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): December 06, 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)**	**(IRS Employer Identification No.)**
780 Brannan Street **San Francisco, California** **(Address of Principal Executive Offices)**		**94103** **(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 December 6, 2023, Olema Pharmaceuticals, Inc. (the "Company") made available on its website a copy of the Company's presentation to be shared with investors and others from time to time beginning on December 6, 2023. The presentation is being furnished as Exhibit 99.1 to this Current Report on Form 8-K.

The information in Exhibit 99.1 attached hereto is intended to be furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act") or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended or the Exchange Act, except as expressly set forth by specific reference in such filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	Investor Presentation, dated December 6, 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, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Olema Pharmaceuticals, Inc.

Date: December 6, 2023

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

Olema SABCS December 2023 Presentation

December 6, 2023

Olema ONCOLOGY

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. 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, expected manufacturing capabilities, 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 combination clinical trial, the potential beneficial characteristics, 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 development of palazestrant, the potential of palazestrant to become a best-in-class treatment option for ER+/HER2- metastatic breast cancer, the endocrine therapy of choice, a backbone therapy, and a transformative therapy for women living with breast cancer, the combinability of palazestrant with other drugs, market size and opportunity, our ability to complete certain milestones, and our financial condition, cash position and runway and sufficiency of our financial resources. Words such as "believe," "anticipate," "plan," "expect," "intend," "will," "may," "goal," "project," "estimate," "potential" and similar expressions are intended to identify forward-looking statements, though not all forward-looking statements necessarily contain 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 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 future filings and reports of the Company with the Securities and Exchange Commission. In light of these risks and uncertainties, the events or circumstances referred to in the forward-looking statements may not occur. The 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 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.

Meeting Participants

Presenting

Sean P. Bohen, M.D., Ph.D.
President and Chief Executive Officer

Q&A

Shane Kovacs, MBA
Chief Operating Officer

Naseem Zojwalla, M.D.
Chief Medical Officer

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

- Palazestrant combines well with CDK4/6 inhibitors
  - In combination with CDK4/6 inhibitors, ribociclib and palbociclib, palazestrant showed **no significant drug-drug interaction**, **no dose-limiting toxicities** and a **tolerability profile consistent with the FDA-approved labels** of the CDK4/6 inhibitor and an endocrine therapy
  - Palazestrant **did not affect the exposure** of either ribociclib or palbociclib in patients, and neither CDK4/6 inhibitor had a meaningful effect on the exposure of palazestrant

- Promising evidence of **anti-tumor activity** and **delay in disease progression**
  - Efficacy data continue to mature
  - Ongoing combination studies support further clinical development of palazestrant in combination with CDK4/6 inhibitors **for first-line treatment**

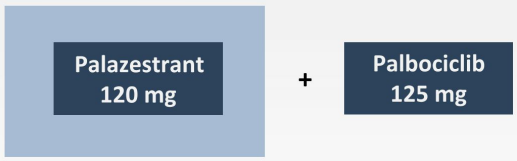
- Competitive landscape has experienced setbacks when combining with CDK4/6 inhibitors
  - Drug-drug interaction and/or enhanced toxicity resulting in dose modifications*
- Potential to initiate 1st-line pivotal trial in combination with CDK4/6 inhibitor by YE2024

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


Olema
ONCOLOGY
Phase 1b/2 Combination
Clinical Studies

Phase 2 Combination Studies Ongoing with CDK4/6 Inhibitors

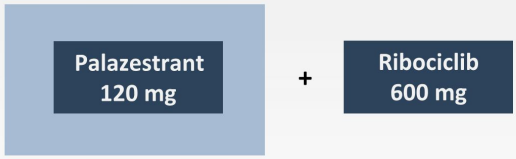
Palazestrant + Palbociclib Phase 2 Ongoing



N=60 patients

Objectives: Safety, tolerability and antitumor activity of palazestrant at RP2D in combination with palbociclib

Palazestrant + Ribociclib Phase 2 Ongoing



N=60 patients

Objectives: Safety, tolerability and antitumor activity of palazestrant at RP2D in combination with ribociclib

Key* Inclusion Criteria:

- ER+/HER2- advanced breast cancer
- Evaluable disease (measurable and non-measurable)
- ≤ 1 (palbociclib) or ≤ 2 (ribociclib) prior hormonal regimen for locally advanced or metastatic disease
- One prior line of chemotherapy for advanced or MBC was allowed
- Can be CDK4/6i naïve or pre-treated

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

* Full eligibility criteria for NCT05266105 and NCT05508906 on clinicaltrials.gov (https://clinicaltrials.gov/study/NCT05266105, https://clinicaltrials.gov/study/NCT05508906)
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

Palazestrant Phase 1b/2 in Combination with Palbociclib

Of 46 patients, 72% had prior CDK4/6i treatment, 43% with baseline ESR1 mutations

Patient Characteristics	Total (N=46)
Median age (years)	64
Range	30–77
ECOG performance status, n (%)	
0	31 (67%)
1	15 (33%)
Measurable disease at baseline, n (%)	36 (78%)
Visceral disease, n (%)	20 (44%)
Prior lines of therapy in advanced setting, n (%)	
0	4 (9%)
1	34 (74%)
2	8 (17%)[a]
Prior lines of endocrine therapy in advanced setting, n (%)	
0	6 (13%)
1	40 (87%)
Types of prior therapy in advanced setting, n (%)	
CDK4/6 inhibitor	33 (72%)[b]
Aromatase inhibitor (AI)	35 (76%)
Fulvestrant	5 (11%)
Chemotherapy	10 (22%)
ESR1 mutations at baseline (ctDNA), n/N (%)	16/37 evaluated (43%)

- 91% of patients were 2/3L+ at study entry; 44% visceral disease; 22% non-measurable disease
- 72% received prior CDK4/6i; 76% received prior AI; 22% received prior chemotherapy
- 43% had activating mutations in ESR1

[a]One patient received chemotherapy, endocrine therapy, and olaparib.
[b]Prior CDK4/6 inhibitors include palbociclib (n=22), ribociclib (n=10), both palbociclib and ribociclib (n=1).
Abbreviations: **AI,** aromatase inhibitor; **CDK4/6i**, cyclin-dependent kinase 4/6 inhibitor; **ctDNA,** circulating tumor DNA; **ECOG**, Eastern Cooperative Oncology Group.
Data Cutoff Date: September 15, 2023

Palazestrant Phase 1b/2 in Combination with Palbociclib

Well tolerated with no DLTs; No dose-related increase in TEAEs

Most Common Treatment-Emergent Adverse Events

TEAEs in ≥20% of Patients	Olema Study 002 Palbociclib + Palazestrant[a]			PALOMA-3 Comparison Palbociclib + Fulvestrant[b,c]		
	All Doses (n=46)			(n=345)		
	All grades	Grade 3	Grade 4	All grades	Grade 3	Grade 4
Neutropenia[d]	40 (87%)	28 (61%)	5 (11%)	96%[e]	56%[e]	11%[e]
Nausea	26 (57%)	0	0	34%	0%	0%
Vomiting	17 (37%)	0	0	19%	1%	0%
Anemia	12 (26%)	1 (2%)	0	30%	4%	0%
Diarrhea	11 (24%)	0	0	24%	0%	0%
Constipation	10 (22%)	1 (2%)	0	NA	NA	NA
Fatigue	10 (22%)	1 (2%)	0	41%	2%	0%
Thrombocytopenia	10 (22%)	0	0	23%	2%	1%

- No dose-limiting toxicities (DLTs) were observed during dose escalation
- No dose-related increases in the incidence or severity of TEAEs was observed
- Overall safety and tolerability profile consistent with palbociclib + aromatase inhibitors 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: September 15, 2023. Data shown are n or n (%). Abbreviations: **DLTs,** dose-limiting toxicities; **TEAE,** treatment-emergent adverse event.

[a]Includes 3 patients at each of 30 mg, 60 mg, and 90 mg palazestrant and 37 patients at 120 mg palazestrant in combination with 125 mg palbociclib.

[b]Source: Palbociclib package insert referencing Paloma-3 trial results. [c]Adverse reactions reported in ≥10% of patients who received palbociclib plus fulvestrant in the PALOMA-3 study.

[d]Combined term includes neutropenia and decreased neutrophil count. [e]Reported as neutrophil count decreased in the laboratory abnormalities in the PALOMA-3 study.

Palazestrant Phase 1b/2 in Combination with Palbociclib

Reduced AEs related to palazestrant or palbociclib

Most Common Treatment-Related Adverse Events

TRAEs in ≥20% of Patients	Olema Study 002 Palbociclib + Palazestrant[a]		
	All Doses (n=46)		
	All grades	Grade 3	Grade 4
Neutropenia[b]	40 (87%)	28 (61%)	5 (11%)
Nausea	23 (50%)	0	0
Vomiting	12 (26%)	0	0
Anemia	11 (24%)	1 (2%)	0
Thrombocytopenia	10 (22%)	0	0

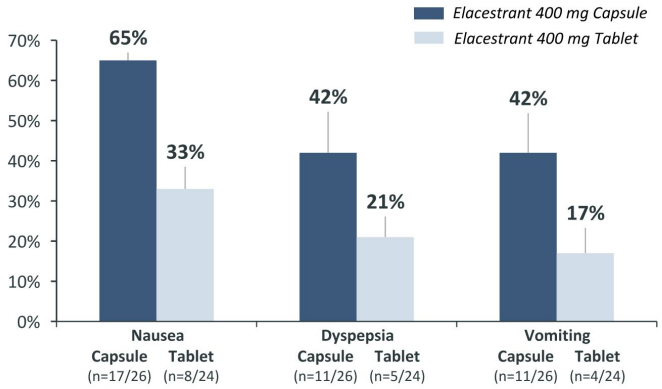
- Most common TRAE is neutropenia with majority occurring in cycle 1
- Patients had utilized capsule formulation; tablet formulation to be utilized going forward

Data Cutoff Date: September 15, 2023.
Data shown are n or n (%).
Abbreviations: **DLTs,** dose-limiting toxicities; **TRAE,** treatment-related adverse event.
[a]Includes 3 patients at each of 30 mg, 60 mg, and 90 mg palazestrant and 37 patients at 120 mg palazestrant in combination with 125 mg palbociclib.
[b]Combined term includes neutropenia and decreased neutrophil count

Elacestrant Experience with Switching from Capsule to Tablet

Potential to improve palazestrant upper GI tolerability with tablet formulation

Elacestrant Upper GI TEAEs in All Patients[2] (All Grades)



- Elacestrant demonstrated less GI tolerability AEs with its tablet formulation vs. capsules[1,2]
  - All GI events were approximately halved in frequency with the tablet compared with capsules
  - Authors suggested the improvement in GI effects with tablets may be due to reduced number of pills required and/or dissolution of the tablet lower in the GI tract

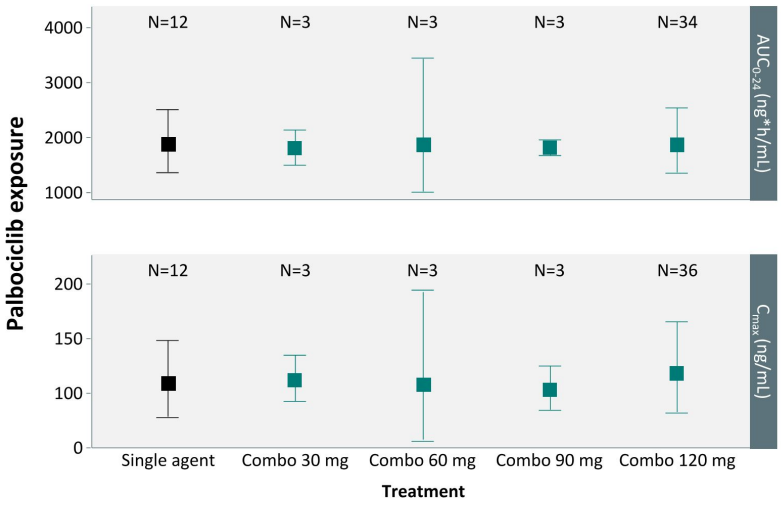
Abbreviations: **GI,** gastrointestional; **TEAE,** treatment-emergent adverse event

Source: (1) Kaklamani, V, et al. "Abstract PD7-07: final analysis of phase 1 study of elacestrant (RAD1901), a novel selective estrogen receptor degrader (SERD), in estrogen receptor positive (ER+), human epidermal growth factor receptor 2 negative (HER2-) advanced breast cancer." Cancer Research 80.4_Supplement (2020): PD7-07; (2) Bardia A, et al. Phase I Study of Elacestrant (RAD1901), a Novel Selective Estrogen Receptor Degrader, in ER-Positive, HER2-Negative Advanced Breast Cancer. CO. 2021;39(12):1360-1370

Palazestrant Phase 1b/2 in Combination with Palbociclib

No effect of palazestrant on palbociclib exposure levels across dose levels

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



Pharmacokinetics

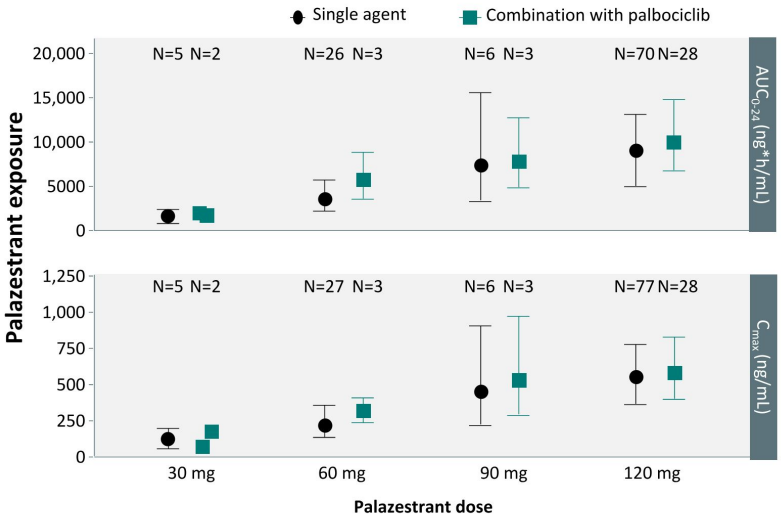
- No drug-drug interaction (DDI) between palbociclib and palazestrant in the dose range of 30 to 120 mg
- Palazestrant did not affect palbociclib 125 mg exposure when compared with published concentrations for single-agent palbociclib
- Exposure of palbociclib was within 90% of reported mean values for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

Data Cutoff Date: September 15, 2023.
Note: Data are geometric mean ± geometric standard deviation.
Abbreviations: **AUC_{0-24}**, area under the curve from 0 to 24 h; **C_{max}**, maximum concentration; **Combo**, combination.

Palazestrant Phase 1b/2 in Combination with Palbociclib

No effect of palbociclib on palazestrant exposure levels compared to monotherapy

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



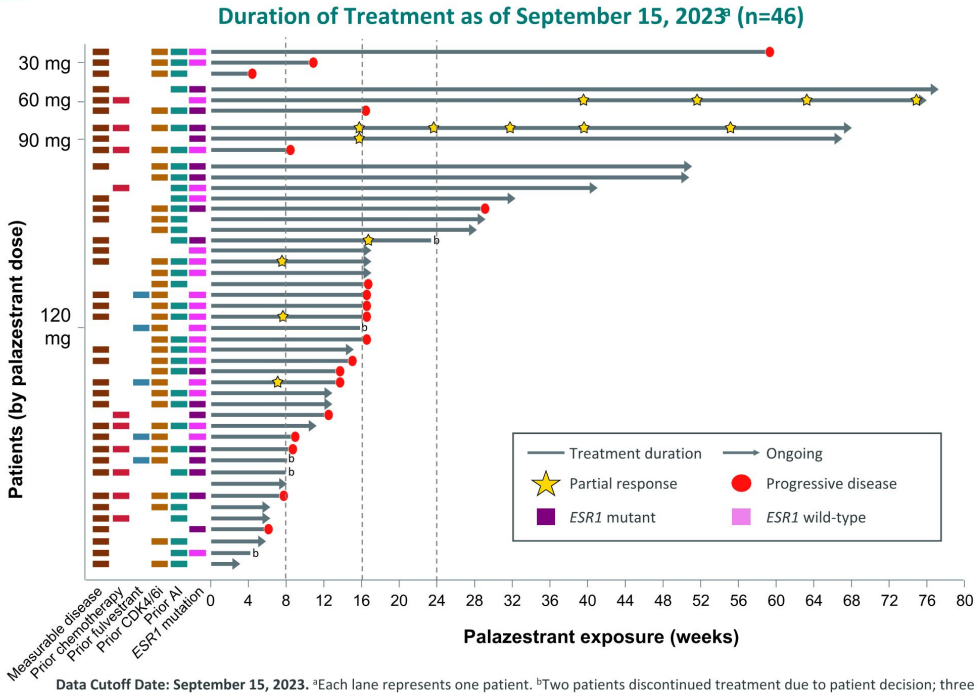
Data Cutoff Date: September 15, 2023.
Note: Data are geometric mean ± geometric standard deviation.
Abbreviations: **AUC_{0-24}**, area under the curve from 0 to 24 h; **C_{max}**, maximum concentration; **Combo**, combination.

Pharmacokinetics

- No DDI between palbociclib and palazestrant in the dose range of 30 to 120 mg
- Palbociclib did not affect palazestrant exposure at any dose level
- Palazestrant was readily bioavailable and demonstrated dose-proportional exposures (across dose range of 30 and 120 mg) and a long half-life
- Steady-state plasma levels show minimal peak-to-trough variability, enabling consistent inhibition of the estrogen receptor for the full dosing interval

Palazestrant Phase 1b/2 in Combination with Palbociclib

Preliminary efficacy signals shown in both wild-type and ESR1 mutant patients



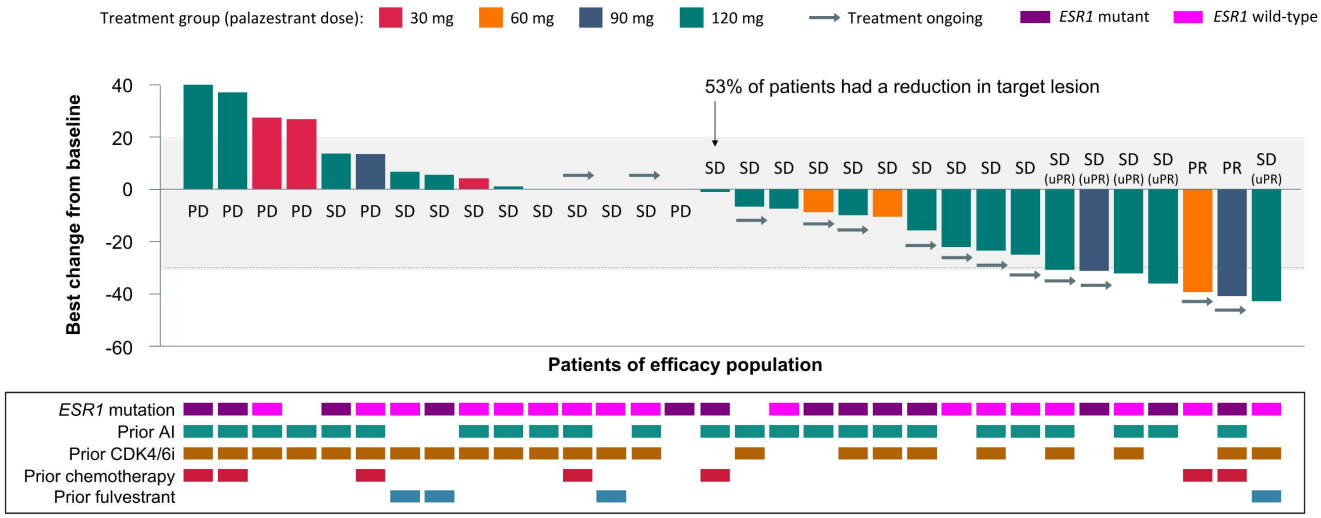
- Activity shown in both wild-type and $ESR1_{MUT}$ patients
- Interim partial responses were observed in seven patients of 32 (two confirmed; five unconfirmed)
- Interim clinical benefit rate^ was:
  - 46% across all patients (12/26 CBR-eligible patients)
  - 60% for $ESR1_{MUT}$ patients (6/10 CBR-eligible patients)
  - 71% for CDK4/6i-naïve patients (5/7 CBR-eligible patients)
- Efficacy data are maturing; 22 patients (48%) remain on treatment and enrollment ongoing
- Longest duration of treatment is 76 weeks and is ongoing; 5 patients remained on therapy >52 weeks

Data Cutoff Date: September 15, 2023. [a]Each lane represents one patient. [b]Two patients discontinued treatment due to patient decision; three discontinued due to physician decision.
Abbreviations: **AI,** aromatase inhibitor; **CDK4/6i,** cyclin-dependent kinase 4/6 inhibitor; **ESR1,** estrogen receptor 1 gene
^ Clinical benefit rate is the proportion of patients who remained on treatment through at least 24 weeks with a confirmed CR or PR, or stable disease.

Palazestrant Phase 1b/2 in Combination with Palbociclib

Anti-tumor activity shown in both wild-type and ESR1 mutant patients

Best percent change from baseline in target lesions and best overall response as of September 15, 2023[a]



53% of patients had any reduction in target lesion size

Data Cutoff Date: September 15, 2023

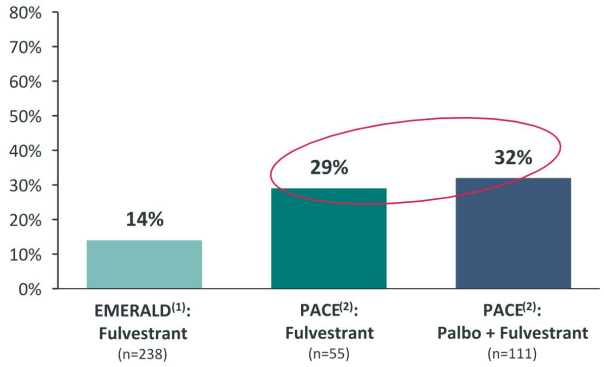
[a]Each lane represents one patient.

Abbreviations: **AI,** aromatase inhibitor; **CDK4/6i,** cyclin-dependent kinase 4/6 inhibitor; **ESR1,** estrogen receptor 1 gen; **PD**, progressive disease; **PR**, partial response (confirmed); **SD**, stable disease; **uPR**, partial response (unconfirmed).

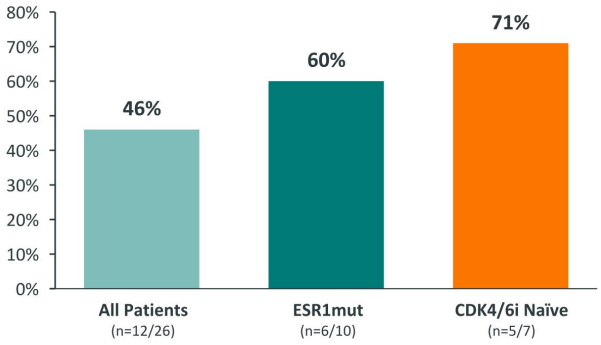
Preliminary Combination Clinical Benefit Rate in 2/3L+ Patients

PACE study indicated palbociclib rechallenge ineffective relative to fulvestrant control

Benchmark Clinical Benefit Rate: Fulvestrant vs. Palbociclib + Fulvestrant



Olema Study 002 Interim Clinical Benefit Rate: Palazestrant + Palbociclib



Promising signals of early efficacy for palazestrant in combination with palbociclib

*** 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: September 15, 2023.

1. Source: SABCS 2021 EMERALD data. Median PFS, CBR, and ORR in control arm.
2. Source: SABCS 2022 PACE data. Median PFS, CBR, and ORR in control arm and in fulvestrant with palbociclib.

Palazestrant Palbociclib Combination – Competitive Landscape

Other SERDs in development have encountered challenges combining with CDK4/6 inhibitors

Treatment	Palazestrant	Camizestrant	Giredestrant	Vepdegestrant
Study	Phase 1b/2	Phase 1 (parts C/D) (SERENA-1)	Phase 1b	Phase 1b (part C)
Dose	120 mg / 125 mg (palbo)	75 mg / "palbo label"	100 mg# / 125 mg (palbo)	200 or 500 mg / 125^ mg (palbo)
Trial Size	46 (37 w/ 120 mg palazestrant)	25	48	46 (21 w/ 200 mg vepdegestrant)
Prior Tx	0 – 2 Lines 72% prior CDK4/6i	68% prior fulvestrant 80% prior CDK4/6i	7% prior fulvestrant **0% prior CDK4/6i**	80% prior fulvestrant 87% prior CDK4/6i
Non-Measurable	22%	32%	NA	33%
$ESR1_{MUT}$	43%	44%	29%	**63%**
Notable TEAEs	• G4 neutropenia (11%) • Nausea (57%) • Vomiting (37%)	• Visual effects (44%) • Bradycardia (16%) • G4 neutropenia (12%)	• Diarrhea (33%) • Bradycardia (31%)	• G4 neutropenia (**38%** @200 mg /**45%** @500 mg) • QT prolongation (19% @200 mg / 30% @500 mg) • 24% palbo discontinuation rate @ 200 mg; 15% @ 500 mg
DDI	No	No	None clinically relevant	46 - 58% increase in palbo exposure
CBR	46% All / 60% for $ESR1_{MUT}$	28%	81%(1)	63%(2)
Source	SABCS 2023	ASCO 2022	ASCO 2020	SABCS 2023

*** 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.**

[1]Less relevant given all patients were CDK4/6i naïve, with lower dose of giredestrant 30mg being explored in future trials.

[2]Less relevant given substantial increase in palbociclib drug exposure, with lower dose palbociclib and vepdegestrant 200 mg being explored in Phase 3 trial.

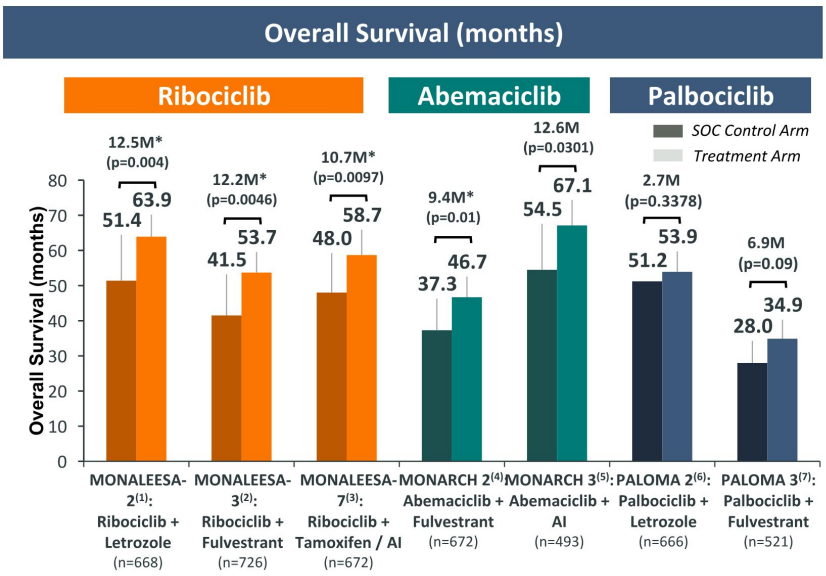
Exploring 30mg dose in future trials given bradycardia and diarrhea. ^ Dose finding palbociclib in future trials given neutropenia.

Note: PALOMA-3 palbociclib + fulvestrant G4 neutropenia (11%), palbociclib + fulvestrant discontinuation rate (6%)

Source: Mittal, A., Filling the Gap after CDK4/6 Inhibitors: Novel Endocrine and Biologic Treatment Options for Metastatic Hormone Receptor Positive Breast Cancer. *Cancers*, 2023; *15*(7), 2015

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

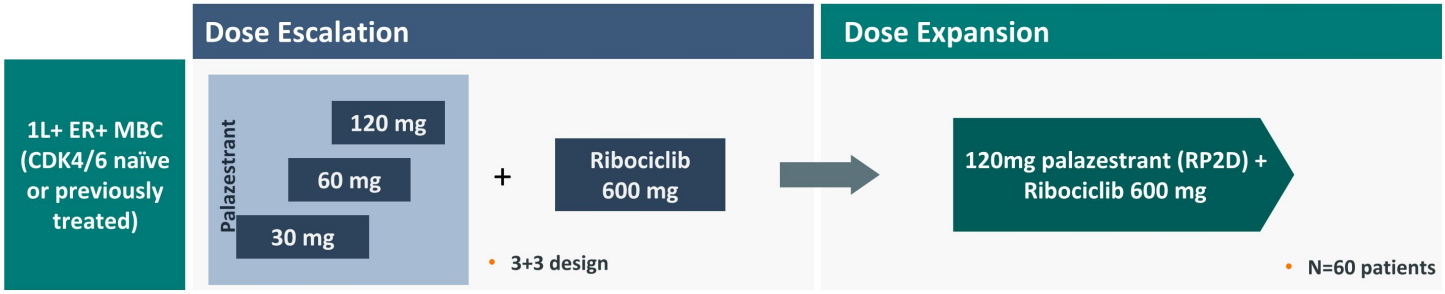


- No statistically significant OS benefit for palbociclib 1L combinations or for abemaciclib + AI
- NCCN guidelines recommend three regimens that have shown OS benefit in Phase 3 randomized controlled studies as **Category 1 preferred** for 1L treatment of patients with HR+/HER2- mBC :
  - ribociclib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

*** 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) Johnston S., et al. MONARCH 3 Final PFS: A Randomized Study of Abemaciclib as Initial Therapy for Advanced Breast Cancer. NPJ Breast Cancer. 2019;5:5; (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

Phase 1b/2 Combination Study with Ribociclib



Primary objectives: Pharmacokinetics, safety and tolerability, identify RP2D of palazestrant for combination with either ribociclib or alpesilib
Secondary objectives: ORR (CR + PR), CBR (CR + PR + SD ≥24 weeks)

Objectives: Safety, tolerability and antitumor activity of palazestrant at RP2D in combination with either ribociclib or alpesilib

Key* Inclusion Criteria:

- ER+/HER2- advanced breast cancer
- Evaluable disease (measurable and non-measurable)
- ≤ 2 prior hormonal regimen for locally advanced or metastatic disease
- One prior line of chemotherapy for advanced or MBC was allowed
- Can be CDK4/6i naïve or pre-treated

* Full eligibility criteria for NCT05508906 on clinicaltrials.gov (https://clinicaltrials.gov/study/NCT05508906)
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

Palazestrant Phase 1b/2 in Combination with Ribociclib

Of 19 patients, 89% had prior CDK4/6i treatment, 29% with baseline ESR1 mutations

Patient Characteristics	Total (N=19)
Median age (years)	59
Range	37–85
ECOG performance status, n (%)	
0	7 (37%)
1	12 (63%)
Measurable disease at baseline, n (%)	12 (63%)
Visceral disease, n (%)	7 (37%)
Prior lines of therapy in advanced setting, n (%)	
1	8 (42%)
2	8 (42%)
3	3 (16%)
Prior lines of endocrine therapy in advanced setting, n (%)	
0	0
1	10 (53%)
2	9 (47%)
Types of prior therapy in advanced setting, n (%)	
CDK4/6 inhibitor	17 (89%)[a]
Aromatase inhibitor (AI)	16 (84%)
Fulvestrant	10 (53%)
Chemotherapy	5 (26%)
ESR1 mutations at baseline (ctDNA), n/N (%)	5/17 evaluated (29%)

- 100% of patients were 2/3L+ at study entry; 37% visceral disease
- 89% received prior CDK4/6i; 84% received prior AI; 26% received prior chemotherapy
- 29% had activating mutations in ESR1

[a]Twelve patients received one prior line of CDK 4/6 inhibitors: palbociclib (n=11), or ribociclib (n=1), five patients received prior lines of therapy that included two CDK4/6 inhibitors: palbociclib and abemaciclib (n=2), palbociclib and ribociclib (n=2), palbociclib and an experimental CDK4/6 inhibitor (n=1).
Abbreviations: **AI**, aromatase inhibitor; **CDK4/6i**, cyclin-dependent kinase 4/6 inhibitor; **ctDNA**, circulating tumor DNA; **ECOG**, Eastern Cooperative Oncology Group.
Data Cutoff Date: November 1, 2023

Palazestrant Phase 1b/2 in Combination with Ribociclib

Well tolerated with no DLTs; No grade 4 TEAEs reported

Most Common Treatment-Emergent Adverse Events

TEAEs in ≥20% of Patients	Olema Study 003 Ribociclib + Palazestrant[a]			MONALEESA-2 Ribociclib + Letrozole[b,c]		
	(n=19)			(n=334)		
	All grades	Grade 3	Grade 4	All grades	Grade 3	Grade 4
Nausea	12 (63%)	1 (5%)	0	52%	2%	0%
Neutropenia[d]	11 (58%)	7 (37%)	0	93%[e]	49%[e]	11%[e]
WBC decr.	8 (42%)	2 (11%)	0	93%[e]	31%[e]	3%[e]
Anemia	7 (37%)	1 (5%)	0	57%[e]	2%[e]	0%[e]
Fatigue	7 (37%)	1 (5%)	0	37%	2%	<1%
Constipation	5 (26%)	0	0	25%	1%	0%
Diarrhea	5 (26%)	0	0	35%	1%	0%
Hyperglycemia	4 (21%)[#]	0	0	NA	NA	NA
Hypotension	4 (21%)	0	0	NA	NA	NA

- No DLTs were observed during dose escalation and MTD was not reached
- No dose-related increases in the incidence or severity of TEAEs was observed
- **No grade 4 TEAEs reported**
- No QTcF values of >500 msec were observed at any time point
- 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: November 1, 2023. Data shown are n or n (%).
Abbreviations: **DLTs,** dose-limiting toxicities; **TEAE,** treatment-emergent adverse event.
[#]All events Grade 1; 3 events unrelated to palazestrant or ribociclib; 1 event related to both drugs
[a]Includes 3 patients at each of 30 mg and 60 mg palazestrant and 13 patients at 120 mg palazestrant in combination with 600 mg ribociclib. [b]Source: NVS Kisqali (ribociclib) Prescribing Information, 2017
[c]Adverse reactions reported in ≥10% of patients who received ribociclib plus letrozole in the MONALEESA-2 study. [d]Combined term includes neutropenia and decreased neutrophil count.
[e]Reported as neutrophil count, hemoglobin, and leukocyte decreased in the laboratory abnormalities in the MONALEESA-2 study.

Palazestrant Phase 1b/2 in Combination with Ribociclib

Reduced AEs related to palazestrant or ribociclib

Most Common Treatment-Related Adverse Events

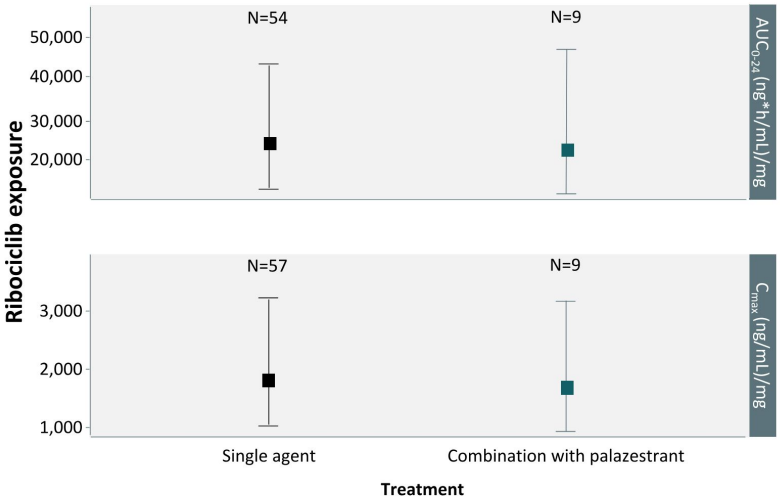
TRAEs in ≥20% of Patients	Olema Study 003 Ribociclib + Palazestrant[a]		
	(n=19)		
	All grades	Grade 3	Grade 4
Neutropenia[b]	11 (58%)	7 (37%)	0
Nausea	11 (58%)	1 (5%)	0
WBC decr.	8 (42%)	2 (11%)	0
Anemia	6 (32%)	1 (5%)	0
Fatigue	5 (26%)	0	0
Diarrhea	4 (21%)	0	0

Data Cutoff Date: November 1, 2023. Data shown are n or n (%).
Abbreviations: **DLTs,** dose-limiting toxicities; **TRAE,** treatment-related adverse event.
[a]Includes 3 patients at each of 30 mg and 60 mg palazestrant and 13 patients at 120 mg palazestrant in combination with 600 mg ribociclib.
[b]Combined term includes neutropenia and decreased neutrophil count.

Palazestrant Phase 1b/2 in Combination with Ribociclib

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))



Pharmacokinetics

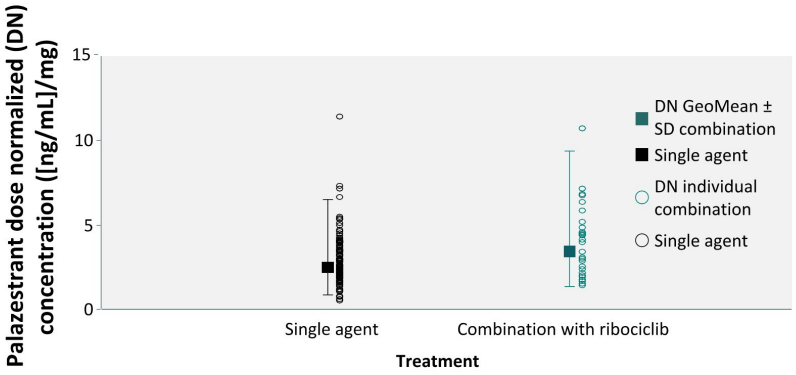
- No drug-drug interaction (DDI) between ribociclib and palazestrant in the dose range of 30 to 120 mg
- Palazestrant did not affect ribociclib 600 mg exposure when compared with published concentrations for single-agent ribociclib
- Exposure of ribociclib was within of reported range of the 600 mg dose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

Data Cutoff Date: November 1, 2023.
Note: Data are geometric mean ± geometric standard deviation.
Abbreviations: **AUC_{0-24}**, area under the curve from 0 to 24 h; **C_{max}**, maximum concentration.

Palazestrant Phase 1b/2 in Combination with Ribociclib

Effect of ribociclib on palazestrant exposure levels not clinically meaningful

Palazestrant (OP-1250) Steady State Trough Concentration (Alone and in Combination with Ribociclib (600 mg)) (n=9)



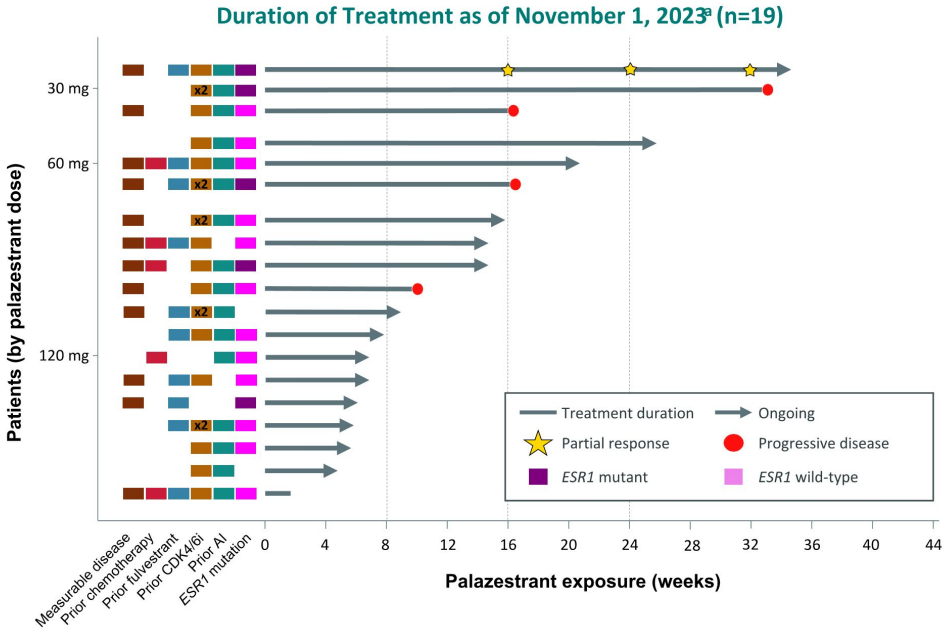
Pharmacokinetics

- Steady-state trough values overlapped between the combination and single agent palazestrant, with a small increase in mean exposure
- Ribociclib has no meaningful effect on palazestrant exposure

Data Cutoff Date: November 1, 2023.
Note: Data are geometric mean ± geometric standard deviation.
Abbreviations: **$AUC_{0\text{-}24}$**, area under the curve from 0 to 24 h; **C_{max}**, maximum concentration.

Palazestrant Phase 1b/2 in Combination with Ribociclib

Preliminary efficacy data, Data are maturing



- Confirmed partial response has been observed in one patient to date (30mg palazestrant)
- Longest duration of treatment is 34 weeks
- Efficacy data are maturing; 14/19 patients (74%) remain on treatment; enrollment ongoing

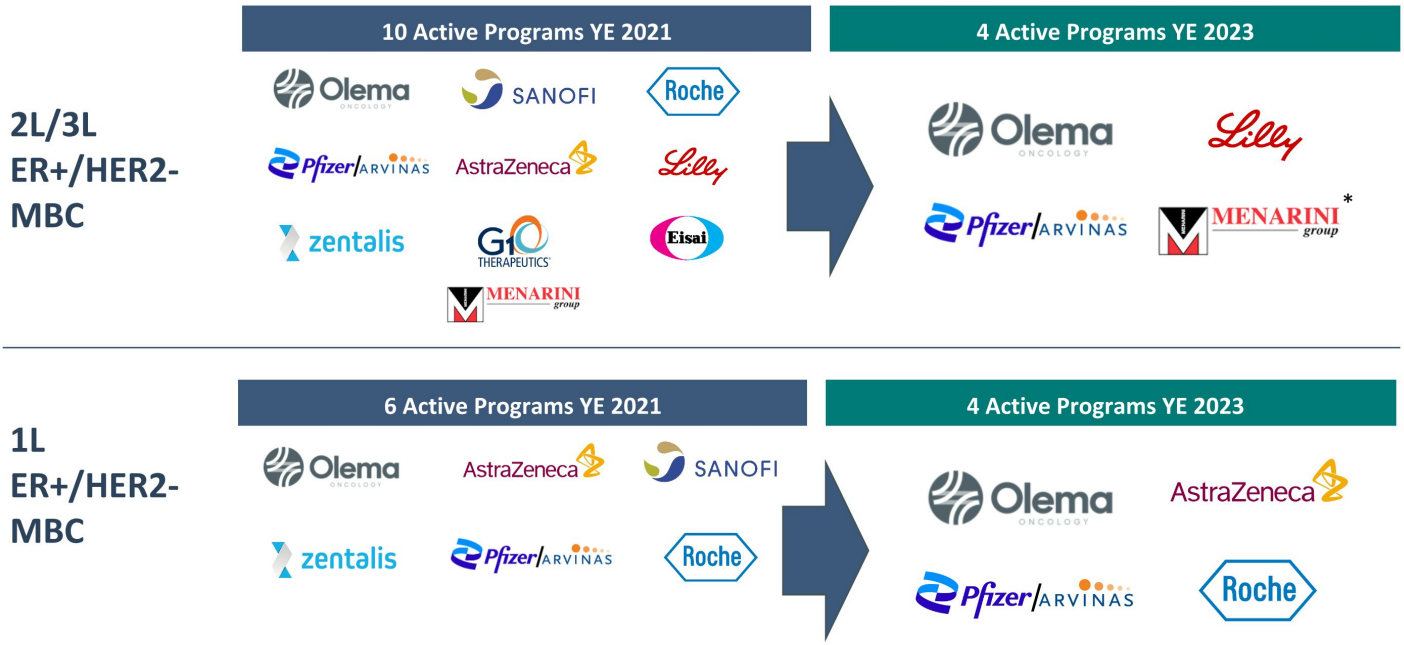
Data Cutoff Date: November 1, 2023.

[a]Each lane represents one patient.

Abbreviations: **AI,** aromatase inhibitor; **CDK4/6i,** cyclin-dependent kinase 4/6 inhibitor; **ESR1,** estrogen receptor 1 gene


Advancing in
Pivotal Phase 3 Trials
Olema
ONCOLOGY

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



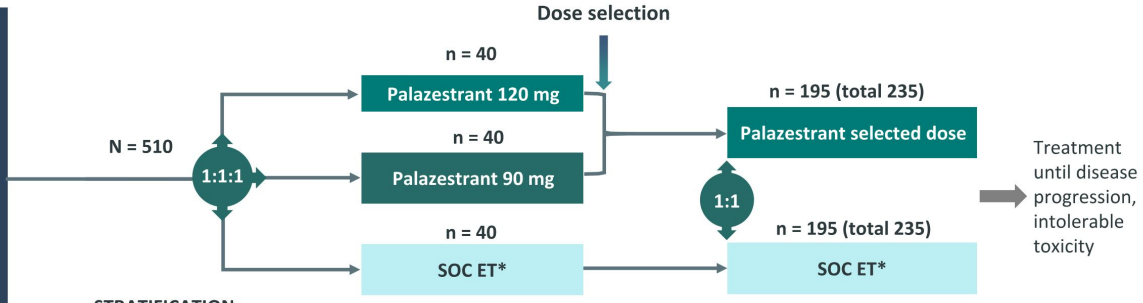
*Menarini's drug ORSERDU (elacestrant) was approved by the U.S. FDA on January 27, 2023.

OPERA-01 Phase 3 Trial Overview

510-patient 2/3L monotherapy trial vs. standard of care

KEY INCLUSION CRITERIA:

- ER+/HER2- mBC
- Evaluable disease (measurable or bone only)
- 1-2 prior lines of endocrine therapy
- Prior treatment with a CDK4/6 inhibitor
- Minimum 6 months on last ET



STRATIFICATION:
1. Visceral metastasis: Yes vs No
2. Prior ET lines: 1 vs 2
3. ESR1 mut vs ESR1 mut-nd

* Fulvestrant (recommended for patients who had not previously received fulvestrant), letrozole, anastrozole or exemestane (with GnRH agonist for premenopausal women or men)

STUDY END POINTS

(Part 1 combined with Part 2)

PRIMARY ENDPOINTS:
PFS (BIRC) ESR1 mut
PFS (BIRC) ESR1 mut-nd

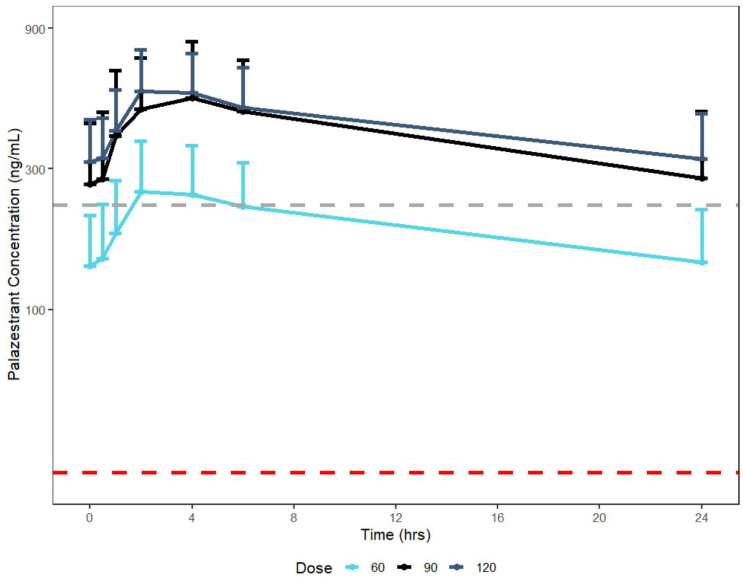
KEY SECONDARY ENDPOINTS:
OS ESR1 mut
OS ESR1 mut-nd

SECONDARY:
PFS (local) ESR1 mut / ESR1 mut-nd / all
ORR/CBR/DOR (BIRC and local) in ESR1 mut / ESR1 mut-nd / all
Safety
PK
PRO (QLQ-C30, EQ-5D)

Abbreviations: **BIRC,** Blinded Independent Central Review; **CBR,** clinical benefit rate; **CDK,** cyclin-dependent kinase; **DOR,** duration of response; **ER+,** estrogen receptor-positive; **ESR1,** estrogen receptor 1; **ESR1 mut,** ESR1 mutated; **ET,** endocrine therapy; **GnRH,** gonadotropin-releasing hormone; **HER2–,** human epidermal growth factor receptor 2-negative; **mBC,** metastatic breast cancer; **mut-nd,** without detectable ESR1 mutation; **ORR,** overall response rate; **OS;** overall survival; **PFS,** progression free survival; **PK,** pharmacokinetics; **PRO,** patient reported outcomes; **SOC,** standard of care

Palazestrant 90 mg and 120 mg Steady State Exposures are Above Target

Steady-state Palazestrant Single Agent and Combination Data[a]

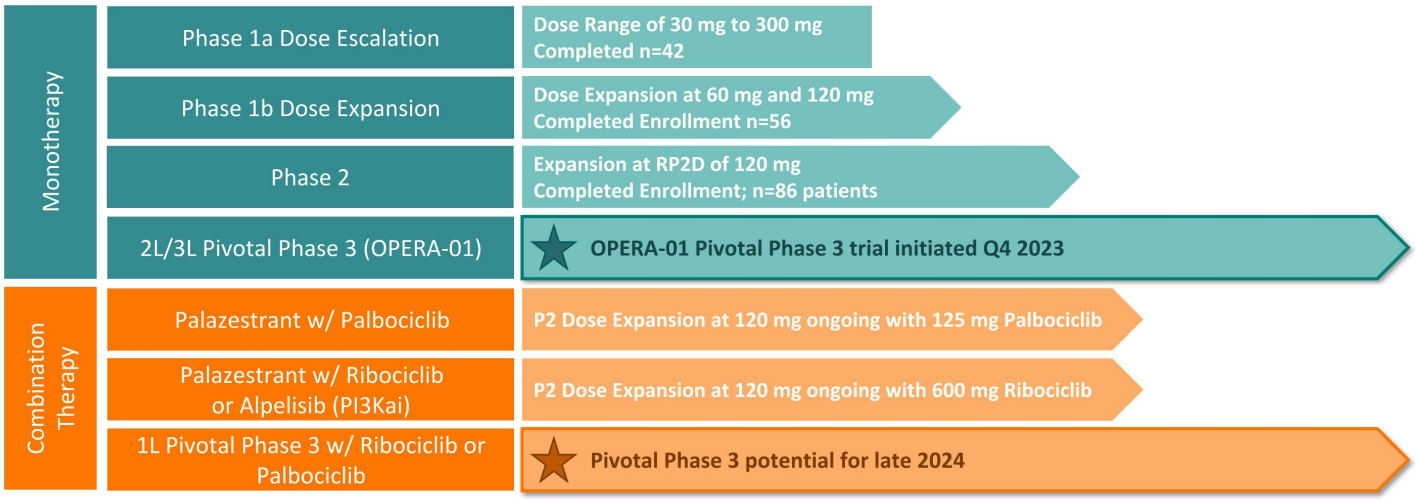


Dashed grey line =Target efficacious exposure based on estradiol supplemented preclinical models Cmin =226 ng/mL
Dashed red line=Cmax for fulvestrant at steady state[b]

a. Data from studies OP-1250-001 and OP-1250-002 combined
b. Fulvestrant product insert Faslodex (fulvestrant) injection label (fda.gov)

- High oral bioavailability and steady-state plasma levels with minimal peak-to-trough variability allowing complete inhibition of the ER for the full dosing interval
- Dosing at the RP2D of 120 mg and at 90 mg yields drug exposures that exceed the predicted efficacious threshold based on pre-clinical models
- Mean terminal half-life ($T_{1/2}$)= 8 days, supporting once-daily dosing

Advancing Palazestrant in Pivotal Phase 3 Studies



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

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 ribociclib or palbociclib – no clinically meaningful DDI* and overall tolerability profile consistent with expected profile of CDK4/6i plus endocrine therapy

CNS Penetration

Demonstrated activity in nonclinical brain metastases studies

*As of September 15, 2023 (palbociclib combination) and as of November 1, 2023 (ribociclib combination), interim update of combination study with Palbociclib or Ribociclib at SABCS 2023. DDI = Drug-Drug Interaction.

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 ~$276.9M of cash and cash equivalents as of September 30, 2023[1]

[1] Cash position as of September 30, 2023. Management believes that the Company's cash, cash equivalents, marketable securities, and the amounts available under the Loan and Security Agreement with Silicon Valley Bank will be sufficient to fund the Company's current operating plan into 2027.

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