SABCS 2024

Palazestrant in Combination with Ribociclib Clinical Update

December 10, 2024

Legal disclaimer

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 candidates or any other future product candidates, strategy, market size and opportunity, clinical trial designs, regulatory matters, including the timing and likelihood of success of obtaining drug approvals, the timelines for the potential initiation of clinical trials and the results of any such 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 timelines for potential commercial launch and related preparatory work, the sufficiency and potential beneficial characteristics, profile, safety, tolerability, efficacy and therapeutic effects of palazestrant as a monotherapy and in combination trials, the progression-free survival rate under palazestrant in combination trials, the potential of palazestrant to become a therapeutic leader and a best-in-class treatment option for ER+/HER2- metastatic breast cancer and a backbone therapy for women living with breast cancer and beyond, the combinability of palazestrant with other drugs, the timelines for initiation of potential clinical trials for and the results of any such clinical trials in connection with our KAT6 inhibitor program, including OP-3136, the potential value and impact of a KAT6 inhibitor program, the best-in-class potential for OP-3136, the potential beneficial characteristics, profile, safety, efficacy, tolerability, and therapeutic effects of OP-3136, our ability to complete certain milestones, our financial condition, our opportunity in breast cancer and beyond, our ability to impact treatment for endocrine-driven cancers, cash position and runway and sufficiency of our financial resources, and the sufficiency and expertise 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, or OP-3136 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.

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— We are on a mission to elevate patient care in breast cancer and beyond

Molecular Advantage

Expertise in endocrine-driven cancers with mechanistically superior scientific approach that fully inactivates estrogen receptors

Lead Asset – Palazestrant

OP-1250, a promising potential backbone therapy for ER+/HER2- breast cancer in late-stage clinical development, forms basis of breast cancer program

OP-3136 Expands Pipeline

Exciting new and potent KAT6 inhibitor with potential to significantly impact breast cancer treatment; IND cleared by FDA and initiation of Phase 1 clinical trial anticipated early 2025

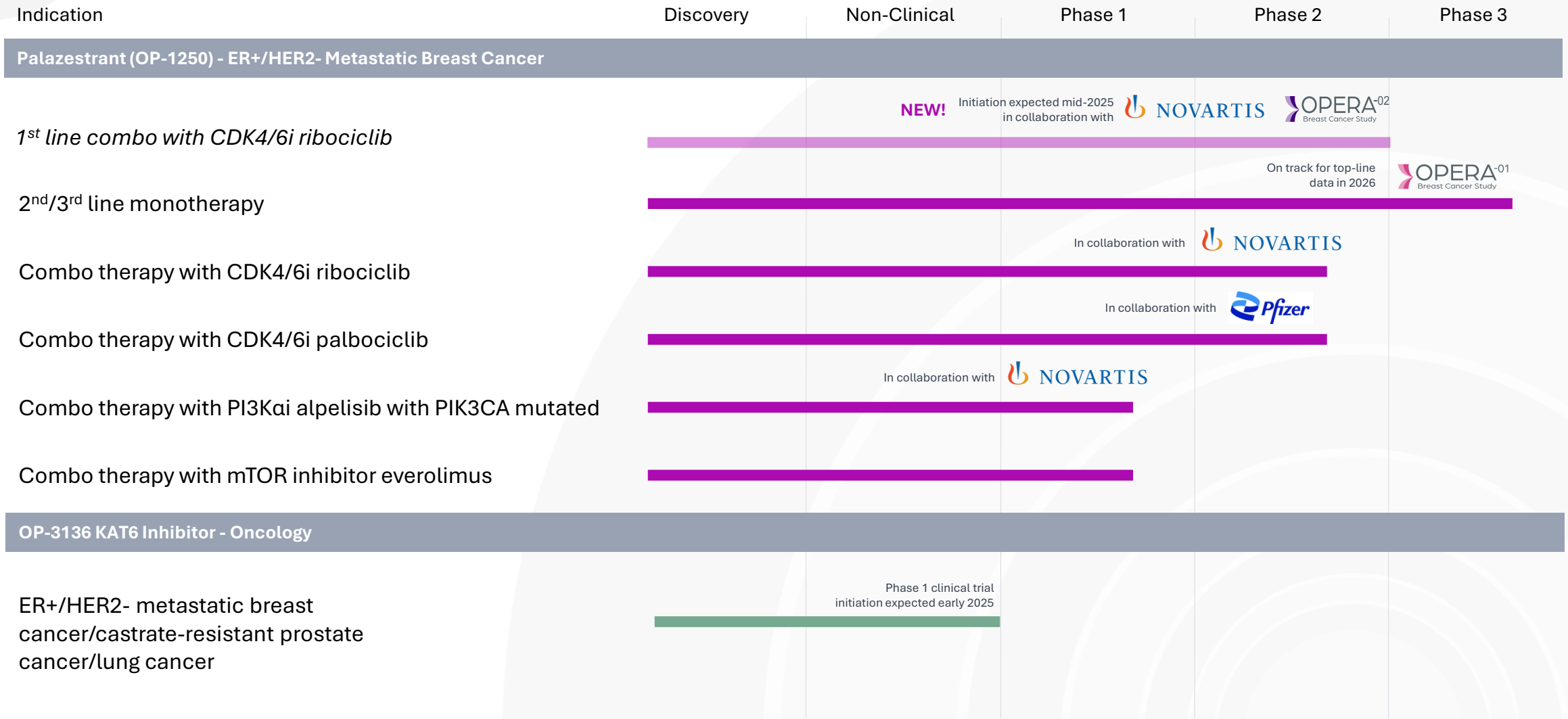
Proven Leadership

Management and Board with deep expertise developing and commercializing oncology medicines

Olema ONCOLOGY

Rapidly advancing clinical pipeline

Palazestrant second/third-line and first-line clinical trials in metastatic breast cancer



KAT6 = lysine acetyltransferase 6; **ER** = estrogen receptor; **HER2** = human epidermal growth factor receptor 2; **CDK4/6i** = cyclin-dependent kinase 4/6 inhibitor; **PI3Kαi** = phosphatidylinositol 3-kinase alpha inhibitor; **mTORi** = mammalian target of rapamycin inhibitor; **PI3Kαi** = phosphoinositide-3 kinase alpha-specific inhibitors; **PI3KCA** = phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha

“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 (ER+/HER2-), advanced or metastatic breast cancer”

SABCS 2024 Poster #P2-09-16

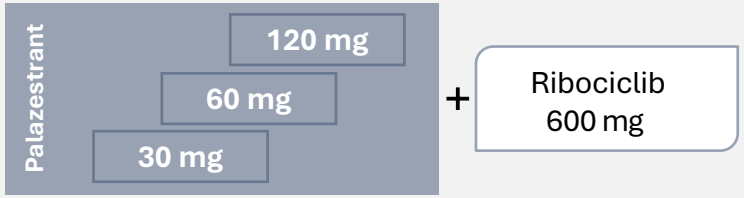
Phase 1b/2 combination study design

ER+/HER2- advanced or metastatic breast cancer (CDK4/6i-naïve or previously treated)

Key eligibility criteria

- Women or men with ER+/HER2– advanced or metastatic breast cancer
- Up to 2 prior endocrine therapies ± a CDK4/6i for locally advanced or metastatic disease; up to 1 prior line of chemotherapy for advanced or metastatic breast cancer was allowed
- Evaluable disease (measurable by RECIST v1.1 or bone only)
- Screening QTcF <450 ms, resting heart rate 50-90 beats/min

Part 1: Dose escalation



Primary endpoints: DLTs, MTD and/or RP2D of palazestrant when administered in combination with ribociclib, incidence and severity of adverse events, PK

Secondary endpoints: ORR (CR + PR), CBR (CR + PR + SD ≥ 24 weeks), DOR

Part 2: Dose expansion

Palazestrant 120 mg + Ribociclib 600 mg

Primary endpoints: incidence and severity of adverse events, PK

Secondary endpoints: ORR (CR + PR), CBR (CR + PR + SD ≥ 24 weeks), DOR, time to progression, PFS

CDK4/6i = cyclin-dependent kinase 4/6 inhibitor; **CBR** = clinical benefit rate; **CR** = complete response; **ctDNA** = circulating tumor DNA; **DLT** = dose-limiting toxicity; **DOR** = duration of response; **MTD** = maximum tolerated dose; **ORR** = objective response rate; **PK =** pharmacokinetics; **PR** = partial response; **QTcF** = QT corrected for heart rate using Fridericia's formula **RECIST** = response evaluation criteria in solid tumors; **RP2D** = recommended Phase 2 dose; **SD** = stable disease

Demographics

Patient Characteristics	Total (N=62)
Median age (years)	61
Range	28–85
Female sex	62 (100%)
Premenopausal	9 (15%)
ECOG performance status, n (%)	
0	38 (61%)
1	24 (39%)
Measurable disease at baseline, n (%)	42 (68%)
Visceral disease, n (%)	36 (58%)
Prior lines of therapy in advanced setting, n (%)	
0	14 (23%)
1	29 (47%)
2	14 (23%)
3	5 (8%)
Prior lines of endocrine therapy in advanced setting, n (%)	
0	14 (23%)
1	35 (56%)
2	13 (21%)
Types of prior therapy in advanced setting, n (%)	
CDK4/6 inhibitor	46 (74%)
Aromatase inhibitor (AI)	33 (53%)
Fulvestrant	25 (40%)
Chemotherapy	11 (18%)
***ESR1* mutations at baseline (ctDNA), n/N (%)**	17/60[a] evaluated (28%)

- N=62; N=56 at 120 mg
- 58% with visceral disease
- 68% with measurable disease
- 77% received prior endocrine therapy in advanced setting
- **74% received prior CDK4/6i + ET**
  - 34 (55%) patients received 1 prior line of CDK4/6i
    - Palbociclib, n=23; abemaciclib n=7 ribociclib, n=4
  - 12 patients (19%) received 2 prior lines of CDK4/6i
    - Palbociclib → abemaciclib, n=3
    - Palbociclib → palbociclib, n=3
    - Palbociclib → ribociclib, n=3
    - Ribociclib → ribociclib, n=1
    - Abemaciclib → palbociclib, n=1
    - Palbociclib → experimental CDK4/6i, n=1
- **28% with *ESR1* mutation**

Data cutoff date: November 11, 2024.

[a] *ESR1* mutations in ctDNA at baseline were determined centrally using SafeSEQ Breast Cancer Panel (Sysmex Inostics, Baltimore, MD). Two samples were not evaluable.

CDK4/6i = cyclin-dependent kinase 4/6 inhibitor; **ctDNA** = circulating tumor DNA; **ECOG =** Eastern Cooperative Oncology Group; ***ESR1*** = estrogen receptor 1 gene

Well tolerated with no DLTs; safety profile consistent with ribociclib + ET

Treatment-emergent AEs

TEAEs in ≥25% of patients	Palazestrant + Ribociclib** (n = 62)			MONALEESA-2* Letrozole + Ribociclib† (n = 334)		
	All grades‡	Grade 3	Grade 4	All grades	Grade 3	Grade 4
Neutropenia§	51 (82%)	28 (45%)	6 (10%)	93%‖	49%	11%
Nausea	49 (79%)	2 (3%)	0%	52%	2%	0%
Fatigue	37 (60%)	2 (3%)	0%	37%	2%	<1%
Diarrhea	31 (50%)	2 (3%)	0%	35%	1%	0%
Anemia	27 (44%)	1 (2%)	0%	57%‖	2%	0%
WBC decrease	26 (42%)	10 (16%)	1 (2%)	93%‖	31%	3%
Constipation	24 (39%)	0%	0%	25%	1%	0%
Creatinine increased	20 (32%)	0%	0%	20%	1%	0%
Vomiting	20 (32%)	1 (2%)	0%	29%	4%	0%
ECG QT prolonged	19 (31%)	3 (5%)	0%	43%¶	8%¶	NR
Arthralgia	18 (29%)	0%	0%	27%	1%	NR
Lymphocyte count decreased	16 (26%)	5 (8%)	1 (2%)	51%‖	12%	2%
Cough	16 (26%)	0%	0%	20%	0%	0%
LDH increased	16 (26%)	0%	0%	NR	NR	NR

- No patients discontinued only palazestrant due to a treatment-emergent AE; 4 patients discontinued both treatments due to a TEAE; 2 patients discontinued ribociclib but stayed on palazestrant
- 30 (48%) patients still on treatment at the data cut-off
- Overall safety and tolerability profile consistent with ribociclib + endocrine therapy
- No DLTs were observed during dose escalation and the maximum tolerated dose was not reached

Data cutoff date: November 11, 2024. Data shown are n or n (%).

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.

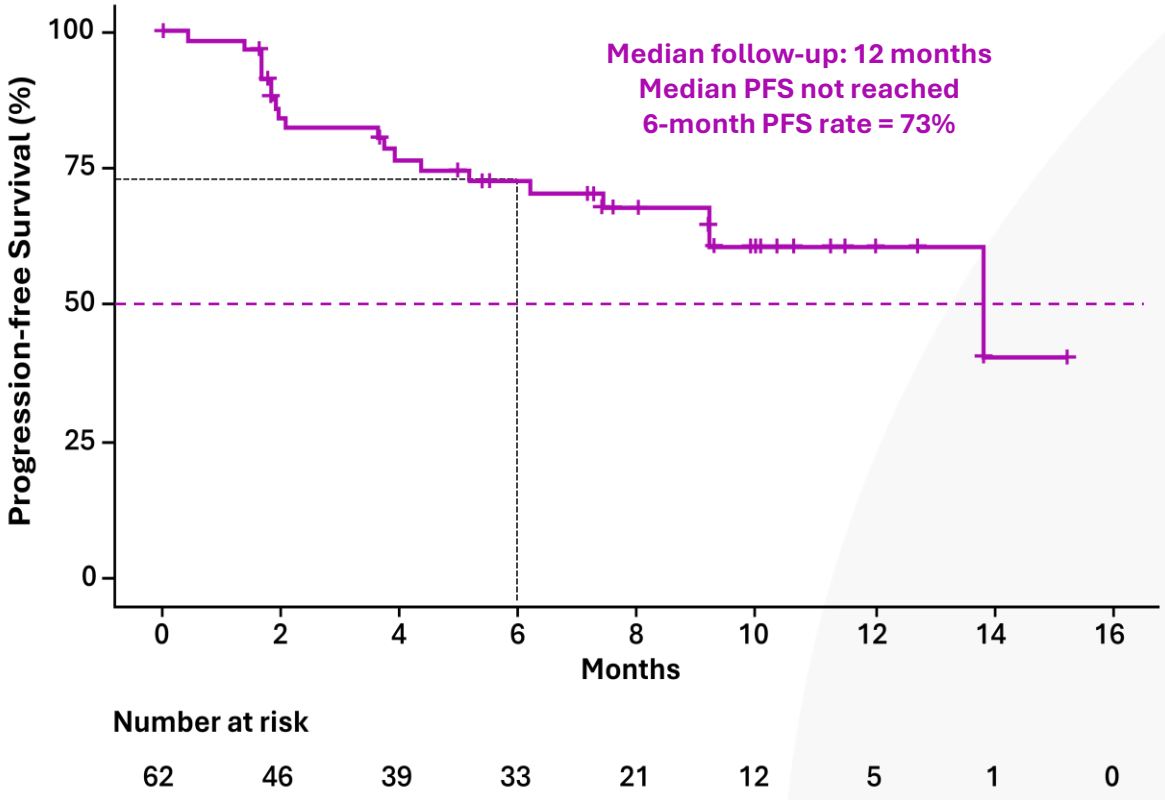
**Includes 3 patients at each of 30 mg and 60 mg palazestrant and 56 patients at 120 mg palazestrant in combination with 600 mg ribociclib. †Adverse reactions reported in ≥10% of patients who received ribociclib plus letrozole in the MONALEESA-2 study.(KISQALI (ribociclib). Prescribing information. Novartis; 2022; Hortobagyi, 2016) ‡Two subjects experienced Grade 5 AEs, heart failure and depressed level of consciousness not related to study drugs but disease progression. §Combined term includes neutropenia, decreased neutrophil count and febrile neutropenia. ‖These values were taken from MONALEESA-2 lab abnormalities data; source: KISQALI (ribociclib). Prescribing information. Novartis; 2022. ¶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%). Aggregate analysis (n=1054 patients) .

AE = adverse event; **DLTs** = dose-limiting toxicity; **ET** = endocrine therapy; **NR** = not reported; **TEAEs** = treatment-emergent adverse events; **WBC** = white blood cell

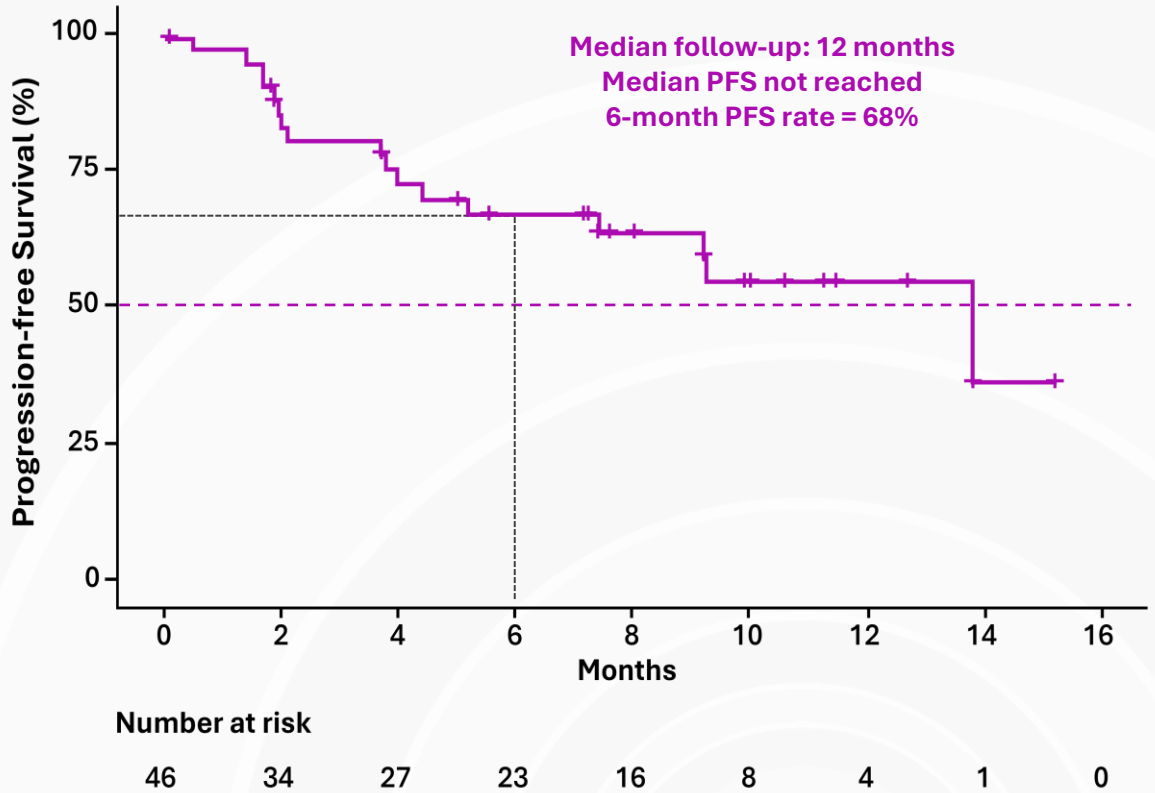
Six-month PFS rate of 73% in all patients, 68% in those with prior CDK4/6i

Median follow-up of 12 months; median PFS not yet reached; 48% of patients remain on study

All patients (N=62)



Patients with prior CDK4/6i plus ET (N=46)



Data cutoff date: November 11, 2024

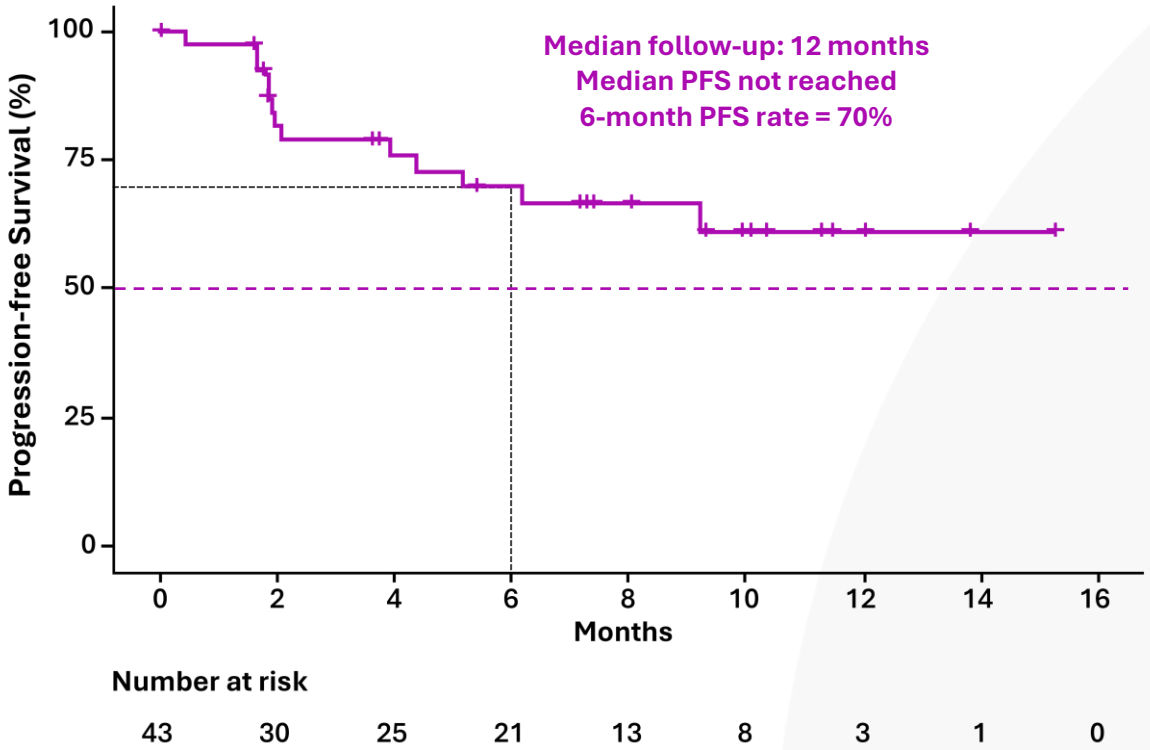
* Follow up was calculated from first dose date to data cutoff date regardless of disease progression status.

CDK4/6i = cyclin-dependent kinase 4/6 inhibitor; **PFS** = progression-free survival

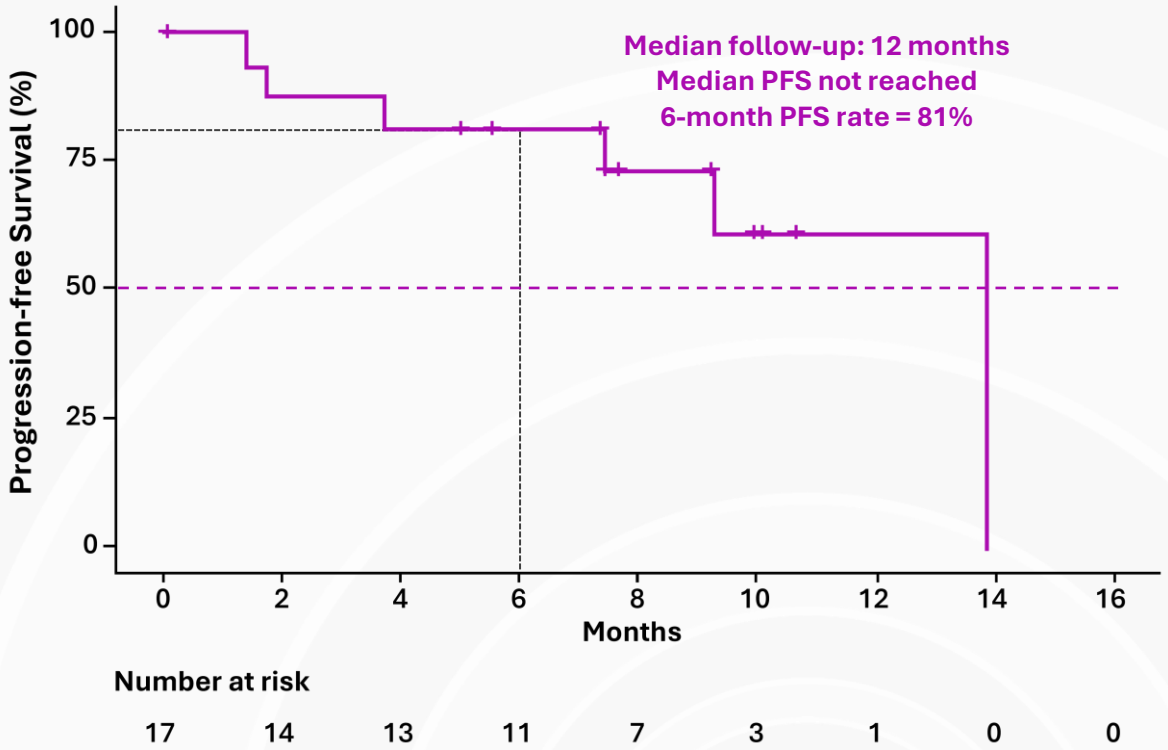
Six-month PFS rate of 81% in *ESR1*-mutant patients, 70% in *ESR1* wild-type

Median follow-up of 12 months; median PFS not yet reached; sustained efficacy regardless of *ESR1* status

ESR1 wild-type (n=43)



ESR1-mutant (n=17)



Data cutoff date: November 11, 2024

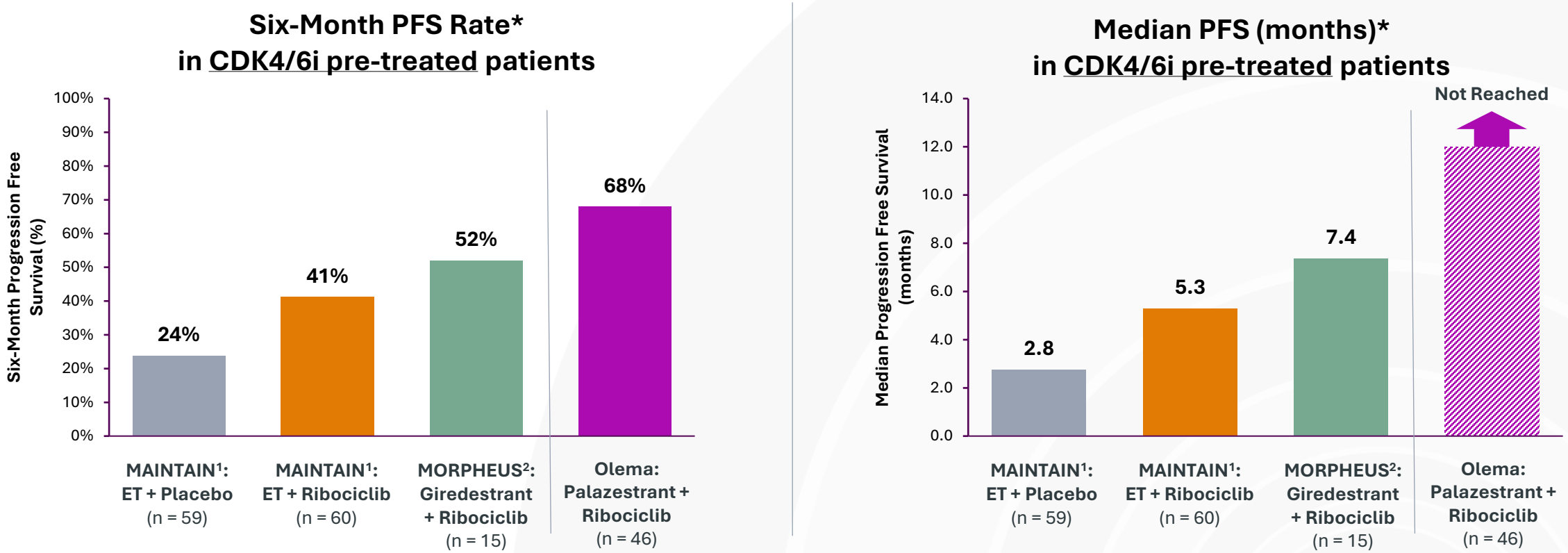
* Follow up was calculated from first dose date to data cutoff date regardless of disease progression status.

ESR1 = estrogen receptor 1 gene; **PFS** = progression-free survival

Efficacy comparison in 2/3L patients vs. competitive landscape

MAINTAIN study of ribociclib plus ET after CDK4/6i progression serves as best clinical benchmark*

Interim efficacy signals for palazestrant in combination with ribociclib



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Data cutoff date: November 11, 2024.

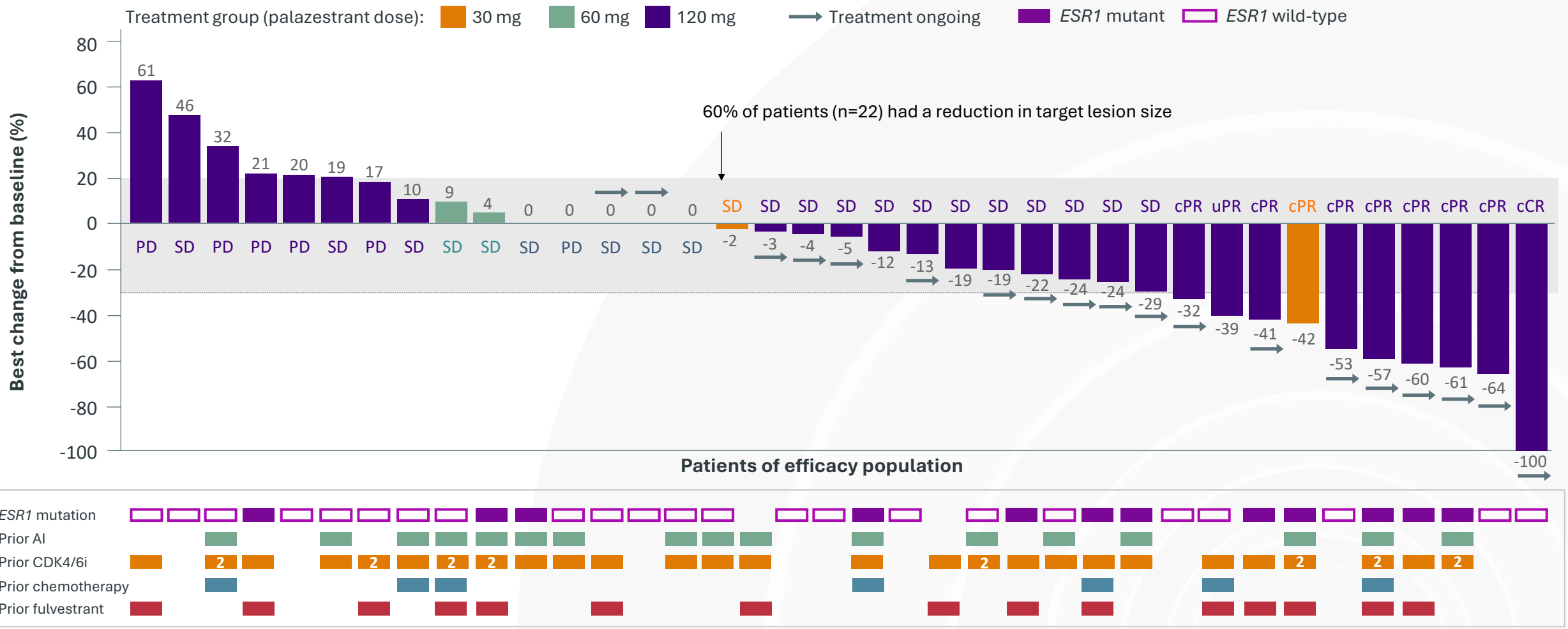
CDK4/6i = cyclin-dependent kinase 4/6 inhibitor; ***ESR1*-mut** = *ESR1*-mutant; ***ESR1*-wt** = *ESR1* wild-type; **ET =** endocrine therapy

[1] ASCO 2022 MAINTAIN data; [2] ASCO 2023 MORPHEUS data

Compelling anti-tumor activity in both wild-type and *ESR1* mutant tumors

60% of patients showed tumor reduction

Best percent change from baseline in target lesions and best overall response



Data cutoff date: November 11, 2024.
Waterfall plot n=37. 2 = 2 prior CDK4/6 inhibitors in metastatic setting.
SD = stable disease; **PD** = progressive disease; **AI** = aromatase inhibitor; **PR** = partial response; **cPR** = confirmed PR; **uPR** = unconfirmed PR; **uCR** = unconfirmed complete response; **cCR** = confirmed complete response; **CDK4/6i =** cyclin-dependent kinase 4/6 inhibitor; ***ESR1*** = estrogen receptor 1 gene

Highly encouraging preliminary efficacy from the combined agents, including in patients with prior CDK4/6i treatment

Efficacy

- **Median follow-up of 12 months with mPFS not yet reached**
- 6-month progression-free survival rate was:
  - 73% across all patients
  - 68% in patients with prior CDK4/6i exposure
  - 70% in patients with ESR1-wt disease
  - 81% in those with ESR1-mut disease
- 11 responses to date (2 confirmed CRs*, 8 confirmed PRs, and 1 unconfirmed PR)
- 27% (10/37) ORR among response-evaluable patients with measurable disease
- Clinical benefit rate (CBR)^:
  - 76% in all patients (37/49 CBR-eligible)
  - 81% in ESR1-mut (13/16 CBR-eligible)
  - 74% in ESR1-wt (23/31 CBR-eligible)
- CBR in patients who received prior CDK4/6i:
  - 71% in all patients (25/35 CBR-eligible)
  - 81% in ESR1-mut (13/16 CBR-eligible)
  - 65% in ESR1-wt (11/17 CBR-eligible)
- Longest duration of treatment 79 weeks and ongoing
- Efficacy data are maturing; 30 (48%) patients remain on treatment

Safety and Tolerability

- Palazestrant (120 mg) in combination with full dose ribociclib was well tolerated
- Safety was consistent with combinations of ribociclib (600 mg) with endocrine therapy

Pharmacokinetics

- No clinically meaningful drug-drug interaction

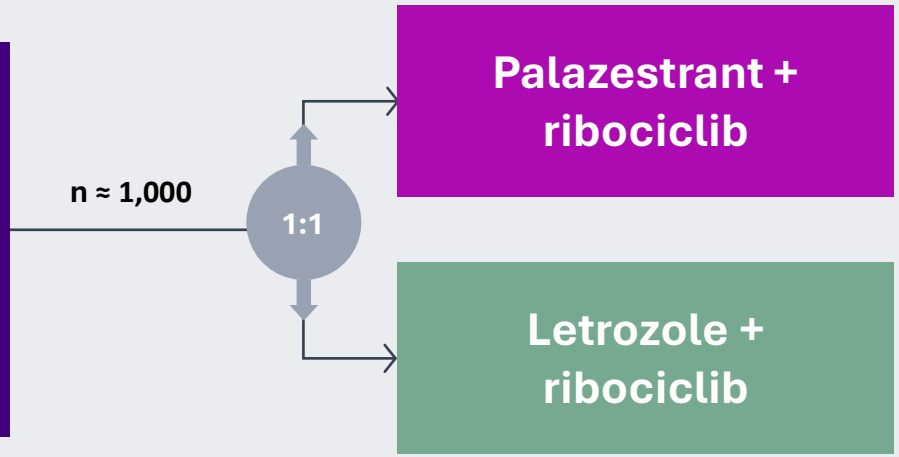
*1 cCR in patient with non-measurable but evaluable disease. ^ CBR is the proportion of patients who remained on treatment through at least 24 weeks with a confirmed complete response or partial response, or stable disease.
Abbreviations: **CDK4/6i =** cyclin-dependent kinase 4/6 inhibitor; ***ESR1*** = estrogen receptor 1 gene; **PR** = partial response; **CR** = complete response.

Proposed OPERA-02 1L Phase 3 pivotal trial in combination with ribociclib

~1,000-patient trial vs. standard of care in preparation for 2025 initiation; in collaboration with Novartis

OPERA-02
Breast Cancer Study

Inclusion criteria:
- ER+/HER2- MBC
- Any menopausal status
- No prior systemic therapy for MBC
- No prior CDK4/6 inhibitor for MBC
- Evaluable disease (measurable or non-measurable)



Study Endpoints

Primary: PFS (BIRC)

Secondary : OS (key)
PFS (Investigator and by *ESR1*mut)
ORR/CBR/DOR (BIRC, Investigator and by *ESR1*mut)
Safety
PK
Health-related PROs

STRATIFICATION:
- Menopausal status: post vs. pre/male
- Visceral metastasis: yes vs. no
- *De novo* metastatic disease vs. recurrent disease after adjuvant ET

CDK4/6i = cyclin-dependent kinase 4/6 inhibitor; **CBR =** clinical benefit rate; **DOR =** duration of response; **ER+ =** estrogen receptor positive; **HER2- =** human epidermal growth factor receptor 2 negative; **MBC =** metastatic breast cancer; **ORR =** objective response rate; **OS =** overall survival; **PFS =** progression free survival; ***ESR1*mut** = *ESR1*-mutant; **ET =** endocrine therapy

Preparing to initiate OPERA-02 in 2025

New clinical trial collaboration and supply agreement with Novartis combined with $250M private placement enables execution of Olema operating plan

- Novartis agreement enables pivotal Phase 3 OPERA-02 clinical trial of palazestrant in combination with ribociclib in frontline ER+/HER2- advanced or metastatic breast cancer
- Ribociclib drug supply expected to be sufficient to conduct the planned OPERA-02 trial; valued at ~$275M
- Olema responsible for the day-to-day operational activities for OPERA-02
- Olema retains global commercial rights to palazestrant
- All clinical data from OPERA-02 will be jointly owned; each party retains rights to its background IP

- $250M equity private placement strengthens Olema's balance sheet
- Participation by new and existing high-quality institutional and accredited investors
- Pro forma cash and cash equivalents expected to fund research and development activities including the execution of OPERA-01, OPERA-02, OP-3136 Phase 1/2, and for working capital and general corporate purposes

Significant opportunity for palazestrant across the spectrum of care

Estimated >$20B ER+/HER2- global metastatic breast cancer market[1]

2L/3L+ ER+/HER2- MBC

OPERA-01 Breast Cancer Study

Patients[2]	~150K
Duration of Therapy[3]	~2-12+ months
Global Market Potential[4]	$5B+

1L ER+/HER2- MBC

OPERA-02 Breast Cancer Study

Patients[2]	~115K
Duration of Therapy[3]	~6-36+ months
Global Market Potential[4]	$10B+

[1] 2025 opportunity estimates for total endocrine therapy market (US and Europe). Olema internal data.
[2] 2025 incidence projection estimates. Olema internal data, Informa ER+/HER2- BC Prevalence Based Market Forecast.
[3] Olema internal data.
[4] Olema internal data.

Olema ONCOLOGY

Olema: a compelling late-stage opportunity in breast cancer and beyond

Changing the treatment paradigm for endocrine-driven cancers

1. Palazestrant anchors Olema's breast cancer program as a potential backbone therapy for metastatic breast cancer
   - Highly differentiated as first oral CERAN/SERD endocrine agent
   - Ongoing 2/3L OPERA-01 Phase 3 trial on track for top-line data in 2026
   - Planned 1L OPERA-02 Phase 3 trial in combination with ribociclib enabled; initiation expected in 2025
   - Go-to-market strategy for potential U.S. launch in 2027
2. OP-3136 expands pipeline with novel and validated KAT6 target
   - IND cleared by FDA; first patient expected to enroll in Phase 1 clinical trial by early 2025
3. Well-capitalized with ~$452M of pro forma cash and cash equivalents as of September 30, 2024[1]

[1] *Pro forma position includes the Company's cash, cash equivalents, and marketable securities as of September 30, 2024, plus net proceeds of approximately $237.5 million from equity private placement which closed on December 4, 2024.*

Thank You

— Advancing medicines for breast cancer and beyond

Olema ONCOLOGY