection estimates. Olema internal data, Informa ER+/HER2- BC Prevalence Based Market Forecast. 26% of adjuvant eligible patients assumed to have Ki-67 ≥ 20%. Early breast cancer incidence includes high risk adjuvant segment. [2]2025 incidence projection estimates. Olema internal data, Informa HER2+ BC Prevalence Based Market Forecast. Forecast based on 2L+ ER+/HER2+ metastatic breast cancer projections. [3]Olema internal data. [4]2025 opportunity estimates for total endocrine therapy market (US and EU5). Olema internal data.

Significantly Fewer Competing Programs for 2/3L and 1L MBC Treatment



*Menarini's drug elacestrant was approved by the U.S. FDA on January 27, 2023.

OP-1250: Best-in-Class Potential for ER+/HER2- Breast Cancer

Clinical dataset with over 190 patients treated with OP-1250 supports opportunity in both monotherapy and combination settings for patients with ER+/HER2- advanced metastatic breast cancer

Complete ER Antagonism

Dual activity as a next-generation CERAN/SERD to drive deeper, more durable responses in both wild-type and mutant ER

Attractive PK Profile

Highly favorable pharmacokinetics, oral bioavailability and 8-day half-life leading to steady-state plasma levels with minimal peak-to-trough variability

Favorable Tolerability

Favorable tolerability profile in heavily pretreated patients

Robust Tumor Shrinkage

Meaningful anti-tumor activity in both wild-type and mutant ER in preclinical models and durable benefit in clinical settings

Combinability w/ CDK4/6i

Combinable with palbociclib – no DDI* and overall tolerability profile consistent with expected profile of palbociclib plus endocrine therapy

CNS Penetratio

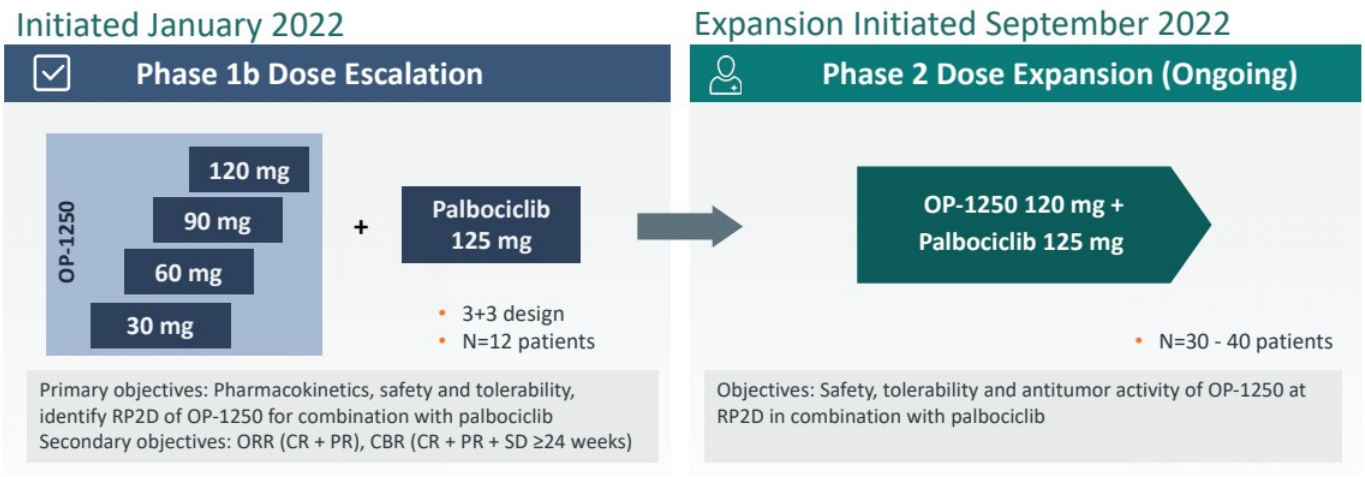
Demonstrated a in nonclinical b metastases stu

*As of May 12, 2023, interim update of combination study with Palbociclib at ESMO Breast Annual Congress 2023. DDI = Drug-Drug Interaction.

Olema ONCOLOGY


Olema
ONCOLOGY
Interim Phase 1b/2
Combination Clinical Update
from ESMO Breast 2023

Phase 1b/2 Combination Study with Palbociclib: Study Design



Key Inclusion Criteria:

- ER+/HER2- advanced breast cancer
- Evaluable disease (measurable and non-measurable)
- ≤ 1 prior hormonal regimen for locally advanced or metastatic disease
- One prior line of chemotherapy for advanced or MBC was allowed
- Can be CDK4/6i naïve or pre-treated

CBR, clinical benefit rate; ORR, objective response rate; CR, complete response; PR, partial response; SD, stable disease; RP2D, recommended phase 2 dose

Olema ONCOLOGY

OP-1250 Phase 1b/2 in Combination with Palbociclib

Of 29 Patients, 20 had prior CDK4/6i treatment, 44% with baseline ESR1 mutations

Patient characteristics	Total (N=29)
Median age (years)	65
Range	49–76
ECOG performance status, n (%)	
0	19 (66)
1	10 (34)
Measurable disease at baseline, n (%)	23 (79)
Visceral disease (liver, lung, peritoneum, pleura, ascites), n (%)	15 (52)
Prior lines of therapy in advanced setting, n (%)	
0	2 (7)
1	20 (69)
2	7 (24)[a]
Prior lines of endocrine therapy in advanced setting, n (%)	
0	4 (14)
1	25 (86)
Types of prior therapy in advanced setting, n (%)	
CDK4/6 inhibitor	20 (69)[b]
Aromatase inhibitor (AI)	22 (76)
Fulvestrant	3 (10)
Chemotherapy	6 (21)
ESR1 mutations at baseline (ctDNA), n/N (%)	8/18 evaluated (44)

[a]One patient received chemotherapy, endocrine therapy, and olaparib.
[b]Prior CDK4/6 inhibitors include palbociclib (n=14), ribociclib (n=5), both palbociclib and ribociclib (n=1).
AI, aromatase inhibitor; CDK4/6, cyclin-dependent kinase 4/6; ECOG, Eastern Cooperative Oncology Group.
*Source: EMERALD Phase 3 trial in CDK4/6 inhibitor-experienced 2/3L patients, Journal of Clinical Oncology.
Data Cutoff Date: March 8, 2023

- 93% of patients were 2/3L+ at study entry; 52% visceral disease
- 69% received prior CDK4/6i; 76% received prior AI; 21% received prior chemotherapy
- 44% had activating mutations in ESR1
- Up to 50% of 2/3L+ patients expected to be endocrine resistant*

Olema ONCOLOGY

OP-1250 Phase 1b/2 in Combination with Palbociclib

Well Tolerated with No DLTs; No dose-related increase in TEAEs

- No DLTs were observed during dose escalation and MTD was not reached
- No dose-related increases in the incidence or severity of TEAEs was observed
- No patients discontinued treatment due to a TEAE
- Overall safety and tolerability profile consistent with palbociclib + aromatase inhibitors prescribing information

Most Common Treatment-Emergent Adverse Events

TEAEs in ≥20% of Patients	OP-1250 Dose										Palbo + Fulvestrant[1]	
	30 mg (n=3)		60 mg (n=3)		90 mg (n=3)		120 mg (n=20)		TOTAL (n=29)		Paloma-3 (n=345)	
	All grades	Grade ≥3	All grades	Grade ≥3	All grades	Grade ≥3	All grades	Grade ≥3	All grades	Grade ≥3	All grades	Grade ≥3
Neutropenia	2	2	3	2	3	2	11	10	**19 (66%)**	**16 (55%)**	**83%**	**66%**
Nausea	2	0	2	0	1	0	9	0	**14 (48%)**	**0**	**34%**	**0%**
Vomiting	1	0	2	0	1	0	4	0	**8 (28%)**	**0**	**19%**	**1%**
Diarrhea	1	0	1	0	0	0	4	0	**6 (21%)**	**0**	**24%**	**0%**
Thrombocytopenia	0	0	1	0	0	0	5	0	**6 (21%)**	**0**	**23%**	**3%**
Constipation	1	0	1	0	0	0	4	0	**6 (21%)**	**0**	**19%**	**0%**
GERD	2	0	1	0	0	0	3	0	**6 (21%)**	**0**	**NR**	**NR**

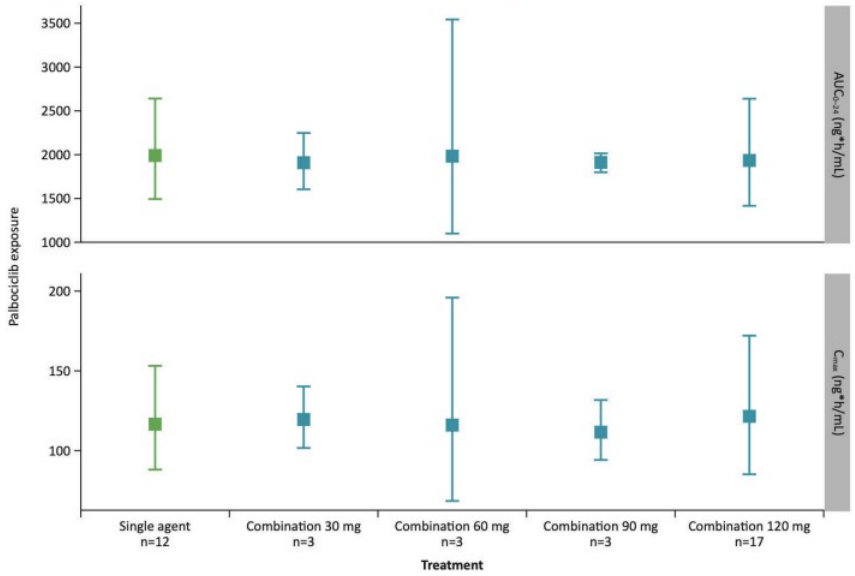
Data shown are n or n (%).
GERD, gastroesophageal reflux disease.
(1) Source: Palbociclib package insert referencing Paloma-3 trial results.

Olema ONCOLOGY

OP-1250 Phase 1b/2 Study in Combination with Palbociclib

No Change in Palbociclib Exposure Levels Across Dose Levels

Palbociclib (125mg) Steady State Exposure ($AUC_{(0-24)}$ and C_{max}) (Alone and in Combination with OP–1250[a])



Note: data are GeoMean±GeoSD.

[a]OP-1250 did not affect steady state palbociclib exposure when compared with published exposures for single-agent palbociclib[8]

AUC_{0-24}, area under the concentration time curve from 0 to 24 h; **C_{max}**, maximum concentration.

Pharmacokinetics

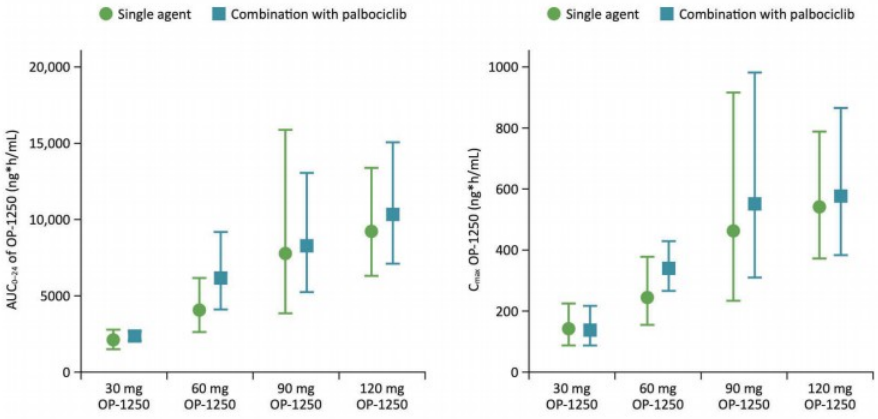
- No drug-drug interaction (DDI) between palbociclib and OP-1250 in the dose range of 30 to 120 mg
- OP-1250 did not affect palbociclib 125 mg exposure when compared with published concentrations for single-agent palbociclib
- Exposure of palbociclib was within 90% of reported mean values for palbociclib

Olema ONCOLOGY

OP-1250 Phase 1b/2 Study in Combination with Palbociclib

No Change in OP-1250 Exposure Levels Compared to Monotherapy

OP-1250 Steady State Exposure (AUC_{0-24} and C_{max}) (Alone and in Combination with Palbociclib (125 mg)[a])



	30 mg OP-1250	60 mg OP-1250	90 mg OP-1250	120 mg OP-1250
Single agent:	n=5	n=26	n=6	n=58
Combination:	n=2	n=3	n=3	n=12

	30 mg OP-1250	60 mg OP-1250	90 mg OP-1250	120 mg OP-1250
Single agent:	n=5	n=27	n=6	n=61
Combination:	n=2	n=3	n=3	n=12

Note: data are GeoMean±GeoSD.

[a]Palbociclib did not affect steady state OP-1250 exposure compared with OP-1250 single-agent exposure seen in an ongoing monotherapy trial.

AUC_{0-24}, area under the concentration time curve from 0 to 24 h; **C_{max}**, maximum concentration.

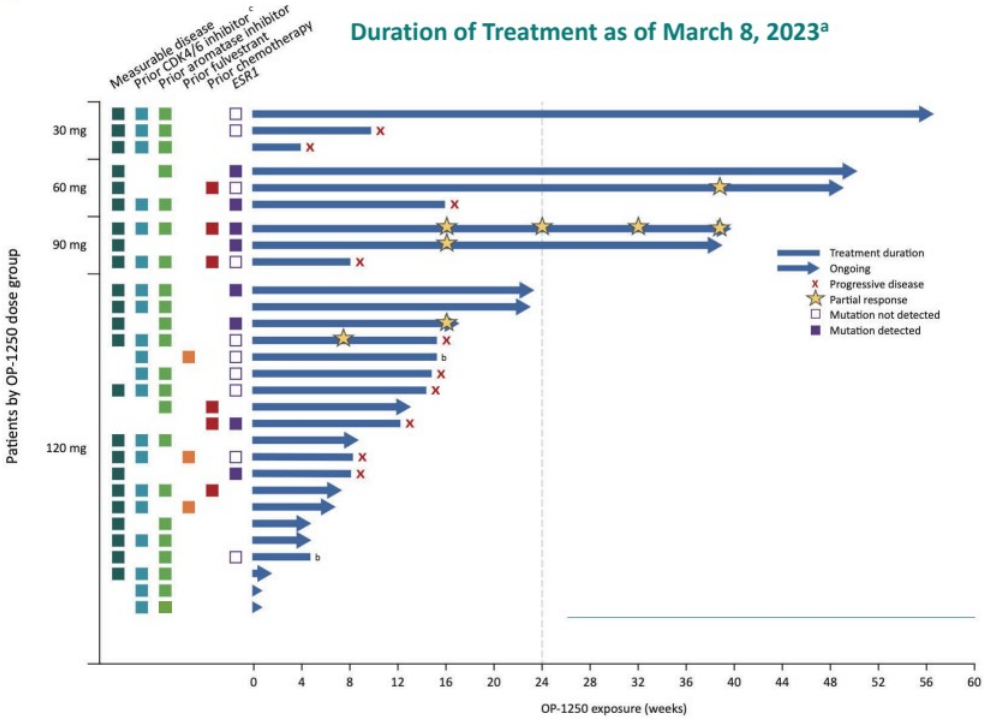
Pharmacokinetics

- No drug-drug interaction (DDI) between palbociclib and OP-1250 in the dose range of 3 to 120 mg
- Palbociclib did not affect OP-1250 exposure at any dose level
- OP-1250 was readily bioavailable and demonstrated dose-proportional exposures an long half-life
- Steady-state plasma levels show minimal peak-trough variability, enabling consistent inhibitio of the estrogen receptor for the full dosing interval

Olema ONCOLOGY

OP-1250 Phase 1b/2 in Combination with Palbociclib

Preliminary Efficacy Demonstrated in Both Wild-type and ESR1 Mutant Patients

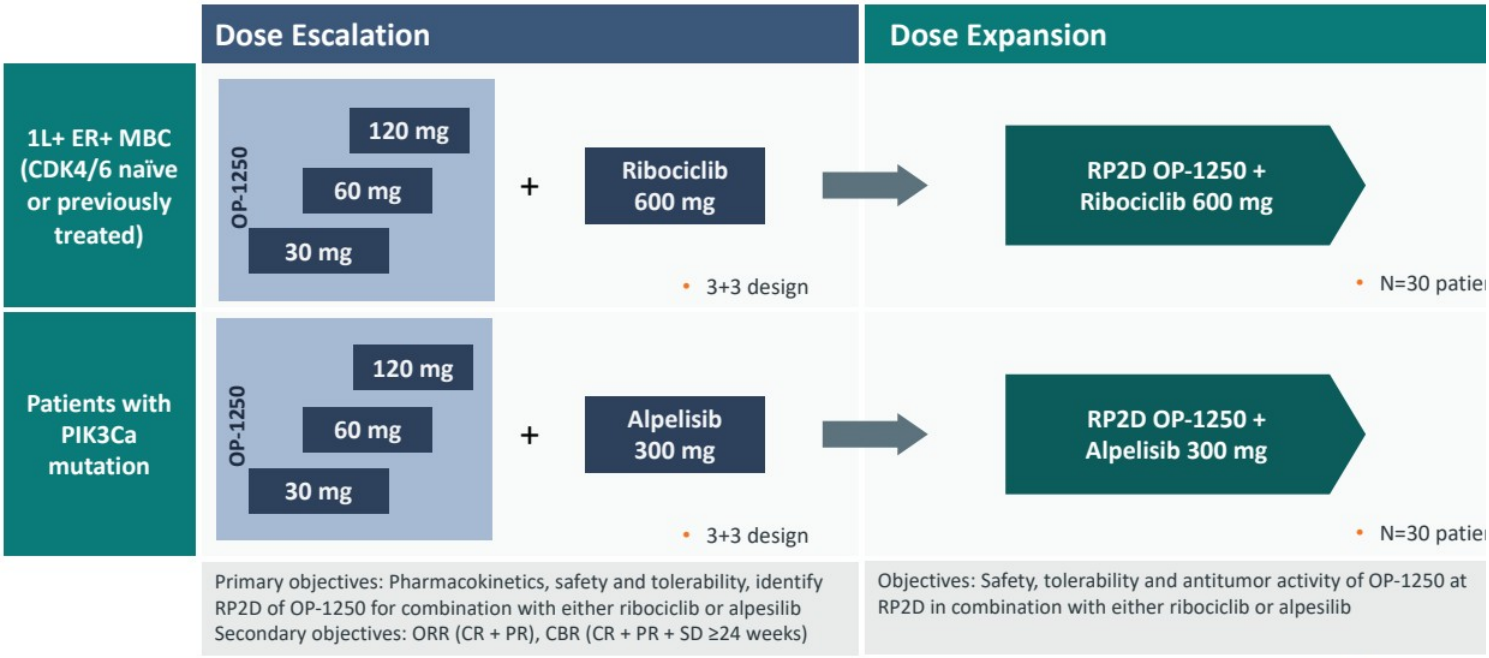


- Activity demonstrated in both wild type and $ESR1_{MUT}$ patients
- Partial responses were observed in five patients to date (one confirmed; four unconfirmed)
- Clinical benefit rate to date was 42% (5/12 CBR-eligible patients)
- Longest duration of treatment is 56 weeks and is ongoing
- Efficacy data are maturing; 17 of 29 patients (59%) remain on treatment; additional enrollment ongoing

[a]Each lane represents one study patient. [b]Two patients discontinued treatment due to patient's decision or physician's decision.
CDK, cyclin-dependent kinase. [c]Prior CDK4/6 inhibitors include palbociclib (n=14), ribociclib (n=5), both palbociclib and ribociclib (n=1).

Phase 1b Combination Study with Ribociclib and Alpelisib

Initiated Q3 2022 (Ongoing)

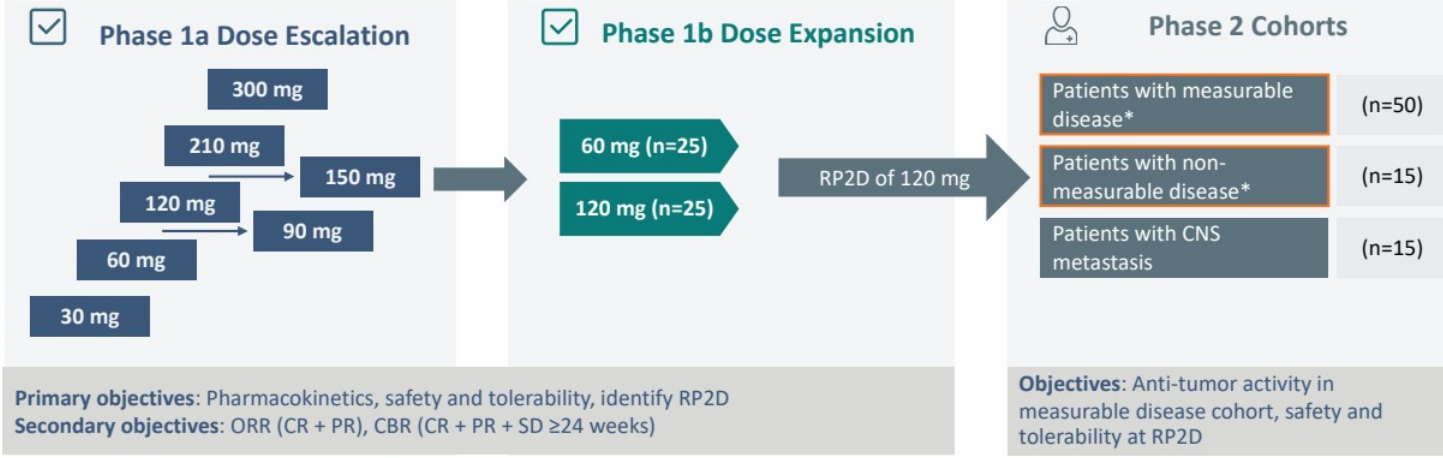


CBR, clinical benefit rate; ORR, objective response rate; CR, complete response; PR, partial response; SD, stable disease; RP2D, recommended phase 2 dose

Olema ONCOLOGY


Phase 1/2 Monotherapy
Clinical Update from
ENA 2022
Olema
ONCOLOGY

OP-1250-001 First-in-Human Phase 1/2 Monotherapy Study: Study Design



Primary objectives: Pharmacokinetics, safety and tolerability, identify RP2D
Secondary objectives: ORR (CR + PR), CBR (CR + PR + SD ≥24 weeks)

Objectives: Anti-tumor activity in measurable disease cohort, safety and tolerability at RP2D

Key Inclusion Criteria:

Phase 1a:
- Tumor must be ER+/HER2 negative
- At least one prior hormone-based therapy for locally advanced, recurrent, or metastatic disease
- 0-2 prior chemotherapy regimens for locally advanced or metastatic disease
- Measurable and non-measurable disease (evaluable disease)

Phase 1b:
- Tumor must be ER+/HER2 negative
- 1-4 prior hormone-based therapy for locally advanced, recurrent, or metastatic disease
- 0-1 prior chemotherapy regimens for locally advanced or metastatic disease
- Measurable disease by RECIST 1.1 Criteria

*Fully-enrolled.
CBR: Includes patients who received at least one cycle of treatment and had at least 1 postbaseline tumor assessment were evaluable for a response, and enrolled ≥24 weeks prior to the data cut-off date. CBR, Clinical Benefit Rate; CR, Confirmed Response; ORR, Objective Response Rate; PR, Partial Response; RP2D, Recommended Phase 2 Dose; SD, Stable Disease

Olema ONCOLOGY

OP-1250 Phase 1/2 Dose Expansion

Patients Received Extensive Prior Therapies

Patient characteristics	60 mg (n=33)	120 mg (n=35)	Total[a] (N=68)
Age, median, years	61	61	61
Range	30–81	39–77	30–81
ECOG performance status, n (%)			
0	22 (67)	17 (49)	39 (57)
1	11 (33)	18 (51)	29 (43)
Measurable disease at baseline, n (%)	32 (97)	34 (97)	66 (97)
Visceral disease (liver, lung, peritoneum, pleura, ascites), n (%)	27 (82)	29 (83)	56 (82)
Prior lines of therapy in advanced setting, n (%)			
1	9 (27)	11 (31)	20 (29)
2	9 (27)	10 (29)	19 (28)
≥3	15 (46)	13 (37)	28 (41)
Missing	0	1 (3)	1 (2)
Prior lines of endocrine therapy in advanced setting, n (%)			
1	13 (39)	12 (34)	25 (36)
2	8 (24)	15 (43)	23 (34)
≥3	11 (33)	7 (20)	18 (27)
Missing	1 (3)	1 (3)	2 (3)
Types of prior therapy in advanced setting, n (%)			
Chemotherapy	14 (42)	8 (23)	22 (32)
AI	26 (79)	29 (83)	55 (81)
Fulvestrant	22 (67)	22 (63)	44 (65)
CDK4/6 inhibitor	32 (97)	33 (94)	65 (96)
ESR1 mutations at baseline (ctDNA), n/N (%)	15/20 (75)	12/26 (46)	27/46 (59)

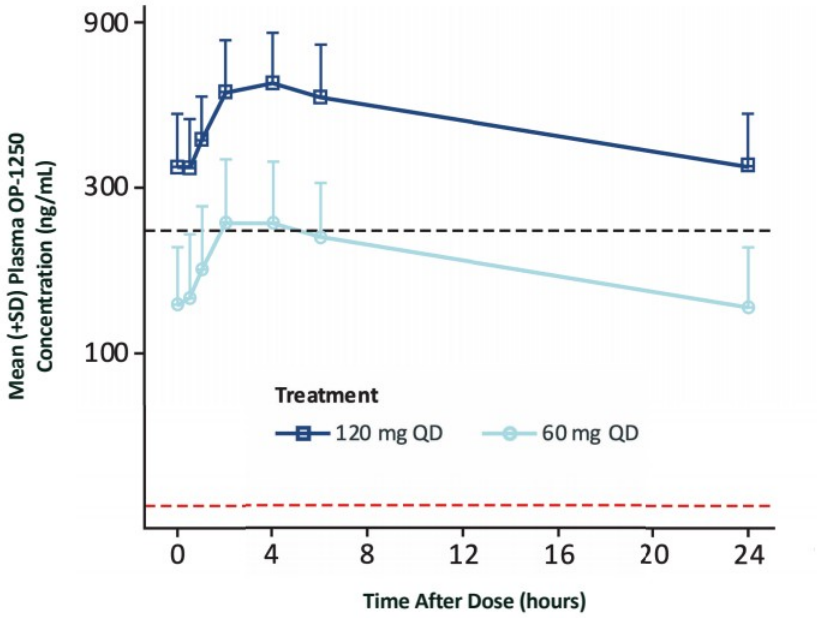
[a]Sums may not total to 100% due to rounding.
*Source: EMERALD Phase 3 trial in CDK4/6 inhibitor-experienced 2/3L patients, Journal of Clinical Oncology.
AI, aromatase inhibitor; CDK4/6, cyclin-dependent kinase 4/6; ECOG, Eastern Cooperative Oncology Group.

- 69% of patients rece 2 or more prior lines therapy in the advar setting; 82% viscera disease
- 96% received prior CDK4/6i; 81% receiv prior AI; 65% receive prior fulvestrant
- 59% had activating mutations in ESR1
- Up to 50% of patien expected to be endocrine resistant*

Olema ONCOLOGY

Dose-Proportional PK with Optimal Steady-State Plasma Concentrations

OP-1250 Steady-state Plasma Concentration-time Profiles



Dashed black line=target efficacious exposure based on estradiol-supplemented preclinical models (C_{min}=226 ng/mL) (8 studies); dotted red line=fulvestrant C_{max}=28mg dosed at 500mg every 28 days QD, once daily.

- High oral bioavailability and steady-state plasma levels with minimal peak-to-trough variability allowing complete inhibition of the ER for the full dosing interval
- Dosing at the RP2D of 120 mg yields drug exposures that exceed the predicted efficacious threshold based on pre-clinical models
- Mean terminal half-life ($T_{1/2}$)= 8 days, supporting once-daily dosing

Olema ONCOLOGY

60 mg and 120 mg Doses Well Tolerated in Phase 1/2 Monotherapy Dose Expansion

TRAEs in ≥15% of Patients in Phase 1a/1b	60 mg (n=33)			120 mg (n=35)			Total (60 mg & 120 mg, n=68)	
	Grade 1	Grade 2	≥Grade 3	Grade 1	Grade 2	≥Grade 3	Grade 1/2	≥Grade 3
Any TRAE	9	7	1	18	3	6	**37 (54%)**	**7 (10%)**
Nausea	8	2	0	18	0	1	**28 (41%)**	**1 (1%)**
Fatigue	5	4	0	5	2	1	**16 (24%)**	**1 (1%)**
Vomiting	2	1	0	7	0	0	**10 (15%)**	**0**

Grade 3/4 Neutropenia

Four out of 68 patients had Grade 3/4 neutropenia, occurring ~4-6 weeks into therapy and have recovered

- 1 patient had Grade 3 neutropenia at 120 mg, discontinued due to concurrent disease progression; neutropenia recovered
- 3 patients had Grade 4 neutropenia at 120 mg:
  - 1 patient's dose was interrupted for 1 week and was restarted at a lower dose (60 mg) with a subsequent cPR and no further neutropenia
  - 1 patient had Grade 4 neutropenia concurrent with disease progression, discontinued, and recovered
  - 1 patient had febrile neutropenia with no evidence of infection, discontinued from treatment, and recovered
- Oncologists are comfortable monitoring for and managing neutropenia in breast cancer patients

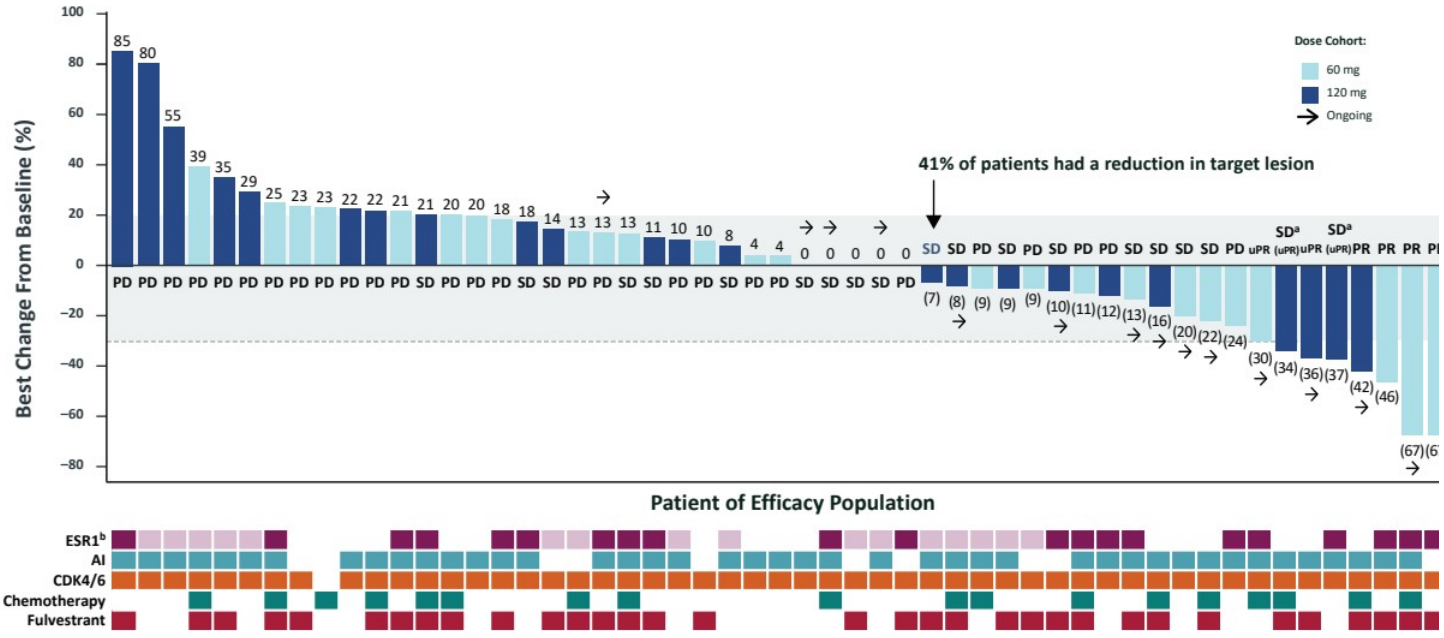
Other Grade 3 Events

- Three additional grade 3 events assessed as potentially related to study drug:
  - Anemia (1 at 60 mg)
  - Nausea (1 at 120 mg)
  - Fatigue (1 at 120 mg)

TRAE, Treatment-Related Adverse Event, cPR, confirmed partial response
Data Cutoff Date: September 2, 2022

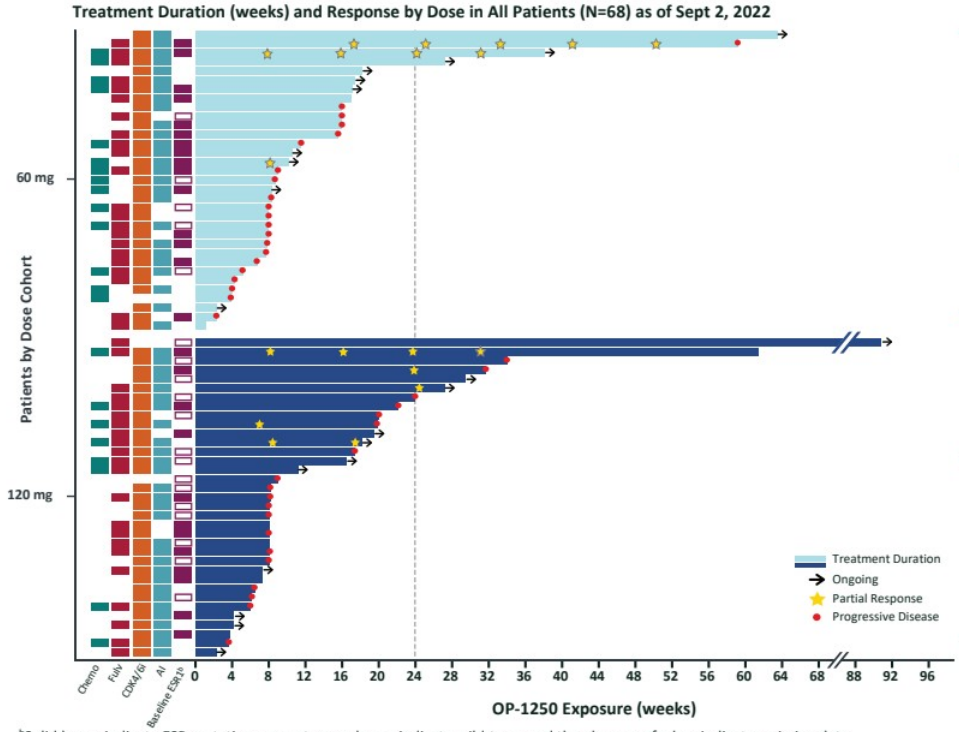
Olema ONCOLOGY

Meaningful Anti-Tumor Activity in OP-1250 Dose Expansion



[a]Patient had an unconfirmed partial response and later progressed at a subsequent scan.
[b]Dark shaded boxes indicate ESR mutation present, light shaded boxes indicate wild-type, and the absence of a box indicates missing data.
AI, aromatase inhibitor; CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; Chemo, chemotherapy; Fulv, fulvestrant; PD, progressive disease; PR, partial response; QD, once daily; SD, stable disease; uPR, unconfirmed partial response.

Clear Efficacy and Durable Clinical Benefit in Heavily Pretreated Population



- Across all patients:
  6 PRs out of 57 response-evaluable patients (4 cPRs and 2 uPRs*)
- In ESR1 mutant patients:
  4 PRs out of 22 response-evaluable patients (3 cPRs and 1 uPR*)
- 39% CBR at RP2D of 120 mg (7/18)
- 32% CBR across both doses (11/34)
- Data maturing with 31% of patients remaining on treatment as of Sept 2022

[b]Solid boxes indicate ESR mutation present, open boxes indicate wild-type, and the absence of a box indicates missing data.
*Unconfirmed partial responses awaiting confirmation at a subsequent scan.
AI, aromatase inhibitor; CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; Chemo, chemotherapy; Fulv, fulvestrant; CBR, Clinical Benefit Rate; PD, progressive disease; PR, partial response.

Olema ONCOLOGY

Phase 1/2 Dose Expansion Summary

OP-1250 is a Phase 3-ready asset with an emerging best-in-class profile

A complete ER-antagonist with attractive PK, high drug exposures and a long-half life

Heavily Pre-treated Patients	
82%	of patients had visceral disease at baseline
96%	of patients were CDK4/6 inhibitor experienced
65%	of patients had prior fulvestrant
69%	2 or More Prior Lines in the Advance Setting

Best-in-Class Emerging Profile	
84%	of TRAEs were Grade 1 / 2 in severity with no MT
41%	of target tumor lesions reduced in size
4 + 2	Confirmed / Unconfirmed partial responses*
39%	CBR at RP2D of 120 mg; 31% of patients still on therapy; efficacy maturing

Up to 50% of patients expected to be endocrine resistant**

Clinically meaningful durable responses in endocrine sensitive patients

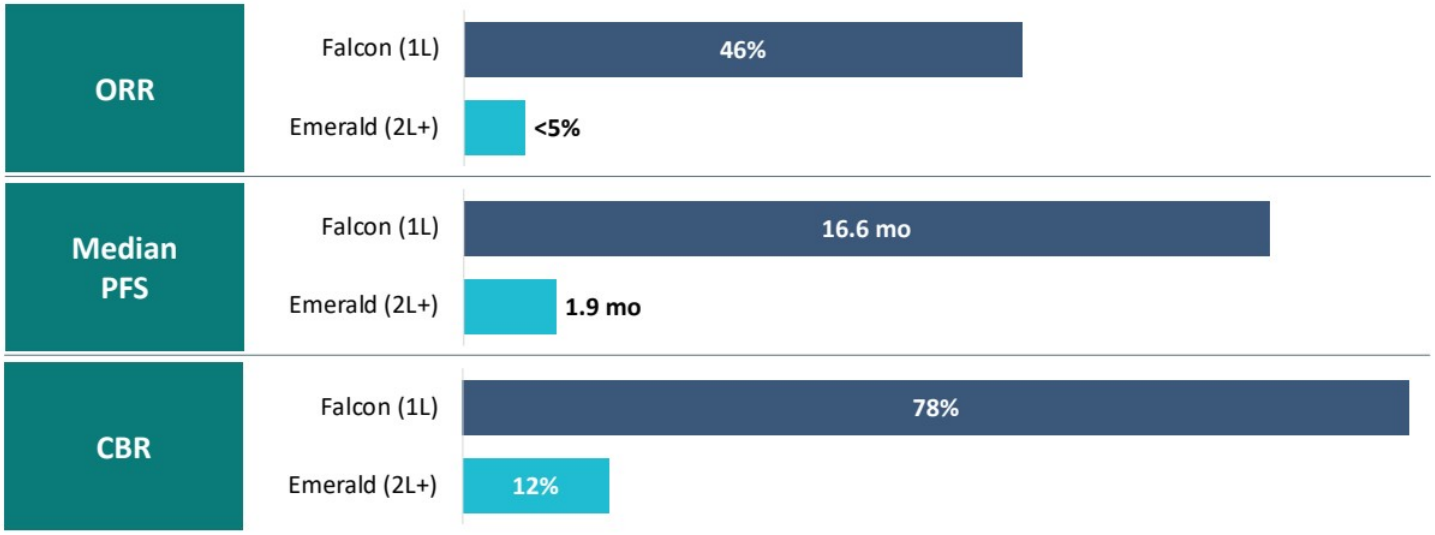
*Unconfirmed partial responses awaiting confirmation at a subsequent scan.
**Source: EMERALD Phase 3 trial in CDK4/6 inhibitor-experienced 2/3L patients, Journal of Clinical Oncology.
Data cut as of September 2, 2022.

Olema ONCOLOGY

Level of Pretreatment Impacts Expected Efficacy in 2L+ ER+/HER2- MBC

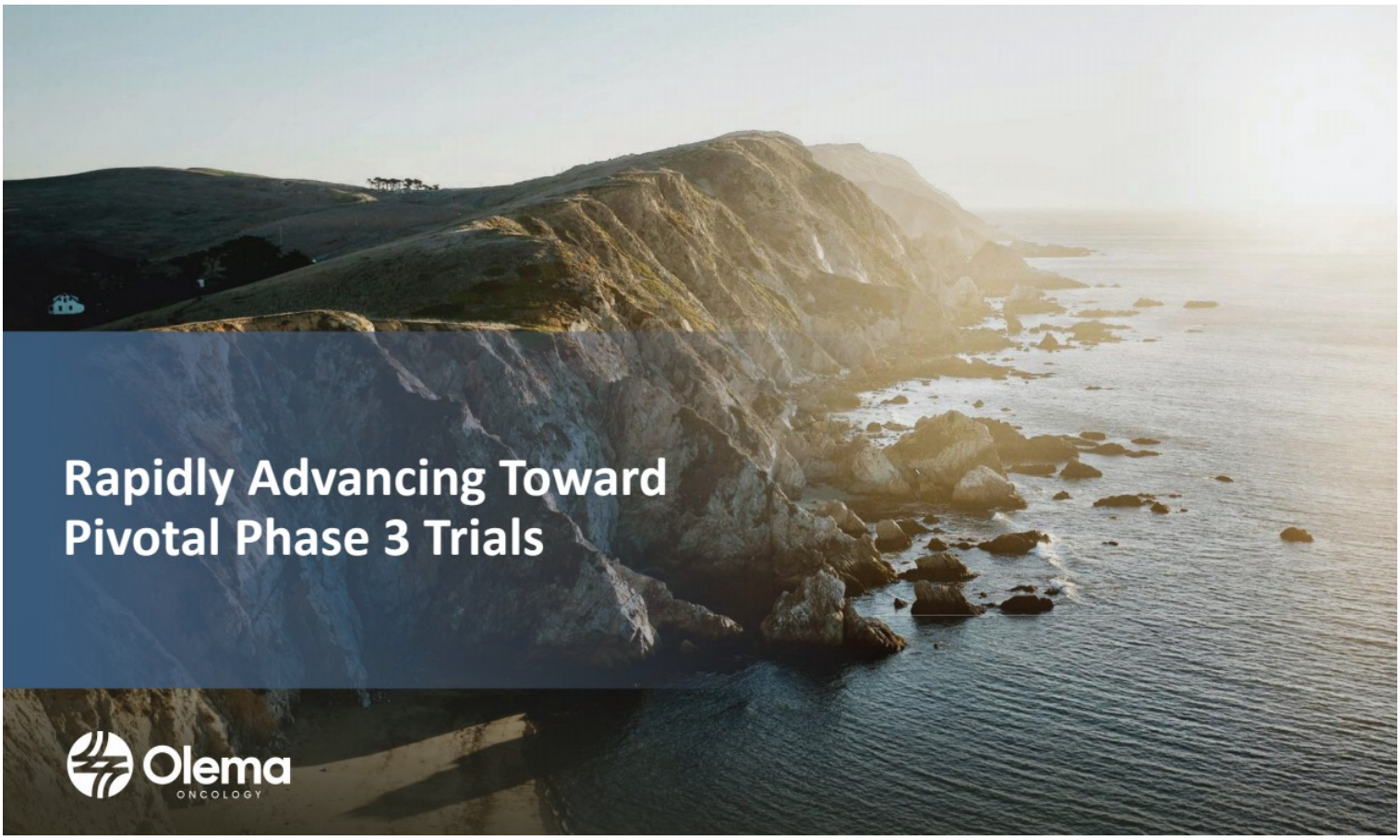
Fulvestrant's efficacy drops significantly in 2L+ post exposure to CDK4/6i in 1L

Performance of Fulvestrant in Falcon (1st line monotherapy) **vs.** **Fulvestrant in Emerald (2L+ monotherapy) demonstrates impact of pretreatment**

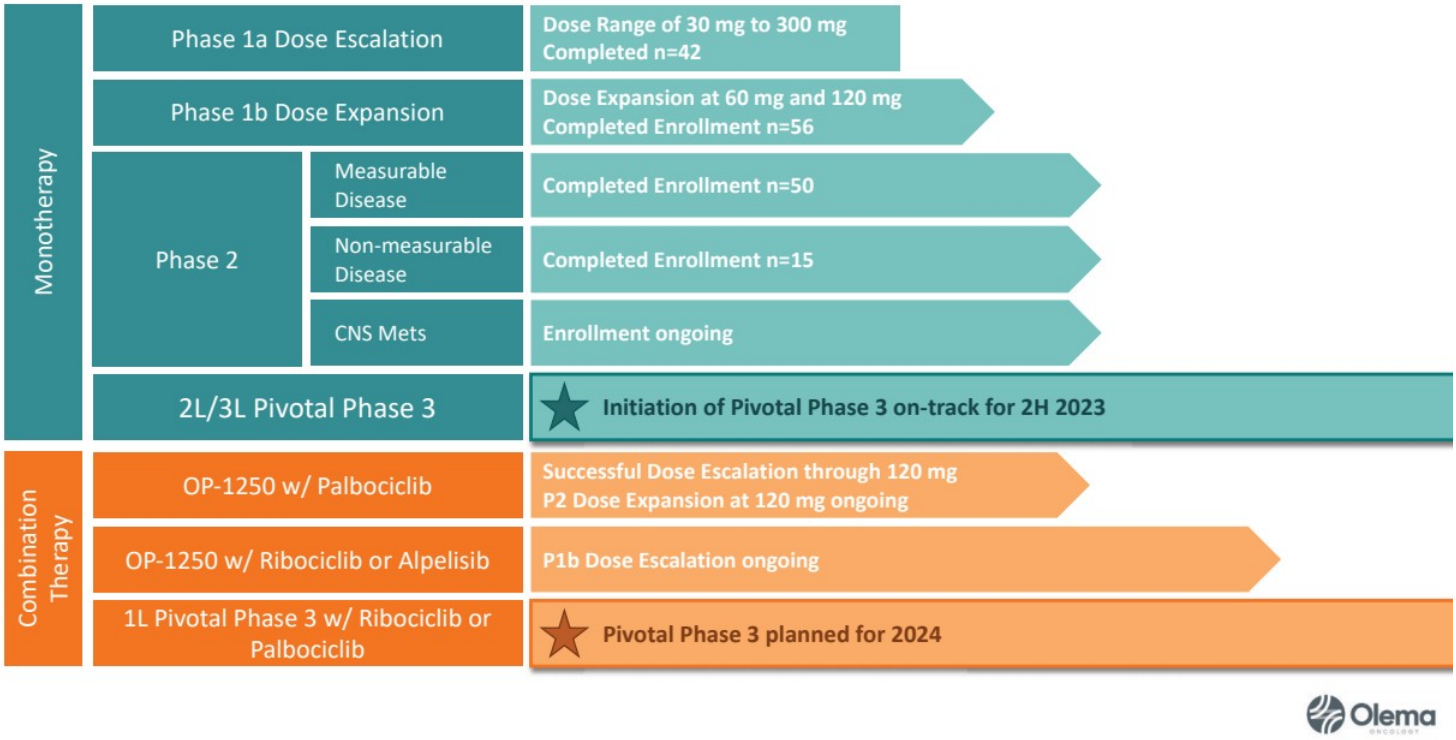


Source: Bidard supplemental documents 2022 JCO; The Lancet Nov 2016.

Olema ONCOLOGY


Rapidly Advancing Toward
Pivotal Phase 3 Trials
Olema
ONCOLOGY

Rapidly Advancing OP-1250 Toward Pivotal Phase 3 Studies



Delivering on Value Creating Milestones in 2023

Strong cash position of $186.0M[(1)] to support clinical development and operations into 2025

(1) As of March 31, 2023.

Olema

Leading the Next Generation of Oral CERAN/SERDs for the Treatment of ER+/HER- Metastatic Breast Cancer (MBC)

OP-1250, Potential Best-in-Class CERAN/SERD for ER+/HER2- MBC

- Completely shuts down estrogen receptor signaling pathways in women with ER+/HER2- MBC
- Internally-discovered, wholly-owned IP with no royalty burden

Clinical Validation as a Monotherapy and in Combo w/ CDK4/6i

- Over 190 patients treated to date with OP-1250
- Highly encouraging Phase 1/2 clinical results in both monotherapy and combination studies

Initiating 1st Pivotal Phase 3 monotherapy trial in 2H 23

- FDA Fast Track designation in 2L+ ER+/HER2- MBC
- Combination studies ongoing with Ibrance®, Kisqali® and Piqray®

Multi-Billion Dollar Commercial Market Opportunity

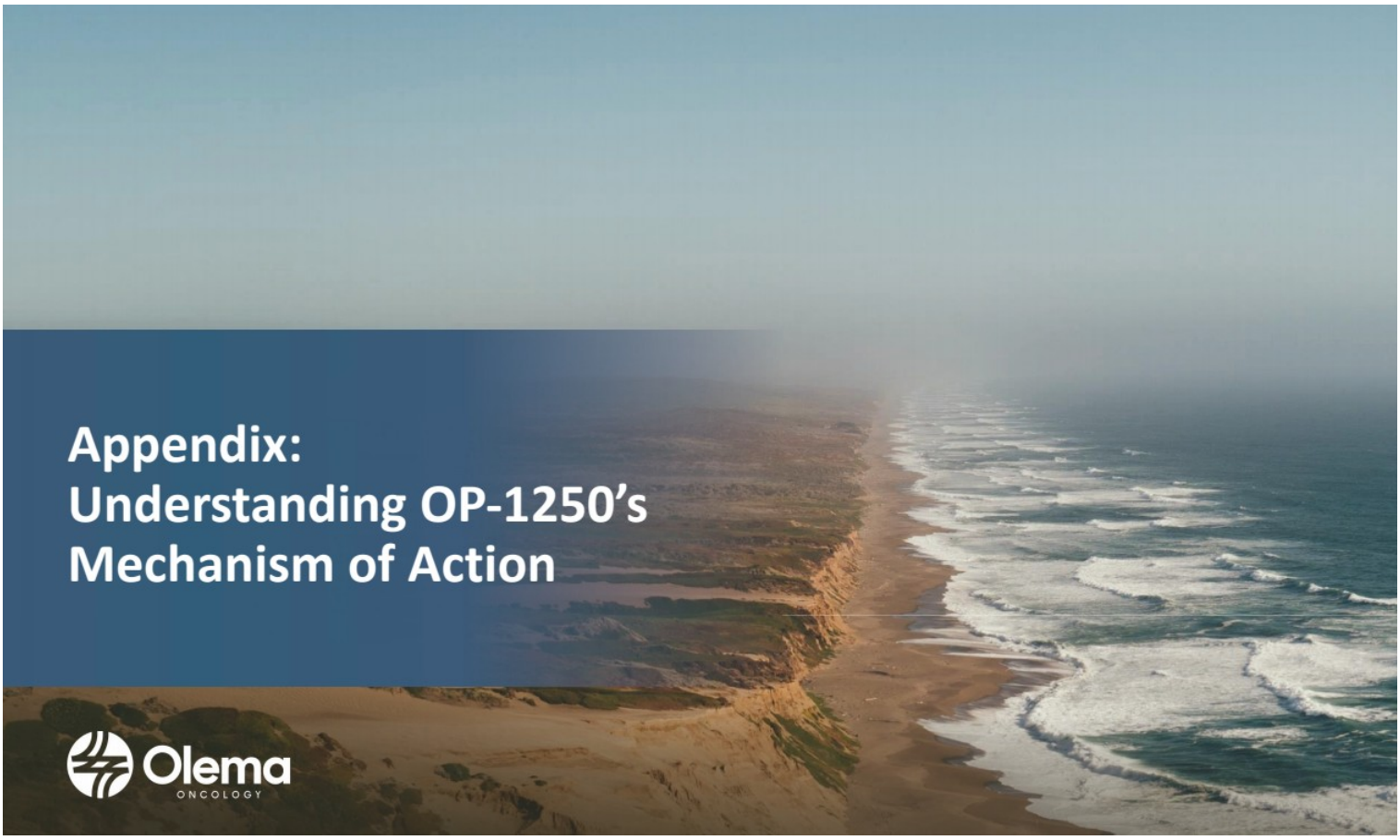
- 2L/3L+ MBC, represents **$3-5B** commercial opportunity
- 1L MBC in combination with CDK4/6i, represents **$5-10B** commercial opportunity

Strong cash position of $186.0M(1) to support clinical development and operations into 2025

(1) As of March 31, 2022.

Olema ONCOLOGY

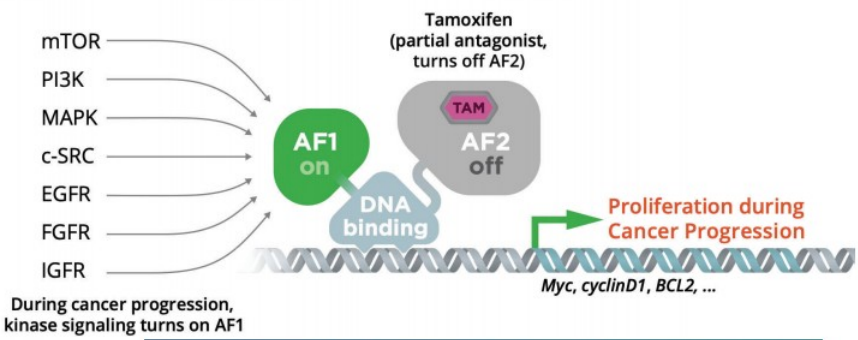

Olema
ONCOLOGY
Investor Relations
ir@olema.com
Media
media@olema.com
Business Development
partnering@olema.com
Careers
careers@olema.com


Appendix:
Understanding OP-1250's
Mechanism of Action
Olema
ONCOLOGY

OP-1250: a Complete Estrogen Receptor ANtagonist (CERAN)

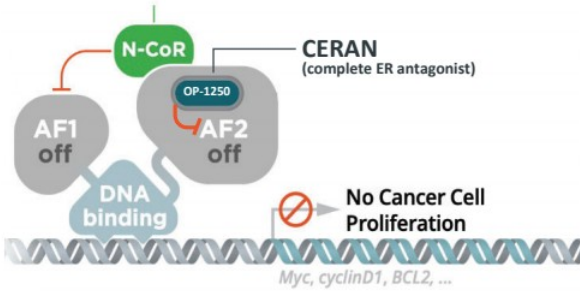
OP-1250 potently and completely inactivates the Estrogen Receptor (ER), blocks ER-driven transcriptional activity, inhibits ER-driven breast cancer cell growth, and strongly induces degradation of ER

Partial Antagonists Have a Short Duration of Response for Treatment of Metastatic Breast Cancer



SERM/SERDs block AF2 activity, but enable AF1 activation

Complete antagonists turn off AF2 and recruit N-CoR to inactivate AF1

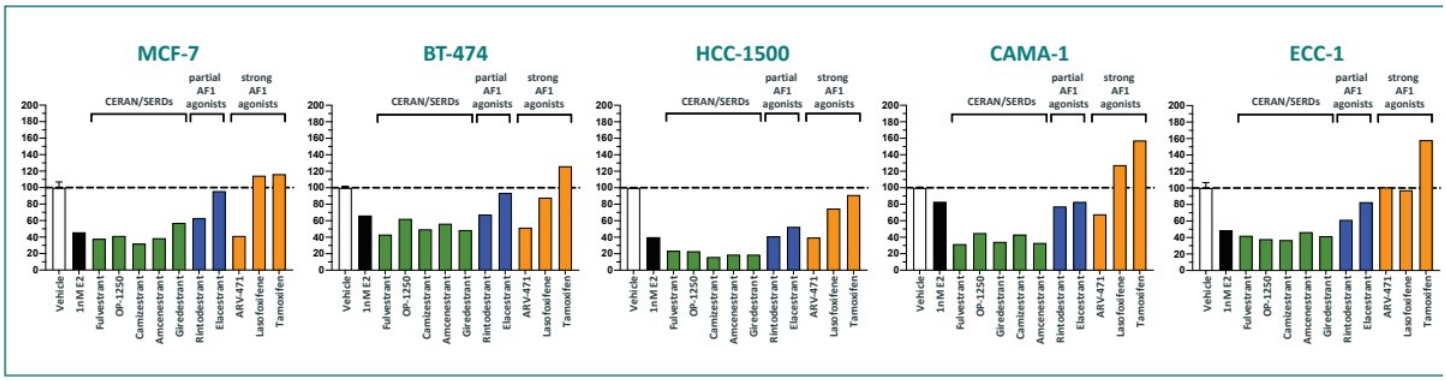


AF1: activation factor 1
AF2: activation factor 2

References: Shang and Brown, *Science*, 2002: Vol. 295, Issue 5564, pp. 2465-2468 ; Webb, Nguyen, and Kushner, *JBC*, 2003: Vol. 278, pp. 6912–6920

Olema ONCOLOGY

Both CERAN/SERDs and SERM/SERDs Are Strong Degraders of ERα



OP-1250 and CERAN/SERDs strongly degraded the estrogen receptor (ER) in five ER+ cell lines

Partial and strong agonists demonstrated variable and inconsistent ER degradation

Estradiol (E2), the prototypical agonist of ERα, degraded ERα in five ER+ cell lines

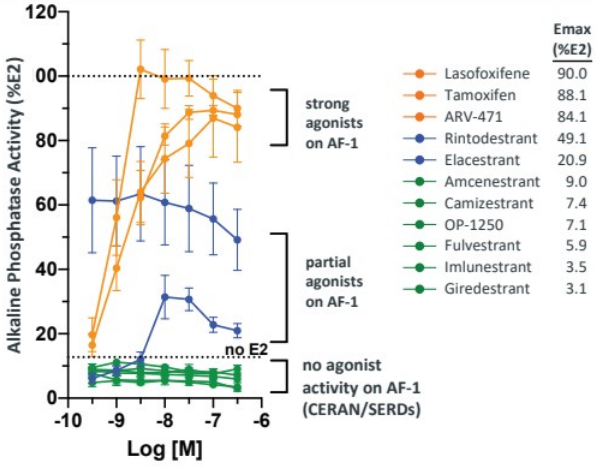
In all cases, none of the compounds achieved full ER degradation; complete ER antagonism is independent from degradation and key to inactivating remaining ER receptor

Reference: Sun et al, Proceedings: 2021 JCA-AACR Precision Cancer Medicine International Conference; September 10-12, 2021.

Olema ONCOLOGY

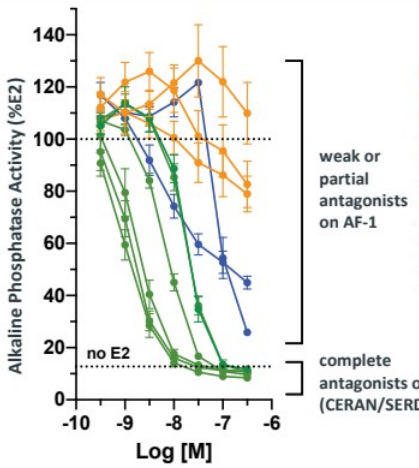
CERAN/SERDs Inactivate Both AF1 & AF2 Activity, While SERM/SERDs Only Inactivate AF2

Agonist Mode (No Estrogen)



	Emax (%E2)
Lasofoxifene	90.0
Tamoxifen	88.1
ARV-471	84.1
Rintodestrant	49.1
Elacestrant	20.9
Amcenestrant	9.0
Camizestrant	7.4
OP-1250	7.1
Fulvestrant	5.9
Imlunestrant	3.5
Giredestrant	3.1

Agonist Mode (+ Estrogen)



	pIC50	Emax (%E2)
Tamoxifen	NA	109.9
Lasofoxifene	NA	82.6
ARV-471	NA	78.9
Elacestrant	6.71	25.9
Rintodestrant	7.00	44.9
Imlunestrant	7.53	11.7
Giredestrant	8.71	10.7
Amcenestrant	7.54	10.5
Camizestrant	8.54	10.5
OP-1250	7.98	9.6
Fulvestrant	8.80	8.4

CERAN/SERDs completely inactivate AF1 activity of the estrogen receptor, while partial and strong agonists (SERM/SERDs) do not fully inhibit AF1 activity.

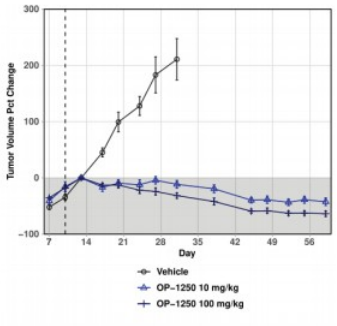
Reference: Sun et al, Proceedings: 2021 JCA-AACR Precision Cancer Medicine International Conference; September 10-12, 2021.

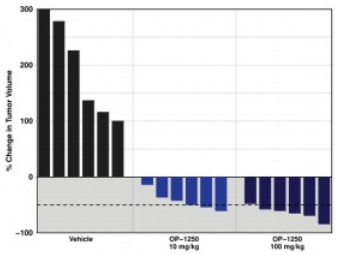
Olema ONCOLOGY

Xenograft Efficacy Studies: OP-1250 vs. Fulvestrant

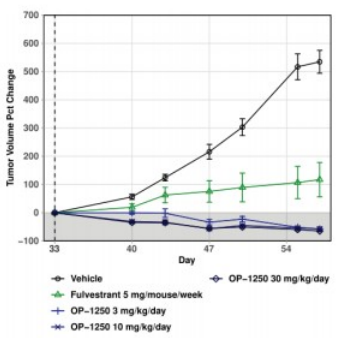
OP-1250 Demonstrates Tumor Shrinkage Across Multiple Xenograft Models

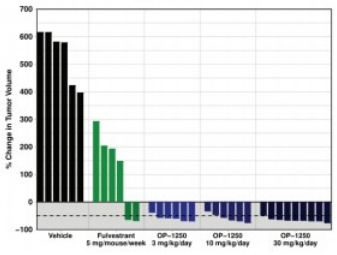
MCF-7 (HER2/neu)



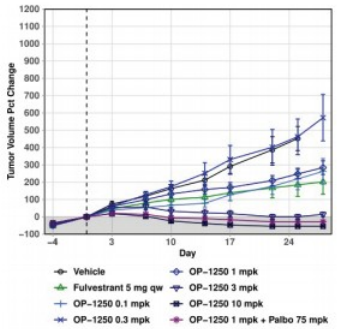


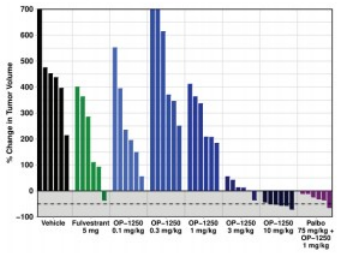
HCC1500



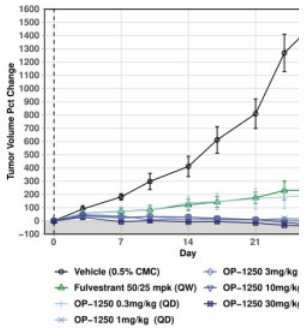


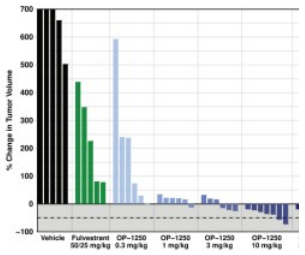
ST941





HCI-013



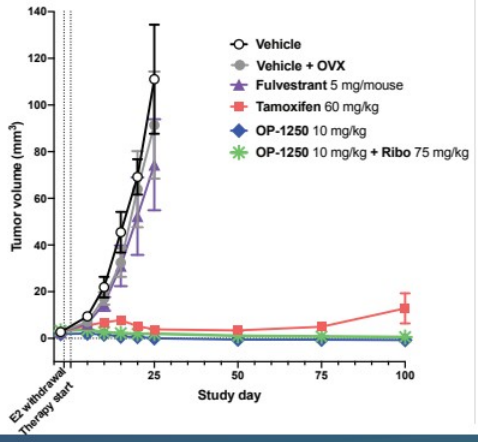


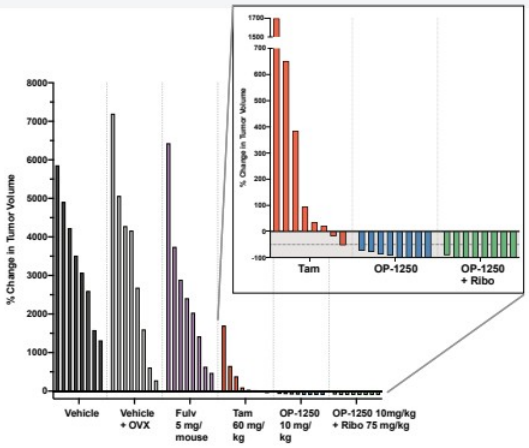
Olema ONCOLOGY

OP-1250 Has Demonstrated Activity in CNS Metastases Models

AACR 2021: Intracranial Breast Cancer Brain Metastases Xenograft Study

10 mg/kg OP-1250 is superior to tamoxifen, fulvestrant and ovariectomy in shrinking mutant ESR1-Y537S tumors in an intracranial model of ER+ br cancer brain metastasis





Treatment	Endpoint	n
Vehicle PO, QD	PD	8
	SD	0
	PR	0
	CR	0
Vehicle + OVX PO, QD	PD	7
	SD	1
	PR	0
	CR	0
5 mg Fulvestrant SC, QW	PD	8
	SD	0
	PR	0
	CR	0
60 mg/kg Tamoxifen PO, QD	PD	6
	SD	1
	PR	1
	CR	0
10 mg/kg OP-1250 PO, QD	PD	0
	SD	0
	PR	4
	CR	4
10 mg/kg OP-1250 + 75 mg/kg Ribociclib PO, QD	PD	0
	SD	0
	PR	1
	CR	7

Endpoint criteria: PD (progressed disease) >20% i tumor size; PR (partial response) >30% decrease i size; CR (complete response): no tumor observed; S disease): does not meet above criteria.

After 100 days, tumors in mice treated with OP-1250 remain small or undetectable while tumors in mice treated with fulvestrant and tamoxifen have started to grow.

Reference: Hodges-Gallagher et al., Proceedings: AACR Annual Meeting 2021; April 9-14, 2021

Olema ONCOLOGY