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): October 22, 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.)
780 Brannan Street San Francisco, California		94103
(Address of principal executive offices)		(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 7.01 Regulation FD Disclosure.

On October 22, 2023, Olema Pharmaceuticals, Inc. (the "Company") announced results from a Phase 2 clinical study of palazestrant (OP-1250), the Company's complete estrogen receptor ("ER") antagonist ("CERAN") and selective ER degrader ("SERD"), for the treatment of metastatic ER+/HER2- breast cancer. 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 the 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 8.01 Other Events.

As described above, on October 22, 2023, the Company announced results from a Phase 2 clinical study of palazestrant (OP-1250), the Company's CERAN and SERD, for the treatment of metastatic ER+/HER2- breast cancer. These results were presented in an oral presentation at the European Society for Medical Oncology ("ESMO") Congress 2023 in Madrid, Spain, on October 22, 2023.

The presentation, titled "Results from the phase 1/2 study of OP-1250, an oral complete estrogen receptor (ER) antagonist (CERAN) and selective ER degrader (SERD) in patients (pts) with advanced or metastatic ER-positive, HER2-negative breast cancer", highlighted that:

- Across 86 heavily pretreated patients, where 42% of patients were 4th line or later at study entry, 120 mg once-daily, monotherapy palazestrant was well tolerated and achieved a median progression-free survival ("PFS") of 4.6 months and clinical benefit rate ("CBR") of 40%, and a median PFS of 5.6 months and CBR of 52% in patients with ESR1 mutations at baseline.
- In a subset analysis of 49 second- or third-line patients with or without prior chemotherapy (the EMERALD trial eligibility criteria), the median PFS was 7.2 months and CBR was 48% across all patients, and the median PFS was 7.3 months and CBR was 59% ESR1-mutant patients.

Phase 2 Clinical Study Results

Enrollment

As of the data cut-off of July 7, 2023, 86 patients with recurrent, locally advanced or metastatic ER+/HER2- breast cancer were treated at the Recommended Phase 2 Dose ("RP2D") of 120 mg. The group was heavily pretreated with 42% of patients being fourth-line or later at study entry, 65% of patients having received two or more prior lines of endocrine therapy for metastatic disease, and 31% having received prior chemotherapy. Almost all patients (97%) received prior treatment with a cyclin-dependent kinase 4/6 ("CDK4/6") inhibitor, and 66% received prior treatment with fulvestrant. Of 75 patients whose circulating tumor DNA ("ctDNA") was assessed, 48% had activating mutations in ESR1 at baseline.

Pharmacokinetics

Palazestrant 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 the ER for the full dosing interval.

Safety and Tolerability

Treatment with palazestrant at the RP2D of 120 mg was well tolerated with no dose-limiting toxicities, and the maximum tolerated dose ("MTD") was not reached. The majority of treatment-emergent adverse events ("TEAEs") were Grade 1 or 2. Of the 86 patients treated, events of Grade 4 neutropenia were observed in six patients, occurring approximately 4–6 weeks into therapy. Of these patients, three had a dose interruption with recovery and subsequent dose reduction (two continued at 90 mg and one continued at 60 mg) without any recurrence, and three had dose discontinuation followed by recovery. All six patients had prior exposure to CDK4/6 inhibitors.

Efficacy Profile

Across all 86 patients, the median PFS was 4.6 months and the CBR was 40% with a 6-month PFS rate of 38%. In patients with an ESR1 mutation, the median PFS was 5.6 months and the CBR was 52% with a 6-month PFS rate of 46%. In ESR1 wild-type patients, the median PFS was 3.5 months and the CBR was 32% with a 6-month PFS rate of 35%.

In a subset analysis of 49 patients that received palazestrant as a second- or third-line therapy with or without prior chemotherapy (the EMERALD trial eligibility criteria), the median PFS was 7.2 months and the CBR was 48% across all patients with a 6-month PFS rate of 54%. In patients with an ESR1 mutation, the median PFS was 7.3 months and CBR was 59% with a 6-month PFS rate of 62%. In ESR1 wild-type patients the median PFS was 5.5 months and the CBR was 38% with a 6-month PFS rate of 44%.

Anti-tumor activity was observed in this heavily pre-treated population, with 40% of patients demonstrating reduction in target lesions and evidence of activity in both ESR1 wild-type and ESR1-mutant patients. Given the advanced and heavily pretreated nature of the patients, many of these patients are expected to be resistant to monotherapy endocrine treatment.

Forward Looking Statements

Statements contained in this Current Report on Form 8-K 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 the potential beneficial characteristics, safety, tolerability, efficacy, and therapeutic effects of palazestrant, the development of palazestrant, the initiation and timing of clinical trials, and palazestrant's combinability with other drugs. 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 June 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.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	Press Release, dated October 22, 2023, of Olema Pharmaceuticals, Inc.
99.2	Investor Presentation, dated October 23, 2023, of Olema Pharmaceuticals, Inc.
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: October 23, 2023

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

Olema Oncology Announces Positive Phase 2 Monotherapy Clinical Study Results for Palazestrant

- *Across all 86 heavily pretreated patients, the median PFS was 4.6 months with a CBR of 40%; in patients with ESR1 mutations at baseline, the median PFS was 5.6 months with a CBR of 52%*
- *In an analysis of 49 second- and third-line patients, the median PFS was 7.2 months with a CBR of 48%; the median PFS was 7.3 months with a CBR of 59% in patients with ESR1 mutations*
- *Results support continued development of palazestrant in the OPERA-01 monotherapy Phase 3 pivotal trial*
- *Olema will host an investor conference call at 8:00 a.m. ET on Monday, October 23, 2023*

SAN FRANCISCO, October 22, 2023 – Olema Pharmaceuticals, Inc. (“Olema”, “Olema Oncology”, or the “Company”, Nasdaq: OLMA), a clinical-stage biopharmaceutical company focused on the discovery, development and commercialization of targeted therapies for women’s cancers, today announced results from a Phase 2 clinical study of palazestrant (OP-1250), the Company’s complete estrogen receptor (ER) antagonist (CERAN) and selective ER degrader (SERD), for the treatment of metastatic ER+/HER2- breast cancer. These results were presented in an oral presentation at the European Society for Medical Oncology (ESMO) Congress 2023 in Madrid, Spain, on October 22, 2023.

The presentation, titled “Results from the phase 1/2 study of OP-1250, an oral complete estrogen receptor (ER) antagonist (CERAN) and selective ER degrader (SERD) in patients (pts) with advanced or metastatic ER-positive, HER2-negative breast cancer”, highlighted that:

- Across 86 heavily pretreated patients, where 42% of patients were 4th line or later at study entry, 120 mg once-daily, monotherapy palazestrant was well tolerated and achieved a median progression-free survival (PFS) of 4.6 months and clinical benefit rate (CBR) of 40%, and a median PFS of 5.6 months and CBR of 52% in patients with ESR1 mutations at baseline.
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“These Phase 2 monotherapy study results demonstrate that palazestrant (OP-1250) has the potential to become a best-in-class endocrine therapy and improve upon current standard of care treatments for women living with metastatic breast cancer. In addition to being well-tolerated, palazestrant has demonstrated compelling progression-free survival as monotherapy in a heavily pretreated patient population,” said Sean P. Bohen, M.D., Ph.D., President and Chief Executive Officer of Olema Oncology. “Going forward, we are in the process of initiating OPERA-01, our first pivotal Phase 3 clinical trial testing palazestrant as monotherapy in second- and third-line metastatic breast cancer.”

Phase 2 Clinical Study Results

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Efficacy

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Anti-tumor activity was observed in this heavily pre-treated population, with 40% of patients demonstrating reduction in target lesions and evidence of activity in both ESR1 wild-type and ESR1-mutant patients. Given the advanced and heavily pretreated nature of the patients, many of these patients are expected to be resistant to monotherapy endocrine treatment.

Company Investor Webcast and Conference Call

Olema will host a webcast and conference call for analysts and investors to review data presented at ESMO 2023 on Monday, October 23, 2023, at 8:00 a.m. ET (5:00 a.m. PT). Dr. Nancy Lin, Associate Chief of the Division of Breast Oncology, Susan F. Smith Center for Women's Cancers, at the Dana-Farber Cancer Institute in Boston, MA, will join Olema management for the call. Please register for the webcast by visiting the Investors & Media section of Olema's website at olema.com.

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

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, palazestrant (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. Palazestrant 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. For more information, please visit us at www.olema.com, or follow us on Twitter and LinkedIn.

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 the potential beneficial characteristics, safety, tolerability, efficacy, and therapeutic effects of palazestrant, the development of palazestrant, the initiation and timing of clinical trials, palazestrant's combinability with other drugs, and the potential of palazestrant to become a best-in-class endocrine therapy in the treatment of ER+/HER2- metastatic breast cancer or improve upon the standard of care treatments 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 Quarterly Report on Form 10-Q for the quarter ended June 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,

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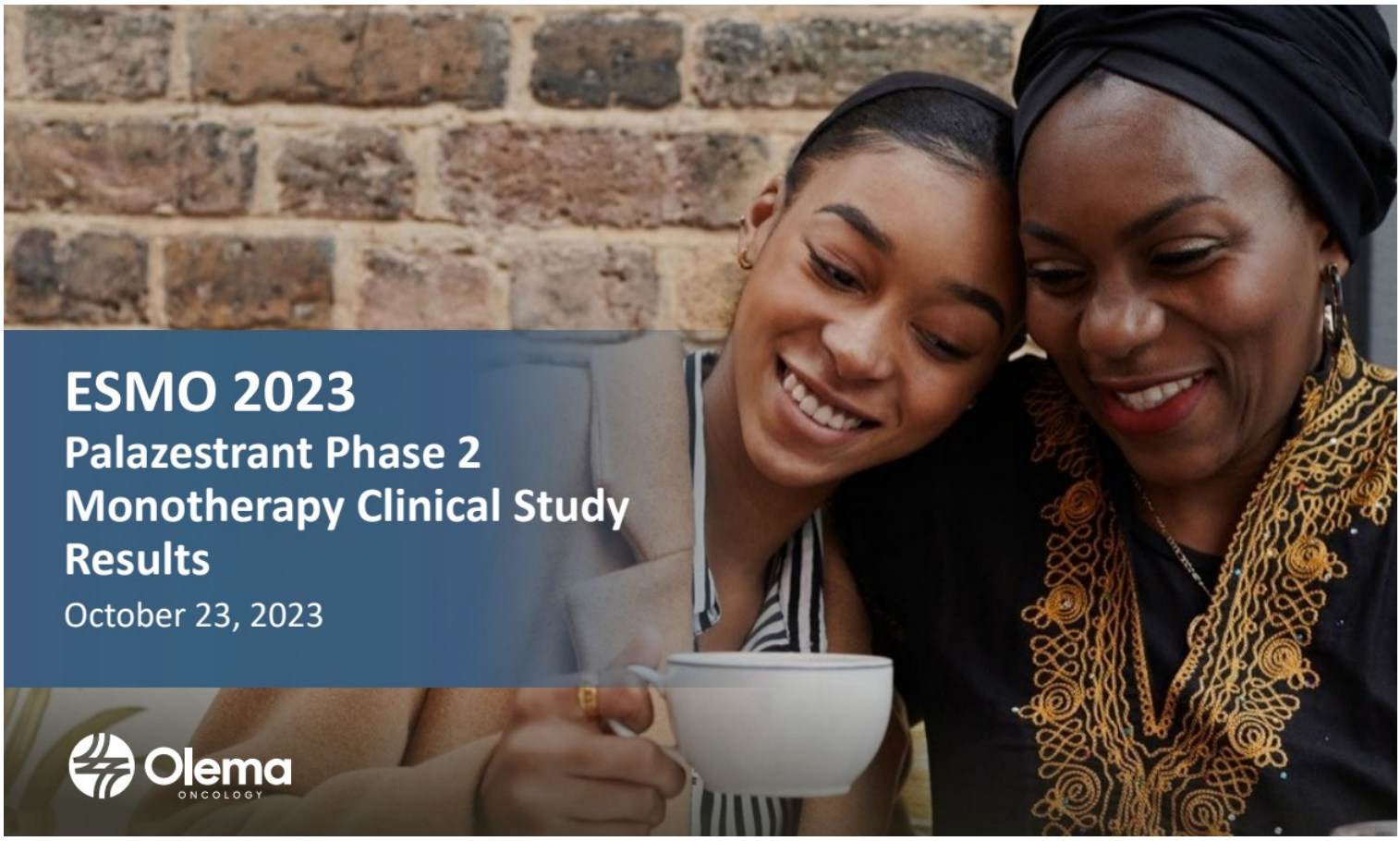
# # #

IR Contact:
Geoffrey Mogilner, Vice President, Investor Relations and Communications
ir@olema.com

Media Contact:
Ignacio Guerrero-Ros, Ph.D., Russo Partners
646-942-5604
ignacio.guerrero-ros@russopartnersllc.com


ESMO 2023
Palazestrant Phase 2
Monotherapy Clinical Study
Results
October 23, 2023
Olema
ONCOLOGY

Forward-Looking Statements and Other Disclaimers

This presentation contains forward-looking statements made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Statements in this presentation that not statements of historical fact are forward-looking statements. Such forward-looking statements include, without limitation, statements regarding our research and clinical development plans, scope, progress, results and costs of developing our product candidate or any other future product candidates, expected manufacturing capabilities, strategy, regulatory matters, including the tir and likelihood of success of obtaining drug approvals, the timelines for potential clinical study results and initiation of clinical trials of palazestrant (OP-1250) as a monotherapy and in combina trials, including OPERA-01, the Company's pivotal Phase 3 monotherapy clinical trial, the potential beneficial characteristics, safety, tolerability, efficacy and therapeutic effects of palazestrant, development of palazestrant, the potential of palazestrant to become a best-in-class treatment option for ER+/HER2- metastatic breast cancer, improve the standard-of-care treatment, or becor transformative therapy for women living with breast cancer, the combinability of palazestrant with other drugs, market size and opportunity, our ability to penetrate the market,, our abilit complete certain milestones, and our financial condition, cash position, cash runway, and sufficiency of our financial resources. Words such as "believe," "anticipate," "plan," "expect," "inte "will," "may," "goal," "project," "estimate," "potential" and similar expressions are intended to identify forward-looking statements, though not all forward-looking statements necessarily con these identifying 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, regulatory, economic competitive risks, uncertainties, contingencies and assumptions about the Company, including, without limitation, risks inherent in developing products and technologies, future results from Company's ongoing and planned clinical trials, the Company's ability to obtain adequate financing to fund its planned clinical trials and other expenses, trends in the industry, the legal regulatory framework for the industry and future expenditures, and other risks and uncertainties affecting the Company, including those described under the caption "Risk Factors" and elsewher the Company's Quarterly Report on Form 10-Q, Annual Report on Form 10-K, and future filings and reports of the Company with the Securities and Exchange Commission. In light of these risks uncertainties, the events or circumstances referred to in the forward-looking statements may not occur. The actual results may vary or differ from the anticipated results and the variation differences may be material. These forward-looking statements should not be taken as forecasts or promises nor should they be taken as implying any indication, assurance or guarantee that assumptions on which such forward-looking statements have been made are correct or exhaustive or, in the case of the assumptions, fully stated in this presentation. You are cautioned not to p undue reliance on these forward-looking statements, which speak only as of the date this 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. No representa is made as to the safety or effectiveness of these product candidates for the use for which such product candidates are being studied.

This presentation incorporates publicly-available third-party data that we have not independently verified. There are risks inherent in conducting cross-trial comparisons. The presentation of third-party data does not represent a head-to-head comparison of how palazestrant performed in a second- or third-line setting relative to elacestrant in the EMERALD study, or any other th party drug candidate or study. Rather, such third-party data has been pulled by us from publicly-available sources for supplemental informational purposes, only. We caution you that comparisons against third-party data set forth herein should not be viewed as a side-by-side comparison, and you should not rely on the completeness or accuracy of our presentation of the res of any third-party drug candidate in these slides, due to differences in study design, how other companies quantify or qualify eligibility criteria, and how results are recorded, among o distinguishing factors and uncertainties. Because we may be unaware of or may not adequately present various distinguishing factors and uncertainties, the comparisons set forth herein may properly present such third-party data, which may differ materially from the data as presented here. Investors are encouraged to independently review third party data and should not rely on presentation of such data (including any such data placed in comparison with the performance of palazestrant) as a single measure to evaluate our business.

The trademarks included herein are the property of the owners thereof and are used for reference purposes only. Such use should not be construed as an endorsement of such products.

Olema

Meeting Participants

Presenting

Sean P. Bohen, M.D., Ph.D.
President and CEO

Dr. Nancy Lin, M.D.
Associate Chief of the Division of Breast Oncology, Susan F. Smith Center for Women's Cancers
Dana-Farber Cancer Institute

Q&A

Shane Kovacs, MBA
Chief Operating
& Financial Officer

Naseem Zojwalla, M.D.
Chief Medical Officer

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Palazestrant (OP-1250) – A Potential Best-in-Class Endocrine Therapy

- Completely shuts-down estrogen receptor signaling pathways, both wild type and ESR1-mutant
- A potential backbone therapy across multiple lines of ER+/HER2- metastatic breast cancer (1L and 2/3L)

- Well tolerated with clinical experience now exceeding 225 patients
- Compelling monotherapy efficacy results in a heavily pretreated patient population
  - **Median PFS of 7.2 months in 2/3L ± chemotherapy subset analysis (EMERALD trial inclusion/exclusi criteria) highly favorable vs. competition**
- OPERA-01 510-patient pivotal Phase 3 trial now underway
  - Opportunity to achieve meaningful PFS benefit in both ESR1-mutant and wild-type patients
  - $5+ billion commercial market opportunity in the US alone for 2/3L monotherapy

- Palazestrant Phase 2 combination studies with each of ribociclib and palbociclib are ongoing
  - New clinical data to be presented in Q4 2023
  - Amcenestrant (SNY), Camizestrant (AZ), Giredestrant (Roche) and Vepdegestrant (Pfizer) have all experienced setbacks when combining with CDK4/6i (DDI, enhanced toxicity) resulting in dose modifications*
- Potential to initiate 1st line pivotal trial in combination with CDK4/6i by YE2024; a $10+ billion market

*Based on publicly available third-party data, which Olema has not independently verified.

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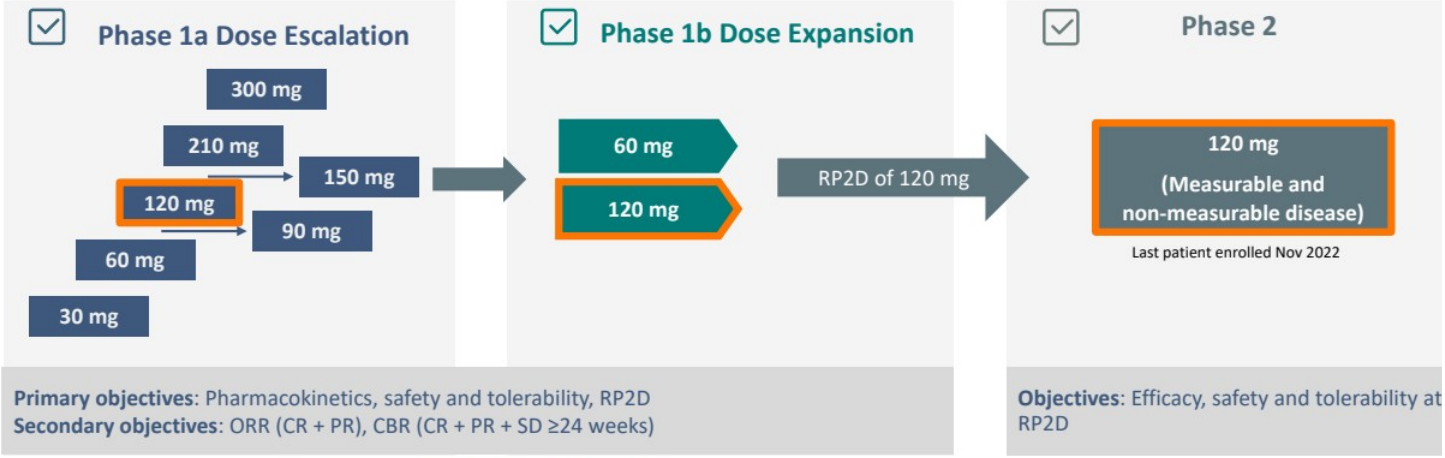
Palazestrant Phase 2
Monotherapy
Clinical Study Results
Olema
ONCOLOGY

Palazestrant (OP-1250) First-in-Human Phase 1/2 Study Design

More Than 150 Patients Treated with Palazestrant in Monotherapy Setting



Key Phase 2 Eligibility Criteria*

- ER+/HER2- advanced breast cancer
- 1–4 prior endocrine therapies for metastatic disease
- Up to 1 line of prior chemotherapy for metastatic disease
- Measurable or non-measurable disease by RECIST v1.1

* Phase 1a dose escalation allowed patients with at least 1 prior line of endocrine therapy and up to 2 prior lines of chemotherapy for metastatic disease.
Abbreviations: **CBR**, clinical benefit rate; **CR**, complete response; **ER+**, estrogen receptor-positive; **HER2**, human epidermal growth factor receptor 2; **ORR**, overall response rate; **PR**, partial response; **RECIST**, Response Evaluation Criteria in Solid Tumours; **RP2D**, recommended phase 2 dose; **SD**, stable disease.

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Patient Demographics and Baseline Characteristics

Patients Received Extensive Prior Therapies

Characteristics	120 mg palazestrant N=86*
Age, median, years (range)	61 (32-85)
Pre- or peri-menopausal, n (%)	7 (8%)
ECOG performance status, n (%)	
0	46 (54%)
1	40 (47%)
Measurable disease at baseline, n (%)	69 (80%)
Visceral disease (liver, lung, peritoneum, pleura, ascites), n (%)	61 (71%)
Prior lines of therapy in advanced setting, n (%)	
1	21 (24%)
2	29 (34%)
3	19 (22%)
4+	17 (20%)
Prior lines of endocrine therapy in advanced setting, n (%)	
1	30 (35%)
2	32 (37%)
3	15 (17%)
4+	9 (10%)
Types of prior therapy in advanced setting, n (%)	
CDK4/6 inhibitor	83 (97%)
Aromatase inhibitor	73 (85%)
Fulvestrant	57 (66%)
Chemotherapy	27 (31%)
mTOR inhibitor	25 (29%)
ESR1 mutations at baseline (ctDNA), n/N (%)	36/75 (48%)

- **42% of patients were 4th line or later at entr**
- 65% of patients received ≥2 prior lines of endocrine therapy for metastatic disease
- 97% received prior CDK4/6 inhibitor
- 66% received prior fulvestrant
- 31% received prior chemotherapy
- 80% had measurable disease
- 71% had visceral disease
- 48% had activating mutations in *ESR1*

*Includes patients from phase 1 (dose escalation and dose expansion) and phase 2 at 120 mg, an patients whose dose was increased from 60 to 120 mg early in treatment.

Abbreviations: **CDK4/6**, cyclin dependent kinase 4/6; **ECOG**, Eastern Cooperative Oncology Group; ***ESR1***, estrogen receptor 1 gene; **mTOR**, mammalian target of rapamycin.

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Safety – Treatment Emergent Adverse Events

Palazestrant is well tolerated with most TEAEs Grade 1 / 2

Treatment Emergent Adverse Events

TEAEs in ≥15% of patients	120 mg palazestrant (n=83)				
	Grade 1	Grade 2	Grade 3	Grade 4	All (%)
Nausea	47	4	3	0	54 (65%)
Vomiting	19	2	4	0	25 (30%)
Fatigue	13	6	3	0	22 (27%)
Neutropenia	6	6	3	6	21 (25%)
Headache	16	1	0	0	17 (20%)
Constipation	13	2	0	0	15 (18%)
AST increased	10	2	1	0	13 (16%)

- **Most AEs were low grade (grade 1/2)**
- Events of grade 4 neutropenia were observed in 6 patients at 120 mg, occurring approximately 4–6 weeks into therapy
  - 3 patients had a dose interruption followed by recovery and dose reduction (2 patients to 90 mg and 1 patient to 60 mg) without any recurrence of neutropenia
  - 3 patients had dose discontinuation followed by recovery
  - No increase in neutropenia in combination with palbociclib

Abbreviations: **AE**, adverse event; **TEAE**, treatment-emergent adverse event; **TRAE**, treatment-related adverse event; **AST**, aspartate aminotransferase.

Data Cutoff Date: July 7, 2023

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Safety – Treatment Related Adverse Events

Treatment Related Adverse Events

TRAEs in ≥15% of patients	120 mg palazestrant (n=83)				
	Grade 1	Grade 2	Grade 3	Grade 4	All n (%)
Nausea	42	2	3	0	47 (57%)
Vomiting	17	2	2	0	21 (25%)
Neutropenia	5	5	3	5	18 (22%)
Fatigue	10	5	2	0	17 (20%)
Headache	13	0	0	0	13 (16%)

- In OPERA-01 pivotal Phase 3 trial, patients will receive tablet formulation instead of the capsules utilized in current dataset
  - Expected to reduce rate and grade of nausea and vomiting
- Clinical pharmacology studies are now successfully completed allowing patients to dose either fed or fasted
  - Patients may also use proton-pump inhibitors

Abbreviations: **AE**, adverse event; **TEAE**, treatment-emergent adverse event; **TRAE**, treatment-related adverse event; **AST**, aspartate aminotransferase.
Data Cutoff Date: July 7, 2023

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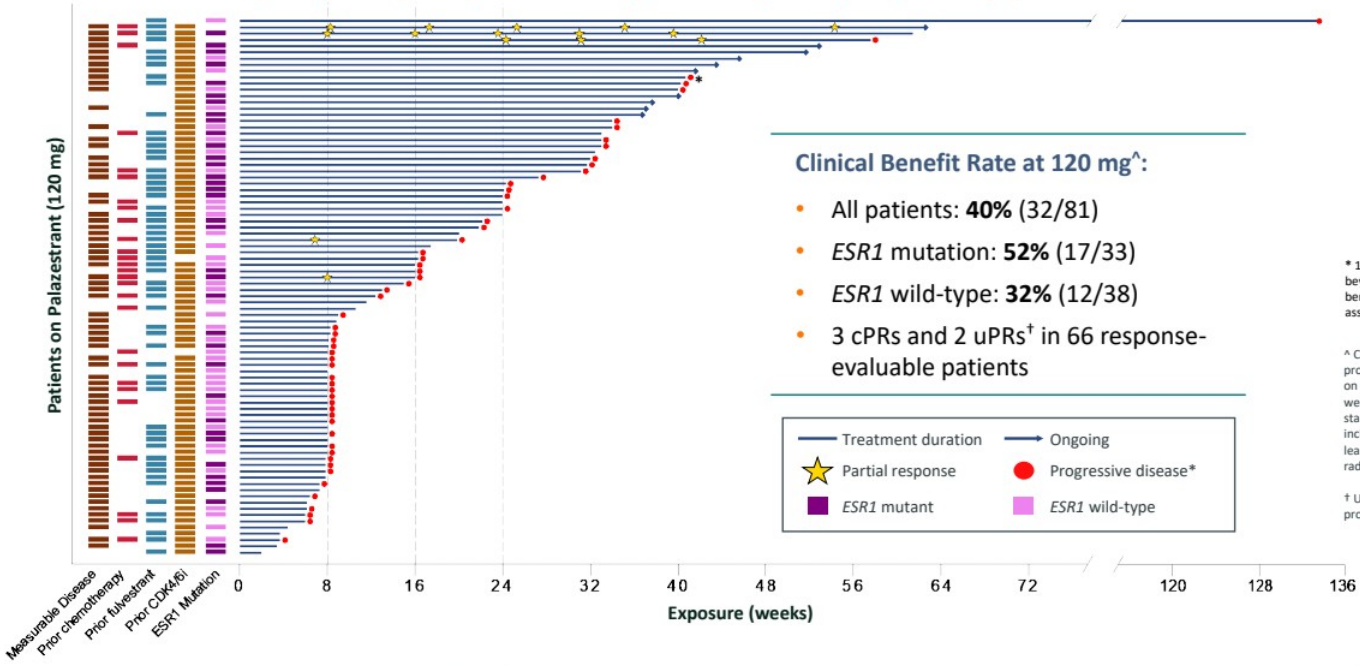
Duration of Treatment

Clinical Benefit Rate of 40% Overall; 52% with ESR1 Mutations; 32% in ESR1 Wild-type

Treatment duration (weeks) and response per RECIST v1.1 by dose in all patients (N=86) as of July 7, 2023



* 1 patient continued treat
beyond progression due to
benefit per principal investi
assessment.

^ Clinical benefit rate is the
proportion of patients who
on treatment through at lea
weeks with a confirmed CR
stable disease. The CBR ana
includes patients who recei
least one evaluable postbas
radiographic assessment.

† Unconfirmed due to disea
progression at a subsequen

Abbreviations: **CDK4/6i**, cyclin dependent kinase 4/6 inhibitor; **cPR**, confirmed partial response; ***ESR1***, estrogen receptor 1 gene; **RECIST**, Response Evaluation Criteria in Solid Tumours; **uPR**, unconfirmed partial response.

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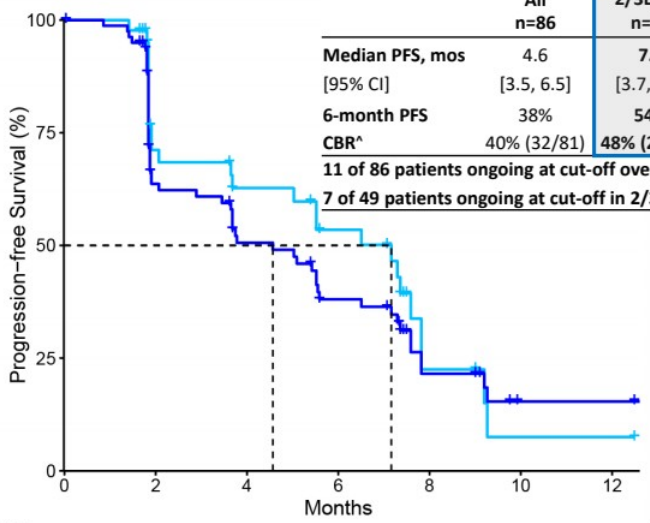
Progression-Free Survival Across All and ESR1-Mutant Patients

Median PFS of 7.2 months overall; 7.3 months in ESR1 mutations in EMERALD-eligible 2/3L ± CT Patients*

All Patients



	All n=86	2/3L ±CT n=49
Median PFS, mos	4.6	**7.2**
[95% CI]	[3.5, 6.5]	[3.7, 7.8]
6-month PFS	38%	**54%**
CBR^	40% (32/81)	**48% (22/46)**

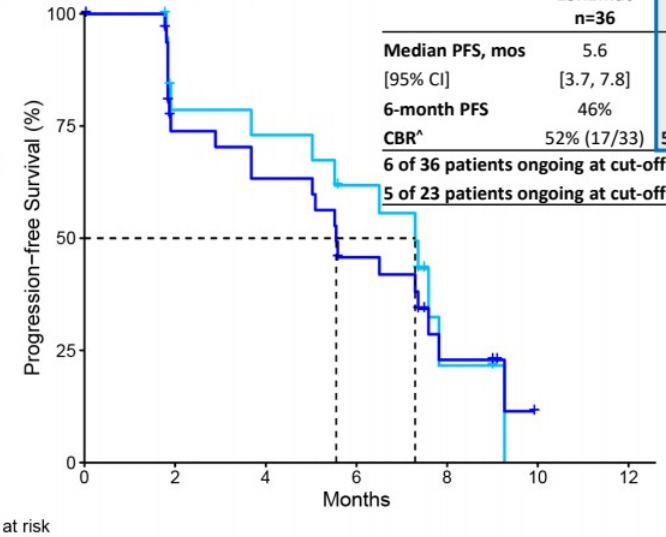
11 of 86 patients ongoing at cut-off overall

7 of 49 patients ongoing at cut-off in 2/3L±CT

Number at risk

All	86	45	33	23	9	3	3
2/3L ±CT	49	26	21	16	4	1	1

Patients with *ESR1 M*utation



	*ESR1*mut n=36	2
Median PFS, mos	5.6	
[95% CI]	[3.7, 7.8]	[
6-month PFS	46%	
CBR^	52% (17/33)	**59**

6 of 36 patients ongoing at cut-off ov

5 of 23 patients ongoing at cut-off in

Number at risk

All	36	21	18	12	4	0	0
2/3L ±CT	23	14	13	10	2	0	0

*** NOTE: This analysis is the aggregation of results across independent studies. There are risks inherent in conducting cross-trial comparisons. Refer to further disclaimers on slide 2.**

Abbreviations: **2/3L**, second/third line; **± CT**, plus/minus chemotherapy; **CBR**, clinical benefit rate; **CI**, confidence interval; ***ESR1***, estrogen receptor 1 gene; **mos**, months; **mut**, mutation; **NA**, not applicable; **PFS**, progression-free survival.

^Clinical Benefit Rate (CBR) is defined as the proportion of subjects who remained on OP-1250 treatment through at least 24 weeks with a confirmed CR or PR, or stable disease. The CBR analysis includes patients who received at least one evaluable postbaseline radiographic assessment. Data cut-off as of July 7, 2023.

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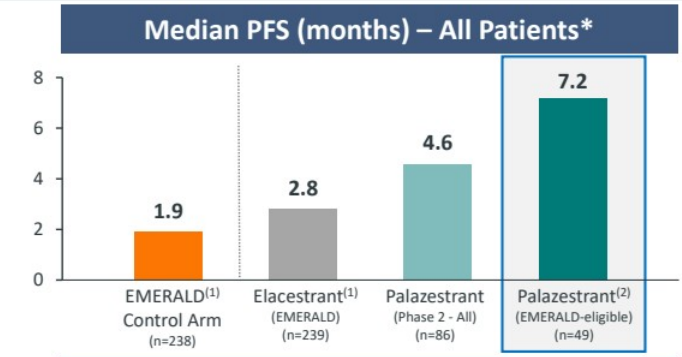
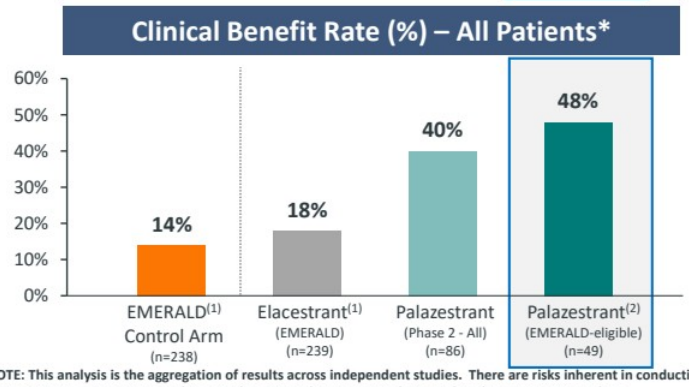
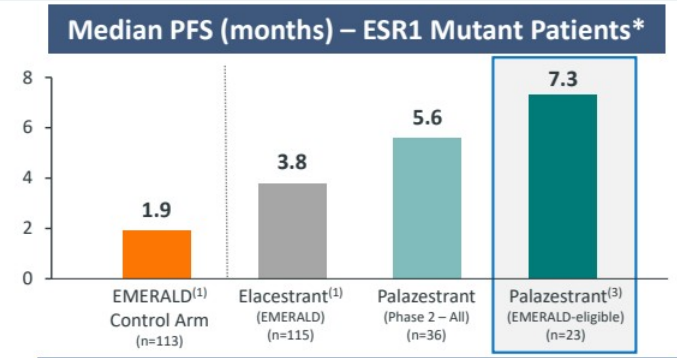
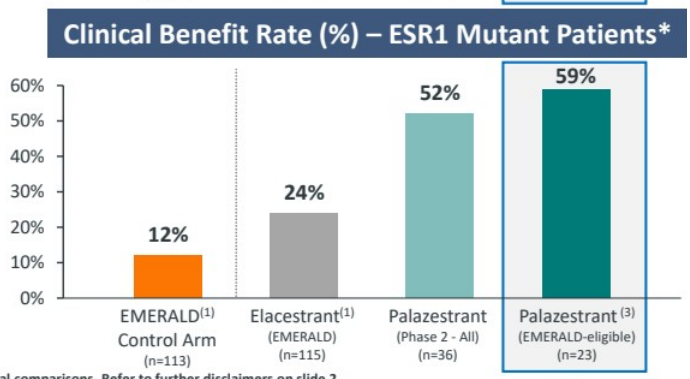
Comparing Across Trials: Palazestrant vs. Elacestrant

Median Progression Free Survival and Clinical Benefit Rate









*** NOTE: This analysis is the aggregation of results across independent studies. There are risks inherent in conducting cross-trial comparisons. Refer to further disclaimers on slide 2.**

1. Source: SABCS 2021 EMERALD data. Median PFS and CBR in control arm and in elacestrant 400 mg dose.
2. Emerald-eligible patient population from palazestrant Phase 2 dataset (2/3L +/-CT).
3. Emerald-eligible patient population from palazestrant Phase 2 dataset (2/3L +/-CT) with ESR1 mutations detected at baseline.

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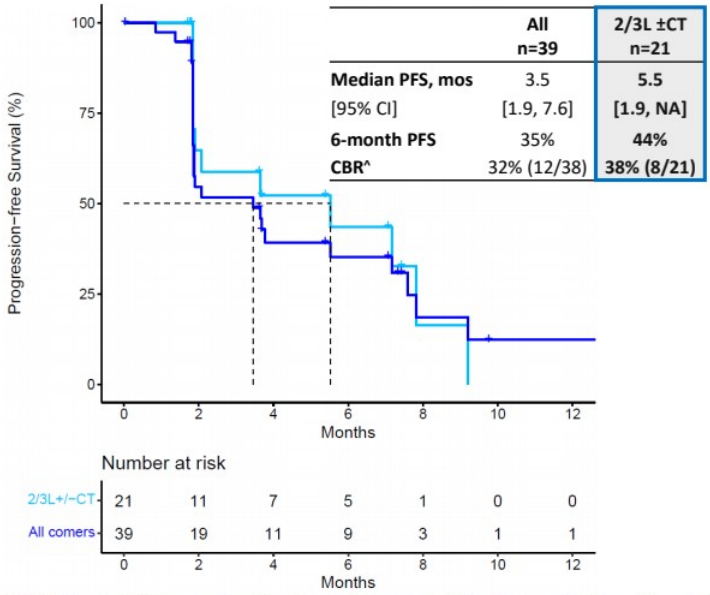
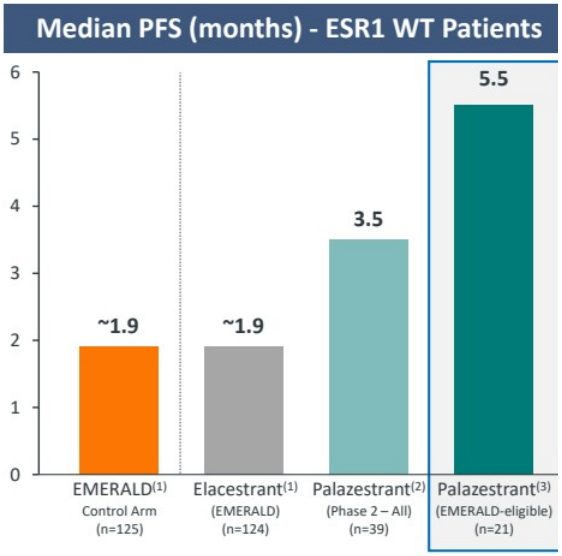
Progression-Free Survival in ESR1 Wild-Type Patients

*Median PFS of 5.5 months in EMERALD-eligible 2/3L ±CT Patients**



	All n=39	2/3L ±CT n=21
Median PFS, mos	3.5	**5.5**
[95% CI]	[1.9, 7.6]	**[1.9, NA]**
6-month PFS	35%	**44%**
CBR^	32% (12/38)	**38% (8/21)**



*** NOTE: This analysis is the aggregation of results across independent studies. There are risks inherent in conducting cross-trial comparisons. Refer to further disclaimers on slide 2.**

Abbreviations: **2/3L**, second/third line; **± CT**, plus/minus chemotherapy; **WT**, wild-type; **CI**, confidence interval; ***ESR1***, estrogen receptor 1 gene; **mos**, months; **NA**, not applicable; **PFS**, progression-free survival.

^Clinical Benefit Rate (CBR) is defined as the proportion of subjects who remained on OP-1250 treatment through at least 24 weeks with a confirmed CR or PR, or stable disease. The CBR analysis includes patients who received at least one evaluable postbaseline radiographic assessment. Data cut-off as of July 7, 2023.

1. Source: 2022 JCO Bidard Supplemental EMERALD data. Median PFS in control arm and in elacestrant 400 mg dose in ESR1 mutant not detected.
2. Source: Palazestrant Phase 2 dataset with ESR1 mutations not detected at baseline.
3. Source: Emerald-eligible patient population from palazestrant Phase 2 dataset (2/3L +/-CT) with ESR1 mutations not detected at baseline.

Palazestrant in the Competitive Landscape – Potential Best-in-Class

*Baseline Patient Characteristics Vary Across Competitor Landscape / Studies**

Treatment	Palazestrant	Elacestrant		Camizestrant		Giredestrant		Vepdegestran
Sponsor	Olema	Menarini		AstraZeneca		Roche		Pfizer / Arvina
Study	Phase 2	Phase 2[1]	EMERALD[2]	Phase 2[3]	Serena-2[4]	Phase 1a/b[5]	Acelera[6]	Veritac[7]
Study Size	n=86	n=50	n=239	n=22	n=74	n=41	n=151	n=71
Dose	120 mg	400 mg	400 mg	75 mg	75 mg	30 mg	30 mg	200 / 500 mg
Prior CDK4/6i	**97%**	**52%**	**100%**	**55%**	**51%**	**66%**	**43%**	**100%**
# Lines Prior ET								
0	0%	NA	0%	NA	**38%**	NA	0%	NA
1	35%	NA	**54%**	NA	**62%**	NA	**68%**	NA
2	37%	NA	**46%**	NA	0%	NA	**31%**	NA
3+	**27%**	NA	0%	NA	0%	0%	0%	NA
4th Line or Later	**44%**	NA	0%	NA	0%	0%	0%	NA
Non-measurable	**20%**	**38%**	25%	**36%**	NA	27%	7%	**38%**
ESR1 mutant	48%	50%	48%	50%	30%	51%	44%	58%

Most Comparable Studies to Palazestrant are EMERALD and Veritac Based on Prior CDK4/6i Experience

*** NOTE: This analysis is the aggregation of results across independent studies. There are risks inherent in conducting cross-trial comparisons. Refer to further disclaimers on slide 2.**

1. **Source: JCO 2021 Phase 1 study of elacestrant (RAD1901), a novel estrogen receptor degrader.**
2. **Source: SABCS 2021 EMERALD data.**
3. **Source:** SABCS 2020 Updated data from Serena-1 Phase 1 dose escalation and expansion study.
4. **Source: 2022 SABCS Serena-2 data.**
5. Source: 2021 ASCO giredestrant Phase 1a/b data.
6. Source: ESMO 2022 Acelera data.
7. Source: SABCS 2022 Veritac data.

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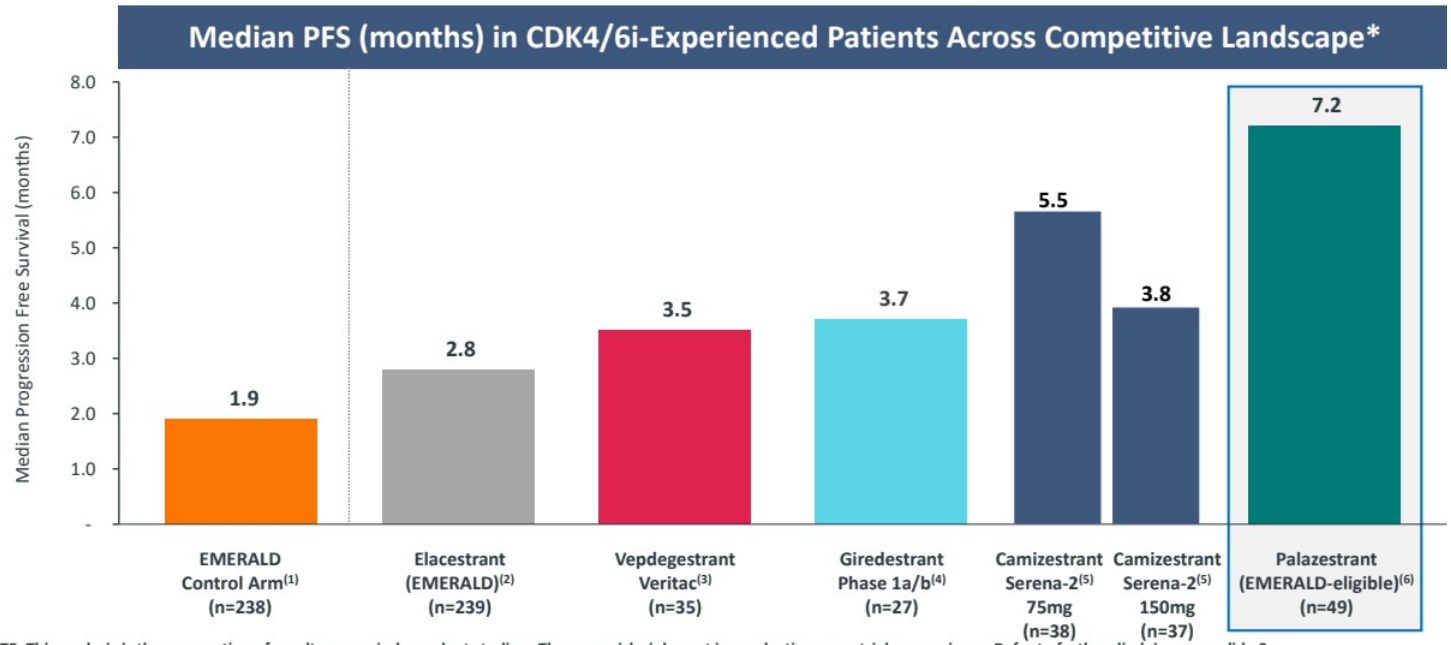
Palazestrant in the Competitive Landscape - Best-in-Class Potential

Median Progression Free Survival Across Comparable, All CDK4/6i-Experienced Patient Populations



*** NOTE: This analysis is the aggregation of results across independent studies. There are risks inherent in conducting cross-trial comparisons. Refer to further disclaimers on slide 2.**

1. Source: SABCS 2021 EMERALD data. Median PFS in control arm. Note: ORR of 4.4% (8/182).
2. Source: SABCS 2021 EMERALD data. Median PFS in elacestrant 400 mg dose. Note: ORR of 4.5% (8/179).
3. Source: SABCS 2022 Veritac data. Median PFS at 200 mg dose across all patients. Note: One cPR at 200 mg dose.
4. Source: ASCO 2021 Phase 1a/b giredestrant results. Median PFS estimated based on subset of giredestrant patients at 30 mg dose with CDK4/6i experience (27 of 41). Note: Six cPRs at 30 mg were all in CDK4/6i-naïve patients.
5. Source: SABCS 2022 Serena-2 data. Median PFS in CDK4/6i-experienced patients at 75 mg (5.5 months) and 150 mg (3.8 months). Represents <2 prior lines of ET-only +/- CT.
   Note: Serena-1 data at 75 mg dose had 2 PRs out of 22 patients; both were CDK4/6i naïve.
6. Source: Emerald-eligible patient population from palazestrant Phase 2 dataset (2/3L +/-CT) with ESR1 mutations detected at baseline

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Perspectives on the
SERD Landscape
Dr. Nancy U. Lin
Dana-Farber
Cancer Institute

Perspectives on Palazestrant as a Next Generation Endocrine Therapy

- Endocrine therapy remains the backbone of treatment for ER+/HER2- breast cancer
  - Shutting off estrogen receptor signaling is a key objective
  - Add additional agents as resistance develops but continue to suppress ER signaling
- Opportunity to improve upon current standard-of-care endocrine therapy
  - Most common resistance mechanism to current 1L standard of care is the development of an ESR1 activating mutation where both aromatase inhibitors and fulvestrant are ineffective
  - EMERALD study results validate the opportunity in ESR1-mutant patients in 2/3L metastatic setting
- Experience to date with palazestrant has been very positive
  - Well tolerated and consistent with oral CERAN/SERDs in development
  - Palazestrant Phase 2 study results are impressive, demonstrating the benefit of complete antagonism with improved PFS in ESR1-mutant patients and demonstrated activity in ESR1 wild-type patients

Dana-Farber Cancer Institute


Summary
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Palazestrant (OP-1250): Best-in-Class Potential for ER+/HER2- Breast Cance

Clinical dataset with over 225 patients treated with palazestrant 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.

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Phase 2 Combination Studies Ongoing with Palbociclib & Ribociclib

Palazestrant - Palbociclib Phase 2 Ongoing

Palazestrant 120 mg + Palbociclib 125 mg

N=50+ patients

Objectives: Safety, tolerability and antitumor activity of OP-1250 at RP2D in combination with palbociclib

Palazestrant - Ribociclib Phase 2 Ongoing

Palazestrant 120 mg + Ribociclib 600 mg

N=50+ patients

Objectives: Safety, tolerability and antitumor activity of OP-1250 at RP2D in combination with ribociclib

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 allow
- Can be CDK4/6i naïve or pre-treated

Phase 1b Dose Escalation Combination Studies Successfully Completed with Each of Palbociclib and Ribociclib

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

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ER+/HER2- Breast Cancer: One of the Largest Commercial Markets in Oncology

OPERA-01 Phase 3 trial targeting 2L/3L therapy; 1L Phase 3 trial in planning

	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]	$5B+	$10B+	~$3-5B	$10B+	~$500M

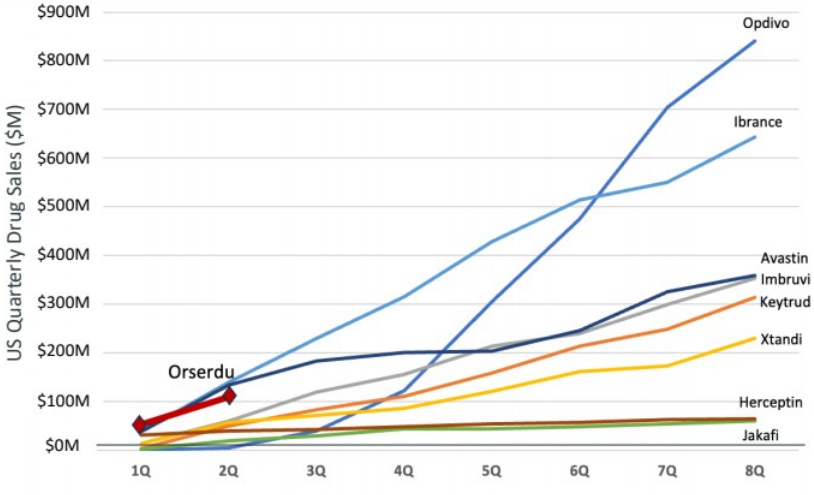
[1]2025 incidence projection estimates. Olema internal data, Informa ER+/HER2- BC Prevalence Based Market Forecast. 26% of adjuvant eligible patients assumed to have Ki-67 ≥ 20%. Early breast cancer incidence includes high risk adjuvant segment. [2]2025 incidence projection estimates. Olema internal 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.

Elacestrant Launch On-track to Rival Top Oncology Product Launches

$400M+ Annualized Sales 6 months into Launch

ORSERDU (Elacestrant) Gross Sales[1]

Precedent Oncology Drug Launches



[1] Source: Symphony data.

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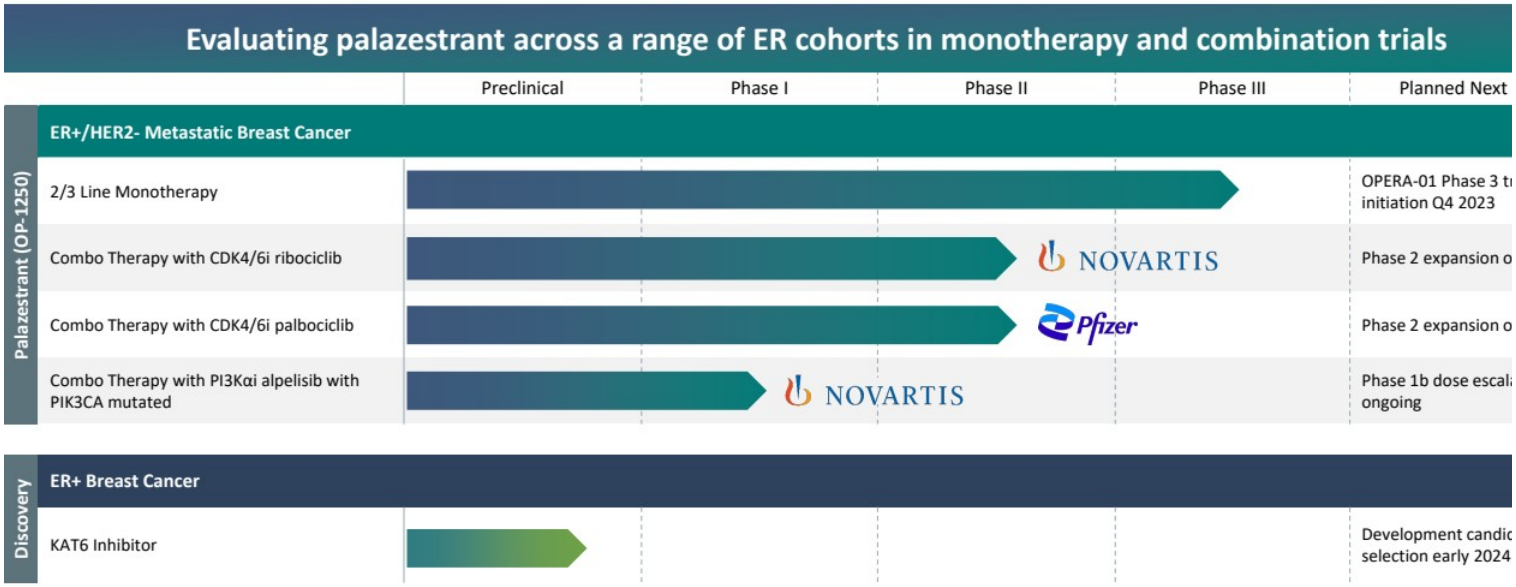
Initiating OPERA-01 Monotherapy Pivotal Phase 3 Trial Q4 2023



MBC = metastatic breast cancer; PI3Kα = phosphatidylinositol 3-kinase alpha; CDK4/6i = CDK4/6 inhibitor

Olema: A Compelling Late-Stage Opportunity in Women's Oncology

- Palazestrant is highly differentiated amongst a new class of endocrine therapies
- Compelling Phase 2 monotherapy data positions OPERA-01 phase 3 trial for success
- Palazestrant combinability with CDK4/6 inhibitors positions it for a potential first-line indication
- Olema's management team and board have deep experience and history of value creation
- Well-capitalized with ~$297.4M of cash and cash equivalents as of June 30, 2023[1]

(1) Cash position as of June 30, 2023, plus pro forma capital from financing announced on September 5, 2023.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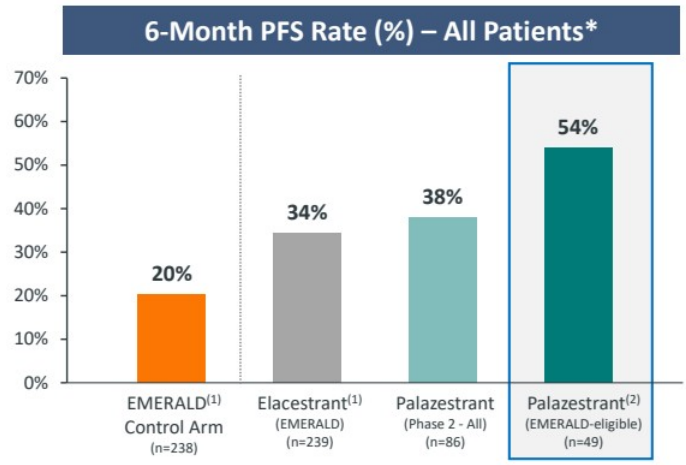
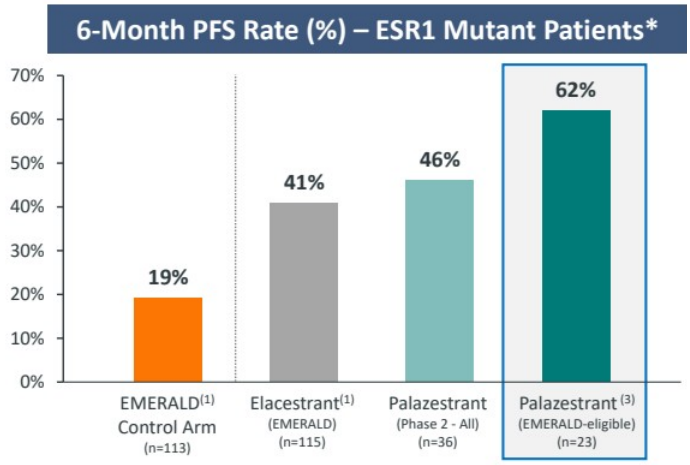
Thank you

Comparing Across Trials: Palazestrant vs. Elacestrant

6-Month Progression Free Survival Rate





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1. Source: SABCS 2021 EMERALD data. Median PFS and CBR in control arm and in elacestrant 400 mg dose.
2. Emerald-eligible patient population from palazestrant Phase 2 dataset (2/3L +/-CT).
3. Emerald-eligible patient population from palazestrant Phase 2 dataset (2/3L +/-CT) with ESR1 mutations detected at baseline.

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Palazestrant in the Competitive Landscape

PRs and ORR in CDK4/6i-Experienced Patients

Partial Responses (PRs) and Objective Response Rate (ORR) in CDK4/6i-Experienced Patients*

Sponsor	Molecule	Study	Dose	# cPRs	# Evaluable	ORR
Olema	Palazestrant[1]	Phase 2	120 mg	3	66	**4.5%**
Menarini	Control Arm[2]	EMERALD	NA	8	182	**4.4%**
Menarini	Elacestrant[2]	EMERALD	400 mg	8	179	**4.5%**
Pfizer / Arvinas	Vepdegestrant[3]	Veritac	200 mg	1	22	**4.5%**
Roche	Giredestrant[4]	Phase 1a/b	30 mg	0	30	**0%**
			90 / 100 mg	1	41	**2.4%**
AstraZeneca	Camizestrant[5]	SERENA-1	75 mg	0	12	**0%**
			150 mg	0	18	**0%**

*** NOTE: This analysis is the aggregation of results across independent studies. There are risks inherent in conducting cross-trial comparisons. Refer to further disclaimers on slide 2.**

1. Palazestrant Phase 2 monotherapy data as of July 7, 2023.
2. Source: SABCS 2021 EMERALD data.
3. Source: SABCS 2022 Veritac data.
4. Source: ASCO 2021 Phase 1-2 Monotherapy giredestrant study results. Note: Six cPRs at 30 mg were all in CDK4/6i-naïve patients; 4 of 5 cPRs at 90/100 mg were in CDK4/6i-naïve patients.
5. Source: SABCS 2020 Serena-1 data. Serena-1 data at 75 mg dose had 2 PRs out of 22 patients; both were CDK4/6i naïve.

Response Rate Does Not Predict Progression-Free Survival When Evaluating Later-stage Endocrine Therapies

Abbreviations: **CDK4/6i**, cyclin dependent kinase 4/6 inhibitor; **cPR**, confirmed partial response; **PR**, partial response; **PFS**, progression-free survival; **ORR**, objective response rate.

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