Olema Oncology

JP Morgan Conference

January 2024

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, 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 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 work for our KAT6 inhibitor, market size and opportunity, our ability to complete certain milestones, and our financial condition, cash position and runway and sufficiency of our financial resources, and the sufficiency of our management team. 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.

Olema's Mission to Transform Breast Cancer Treatment

Potential best-in-class backbone endocrine therapy to improve outcomes for women with ER+/HER2- breast cancer

2023: Established aspirational profile of palazestrant

- **Demonstrated Robust Efficacy and Tolerability** – Presented compelling Phase 2 monotherapy data
- **Demonstrated Combinability –** Presented positive Phase 2 combination data with CDK4/6i's, palbociclib and ribociclib
- **Initiated Phase 3** – Initiated OPERA-01 Pivotal Phase 3 2/3L Monotherapy Trial
- **Extended Cash Runway** – Completed financing for up to $180 million
- **Added New Asset** – Announced discovery of potent KAT6 inhibitor (named OP-3136)

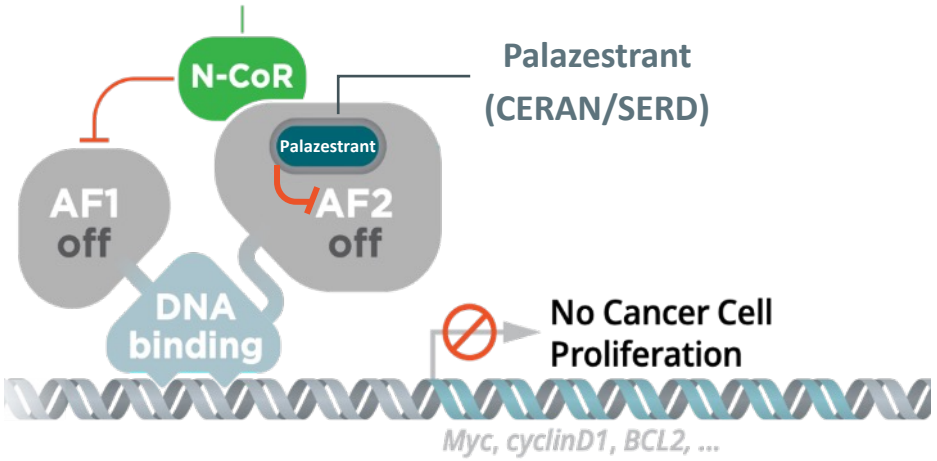
2024: Further unique combinability and execute on pivotal trial

- Complete Palazestrant – Ribociclib Phase 2 Study Enrollment with Updated Clinical Results in H1 2024
- Execute OPERA-01 Pivotal Phase 3 2/3L Monotherapy Trial
- Prepare for OPERA-02 Pivotal Phase 3 1L Combination Trial with CDK4/6i
- Initiate Palazestrant – Everolimus Phase 1b/2 Clinical Study
- File IND and Advance Clinical Development for KAT6i OP-3136 in Late 2024

Palazestrant: A Differentiated Next Generation Endocrine Therapy

Palazestrant, a complete estrogen receptor (ER) antagonist (CERAN), potently and completely inactivates the ER, blocks ER-driven transcriptional activity, inhibits ER-driven breast cancer cell growth, and strongly induces ER degradation

Complete ER antagonists turn off AF2 and recruit N-CoR to inactivate AF1



Complete ER Antagonism — CERAN completely shuts off ER growth and proliferation signal 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

Favorable Tolerability — Favorable tolerability 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 — Combinable with ribociclib or palbociclib at full doses – without DDI* and overall tolerability profile consistent with expected profile of CDK4/6i plus endocrine therapy

CNS Penetration — Demonstrated activity in nonclinical brain metastases models

*Interim update of combination study with Palbociclib or Ribociclib at SABCS 2023. Abbreviations: **AF1,** activation factor 1; **AF2,** activation factor 2; **CDK4/6i, c**yclin dependent kinase 4/6 inhibitor; **DDI,** drug-drug interaction

References: Shang and Brown, *Science*, 2002: Vol. 295, Issue 5564, pp. 2465-2468 ; Webb, Nguyen, and Kushner, *JBC*, 2003: Vol. 278, pp. 6912–6920

Competing Programs and Market Opportunity for 2/3L and 1L MBC Treatment

	Current Active Programs	Market Opportunity for ER+/HER2-[1]	
2L/3L ER+/HER2- MBC	Olema Oncology; Lilly; Pfizer/Arvinas; Menarini group*	Patients	~150K
		Duration of Therapy[2]	~2-12+ months
		Market Potential[3]	$5B+
1L Combo ER+/HER2- MBC	Olema Oncology; AstraZeneca w/palbociclib; Pfizer/Arvinas w/palbociclib; Roche w/palbociclib	Patients	~115K
		Duration of Therapy[2]	~6-36+ months
		Market Potential[3]	$10B+

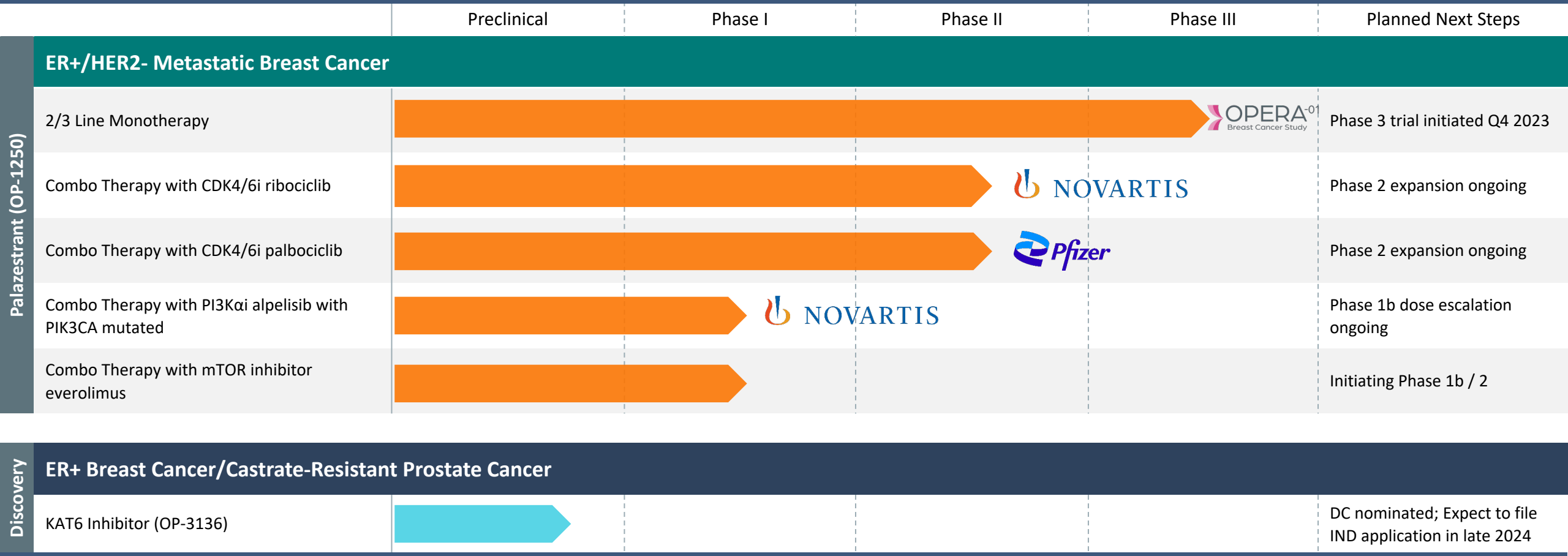
*Menarini's drug ORSERDU (elacestrant) was approved by the U.S. FDA on January 27, 2023 for treatment of ER+/HER2- ESR1-mutated metastatic breast cancer following initial hormonal therapy.

[1]2025 incidence projection estimates. Olema internal data, Informa ER+/HER2- BC Prevalence Based Market Forecast. [2]Olema internal data. [3]2025 opportunity estimates for total endocrine therapy market (US and EU5). Olema internal data.

Expanding Olema's Pipeline Focused on Women's Oncology

OPERA-01 pivotal 2/3L trial ongoing; OPERA-02 pivotal 1L trial in planning

Evaluating palazestrant across a range of ER cohorts in monotherapy and combination trials



Strong cash position of ~$276.9M to support clinical development and operations into 2027[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.

Abbreviations; **MBC,** metastatic breast cancer; **PI3Kα,** phosphatidylinositol 3-kinase alpha; **CDK4/6i,** CDK4/6 inhibitor; **KAT6,** lysine acetyltransferase 6; **mTOR,** mammalian target of rapamycin

Palazestrant Phase 2 Monotherapy Clinical Results (ESMO 2023)

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Monotherapy: Compelling PFS in ESR1-Mutant and Wild-Type Patients

Well tolerated, favorable PK and efficacy in heavily pretreated patients

Palazestrant Phase 2 monotherapy clinical results at ESMO 2023

Demographics

- 86 patients as of data cutoff of July 7, 2023
- Majority had measurable and/or visceral disease
- 42% of patients were 4th line or later at entry
- 97% prior CDK4/6i
- 66% prior fulvestrant
- 31% prior chemotherapy
- 48% activating mutations in *ESR1*

Safety: Well Tolerated

- Palazestrant at RP2D of 120 mg was well tolerated with no dose-limiting toxicities, and maximum tolerated dose (MTD) was not reached
- Most AEs were low grade (1/2)
- Reversible grade 4 neutropenia observed in 6 of 86 patients
- Tablet formulation should reduce upper GI adverse events

Favorable Pharmacokinetics

- High oral bioavailability with daily dosing, dose proportional exposure and a long half-life of eight days
- Steady-state plasma levels showed minimal peak-to-trough variability

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

Abbreviations: **CDK4/6i**, cyclin dependent kinase 4/6 inhibitor; ***ESR1***, estrogen receptor 1 gene; **RP2D**, recommended Phase 2 dose; **PFS**, progression-free survival; **PK**, pharmacokinetics

Data Cutoff Date: July 7, 2023

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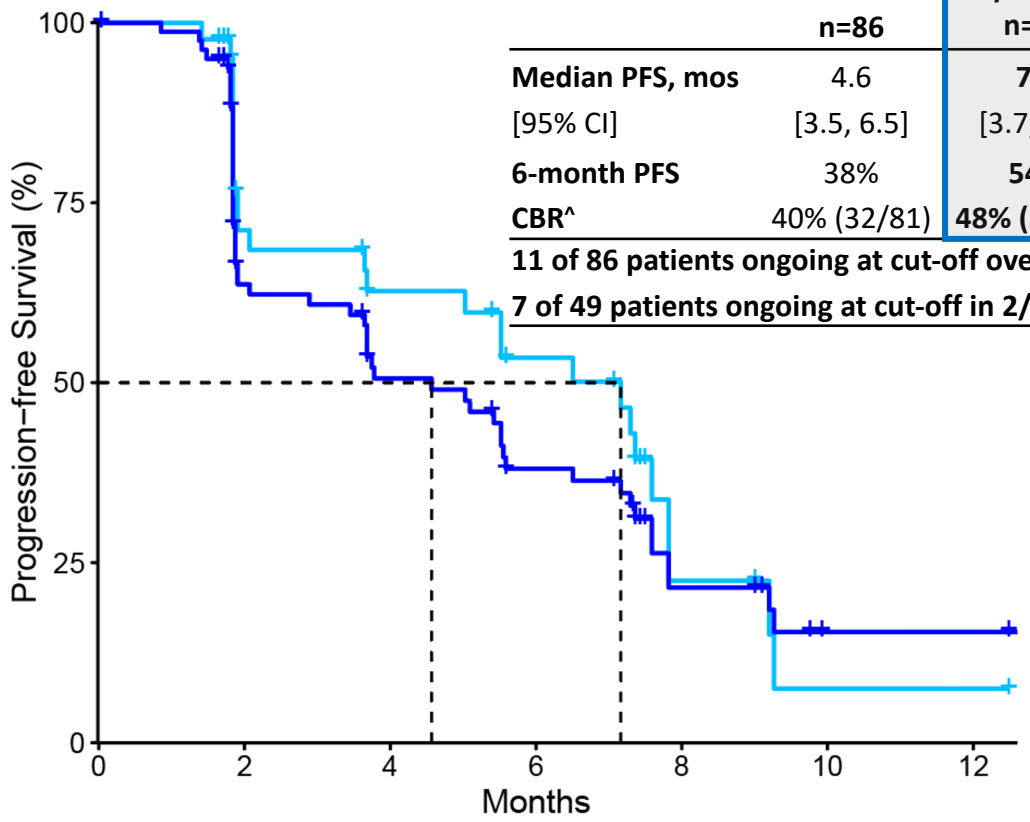
Progression-Free Survival Across All and ESR1-Mutant Patients

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

All Patients



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

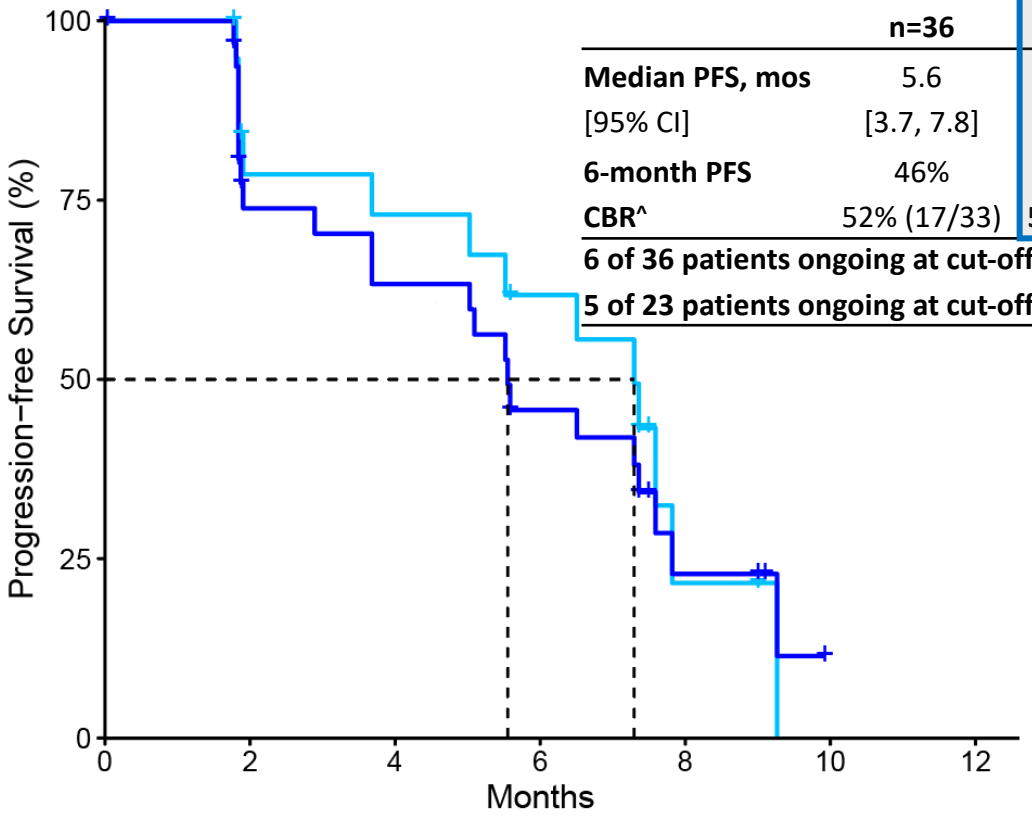
11 of 86 patients ongoing at cut-off overall

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

Number at risk

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

Patients with *ESR1* Mutation



	*ESR1*mut n=36	2/3L ±CT n=23
Median PFS, mos	5.6	**7.3**
[95% CI]	[3.7, 7.8]	[5.0, NA]
6-month PFS	46%	**62%**
CBR^	52% (17/33)	**59% (13/22)**

6 of 36 patients ongoing at cut-off overall

5 of 23 patients ongoing at cut-off in 2/3L±CT

Number at risk

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

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

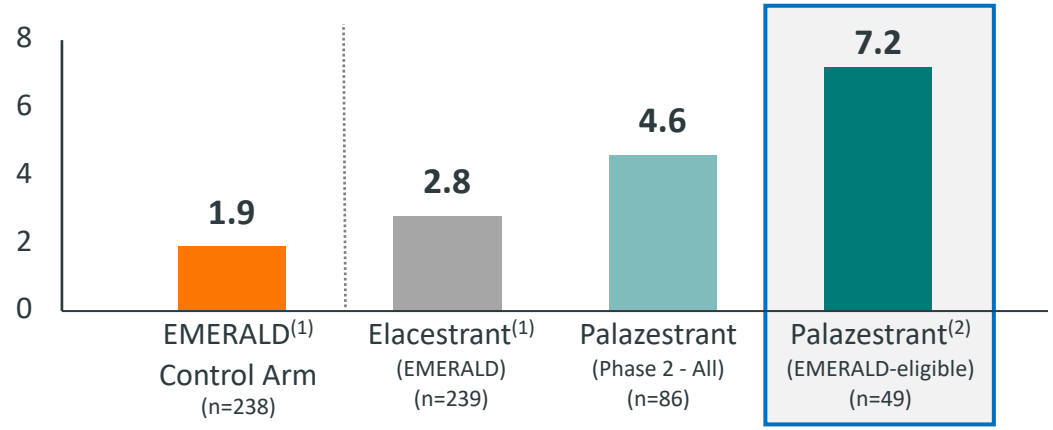
Abbreviations: **2/3L**, second/third line; **± CT**, plus/minus chemotherapy; **CBR**, clinical benefit rate; **CI**, confidence interval; ***ESR1***, estrogen receptor 1 gene; **mos**, months; **mut**, mutation; **NA**, not applicable; **PFS**, progression-free survival.

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

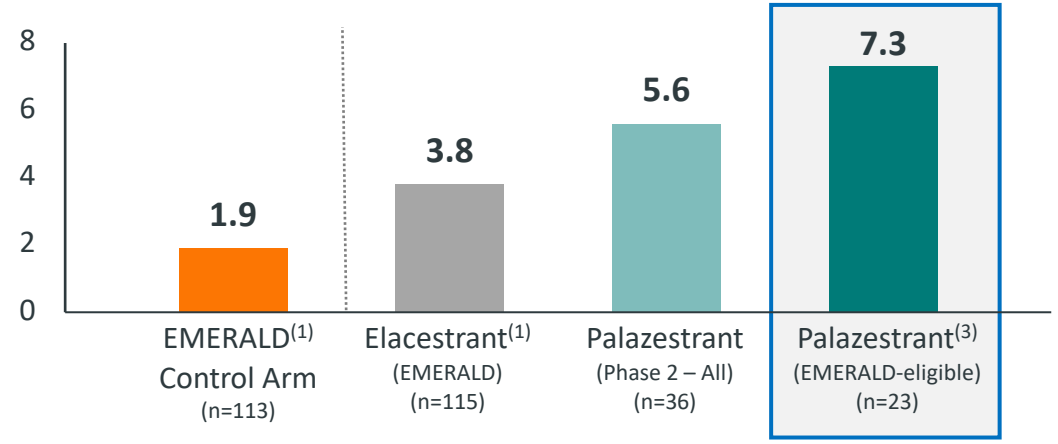
Comparing Across Trials: Palazestrant vs. Elacestrant

Median Progression Free Survival and Clinical Benefit Rate

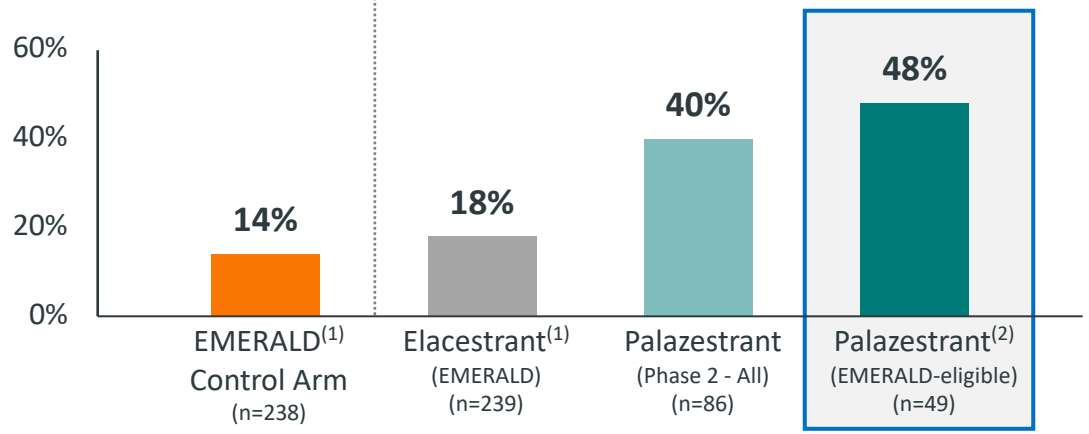
Median PFS (months) – All Patients*



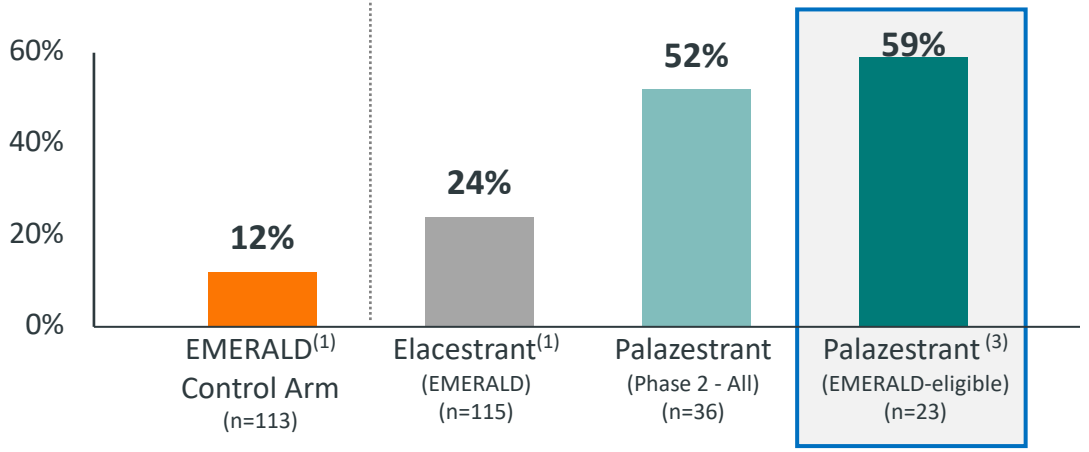
Median PFS (months) – ESR1 Mutant Patients*



Clinical Benefit Rate (%) – All Patients*



Clinical Benefit Rate (%) – ESR1 Mutant Patients*

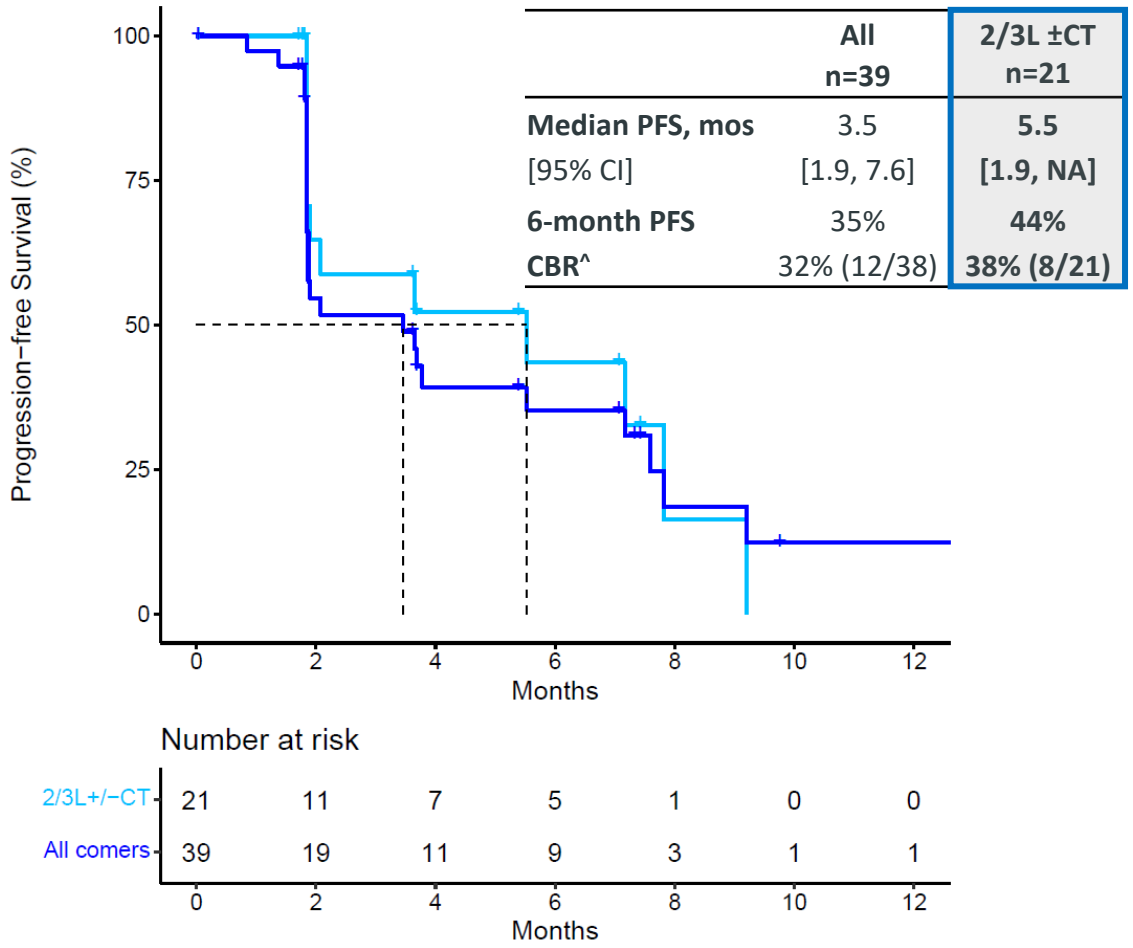


*** NOTE: This analysis is the aggregation of results across independent studies. There are risks inherent in conducting cross-trial comparisons. Refer to further disclaimers on slide 2.**

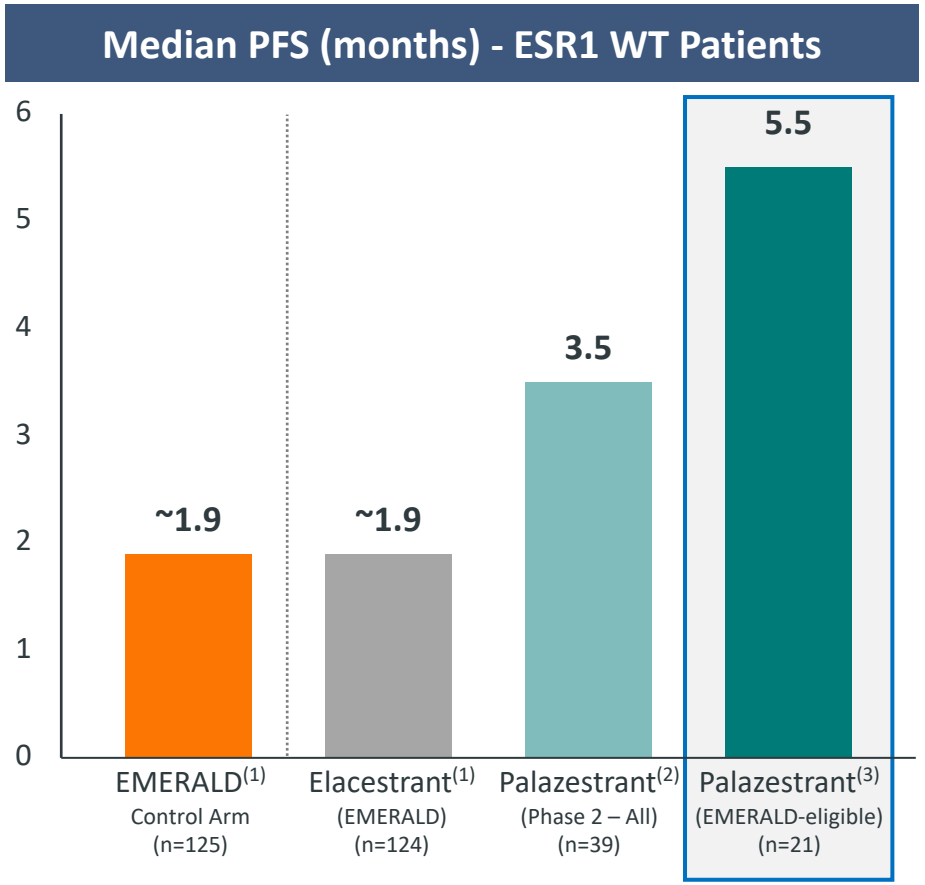
1. Source: SABCS 2021 EMERALD data. Median PFS and CBR in control arm and in elacestrant 400 mg dose.
2. Emerald-eligible patient population from palazestrant Phase 2 dataset (2/3L +/-CT).
3. Emerald-eligible patient population from palazestrant Phase 2 dataset (2/3L +/-CT) with ESR1 mutations detected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

Progression-Free Survival in ESR1 Wild-Type Patients

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



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



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

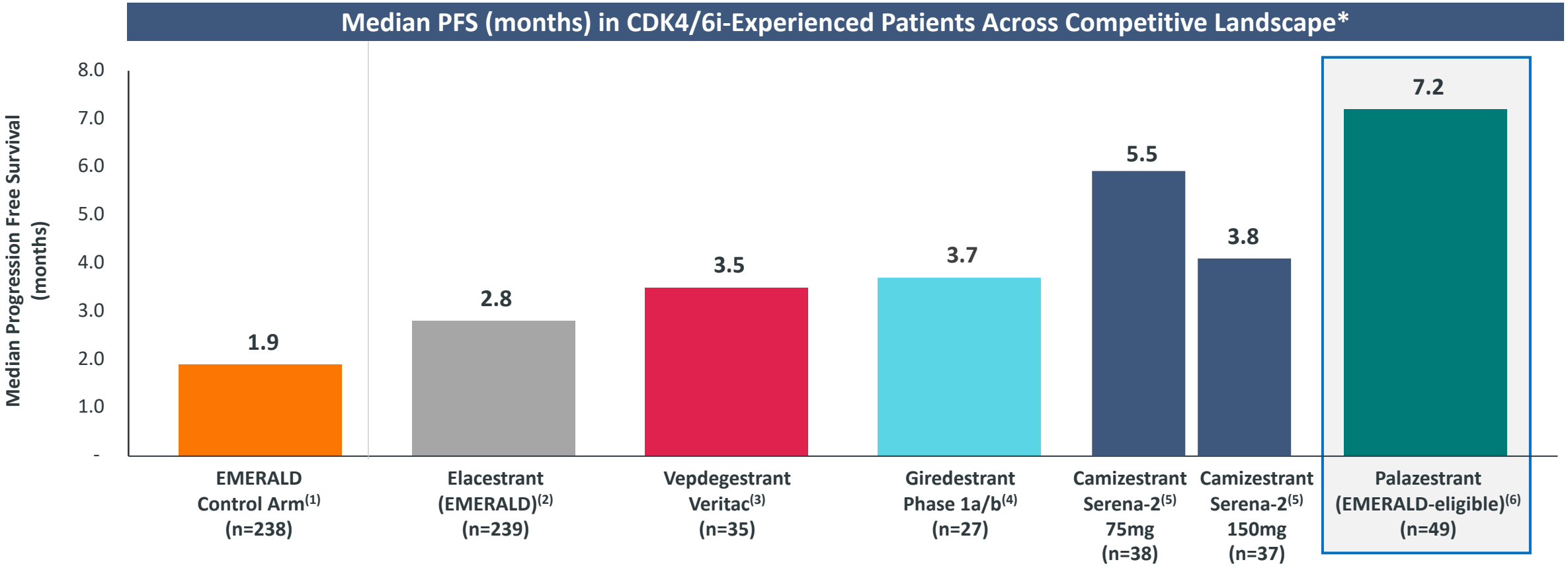
Abbreviations: **2/3L**, second/third line; **± CT**, plus/minus chemotherapy; **WT**, wild-type; **CI**, confidence interval; ***ESR1***, estrogen receptor 1 gene; **mos**, months; **NA**, not applicable; **PFS**, progression-free survival.

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

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

Monotherapy Competitive Landscape – Best-in-Class Potential

Median PFS across comparable, all CDK4/6i-experienced patient populations



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

1. Source: SABCS 2021 EMERALD data. Median PFS in control arm. Note: ORR of 4.4% (8/182).
2. Source: SABCS 2021 EMERALD data. Median PFS in elacestrant 400 mg dose. Note: ORR of 4.5% (8/179).
3. Source: SABCS 2023 Veritac data. Median PFS at 200 mg dose across all patients.
4. Source: ASCO 2021 Phase 1a/b giredestrant results. Median PFS estimated based on subset of giredestrant patients at 30 mg dose with CDK4/6i experience (27 of 41). Note: Six cPRs at 30 mg were all in CDK4/6i-naïve patients.
5. Source: SABCS 2022 Serena-2 data. Median PFS in CDK4/6i-experienced patients at 75 mg (5.5 months) and 150 mg (3.8 months). Represents <2 prior lines of ET-only +/- CT.
Note: Serena-1 data at 75 mg dose had 2 PRs out of 22 patients; both were CDK4/6i naïve.
6. Source: Emerald-eligible patient population from palazestrant Phase 2 dataset (2/3L +/-CT) with ESR1 mutations detected at baseline

Phase 1b/2 Combination Clinical Results (SABCS 2023)

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Phase 2 Combination Studies Ongoing with CDK4/6 Inhibitors

Palazestrant + Palbociclib Phase 2 Ongoing

Palazestrant 120 mg + Palbociclib 125 mg

N=60 patients

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

Palazestrant + Ribociclib Phase 2 Ongoing

Palazestrant 120 mg + Ribociclib 600 mg

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

Palbociclib Combination: Attractive Combinability with No DLTs, No DDIs

Preliminary efficacy signals and anti-tumor activity shown in both wild-type and ESR1 mutant

Palbociclib combination Phase 1b/2 clinical results from SABCS 2023, enrollment ongoing

Demographics

- 46 heavily pretreated patients as of data cut-off of September 15, 2023
- 91% were 2/3L+ at study entry
- 44% visceral disease; 22% non-measurable disease
- 72% had prior CDK4/6i treatment
- 22% received prior chemotherapy
- 43% activating mutations in *ESR1*

Safety: Well tolerated

- 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 established profile of palbociclib + aromatase inhibitors

Favorable Pharmacokinetics

- No drug-drug interaction (DDI) between palbociclib and palazestrant
- Palazestrant did not affect palbociclib 125 mg exposure, and palbociclib did not affect palazestrant exposure at any dose level

SAN ANTONIO BREAST CANCER SYMPOSIUM®

Abbreviations: **CDK4/6i**, cyclin dependent kinase 4/6 inhibitor; ***ESR1***, estrogen receptor 1 gene; **TEAE,** treatment-emergent adverse event;
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] (n=46)			PALOMA-3 Comparison Palbociclib + Fulvestrant[b,c] (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.

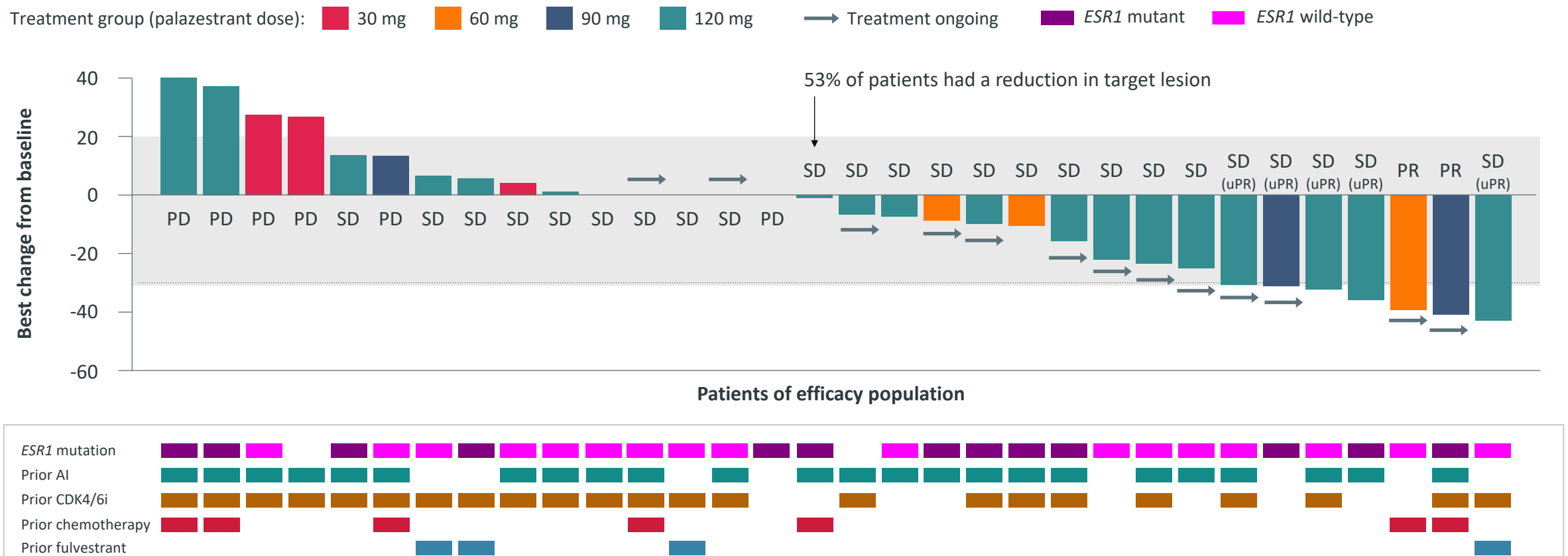
[b]Source: Palbociclib package insert referencing Paloma-3 trial results. [c]Adverse reactions reported in ≥10% of patients who received palbociclib plus fulvestrant in the PALOMA-3 study.

[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

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

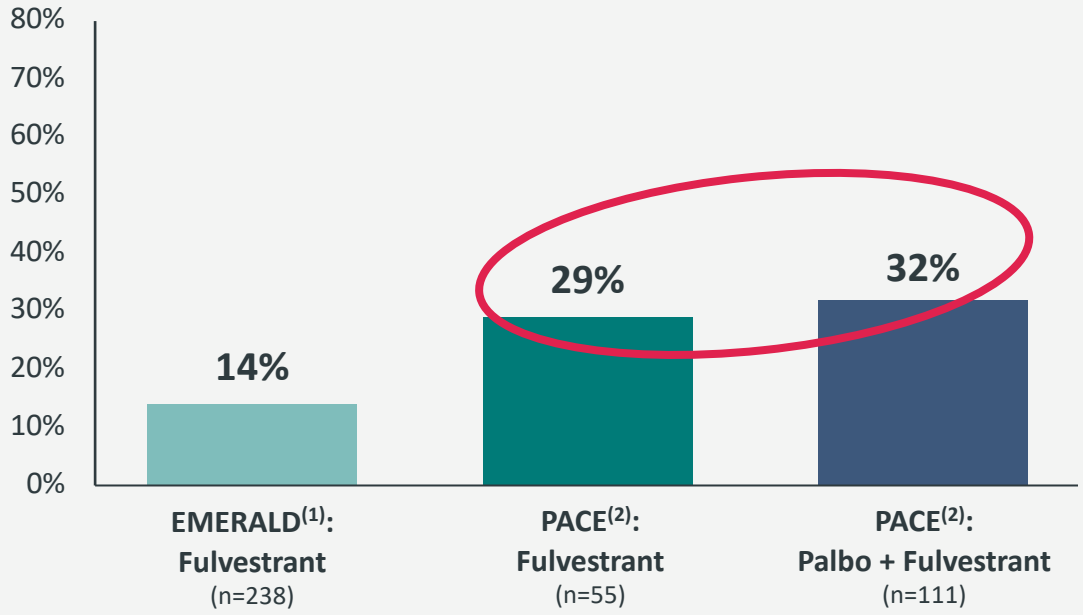
[a]Each lane represents one patient.

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).

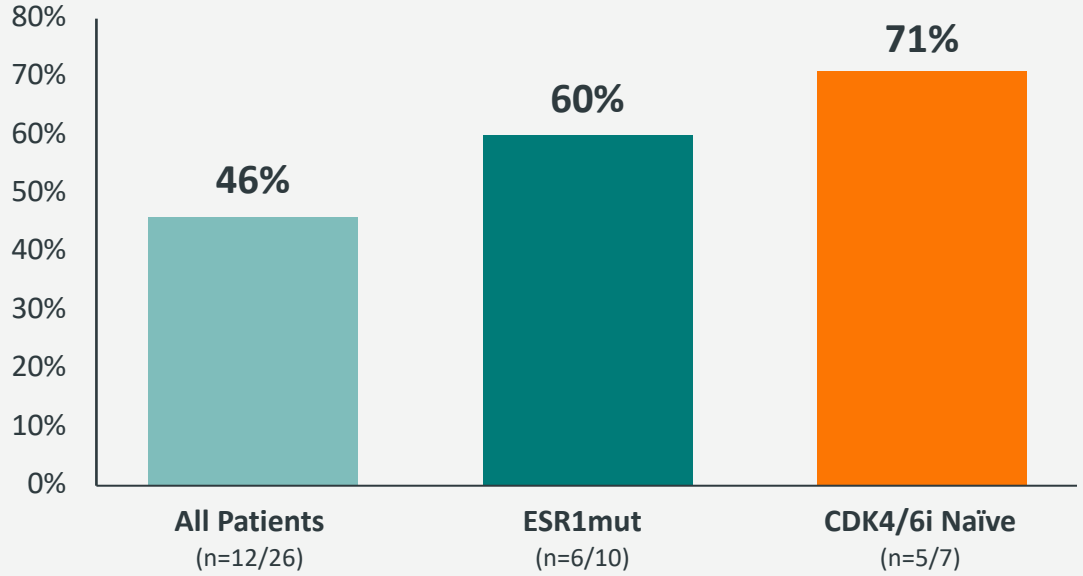
Preliminary Combination Clinical Benefit Rate in 2/3L+ Patients

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 – Potential Best-in-Class Combinability

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

Treatment	Palazestrant	Fulvestrant (PALOMA-3)	Camizestrant	Giredestrant	Vepdegestrant
Study	Phase 1b/2	Phase 3	Phase 1 (parts C/D) (SERENA-1)	Phase 1b	Phase 1b (part C)
Dose	120 mg / 125 mg (palbo)	500 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)	521 (randomized palbo vs. Pbo, 2:1)	25	48	46 (21 w/ 200 mg vepdegestrant)
Prior Tx	0 – 2 Lines 72% prior CDK4/6i	75% prior therapy	68% prior fulvestrant 80% prior CDK4/6i	7% prior fulvestrant **0% prior CDK4/6i**	80% prior fulvestrant 87% prior CDK4/6i
Non-Measurable	22%	22%	32%	NA	33%
$ESR1_{MUT}$	43%	ND	44%	29%	**63%**
Notable TEAEs	• G4 neutropenia (11%) • G1/2 nausea (57%) • G1/2 vomiting (37%) • G1/2 diarrhea (24%)	• G4 neutropenia (11%) • G1/2 nausea (34%) • G1/2 diarrhea (24%) • G1/2 vomiting (19%)	• G4 neutropenia (12%) • Visual effects (44%) • Bradycardia (16%)	• G3/4 neutropenia (60%; G4 not disclosed) • 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	No	No	46 - 58% increase in palbo exposure
CBR	46% All / 60% for $ESR1_{MUT}$	Not reported	28%	81%(1)	63%(2)
Source	SABCS 2023	Ibrance USPI	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]All patients were CDK4/6i naïve, with lower dose of giredestrant 30mg in current trials.

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

30mg dose in current trials given bradycardia and diarrhea. ^ Dose finding at lower doses of 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 Combination: Combinability with the CDK4/6i-of-Preference

No significant DDIs, no DLTs, overall safety profile consistent with expected of ribociclib plus ET

Ribociclib Phase 1b combination data from SABCS 23, enrollment ongoing

Demographics

- 19 heavily pretreated patients as of data cut-off of November 1, 2023
- 100% were 2/3L+ at study entry
- 37% visceral disease
- 89% had prior CDK4/6i treatment
- 26% received prior chemotherapy
- 29% with activating mutations in *ESR1*

Safety: Well-tolerated with no DLTs

- Overall safety and tolerability profile consistent with ribociclib + endocrine therapy
- 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

Favorable Pharmacokinetics

- Palazestrant did not affect ribociclib drug exposure in patients, and ribociclib had no clinically meaningful effect on palazestrant drug exposure

SAN ANTONIO BREAST CANCER SYMPOSIUM®

Abbreviations: **CDK4/6i**, cyclin dependent kinase 4/6 inhibitor; ***ESR1***, estrogen receptor 1 gene; **DLT**, dose-limiting toxicity; **MTD**, maximum tolerated dose; **TEAE,** treatment-emergent adverse event
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] (n=19)			MONALEESA-2 Ribociclib + Letrozole[b,c] (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

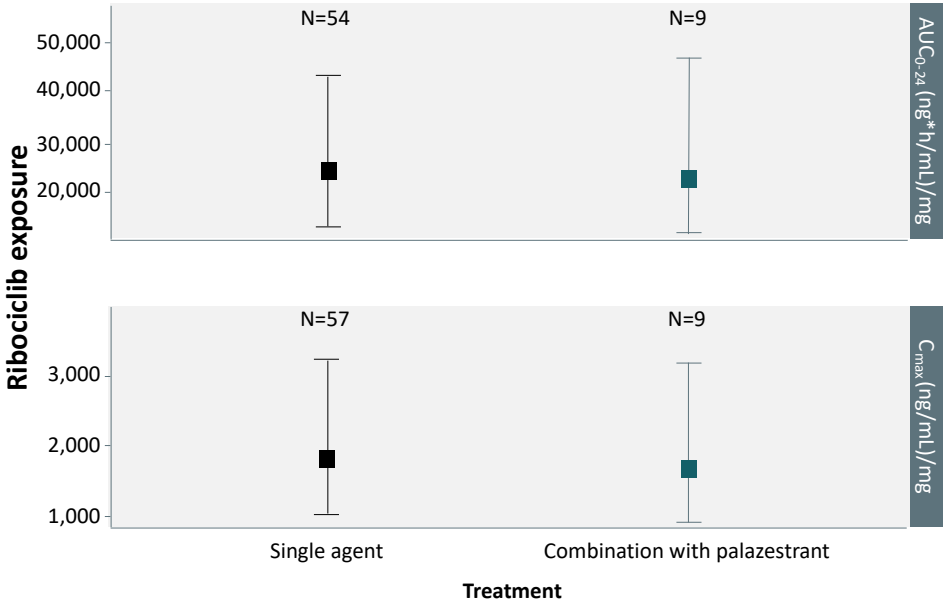
- No DLTs were observed during dose escalation and MTD was not reached
- No dose-related increases in the incidence or severity of TEAEs was observed
- **No grade 4 TEAEs reported**
- No QTcF values of >500 msec were observed at any time point
- Overall safety and tolerability profile consistent with 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

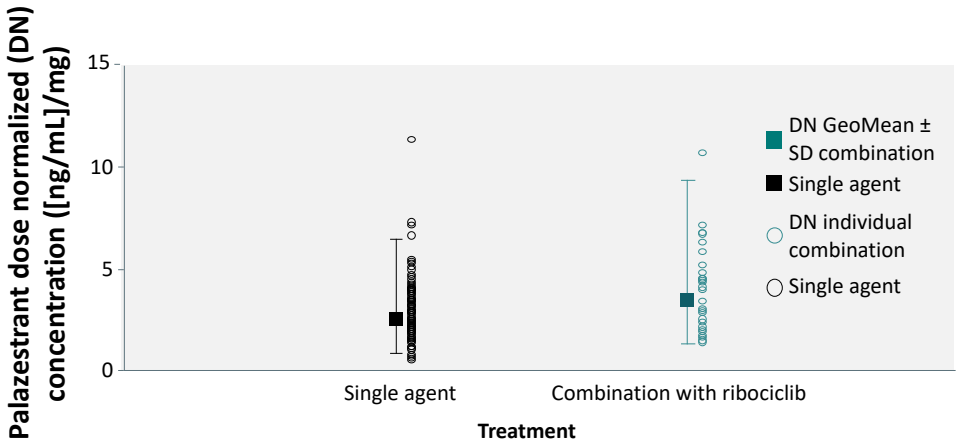
No significant effect on exposure levels

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



- 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

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



- 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

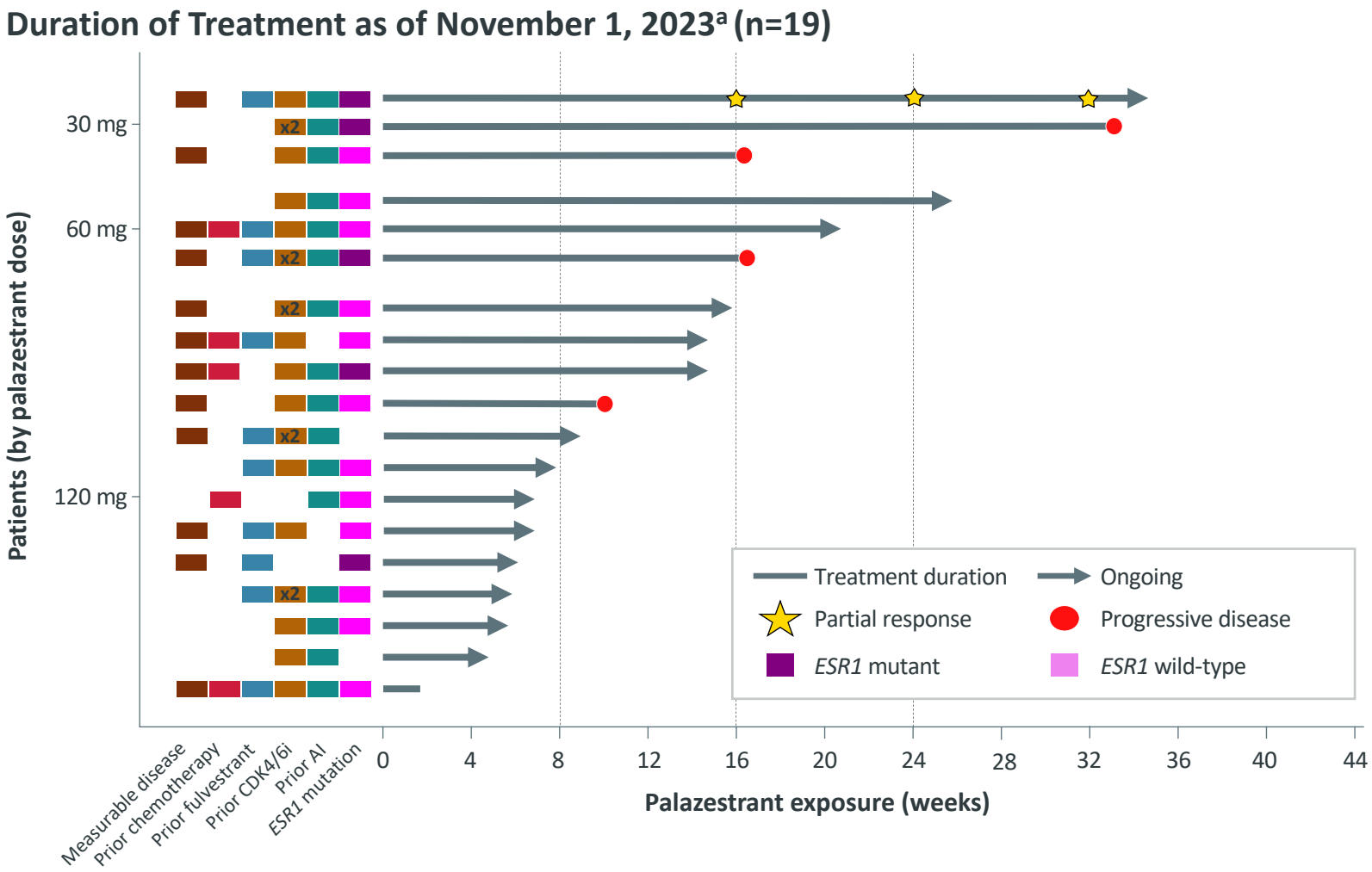
Data Cutoff Date: November 1, 2023.

Note: Data are geometric mean ± geometric standard deviation.

Abbreviations: **AUC_{0-24}**, 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

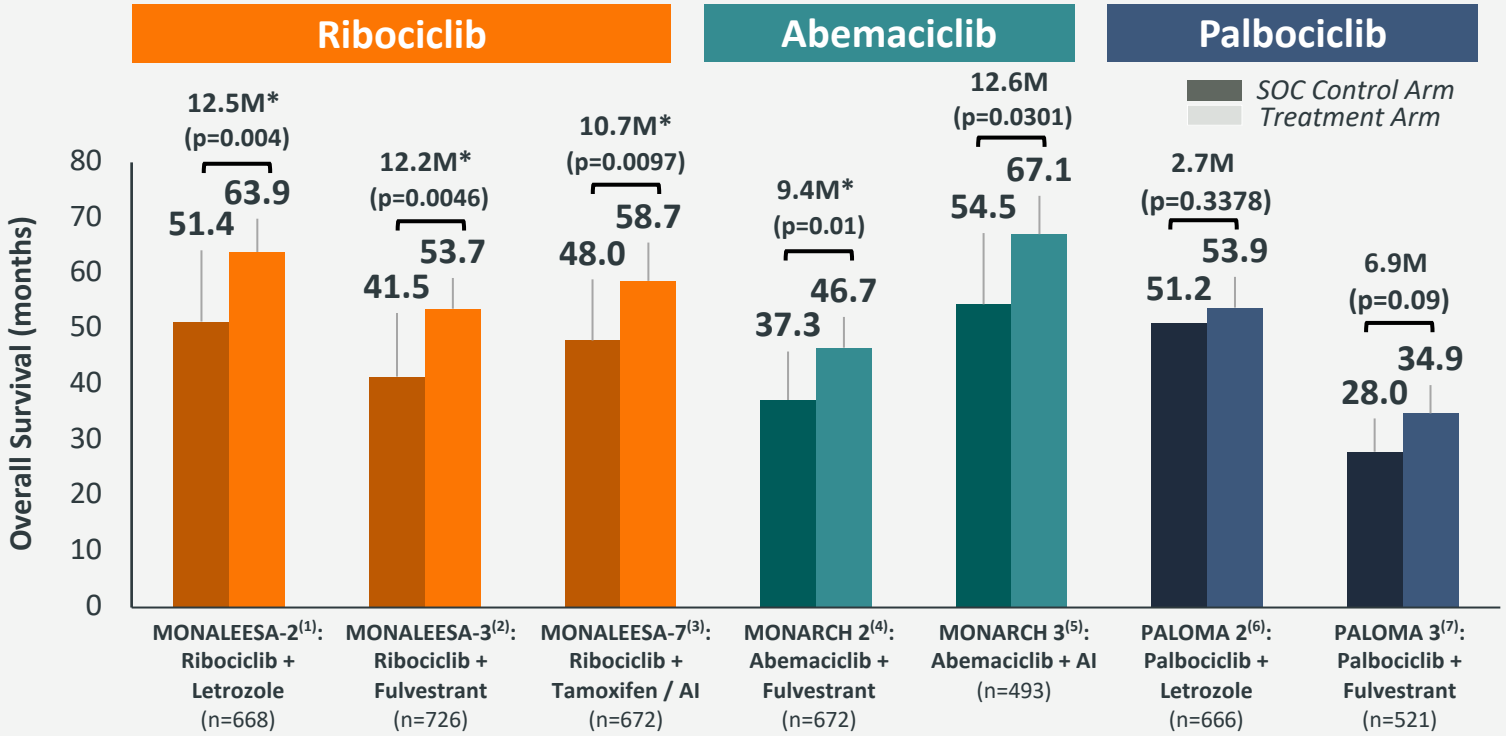
Data Cutoff Date: November 1, 2023.

[a]Each lane represents one patient.

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

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

Palazestrant will be the only novel ET combined with ribociclib in a pivotal trial; all other 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.**

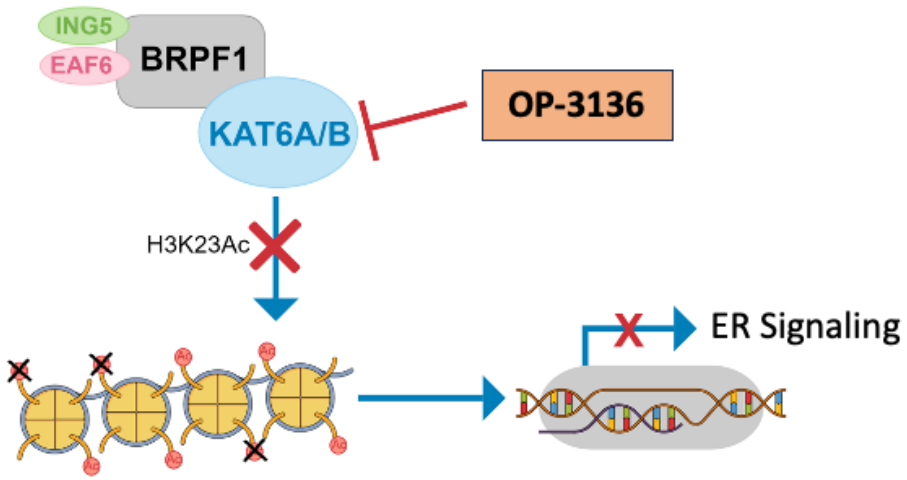
Source: (1) Hortobagyi G.N., et al. Overall Survival with Ribociclib plus Letrozole in Advanced Breast Cancer. NEJM. 2022;386:942-950; (2) Salmon D.J., et al. Overall Survival with Ribociclib plus Fulvestrant in Advanced Breast Cancer. NEJM. 2020;382:514–524; (3) Im S.-A., et al. Overall Survival with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

Advancing in Pivotal Phase 3 Trials

Olema ONCOLOGY

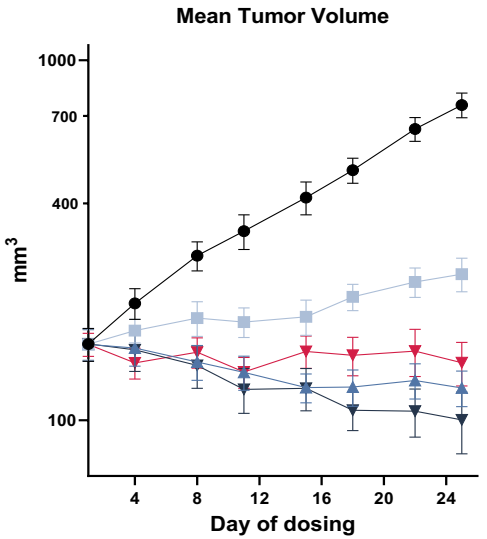
OP-3136 – Olema KAT6 Inhibitor Development Candidate

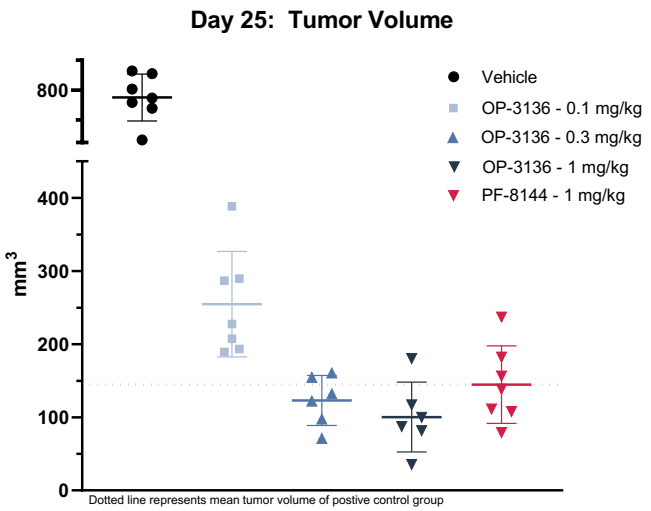
Anti-tumor Activity in Xenograft Models



- KAT6 is a clinically validated target[1] and its overexpression correlated with worse clinical outcome in ER+ breast cancer[2]
- KAT6 inhibition downregulates genes involved **in estrogen receptor signaling** and other signaling pathways[3]

OP-3136 demonstrates anti-tumor activity in xenograft models





- OP-3136 is potent and selective against KAT6A/B
- Orally bioavailable with high levels of free drug exposure
- **OP-3136 synergizes with palazestrant** and CDK4/6 inhibitors in preclinical models

OP-3136 demonstrates activity in both ESR1 wild-type and mutant breast cancer cell lines, synergizes with ERα and CDK4/6 inhibitors, and causes tumor reduction in ER+ breast cancer models

Abbreviations: **CDK4/6i**, cyclin dependent kinase 4/6 inhibitor; **ER+**, estrogen receptor-positive; ***ESR1***, estrogen receptor 1 gene; **KAT6i,** lysine acetyltransferase 6 inhibitor

References: 1. Sommerhalder D, et al. First-in-human ph 1 dose escalation study of the KAT6 inhibitor PF-07248144 in patients with advanced solid tumors. JCO. 2023. 41(16)1054-1054;
2. Yu L, et, al. Identification of MYST3 as a novel epigenetic activator of ERα frequently amplified in breast cancer. Oncogene. 2017 May 18;36(20):2910-2918
3. Sharma S, et al. Discovery of a highly potent, selective, orally bioavailable inhibitor of KAT6A/B histone acetyltransferases with efficacy against KAT6A-high ER+ breast cancer. Cell Chemical Biology. 30, 1–20

Note: Olema KAT6 inhibitors discovered in collaboration with Aurigene

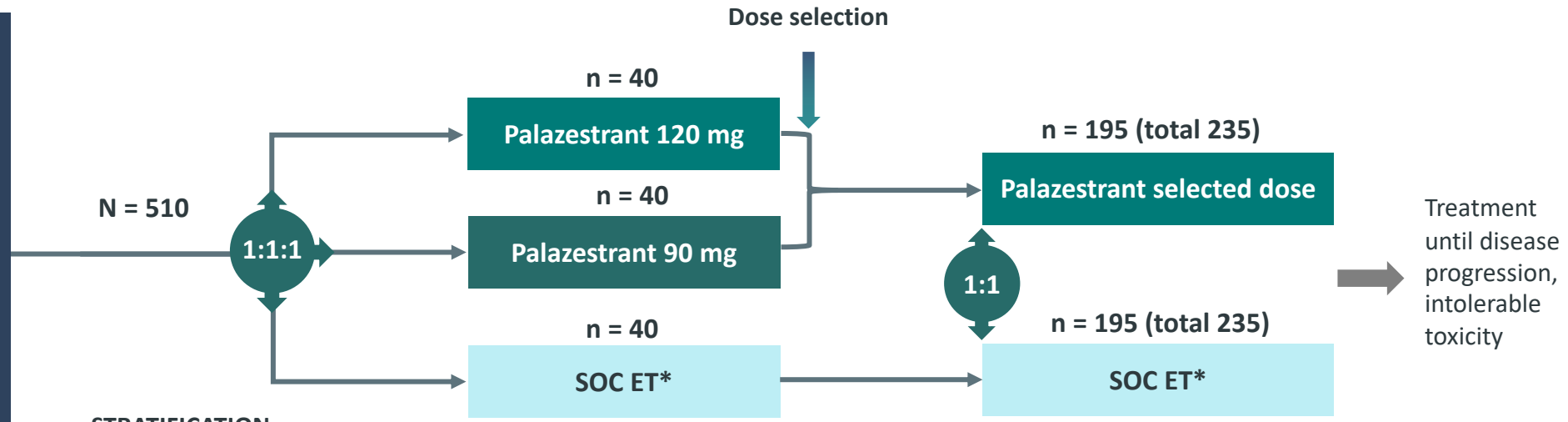
OPERA-01 Phase 3 Trial Overview

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

OPERA-01 Breast Cancer Study

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

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

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 ~$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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