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 15, 2024

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)**	**(IRS Employer Identification No.)**

780 Brannan Street **San Francisco, California**	**94103**
(Address of Principal Executive Offices)	**(Zip Code)**

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

N/A
(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:

☐ 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, par value $0.0001 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 May 15, 2024, Olema Pharmaceuticals, Inc. (the "Company" or "Olema") announced interim results from an ongoing Phase 1b/2 clinical study of palazestrant (OP-1250) in combination with CDK 4/6 inhibitor ribociclib for the treatment of ER+/HER2- metastatic 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 May 15, 2024, the Company announced interim results from an ongoing Phase 1b/2 clinical study of palazestrant in combination with CDK 4/6 inhibitor ribociclib for the treatment of ER+/HER2- metastatic breast cancer. These results, as of the data cut-off of March 13, 2024, will be presented in a poster session at the 2024 ESMO Breast Cancer Annual Congress in Berlin, Germany ("ESMO Breast") on May 16, 2024.

The poster, titled "A Phase 1b/2 Study of Palazestrant (OP-1250) in Combination with Ribociclib in Patients with Estrogen Receptor-Positive, Human Epidermal Growth Factor Receptor 2-Negative, Advanced and/or Metastatic Breast Cancer", highlighted that:

- Across 50 treated patients, the combination of up to 120 mg of palazestrant with the full and approved dose of 600 mg of ribociclib daily was well tolerated, with no new safety signals or enhancement of toxicity and an overall safety profile consistent with the established safety profile of ribociclib plus an endocrine therapy.
- Palazestrant did not affect ribociclib drug exposure and ribociclib had no clinically meaningful effect on palazestrant drug exposure.
- Favorable preliminary efficacy profile was observed to date with a clinical benefit rate ("CBR") of 85% across all CBR-eligible patients (11/13), 83% in ESR1-mutant patients (5/6), 86% in ESR1-wild-type patients (6/7), and 83% in prior CDK4/6 inhibitor patients (10/12).
- Partial responses were observed in five patients through the data cut-off (2 confirmed, 3 unconfirmed) among 23 response-evaluable patients.
- Findings from this study support the continued clinical development of palazestrant in combination with ribociclib for the first-line treatment of ER+/HER2- advanced or metastatic breast cancer.

Phase 1b/2 Clinical Study Results

Enrollment

As of the data cut-off of March 13, 2024, 50 patients with recurrent, locally advanced or metastatic ER+/HER2- breast cancer with at least four weeks of follow-up were treated with palazestrant (3 patients each at 30 mg once daily and 60 mg once daily, 44 patients at the palazestrant recommended Phase 2 dose ("RP2D") of 120 mg once daily) plus ribociclib 600 mg once daily (three weeks followed by one week off treatment). The majority of patients (37 or 74%) were 2nd/3rd line+, with 37 (74%) patients having received prior endocrine therapy for metastatic breast cancer, 35 (70%) patients having received prior CDK4/6 inhibitors (11 or 22% having received two prior lines of CDK4/6 inhibitors), and nine (18%) patients having received chemotherapy for metastatic breast cancer. Of 48 patients whose circulating tumor DNA ("ctDNA") was assessed as of the data cut-off, 27% had activating mutations in ESR1 at baseline. The study is now fully enrolled with 60 patients.

Pharmacokinetics

Palazestrant demonstrated favorable pharmacokinetics characterized by high oral bioavailability, dose proportional exposure and a half-life of eight days as a single agent, with steady-state plasma levels showing minimal peak-to-trough variability enabling consistent inhibition of ER for the full dosing interval. Palazestrant did not affect ribociclib 600 mg drug exposure when compared with published exposure data for single-agent ribociclib. Steady-state trough values showed no clinically significant difference between the combination and single-agent palazestrant.

Safety and Tolerability Profile

Treatment with palazestrant up to 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, and the severity and incidence of adverse events were consistent with the expected safety profile of ribociclib plus endocrine therapy. Ten patients had dose reduction of ribociclib only, due to QTcF prolongation (n=4), neutropenia (n=4) or fatigue (n=2). No patients discontinued palazestrant due to a treatment-related adverse event, and two patients discontinued ribociclib for neutropenia without discontinuation of palazestrant in the 120 mg cohort. Neutropenia was reversible in all patients and the timing was consistent with ribociclib-related neutropenia.

Efficacy Profile

In a maturing dataset, palazestrant showed anti-tumor activity and prolonged disease stabilization in patients both with ESR1 wild-type and ESR1 activating mutations at baseline and in those previously treated with one or two lines of CDK4/6 inhibitors. Partial responses were observed in five patients (two confirmed, three unconfirmed as of data cut-off) out of 23 response-evaluable patients. Across patients who were CBR-eligible, the CBR was 85% (11/13) for all patients, 83% (5/6) for patients with ESR1-mutations, 86% (6/7) for patients that were ESR1 wild-type, and for CDK4/6i-pretreated patients the CBR was 83% (10/12). The longest duration on treatment is 44 weeks through the data cut-off, and 66% (33/50) of patients in this data set remain on treatment as of the data cut-off date.

Forward Looking Statements

Statements contained in this Current Report on Form 8-K, including the exhibits furnished herewith, 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, the potential of palazestrant to become a backbone endocrine therapy in the treatment of ER+/HER2- metastatic breast cancer, and Olema's potential to transform the endocrine therapy 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 March 31, 2024, and other 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 May 15, 2024, of Olema Pharmaceuticals, Inc.
99.2	Investor Presentation, dated May 15, 2024, 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, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

OLEMA PHARMACEUTICALS, INC.

Date: May 15, 2024

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

Olema Oncology Announces Promising New Data for Palazestrant in Combination with Ribociclib Presented at the 2024 ESMO Breast Cancer Congress

- *Across 50 treated patients, palazestrant (OP-1250) in combination with ribociclib was well tolerated with no new safety signals or increased toxicity and no clinically meaningful impact on drug exposure of either therapy*
- *85% clinical benefit rate (CBR) observed to date across all CBR-eligible patients supports promising preliminary efficacy profile of the palazestrant-ribociclib combination*
- *Olema will host an investor conference call today at 8:00 a.m. ET*

SAN FRANCISCO, May 15, 2024 – Olema Pharmaceuticals, Inc. ("Olema" or "Olema Oncology," Nasdaq: OLMA), a clinical-stage biopharmaceutical company focused on the discovery, development and commercialization of targeted therapies for women's cancers, today announced interim results from an ongoing Phase 1b/2 clinical study of palazestrant (OP-1250) in combination with CDK4/6 inhibitor ribociclib for the treatment of ER+/HER2- metastatic breast cancer. These results, as of the data cut-off of March 13, 2024, will be presented on May 16, 2024, in a poster session at the 2024 ESMO Breast Cancer Annual Congress in Berlin, Germany (ESMO Breast).

The poster, titled "A Phase 1b/2 Study of Palazestrant (OP-1250) in Combination with Ribociclib in Patients with Estrogen Receptor-Positive, Human Epidermal Growth Factor Receptor 2-Negative, Advanced and/or Metastatic Breast Cancer", highlighted that:

- Across 50 treated patients, the combination of up to 120 mg of palazestrant with the full and approved dose of 600 mg of ribociclib daily was well tolerated, with no new safety signals or enhancement of toxicity and an overall safety profile consistent with the established safety profile of ribociclib plus an endocrine therapy.
- Palazestrant did not affect ribociclib drug exposure and ribociclib had no clinically meaningful effect on palazestrant drug exposure.
- Promising preliminary efficacy was observed to date with a clinical benefit rate (CBR) of 85% across all CBR-eligible patients (11/13), 83% in *ESR1*-mutant patients (5/6), 86% in *ESR1*-wild-type patients (6/7), and 83% in prior CDK4/6 inhibitor patients (10/12).
- Partial responses were observed in five patients through the data cut-off (2 confirmed, 3 unconfirmed) among 23 response-evaluable patients.
- Findings from this study support the continued clinical development of palazestrant in combination with ribociclib for the first-line treatment of ER+/HER2- advanced or metastatic breast cancer.

"The data we are presenting at the ESMO Breast Cancer Annual Congress in Berlin add further support to our thesis that palazestrant possesses key characteristics that make it a potential backbone endocrine therapy of preference for ER+/HER2- breast cancer, both as a

monotherapy and in combination with other targeted agents," said Sean P. Bohen, M.D., Ph.D., President and Chief Executive Officer of Olema Oncology. "We are grateful to the approximately 300 women to date that have participated across our clinical trials. We are excited with the progress we are making, and we look forward to advancing toward our goal of transforming the endocrine therapy standard of care for breast cancer."

Phase 1b/2 Clinical Study Results

Enrollment

As of the data cut-off of March 13, 2024, 50 patients with recurrent, locally advanced or metastatic ER+/HER2- breast cancer with at least four weeks of follow-up were treated with palazestrant (3 patients each at 30 mg once daily and 60 mg once daily, 44 patients at the palazestrant recommended Phase 2 dose (RP2D) of 120 mg once daily) plus ribociclib 600 mg once daily (three weeks followed by one week off treatment). The majority of patients (37 or 74%) were 2nd/3rd line+, with 37 (74%) patients having received prior endocrine therapy for metastatic breast cancer, 35 (70%) patients having received prior CDK4/6 inhibitors (11 or 22% having received two prior lines of CDK4/6 inhibitors), and nine (18%) patients having received chemotherapy for metastatic breast cancer. Of 48 patients whose circulating tumor DNA (ctDNA) was assessed as of the data cut-off, 27% had activating mutations in *ESR1* at baseline. The study is now fully enrolled with 60 patients.

Pharmacokinetics

Palazestrant demonstrated favorable pharmacokinetics characterized by high oral bioavailability, dose proportional exposure and a half-life of eight days as a single agent, with steady-state plasma levels showing minimal peak-to-trough variability enabling consistent inhibition of ER for the full dosing interval. Palazestrant did not affect ribociclib 600 mg drug exposure when compared with published exposure data for single-agent ribociclib. Steady-state trough values showed no clinically significant difference between the combination and single-agent palazestrant.

Safety and Tolerability

Treatment with palazestrant up to 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, and the severity and incidence of adverse events were consistent with the expected safety profile of ribociclib plus endocrine therapy. Ten patients had dose reduction of ribociclib only, due to QTcF prolongation (n=4), neutropenia (n=4) or fatigue (n=2). No patients discontinued palazestrant due to a treatment-related adverse event, and two patients discontinued ribociclib for neutropenia without discontinuation of palazestrant in the 120 mg cohort. Neutropenia was reversible in all patients and the timing was consistent with ribociclib-related neutropenia.

Efficacy

In a maturing dataset, palazestrant showed anti-tumor activity and prolonged disease stabilization in patients both with *ESR1* wild-type and *ESR1* activating mutations at baseline and in those previously treated with one or two lines of CDK4/6 inhibitors. Partial responses were observed in five patients (two confirmed, three unconfirmed as of data cut-off) out of 23 response-evaluable patients. Across patients who were CBR-eligible, the CBR was 85% (11/13) for all patients, 83% (5/6) for patients with *ESR1*-mutations, 86% (6/7) for patients that were *ESR1* wild-type, and for CDK4/6i-pretreated patients the CBR was 83% (10/12). The longest duration on treatment is 44 weeks through the data cut-off, and 66% (33/50) of patients in this data set remain on treatment as of the data cut-off date.

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

Company Investor Webcast and Conference Call

Olema will host a webcast and conference call for analysts and investors to review the data being presented at ESMO Breast Cancer Annual Congress 2024 today, Wednesday, May 15, 2024, at 8:00 a.m. ET (2:00 p.m. CEST). Please register for the webcast by visiting the Investors & Media section of Olema's website at olema.com.

About Palazestrant (OP-1250)

Palazestrant (OP-1250) is a novel, orally-available small molecule with dual activity as both a complete estrogen receptor (ER) antagonist (CERAN) and selective ER degrader (SERD). It is currently being investigated in patients with recurrent, locally advanced or metastatic ER-positive (ER+), human epidermal growth factor receptor 2-negative (HER2-) breast cancer. In clinical studies, palazestrant completely blocks ER-driven transcriptional activity in both wild-type and mutant forms of metastatic ER+ breast cancer and has demonstrated anti-tumor efficacy along with attractive pharmacokinetics and exposure, favorable tolerability, CNS penetration, and combinability with CDK4/6 inhibitors. Palazestrant has been granted U.S. Food and Drug Administration (FDA) Fast Track designation for the treatment of ER+/HER2- metastatic breast cancer that has progressed following one or more lines of endocrine therapy with at least one line given in combination with a CDK4/6 inhibitor. It is being evaluated both as a single agent in an ongoing Phase 3 clinical trial, OPERA-01, and in Phase 1/2 combination studies with CDK4/6 inhibitors (palbociclib and ribociclib), a PI3Ka inhibitor (alpelisib), and an mTOR inhibitor (everolimus). For more information, please visit www.opera01study.com.

About Olema Oncology

Olema Oncology is a clinical-stage biopharmaceutical company committed to transforming the standard of care and improving outcomes for women living with cancer. Olema is advancing a pipeline of novel therapies by leveraging our deep understanding of endocrine-driven cancers, nuclear receptors, and mechanisms of acquired resistance. In addition to our lead product candidate, palazestrant (OP-1250), a proprietary, orally-available complete estrogen receptor (ER) antagonist (CERAN) and a selective ER degrader (SERD), Olema is developing a potent

KAT6 inhibitor (OP-3136). Olema is headquartered in San Francisco and has operations in Cambridge, Massachusetts. For more information, please visit us at www.olema.com.

Forward Looking Statements

Statements contained in this press release regarding matters that are not historical facts are “forward-looking statements” within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. Words such as “anticipate,” “expect,” “will,” “may,” “goal,” “potential” and similar expressions (as well as other words or expressions referencing future events, conditions or circumstances) are intended to identify forward-looking statements. These statements include those related to 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, the potential of palazestrant to become a backbone endocrine therapy in the treatment of ER+/HER2- metastatic breast cancer, and Olema’s potential to transform the endocrine therapy 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 March 31, 2024, and other 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.

# # #

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

ESMO Breast Cancer 2024

Palazestrant-Ribociclib Combination Interim Results

May 15, 2024

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 this presentation that are not statements of historical fact are forward-looking statements. Words such as “anticipate,” “believe,” “estimate,” “expect,” “goal,” “intend,” “may,” “plan,” “potential,” “project,” “will,” and similar expressions are intended to identify forward-looking statements, though not all forward-looking statements necessarily contain these identifying words. Such forward-looking statements include, without limitation, statements regarding our research and clinical development plans, the scope, progress, results and costs of developing our product candidate or any other future product candidates, strategy, regulatory matters, including the timing and likelihood of success of obtaining drug approvals, the timelines for potential clinical study results and clinical trials of palazestrant (OP-1250) as a monotherapy and in combination trials, including OPERA-01, the Company’s pivotal Phase 3 monotherapy clinical trial, and OPERA-02, the Company's potential pivotal Phase 3 clinical trial of palazestrant in combination with ribociclib, the potential beneficial characteristics, profile, safety, tolerability, efficacy and therapeutic effects of palazestrant as a monotherapy and in combination trials, the potential beneficial characteristics and tolerability of a tablet formulation, the potential of palazestrant to become a best-in-class treatment option for ER+/HER2- metastatic breast cancer and a backbone therapy for women living with breast cancer, the combinability of palazestrant with other drugs, the timelines for potential preclinical studies and clinical trials for our KAT6 inhibitor, market size and opportunity, our ability to complete certain milestones, our financial condition, cash position and runway and sufficiency of our financial resources, and the sufficiency of our management team. 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 the 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 and competitive risks, uncertainties, contingencies and assumptions about the Company, including, without limitation, risks inherent in developing products and 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 other expenses, trends in the industry, the legal and 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 elsewhere in the Company’s Quarterly Reports on Form 10-Q, Annual Report on Form 10-K, and other filings and reports the Company files with the Securities and Exchange Commission from time to time. In light of these risks and uncertainties, the events or circumstances referred to in the forward-looking statements may not occur. The actual 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 be 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 case of 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 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 representation 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 and the results should be interpreted with caution. The presentation of such third-party data does not represent a head-to-head comparison of how palazestrant, in monotherapy or in combination, performed against any other third-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 any 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 results 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 other 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 not 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 our 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.

Unmatched Combinability and Promising Efficacy for Palazestrant-Ribociclib Combo

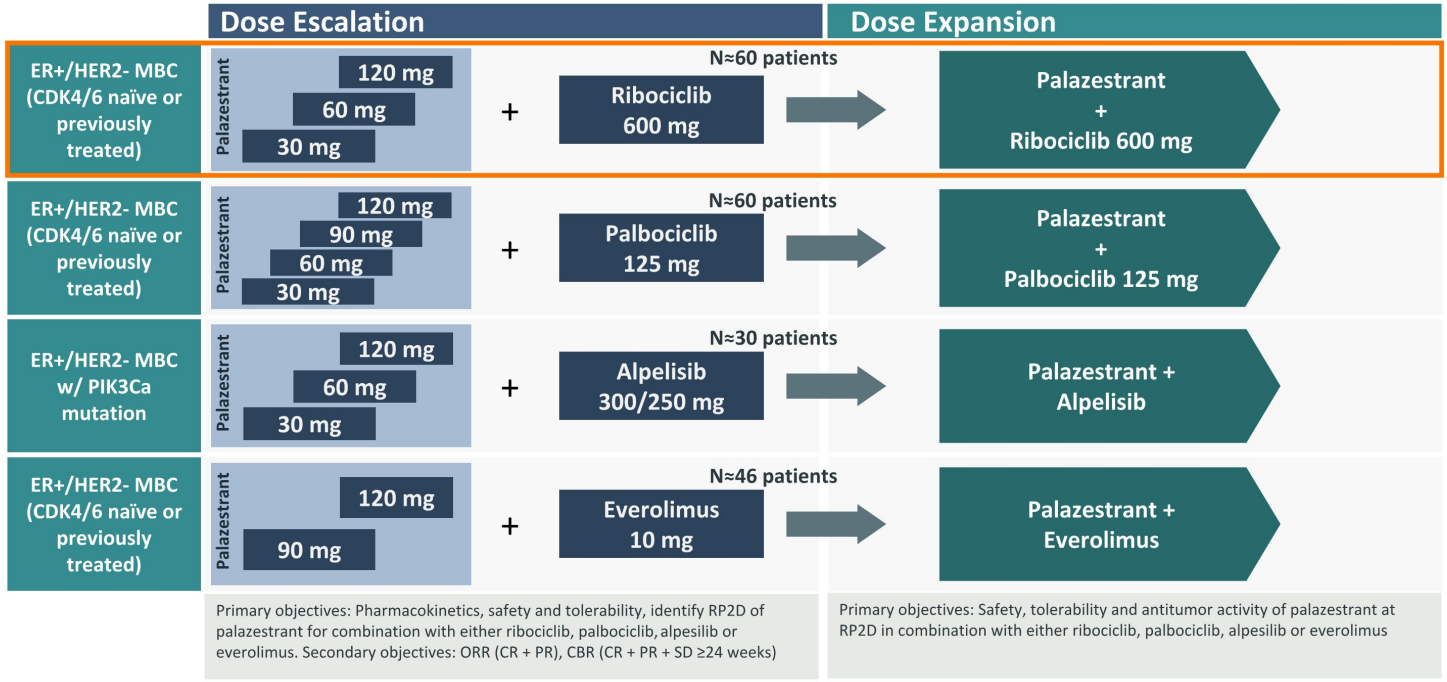
- Interim Phase 1b/2 data across 50 patients (on treatment for >4wks); 60-patient study now fully enrolled
  - Strong investigator enthusiasm resulted in rapid study enrollment
  - Largest data set for any CERAN/SERD in combination with ribociclib to be presented
- **Compelling combinability**
  - Well tolerated with no DLTs, no new safety signals or increased toxicity
  - No clinically meaningful impact on drug exposure of either therapy

- **Promising preliminary efficacy** shows best-in-class potential
  - **85% clinical benefit** rate (CBR) across all CBR-eligible patients
  - 83% in ***ESR1*-mutant** patients, 86% in ***ESR1*-wild-type** patients, and 83% in **CDK4/6i-pretreated** patients
  - Efficacy data continues to mature

- Palazestrant has shown best-in-class potential and significant differentiation based both on **monotherapy efficacy** and an ability to **effectively combine with CDK4/6 inhibitors**
- Results support continued clinical development of palazestrant in combination with ribociclib in a **1st-line pivotal Phase 3 trial**


Phase 1b/2 Palazestrant-Ribociclib
Combination Clinical Study

Demonstrating Palazestrant's Combinability with Other Targeted Agents



Abbreviations: **CBR,** clinical benefit rate; **CR,** complete response; **ER+**, estrogen receptor positive; **HER2-**, human epidermal growth factor receptor 2 negative; **MBC**, metastatic breast cancer; **PR,** partial response; **SD,** stable disease; **RP2D,** recommended phase 2 dose; **ORR**, objective response rate

Palazestrant-Ribociclib Demographics

Of 50 patients, 70% had prior CDK4/6i treatment, 27% with baseline ESR1 *mutations*

Demographic and disease characteristics	Total(N=50)^
Median age (years) (min-max)	62 (37–85)
ECOG performance status, n (%)	
0	24 (48%)
1	22 (44%)
Not reported	4 (8%)
Measurable disease at baseline, n (%)	31 (62%)
Visceral disease, n (%)	29 (58%)
Prior lines of therapy in advanced setting, n (%)	
0	13 (26%)
1	20 (40%)
2	12 (24%)
3	5 (10%)
Prior lines of endocrine therapy in advanced setting, n (%)	
0	13 (26%)
1	24 (48%)
2	13 (26%)
Types of prior therapy in advanced setting, n (%)	
CDK4/6 inhibitor	35 (70%)
Aromatase inhibitor	29 (58%)
Fulvestrant	18 (36%)
Chemotherapy	9 (18%)
***ESR1* mutations at baseline (ctDNA), n/N (%)**	13/48* (27%)

^ Patients included in this analysis (n=50) include patients who have been on treatment for at least one cycle, or 4 weeks, which allows for an assessment of combination safety and tolerability

*Two samples not evaluable

Abbreviations: **AI,** aromatase inhibitor; **CDK4/6i**, cyclin-dependent kinase 4/6 inhibitor; **ECOG**, Eastern Cooperative Oncology Group; **ctDNA**, circulating tumor DNA.

Data Cutoff Date: March 13, 2024

- 60 patients were enrolled as of March 13, 2024; analysis includes 50 patients with ≥4 weeks of follow-up
  - 3 patients at each of 30 mg and 60 mg, 44 at RP2D of 120 mg
- 58% had visceral disease, and 62% had measurable disease
- 74% received prior endocrine therapy for metastatic breast cancer
- 70% received prior CDK4/6 inhibitor
  - 24 (48%) had one prior CDK4/6i
  - 11 (22%) had two prior CDK4/6i
- 27% had activating mutations in *ESR1*

Palazestrant-Ribociclib Treatment Emergent Adverse Events

Well tolerated with no DLTs, safety and tolerability profile consistent with ribociclib + ET

Most Common Treatment-Emergent Adverse Events

TEAEs in ≥20% of patients	Ribociclib + Palazestrant[1] (n=50)			MONALEESA-2* Ribociclib + Letrozole[2] (n=334)		
	All grades	Grade 3	Grade 4	All grades	Grade 3	Grade 4
Neutropenia[a]	38 (76%)	24 (48%)	5 (10%)	93%[b]	49%	11%
Nausea	37 (74%)	1 (2%)	0%	52%	2%	0%
Fatigue	25 (50%)	1 (2%)	0%	37%	2%	<1%
Diarrhea	23 (46%)	1 (2%)	0%	35%	1%	0%
Anemia	18 (36%)	1 (2%)	0%	57%[b]	2%	0%
WBC decreased	18 (36%)	8 (16%)	0%	93%[b]	31%	3%
Constipation	15 (30%)	0%	0%	25%	1%	0%
Creatinine increased	12 (24%)	0%	0%	20%[b]	1%	0%
ECG QT prolonged	12 (24%)	3 (6%)	0%	43%[c]	8%[c]	0%
Thrombocytopenia	10 (20%)	0%	0%	29%[b]	1%	0%

- No DLTs were observed during dose escalation and the maximum tolerated dose was not reached
- No patients discontinued palazestrant due to a treatment-related AE; 2 patients discontinued ribociclib but stayed on palazestrant
- Overall safety and tolerability profile consistent with ribociclib + endocrine therapy prescribing information

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

Data Cutoff Date: March 13, 2024. Data shown are n or n (%).

Abbreviations: **DLTs,** dose-limiting toxicities; **TEAE,** treatment-emergent adverse event; **ECG,** electrocardiogram; **WBC,** white blood cells; **ET,** endocrine therapy.

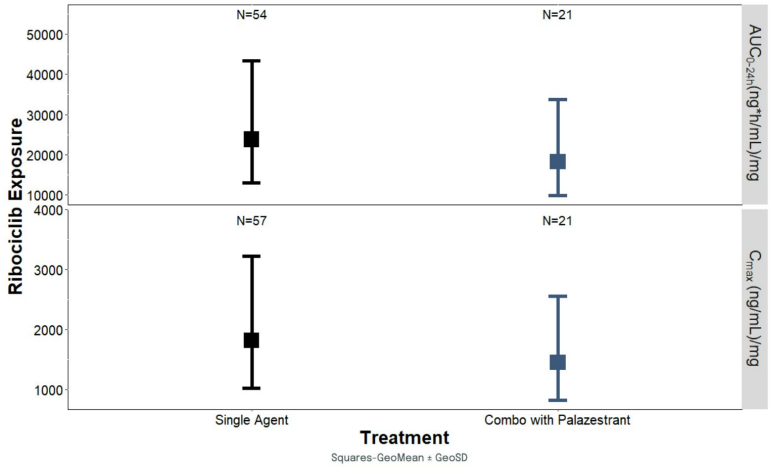
(1) Includes 3 patients at each of 30 mg and 60 mg palazestrant and 44 patients at 120 mg palazestrant in combination with 600 mg ribociclib. Two patients experienced Grade 5 AEs (myocarditis due to COVID-19; depressed level of consciousness not related to study drug) (2) Source: Novartis Kisqali (ribociclib) Prescribing Information, 2022

[a]Combined term includes neutropenia and decreased neutrophil count; [b]These values were taken from MONALEESA-2 lab abnormalities data. [c] Ribociclib + fulvestrant in MONALEESA-3 per the Ribociclib Approval Package (NUMBER:209092Orig1s001, June 2018); ribociclib + non-steroidal aromatase inhibitors in MONALEESA-7: all grade QTcF prolongation was 46.5% (Grade 2, 5.3%; Grade 3, 9%)

Palazestrant-Ribociclib Pharmacokinetics

No effect of palazestrant on ribociclib exposure levels across dose levels

Ribociclib (600mg) Steady State Exposure ($AUC_{(0-24)}$ and C_{max})* (Alone and in Combination with Palazestrant (OP-1250))



$AUC_{(0-24)}$, area under the curve from 0 to 24 h; **C_{max}**, maximum concentration; **GeoMean,** geometric mean; **GeoSD**, geometric standard deviation
Data Cut-off Date: March 20, 2024
* Single Agent Steady State exposure levels for ribociclib (Yan J, et al. Presented at SABCS 2019; December 10-14, 2019 (poster number P1-19-37))

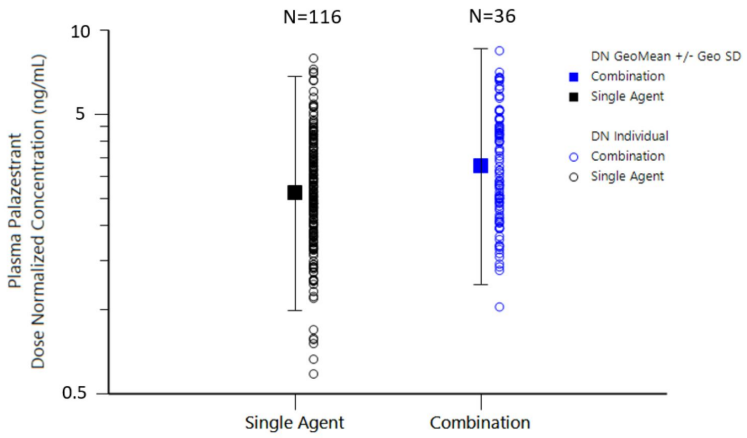
Pharmacokinetics

- No drug-drug interaction (DDI) between ribociclib and palazestrant in the dose range of 30 to 120 mg
- Palazestrant did not affect ribociclib 600 mg exposure when compared with published exposure data for single-agent ribociclib
- Exposure of ribociclib was within the reported range of the 600 mg dose single agent exposures at steady state

Palazestrant-Ribociclib Pharmacokinetics

Effect of ribociclib on palazestrant exposure is not clinically meaningful

Palazestrant (OP-1250) Steady State Trough Concentration (Alone and in Combination with Ribociclib (600 mg))



Data Cut-off Date: March 20, 2024

Note: Pre-dose samples at C2D1, C2D15, C3D1, C5D1, C7D1, and C9D1 included for both studies.

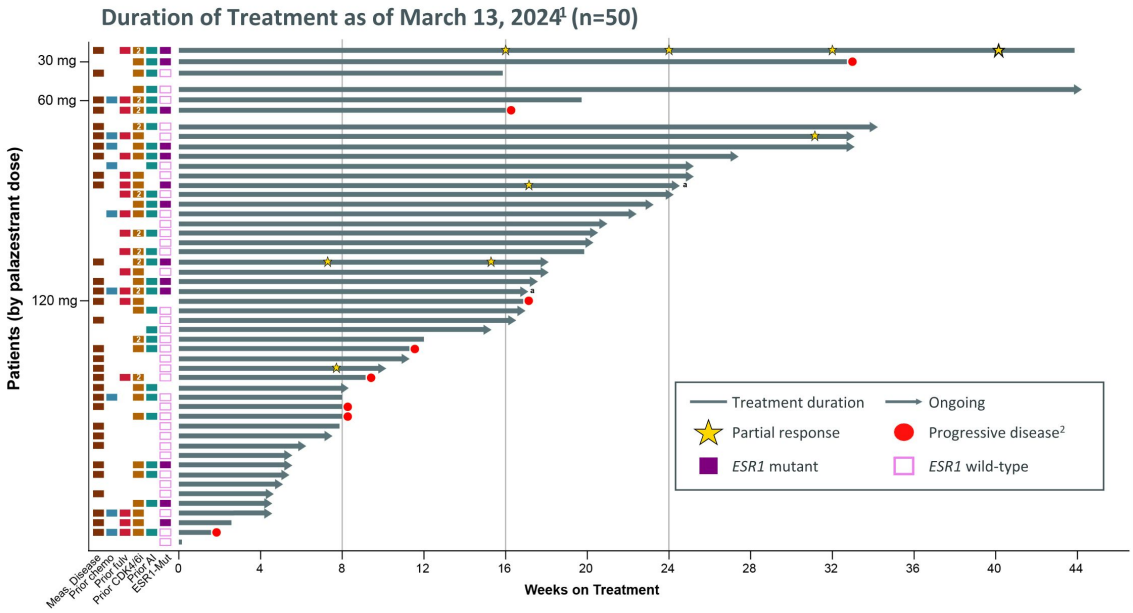
DN, dose normalized; **GeoMean**, geometric mean; **GeoSD**, geometric standard deviation.

Pharmacokinetics

- Steady-state trough values between the combination and single-agent palazestrant were overlapping.
- Ribociclib had no clinically meaningful effect on palazestrant exposure

Palazestrant-Ribociclib Preliminary Efficacy

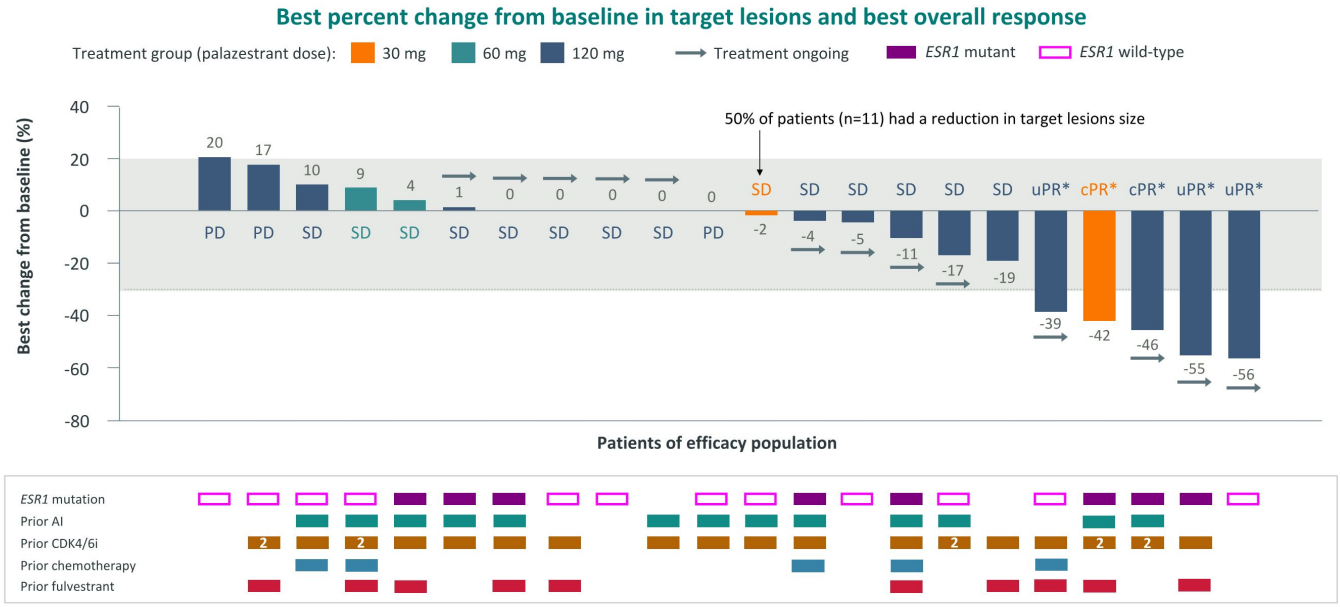
85% Clinical Benefit Rate Across Wild-type and ESR1 *Mutant Patients*



- Activity shown in both wild-type and *ESR1*-mut patients
- 5 partial responses to date of 23 eligible (2 cPR, 3 uPR)
- **Clinical benefit rate (CBR)**^:
  - **85% in all patients** (11/13 CBR-eligible)
  - **83% in *ESR1*-mut** (5/6 CBR-eligible)
  - **86% in *ESR1*-wt** (6/7 CBR-eligible)
  - **83% for prior CDK4/6i** (10/12 CBR-eligible)
- Longest duration of treatment 44 weeks
- Efficacy data are maturing; 33 (66%) of 50 patients remain on treatment; 60 patients have been enrolled

[1]Each lane represents one patient. [2] Progression by radiographic assessment only.
a: Two patients discontinued ribociclib but continued palazestrant.
2: 2 prior CDK4/6 inhibitors in metastatic setting.
Abbreviations: **AI,** aromatase inhibitor; **CDK4/6i,** cyclin-dependent kinase 4/6 inhibitor; **ESR1,** estrogen receptor 1 gene; **cPR**, confirmed partial response; **uPR**, unconfirmed partial response
^ Clinical benefit rate (CBR) is the proportion of patients who remained on treatment through at least 24 weeks with a confirmed CR or PR or stable disease

Palazestrant-Ribociclib Preliminary Efficacy
Anti-tumor Activity Shown Both in Wild-Type and ESR1 *Mutant Patients*



Data cut-off: March 13, 2024

* cPR, confirmed PR; uPR, unconfirmed PR

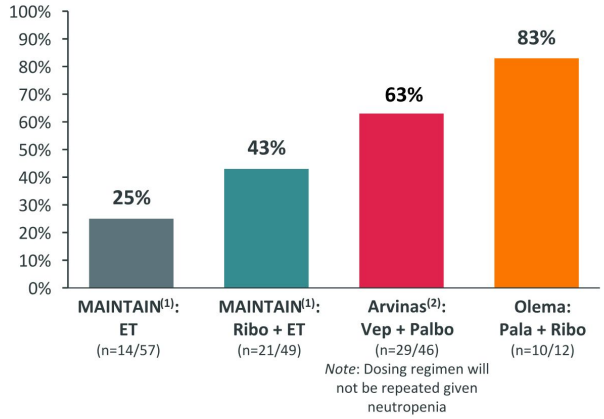
2: 2 prior CDK4/6 inhibitors in metastatic setting.

Waterfall plot n=22. **AI,** aromatase inhibitor; **CDK4/6i,** cyclin-dependent kinase 4/6 inhibitor; ***ESR1,*** estrogen receptor 1 gene; **SD**, stable disease; **PD**, progressive disease

Comparison of Combination Efficacy in 2/3L+ Patients

MAINTAIN study of ribociclib after CDK4/6i progression serves as clinical benchmark for patient population

Benchmark Clinical Benefit Rate*^ in CDK4/6i pre-treated patients



- Palazestrant + ribociclib combination showed efficacy in *ESR1*-mut and wild-type patients
  - 85% in all patients (11/13 CBR-eligible)
  - 83% for *ESR1*-mut (5/6 CBR-eligible)
  - 86% for *ESR1*-wt (6/7 CBR-eligible)
  - *83% for prior CDK4/6i (10/12 CBR-eligible)*
- MAINTAIN study indicated potential benefit of ribociclib after CDK4/6 inhibitor progression with increase in clinical benefit rate, but was not statistically significant (p=0.06)

Early signals of efficacy for palazestrant in combination with ribociclib

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

Data Cutoff Date: March 13, 2024.

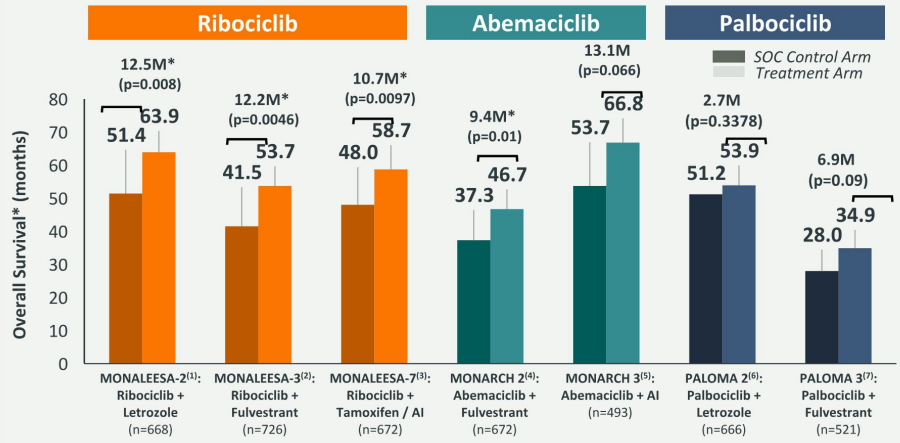
Abbreviations: **ET,** endocrine therapy; **Ribo**, ribociclib; **Vep**, vepdegestrant; **Palbo**, Palbociclib; **Pala**, palazestrant; **ESR1-mut**, ESR1-mutant; **ESR1-wt**, ESR1 wild-type; **CDK4/6i**, CDK4/6 inhibitor

1. Source: ASCO 2022 MAINTAIN data. Median PFS, CBR, and ORR in control arm and in ET with ribociclib.
2. Source: SABCS 2023 Phase 1b data. Median PFS, CBR, and ORR in control arm and in vepdegestrant with palbociclib

^ Clinical benefit rate (CBR) is the proportion of patients who remained on treatment through at least 24 weeks with a confirmed CR or PR or stable disease

Ribociclib Only CDK4/6i with Confirmed OS Benefit in Combo with AI

CDK4/6is were approved with PFS but ribociclib has strongest evidence of OS benefit



- No statistically significant OS benefit for palbociclib 1L combinations or for abemaciclib + AI
- NCCN guidelines recommend three regimens that have shown OS benefit in Phase 3 randomized controlled studies as **Category 1 preferred** for 1L treatment of patients with HR+/HER2- mBC :
  - ribociclib + endocrine therapy
  - ribociclib + fulvestrant
  - abemaciclib + fulvestrant
- The CDK 4/6 inhibitors have varying potency, selectivity, and PK which also impacts tolerability profiles

If first-line Phase 3 clinical trial initiated, palazestrantwill be the only novel ET combined with ribociclib in a pivotal trial; all other current combinations include palbociclib or physician choice CDK4/6i

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

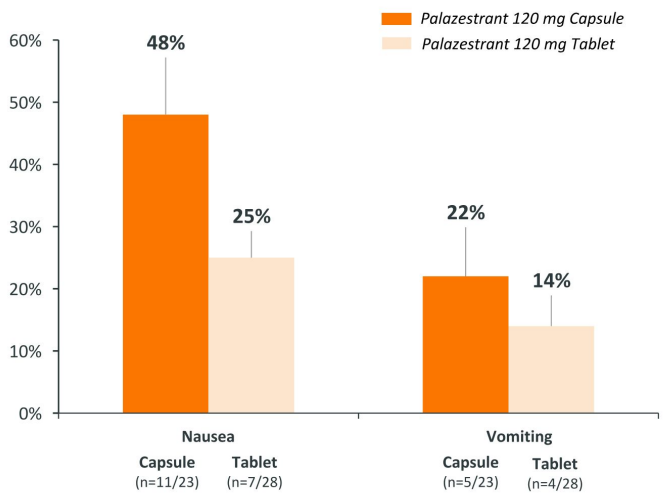
Source: (1) Hortobagyi G.N., et al. Overall Survival with Ribociclib plus Letrozole in Advanced Breast Cancer. NEJM. 2022;386:942-950; (2) Salmon D.J., et al. Overall Survival with Ribociclib plus Fulvestrant in Advanced Breast Cancer. NEJM. 2020;382:514–524; (3) Im S.-A., et al. Overall Survival with Ribociclib plus Endocrine Therapy in Breast Cancer. NEJM. 2019;381:307–316; (4) Sledge G.W., Jr., et al. MONARCH 2: Abemaciclib in Combination with Fulvestrant in Women with HR+/HER2– Advanced Breast Cancer Who Had Progressed While Receiving Endocrine Therapy. J. Clin. Oncol. 2017;35:2875–2884; (5) Toi M., et al. MONARCH 3: Final Overall Survival Results of Abemaciclib Plus a Nonsteroidal AI as First-line Therapy for HR+, HER2- Advanced Breast Cancer. SABCS 2023 GS01-12 (; (6) Finn R.S., et al. Palbociclib and Letrozole in Advanced Breast Cancer. NEJM. 2016;375:1925–1936; (7) Cristofanilli M., et al. Fulvestrant plus palbociclib versus fulvestrant plus placebo for treatment of hormone-receptor-positive, HER2-negative metastatic breast cancer that progressed on previous endocrine therapy (PALOMA-3): Final analysis of the multicentre, double-blind, phase 3 randomised controlled trial. Lancet Oncol. 2016;17:425–439

Improvement in Upper GI Adverse Events with Palazestrant Tablets

Up to 50% of nausea and vomiting incidence reduced vs. capsule formulation

- Palazestrant tablet formulation introduced in February 2023
  - 23 subjects were treated with 120 mg capsules
  - 28 subjects treated with 120 mg tablets only
- Overall incidence of treatment-emergent or palazestrant-related nausea/vomiting has decreased with tablet formulation
  - Incidence of Grade 2 events has decreased with tablet formulation
  - No upper GI Grade 3 events reported in this study

Palazestrant Upper GI TRAEs in All Patients (All Grades)



Data Cutoff Date: March 20, 2024.

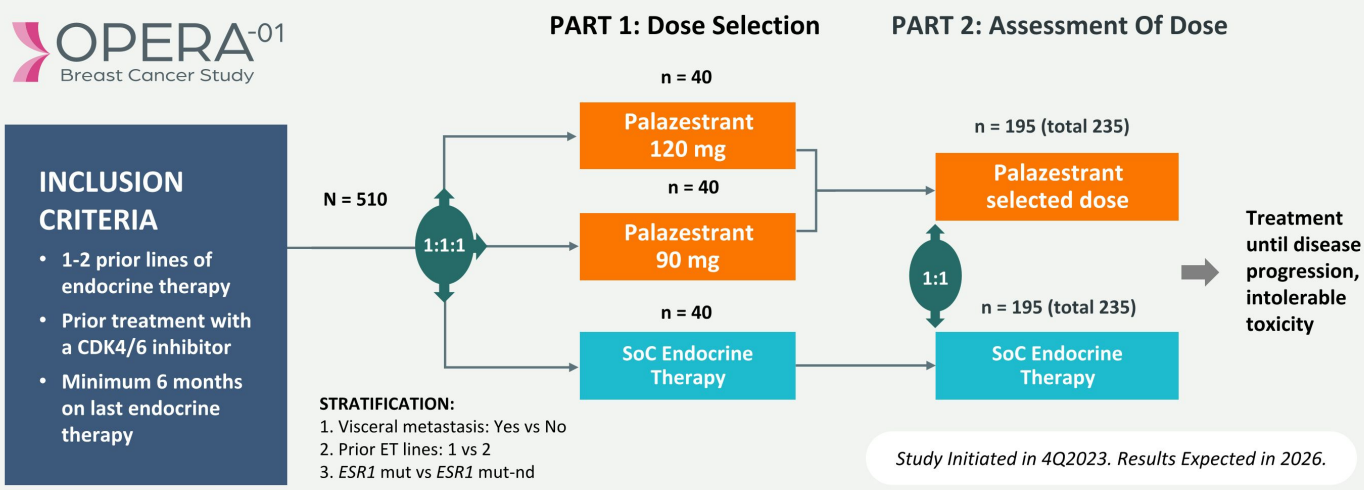
Abbreviations: **GI,** gastrointestinal; **TRAE,** treatment-related adverse event

Advancing Value – Palazestrant and Pipeline

Olema ONCOLOGY

OPERA-01 Designed to Show Effectiveness over Standard of Care

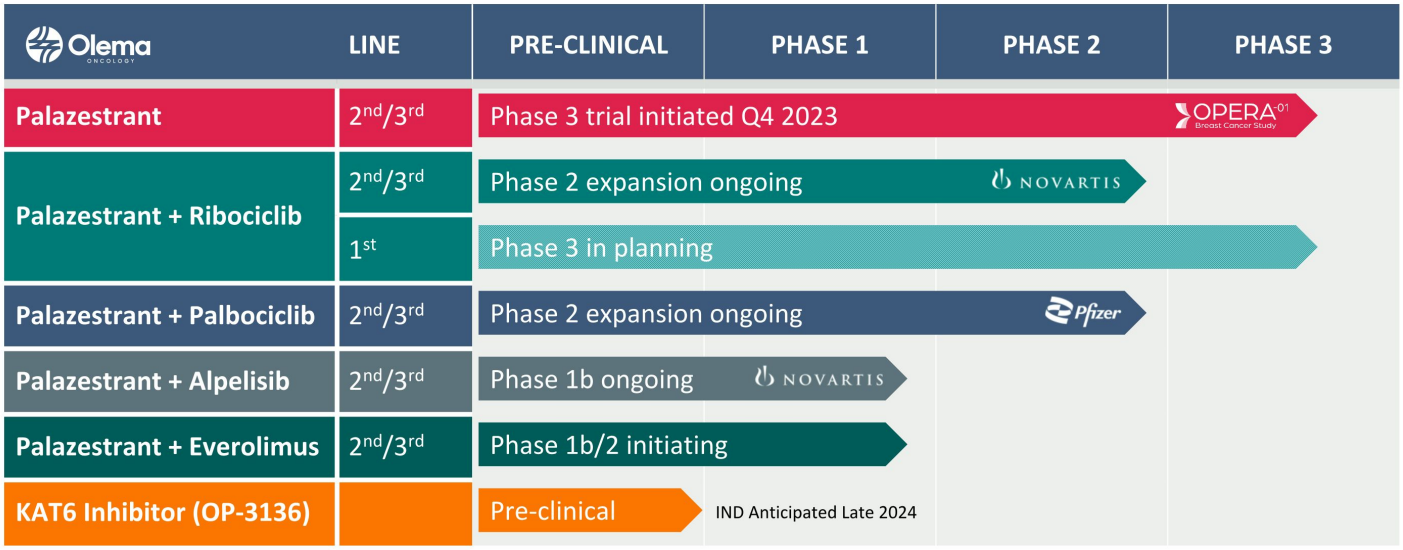
510-Patient Phase 3 2/3L Monotherapy Trial vs. Standard of Care (SoC)



For more details on this trial, please visit www.opera01study.com.
Abbreviations: **CDK4/6i**, cyclin dependent kinase 4/6 inhibitor; ***ESR1***, estrogen receptor 1 gene; **SoC**, standard of care; **ET**, endocrine therapy; **mut**, mutation; **mut-nd**, mutation not detected

Olema's Expanding Pipeline Focused on Women's Oncology

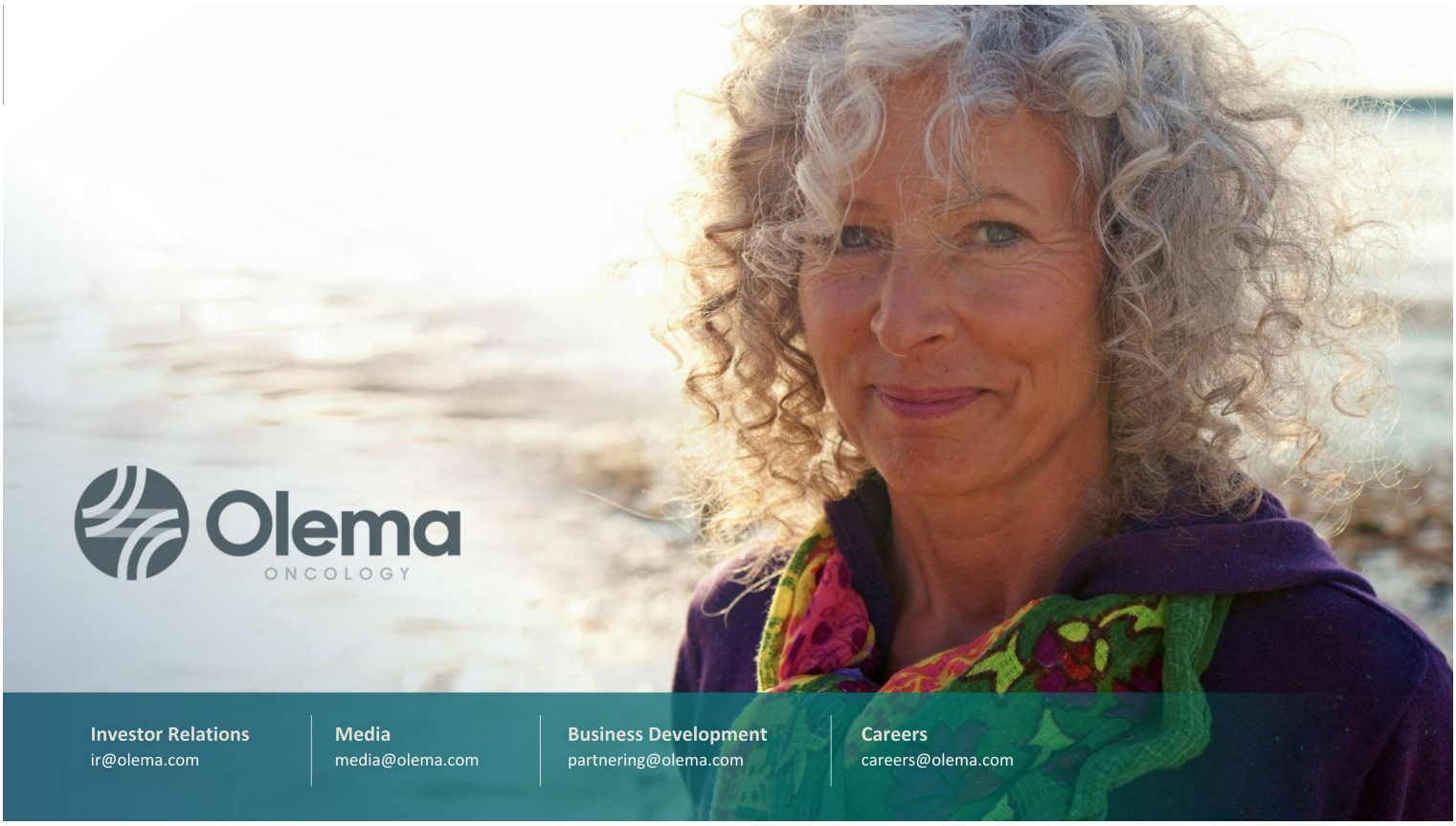
Advancing Palazestrant in 2nd/3rd Line and in 1st Line Metastatic Breast Cancer



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

- Palazestrant is highly differentiated within the new class of endocrine therapies
- Compelling Phase 2 monotherapy data positions OPERA-01 phase 3 trial for success
- Palazestrant full-dose combinations with CDK4/6 inhibitors position it for first-line indication
- Management and Board with deep experience and history of success
- Well-capitalized with ~$249M of cash and cash equivalents as of March 31, 2024[1]

[1] Cash position as of March 31, 2024, includes the Company's cash, cash equivalents, and marketable securities.



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