Olema ONCOLOGY

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.

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Unmatched Combinability and Promising Efficacy for Palazestrant-Ribociclib Combo

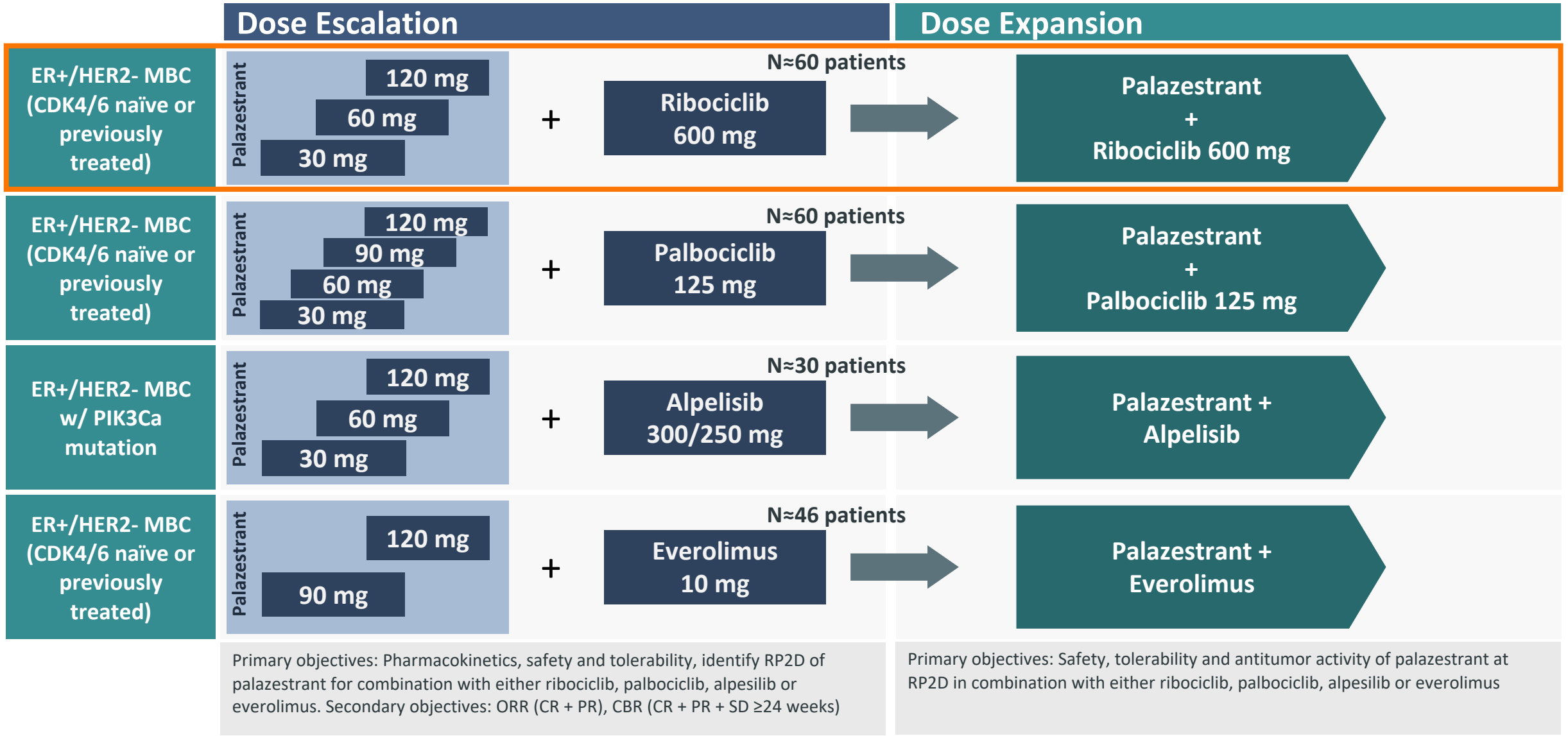
- Interim Phase 1b/2 data across 50 patients (on treatment for ≥ 4wks); 60-patient study now fully enrolled
  - Strong investigator enthusiasm resulted in rapid study enrollment
  - Largest data set for any CERAN/SERD in combination with ribociclib to be presented
- **Compelling combinability**
  - Well 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



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

Primary objectives: Safety, tolerability and antitumor activity of palazestrant at RP2D in combination with either ribociclib, palbociclib, alpesilib or everolimus

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%)

- 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*

^ 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; **RP2D**, recommended Phase 2 dose; **ctDNA**, circulating tumor DNA.

Data Cutoff Date: March 13, 2024

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.

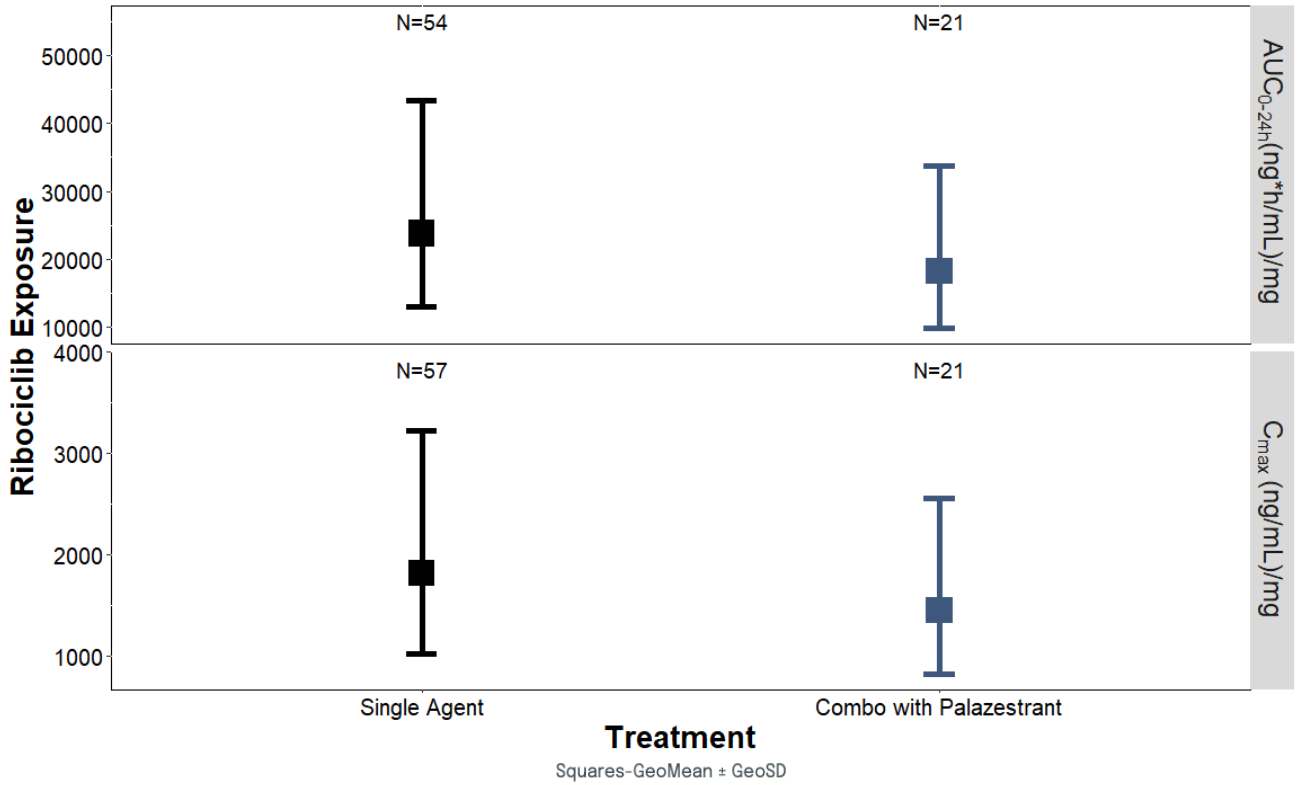
(1) Includes 3 patients at each of 30 mg and 60 mg palazestrant and 44 patients at 120 mg palazestrant in combination with 600 mg ribociclib. Two patients experienced Grade 5 AEs (myocarditis due to COVID-19; depressed level of consciousness not related to study drug) (2) Source: Novartis Kisqali (ribociclib)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

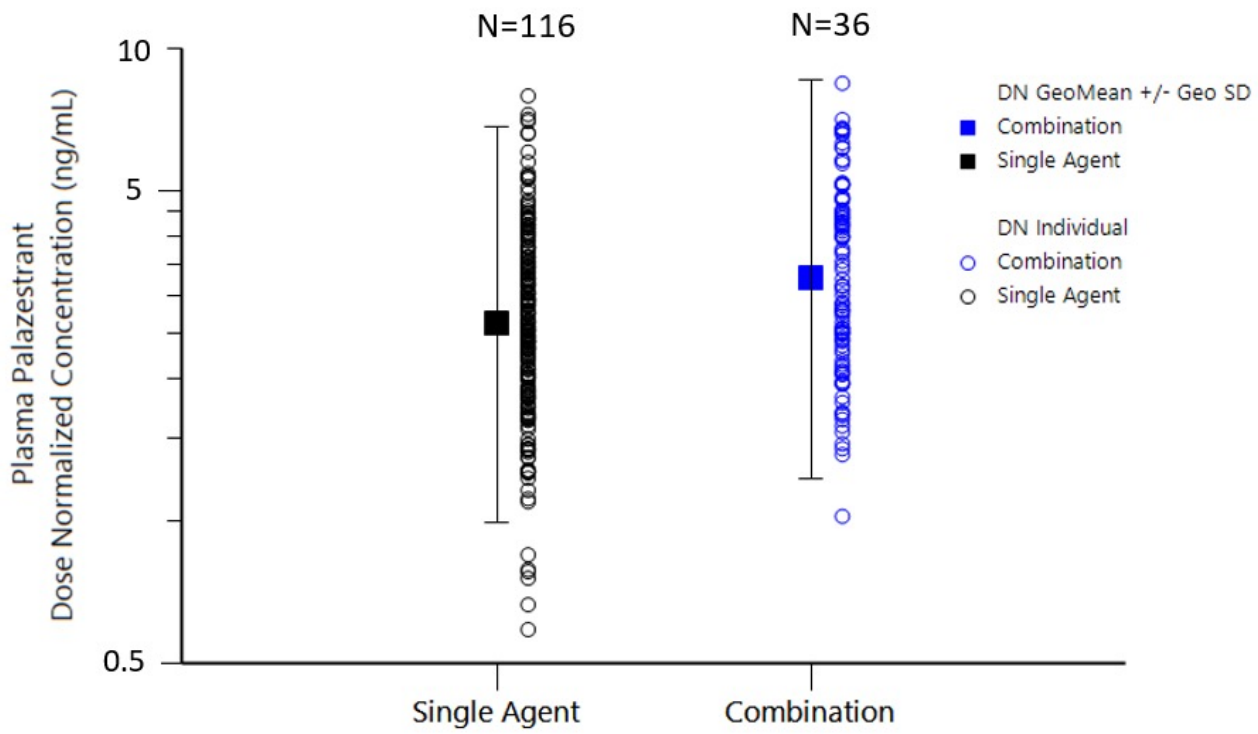
Pharmacokinetics

- 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.

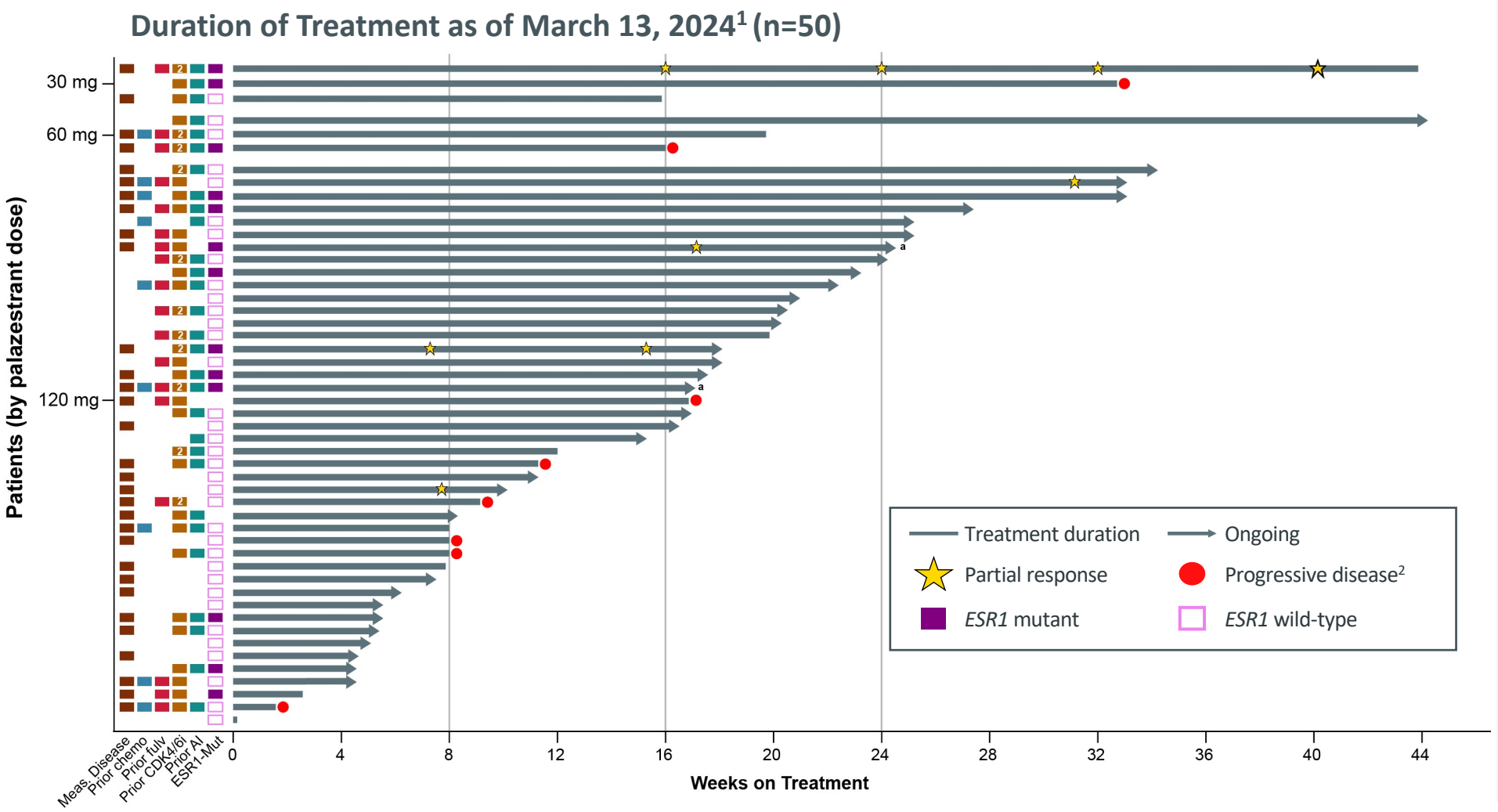
DN, dose normalized; **GeoMean**, geometric mean; **GeoSD**, geometric standard deviation.

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*



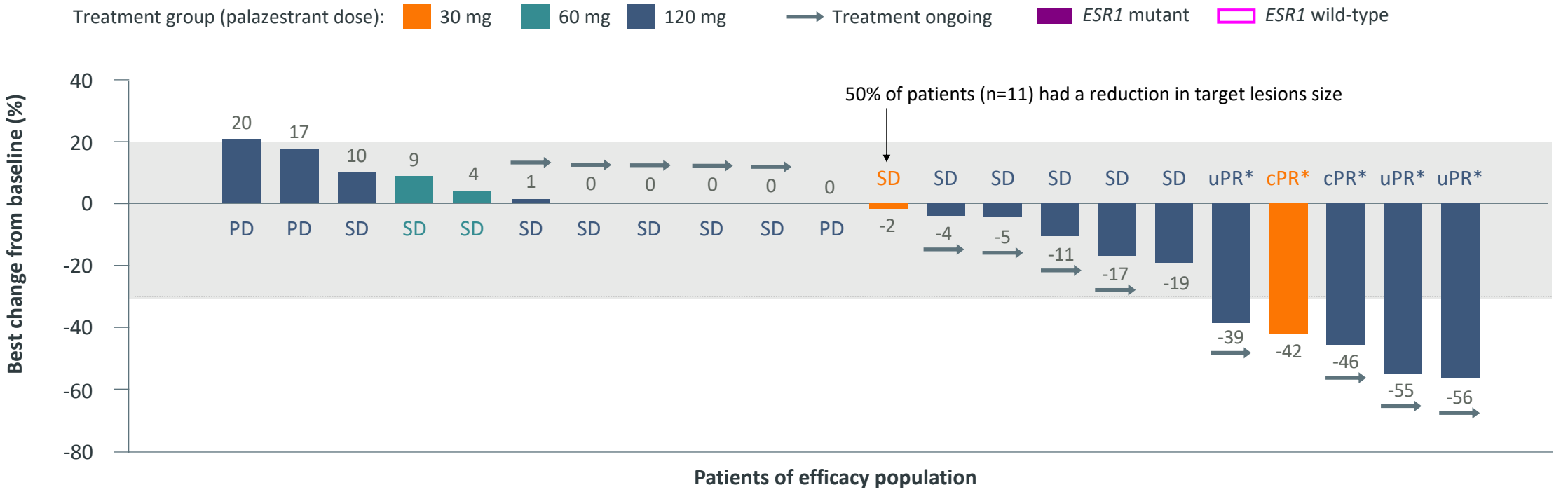
- Activity shown in both wild-type and *ESR1*-mut patients
- 5 partial responses to date of 23 eligible (2 cPR, 3 uPR)
- **Clinical benefit rate (CBR)**^:
  - **85% in all patients** (11/13 CBR-eligible)
  - **83% in *ESR1*-mut** (5/6 CBR-eligible)
  - **86% in *ESR1*-wt** (6/7 CBR-eligible)
  - **83% 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

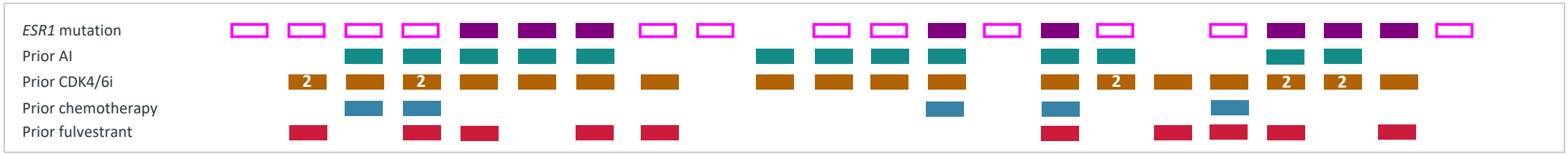
[1]Each lane represents one patient. [2] Progression by radiographic assessment only.
a: Two patients discontinued ribociclib but continued palazestrant.
2: 2 prior CDK4/6 inhibitors in metastatic setting.
Abbreviations: **AI,** aromatase inhibitor; **CDK4/6i,** cyclin-dependent kinase 4/6 inhibitor; **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*

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





Data cut-off: March 13, 2024

* cPR, confirmed PR; uPR, unconfirmed PR

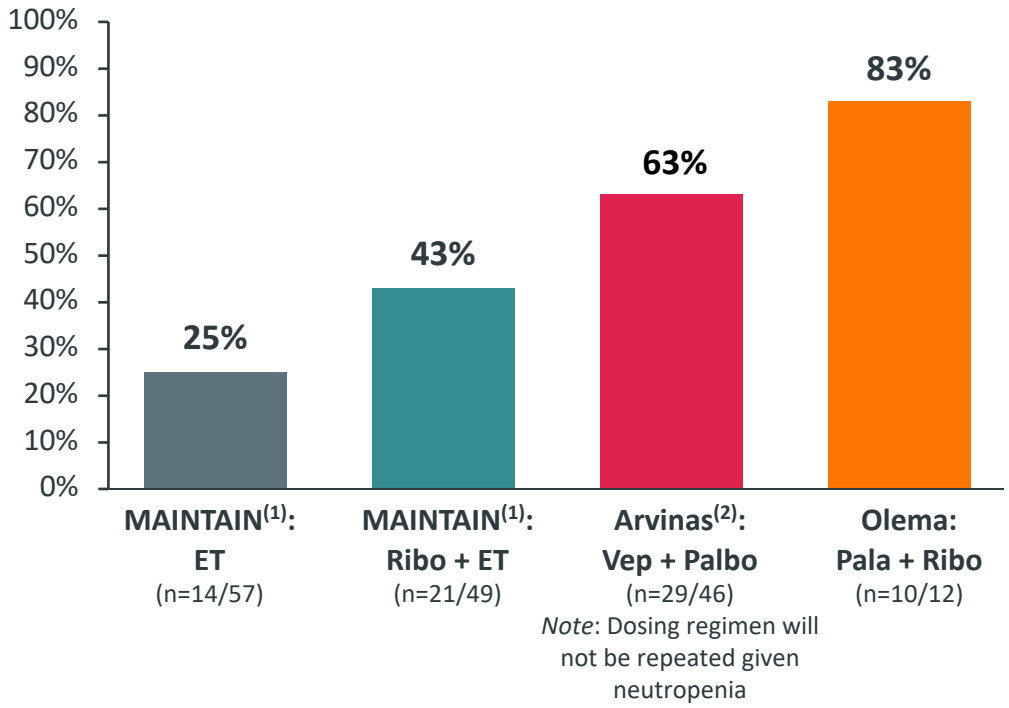
2: 2 prior CDK4/6 inhibitors in metastatic setting.

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



Note: Dosing regimen will not be repeated given neutropenia

- 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.

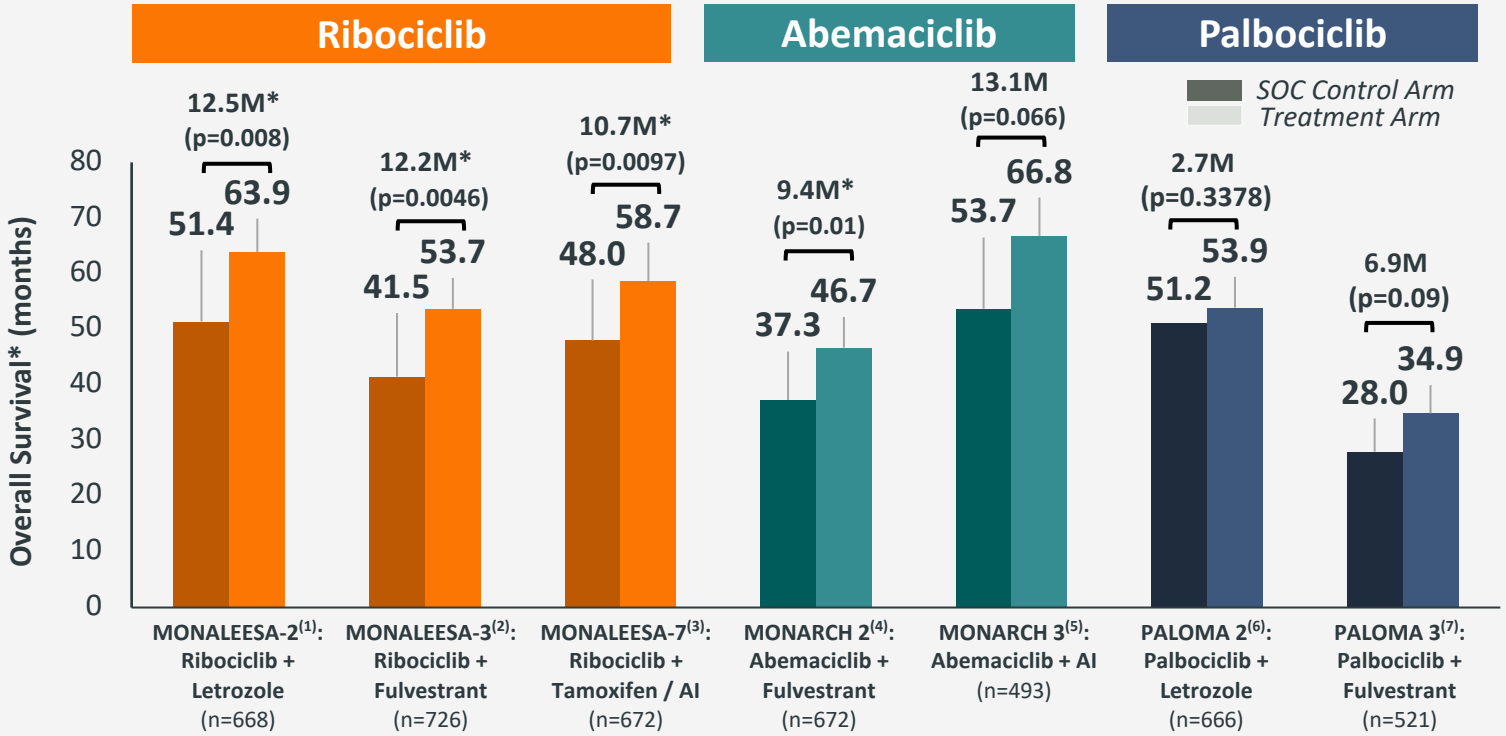
Abbreviations: **ET,** endocrine therapy; **Ribo**, ribociclib; **Vep**, vepdegestrant; **Palbo**, Palbociclib; **Pala**, palazestrant; **ESR1-mut**, ESR1-mutant; **ESR1-wt**, ESR1 wild-type; **CDK4/6i**, CDK4/6 inhibitor

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, palazestrant will 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.**

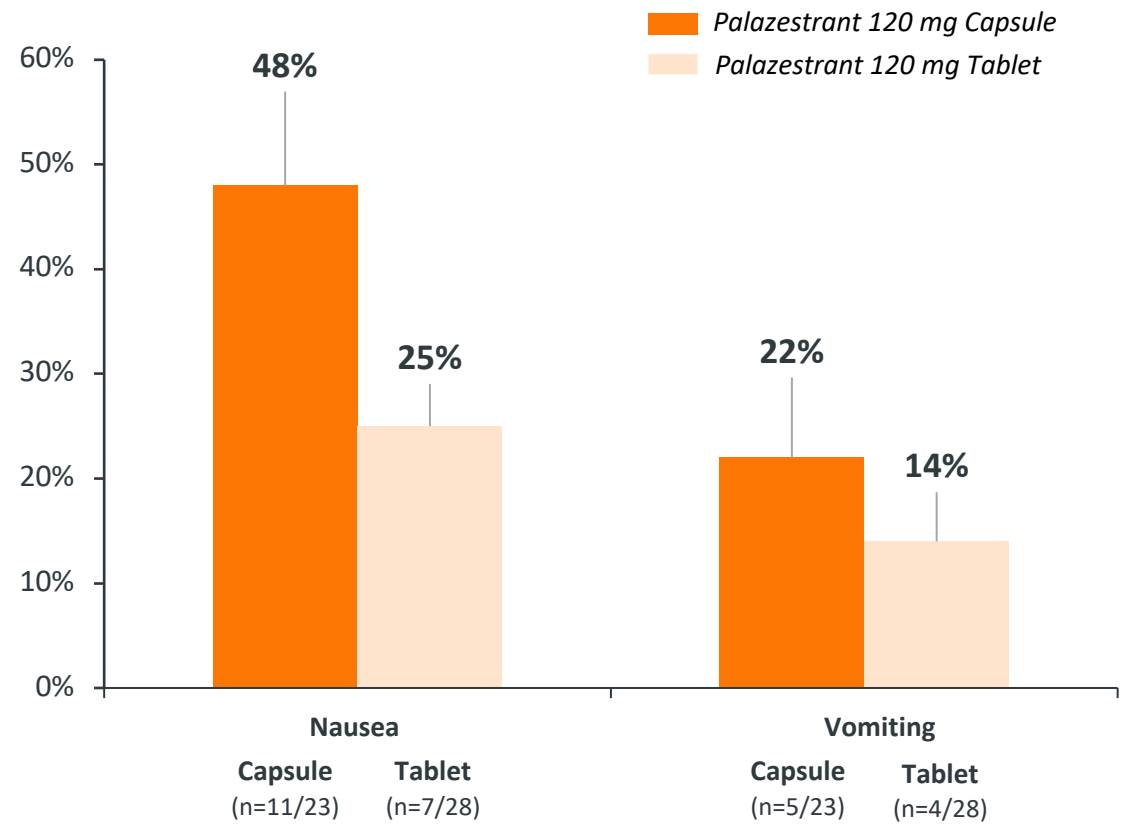
Source: (1) Hortobagyi G.N., et al. Overall Survival with Ribociclib plus Letrozole in Advanced Breast Cancer. NEJM. 2022;386:942-950; (2) Salmon D.J., et al. Overall Survival with Ribociclib plus Fulvestrant in Advanced Breast Cancer. NEJM. 2020;382:514–524; (3) Im S.-A., et al. Overall Survival with 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

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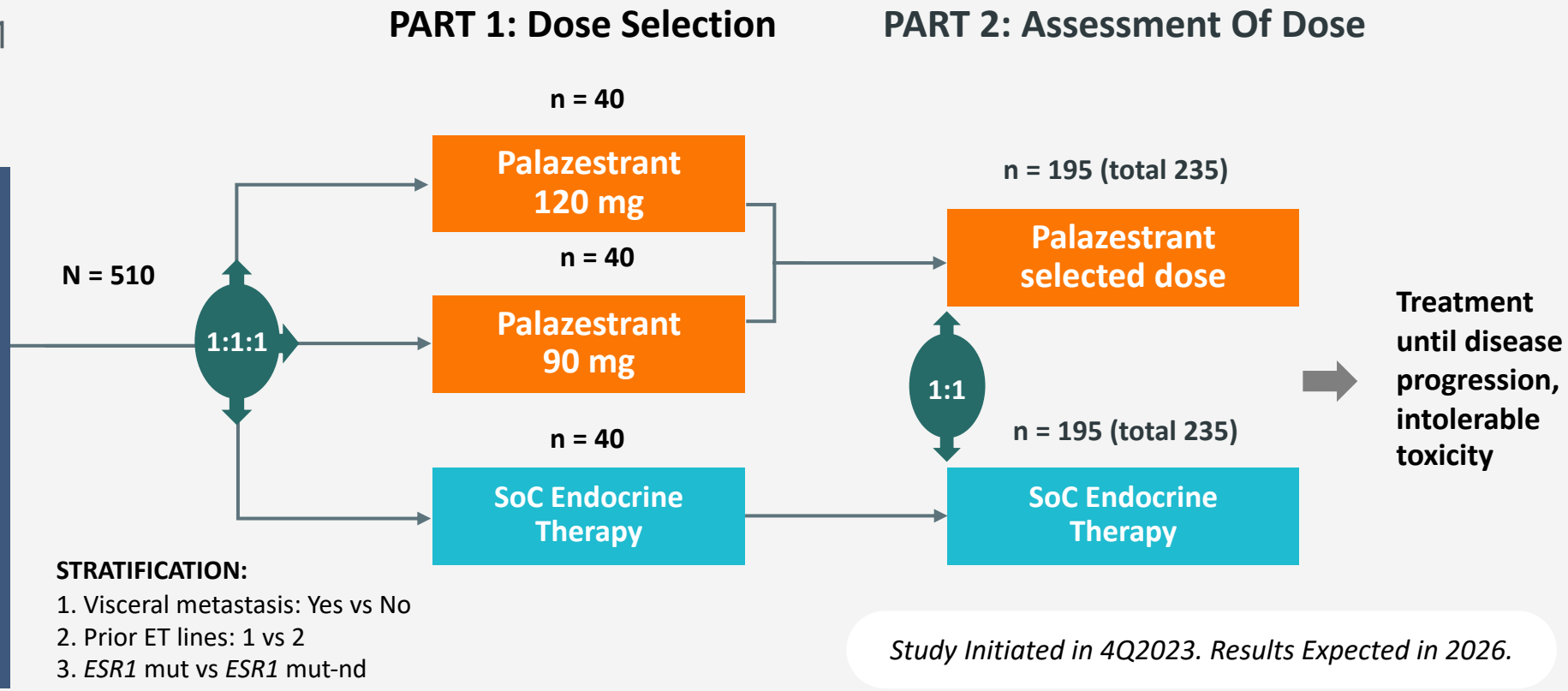
OPERA-01 Designed to Show Effectiveness over Standard of Care

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

OPERA-01 Breast Cancer Study

INCLUSION CRITERIA

- 1-2 prior lines of endocrine therapy
- Prior treatment with a CDK4/6 inhibitor
- Minimum 6 months on last endocrine therapy



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

Study Initiated in 4Q2023. Results Expected in 2026.

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 Oncology	LINE	PRE-CLINICAL	PHASE 1	PHASE 2	PHASE 3
Palazestrant	2nd/3rd	Phase 3 trial initiated Q4 2023			OPERA-01 Breast Cancer Study
Palazestrant + Ribociclib	2nd/3rd			Phase 2 expansion ongoing (Novartis)	
	1st				Phase 3 in planning
Palazestrant + Palbociclib	2nd/3rd			Phase 2 expansion ongoing (Pfizer)	
Palazestrant + Alpelisib	2nd/3rd		Phase 1b ongoing (Novartis)		
Palazestrant + Everolimus	2nd/3rd		Phase 1b/2 initiating		
KAT6 Inhibitor (OP-3136)		Pre-clinical	IND Anticipated Late 2024		

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.

Olema ONCOLOGY

Investor Relations
ir@olema.com

Media
media@olema.com

Business Development
partnering@olema.com

Careers
careers@olema.com