Olema ONCOLOGY

Corporate Overview

Advancing medicines for breast cancer and beyond

December 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 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 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 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 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 potential preclinical studies and clinical trials for 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.

— 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

What drives us: we are all impacted by breast cancer

The most common cancer diagnosed and the second leading cause of cancer death among women

1 in 8*

Women in the U.S. will be diagnosed with invasive breast cancer in her lifetime

~311k*

Estimated women in the U.S. that will be diagnosed with breast cancer in 2024

~42k*

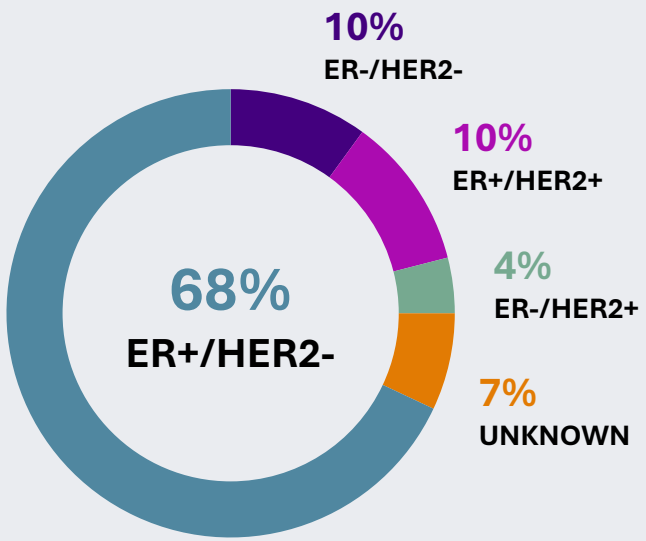
Estimated women in the U.S. will die of metastatic breast cancer in 2024

*Source: American Cancer Society

Today's therapies are insufficient to meet patient needs

Patient outcomes reflect limitations and discontinuations of currently available therapies

A majority of all breast cancers are estrogen receptor positive (ER+)*



Current ER targeting agents have significant deficiencies

AIs
SERMs
SERDs

- **Incomplete ER antagonism**
- **Sub-optimal PK profile**
- **Limited CNS penetration**
- **Tolerability issues**

Common targeted Tx used in combination with an endocrine agent

- abemaciclib (CDK4/6i)
- palbociclib (CDK4/6i)
- ribociclib (CDK4/6i)
- alpelisib (PI3Kai)
- everolimus (mTORi)
- capivasertib (AKTi)

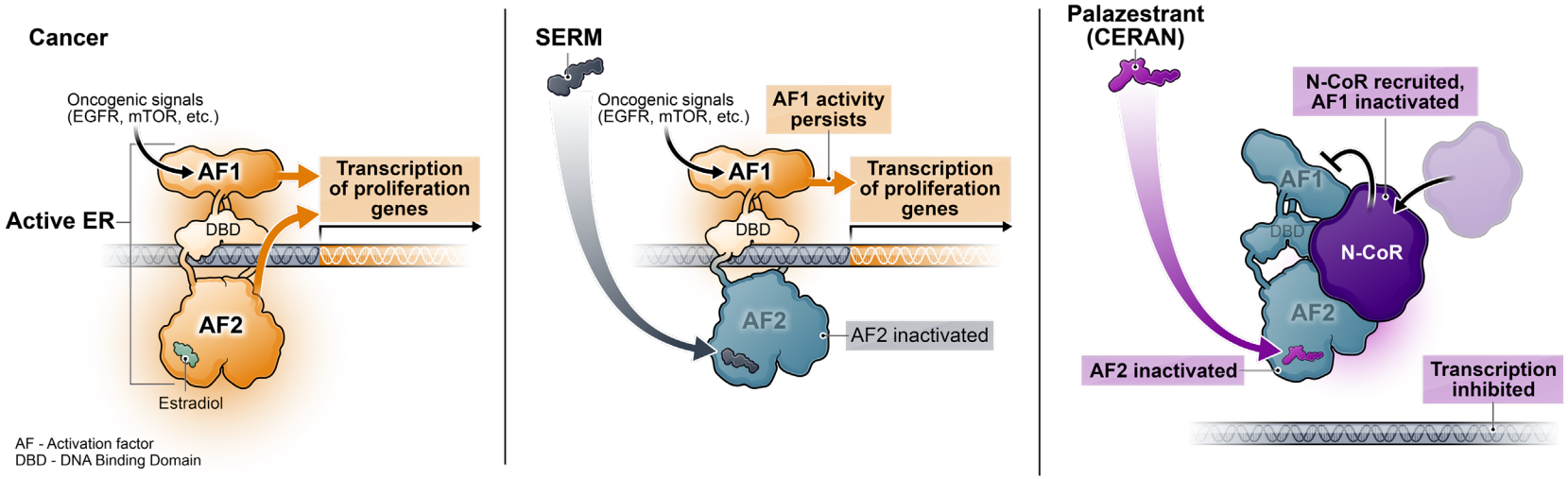
"Aromatase inhibitors are **life-saving** … but **life-eroding** and really difficult to be on."
– ER+/HER2- Stage 3A patient

Source: National Breast Cancer Foundation, World Health Organization; American Cancer Society. Facts and Figures 2024; SEER database
***ER** = estrogen receptor; **HER2** = human epidermal growth factor receptor 2; **AI** = aromatase inhibitor; **SERM** = selective estrogen receptor modulator; **SERD** = selective estrogen receptor degrader; **CDK4/6i** = cyclin-dependent kinase 4/6 inhibitor; **PI3Kαi** = phosphatidylinositol 3-kinase alpha inhibitor; **mTORi** = mammalian target of rapamycin inhibitor; **AKTi** = serine/threonine protein kinase 1*

Palazestrant (OP-1250) has the attributes of a therapeutic class leader

A differentiated oral CERAN/SERD targeting metastatic breast cancer with experience in over 400 patients to date

Growth and Proliferation Mechanism Driving ER+ Breast Cancer



Activated ER **drives cancer cell** growth

SERMs and SERDs **partially** inactivate ER

Palazestrant **completely** inactivates ER

Palazestrant delivers what patients need

- Once-daily oral delivery
- Favorable tolerability
- Combinability
- Complete ER antagonism
- Robust tumor shrinkage
- Attractive PK profile
- CNS penetration

Our goal: helping patients **feel better, longer**

***CERAN** = complete estrogen receptor antagonist; **SERM** = selective estrogen receptor modulator; **SERD** = selective estrogen receptor degrader*

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

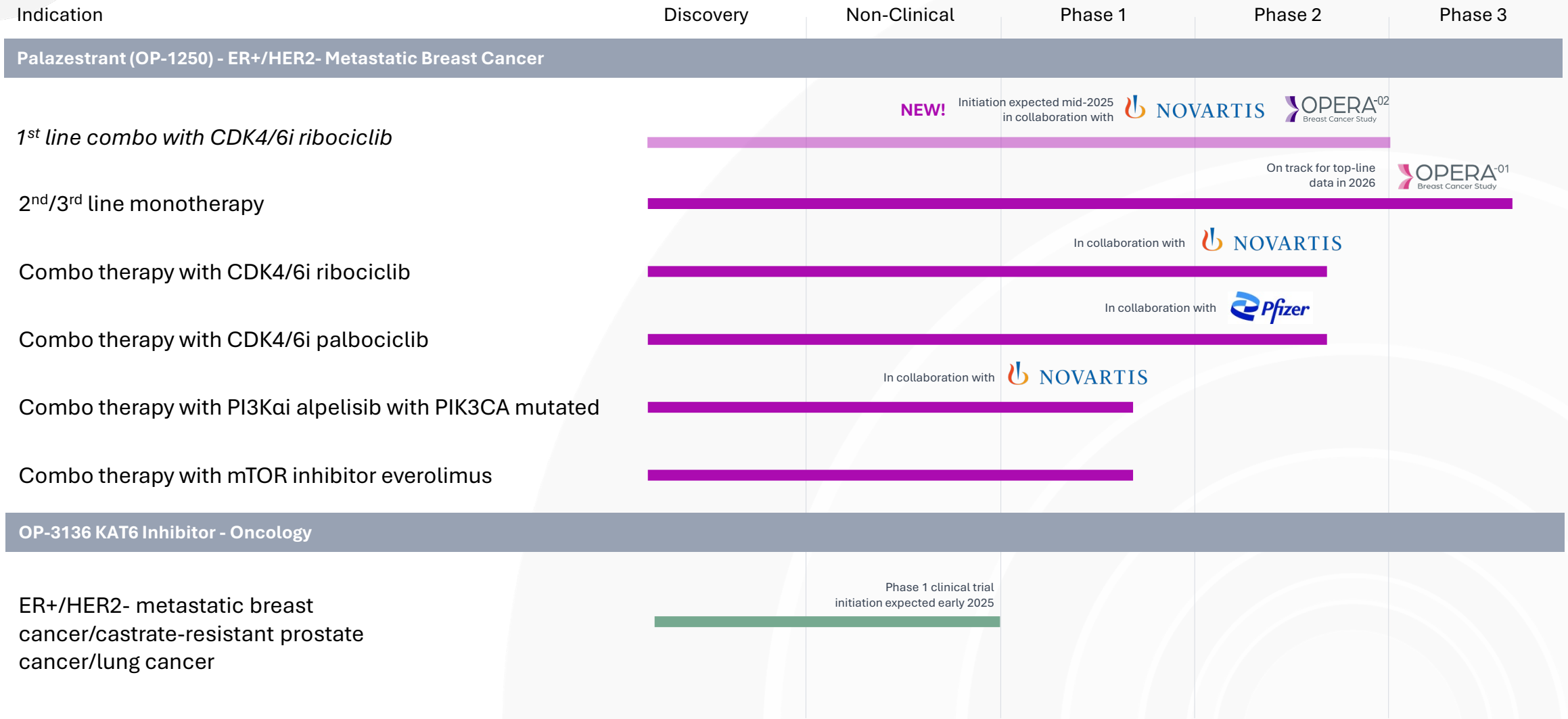
OPERA-02 Breast Cancer Study

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 EU5). 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.*

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*

Strategy driven by leaders positioned to go the distance

Oncology and industry experts with track record of advancing programs from clinical to commercial

Executive Leadership Team

Sean Bohen, M.D., Ph.D.
President and CEO

Shane Kovacs
Chief Operating and Financial Officer

Naseem Zojwalla, M.D.
Chief Medical Officer

David Myles, Ph.D.
Chief Discovery and Non-Clinical Development Officer

Julie Dexter
Senior Vice President and Head of People

Experience

AstraZeneca
BlueRock Therapeutics
Peloton Therapeutics
Abbott
ImClone Systems
KOSAN BIOSCIENCES
PTC Therapeutics
Eisai
ONYX Pharmaceuticals
Turning Point Therapeutics
Roche
Genentech
RBC Capital Markets
CREDIT SUISSE
pharmacyclics An AbbVie Company
CHIRON

Board of Directors

- Ian Clark
  Chairman of the Board
- Sean Bohen, M.D., Ph.D.
  President and CEO
- Sandra Horning, M.D., FACP, FASCO
- Cindy Butitta
- Scott Garland
- Cyrus Harmon, Ph.D.
- Gorjan Hrustanovic, Ph.D.
- Yi Larson
- Andy Rappaport
- Graham Walmsley, M.D., Ph.D.

CORPORATE PRIORITIES AND ANTICIPATED MILESTONES

Q4 2024

- Execute OPERA-01 pivotal Phase 3 2/3L monotherapy trial
- Enroll palazestrant + everolimus Phase 1b/2 clinical study
- Presented OP-3136 KAT6i non-clinical data at ENA 2024 (October)
- Announced new Novartis agreement (December)
- Presented palazestrant + ribociclib efficacy data at SABCS (December)
- IND for OP-3136 KAT6i cleared (December)

2025

- Initiate OP-3136 KAT6i Phase 1/2 clinical study (early 2025)
- Continue to execute OPERA-01 pivotal Phase 3 2/3L monotherapy trial
- Initiate OPERA-02 palazestrant + ribociclib 1L pivotal Phase 3 trial (mid-year)

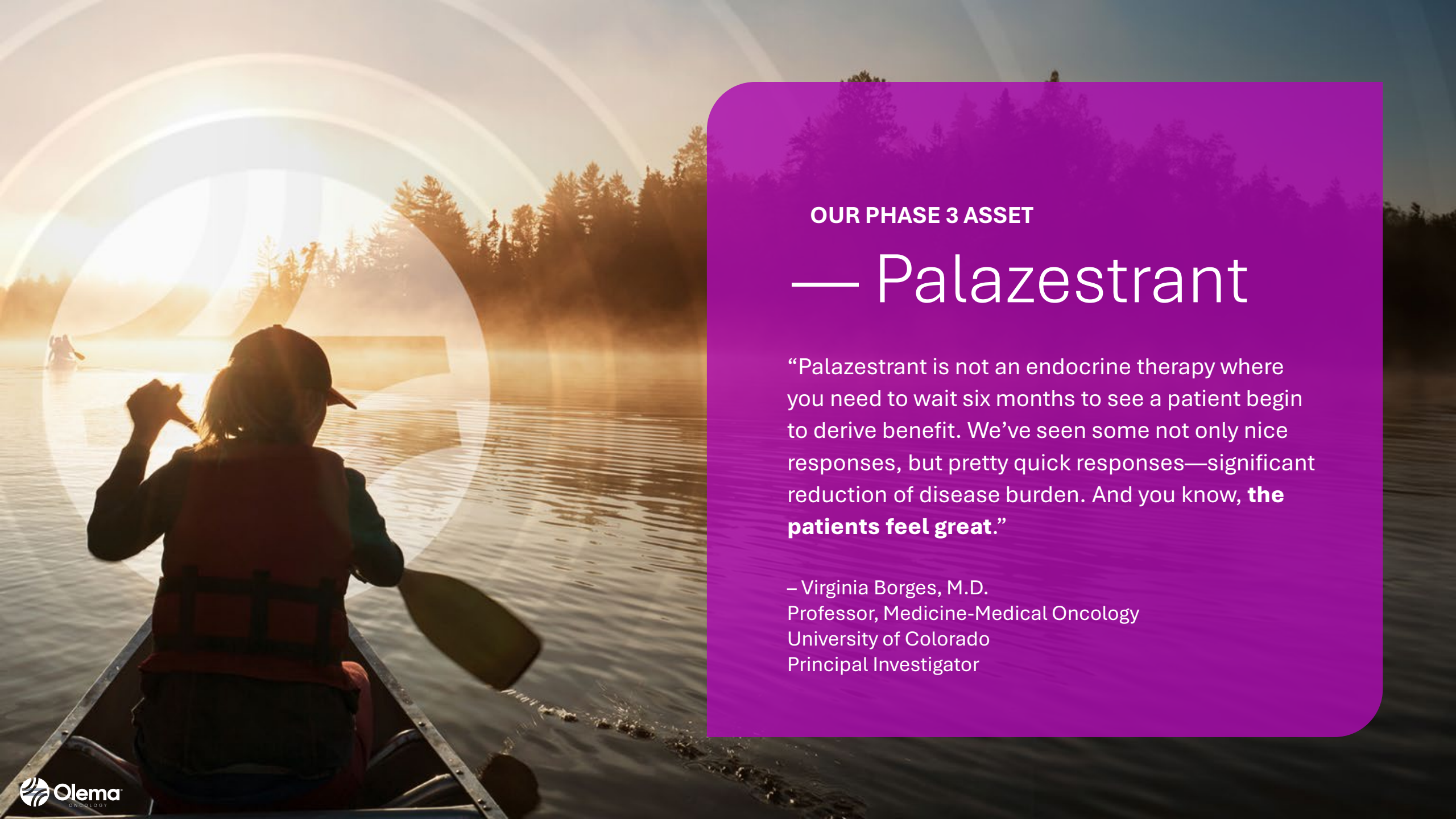
2026

- Announce OPERA-01 pivotal Phase 3 2/3L monotherapy top-line results
- Anticipate OP-3136 KAT6i initial clinical data from Phase 1/2 clinical study
- File NDA for palazestrant for 2/3L monotherapy approval
- Prepare for commercial launch

2027

- Anticipated U.S. commercial launch

KAT6i *= lysine acetyltransferase 6 inhibitor*



OUR PHASE 3 ASSET

— Palazestrant

"Palazestrant is not an endocrine therapy where you need to wait six months to see a patient begin to derive benefit. We've seen some not only nice responses, but pretty quick responses—significant reduction of disease burden. And you know, **the patients feel great**."

– Virginia Borges, M.D.
Professor, Medicine-Medical Oncology
University of Colorado
Principal Investigator

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Clinical development strategy to unlock the potential of palazestrant

Potential best-in-class backbone therapy designed to preserve and prolong a higher quality of life

Establishing palazestrant as the backbone endocrine therapy of choice across the metastatic setting

2/3L+

OPERA-01

- Ongoing 510-patient Phase 3 trial
- Monotherapy trial vs. SoC
- Phase 1/2 monotherapy data support potentially differentiated opportunity
- Top-line results expected 2026

1L

OPERA-02

- Proposed ~1,000 patient Phase 3 trial
- Palazestrant in combination with ribociclib vs. SoC
- Phase 1/2 palazestrant + ribociclib combination data demonstrate no significant DDI and tolerability profile consistent with the FDA-approved label of ribociclib; efficacy maturing
- Successfully completed FDA interactions
- Preparing for initiation in 2025

__SoC__ = standard of care; __DDI__ = drug-drug interaction

Palazestrant monotherapy Phase 2 data supports ongoing Phase 3 trial

Data demonstrate palazestrant is well-tolerated with favorable PK and differentiated efficacy profile

Differentiated Efficacy Profile

- Median PFS of 7.3 months in 2/3L ±CT *ESR1*-mutant
- Median PFS of 5.5 months in 2/3L ±CT *ESR1*-wild-type

Favorable Pharmacokinetics

- High oral bioavailability with daily dosing
- Dose proportional exposure
- Long half-life supports once-daily dosing

Summary Safety

- Well-tolerated
- Most AEs were low grade (1/2)

For more details on this data milestone, please refer to the oral presentation at this link.
***CT** = chemotherapy; **ESR1** = estrogen receptor 1 gene; **PFS** = progression free survival*
Data cutoff date: July 7, 2023

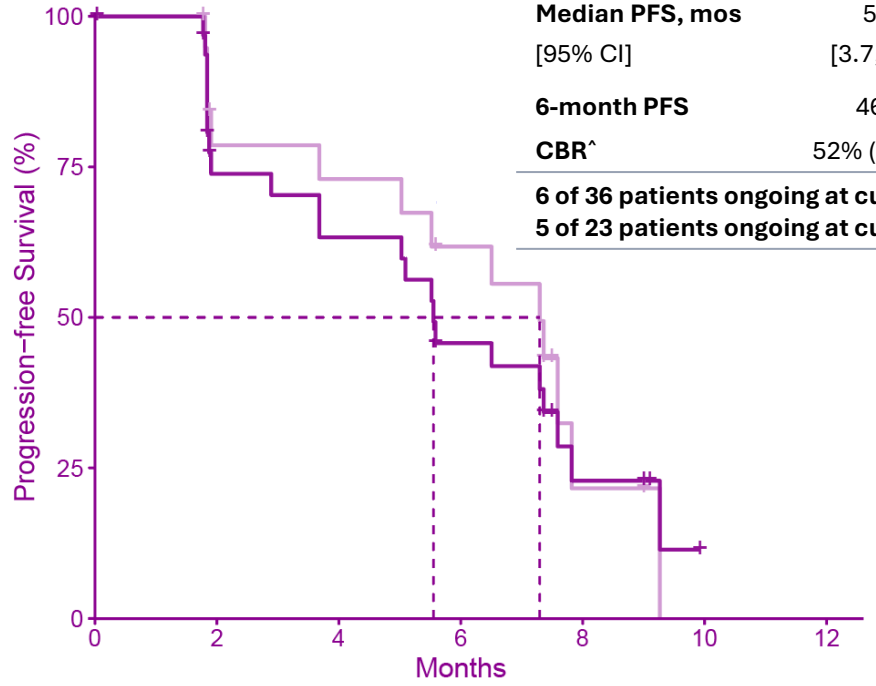
Compelling palazestrant Phase 2 data supports ongoing Phase 3 trial

7.3 months mPFS in *ESR1*-mutant; 5.5 months in wild-type for EMERALD-eligible 2/3L ± CT Patients*

Patients with *ESR1* Mutation[1]

	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

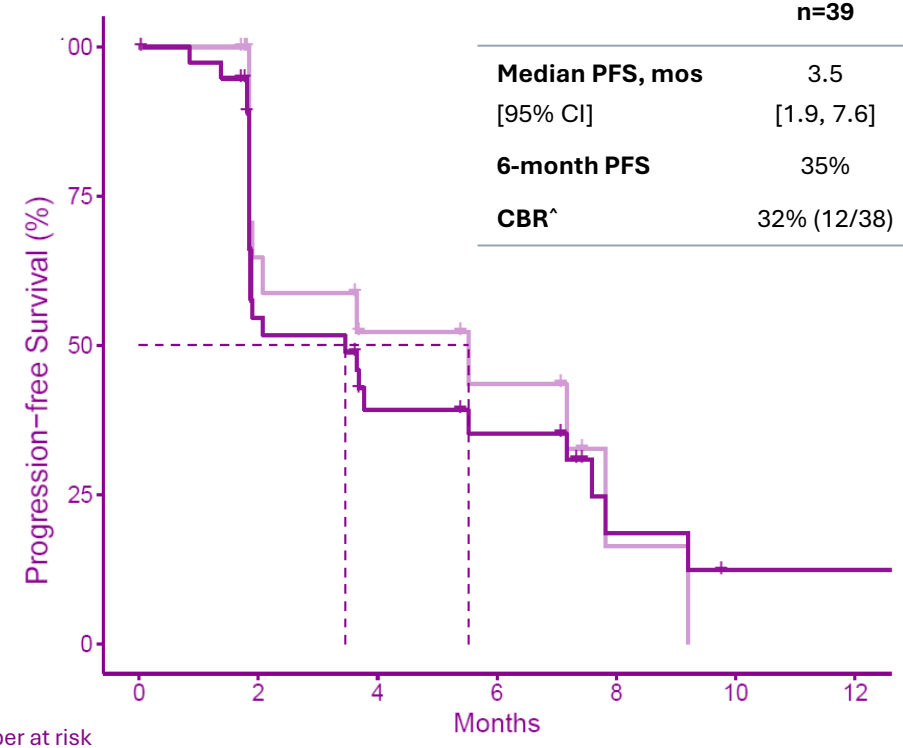


Number at risk

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

Patients with *ESR1* Wild-Type[2]

	ESR1 WT 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)**



Number at risk

All comers	39	19	11	9	3	1	1
2/3L+/−CT	21	11	7	5	1	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***

***2/3L** = second/third line; **± CT** = plus/minus chemotherapy; **CBR** = clinical benefit rate; **CI** = confidence interval; **ESR1** = estrogen receptor 1 gene; **mos**= months; **WT**= wild-type; **mut** = mutation; **NA** = not applicable; **mPFS** = median progression-free survival*

[1] Palazestrant Phase 2 dataset with ESR1 mutations detected at baseline

[2] Palazestrant Phase 2 dataset with ESR1 mutations not detected at baseline

^ 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 post-baseline radiographic assessment. Data cut-off as of July 7, 2023.

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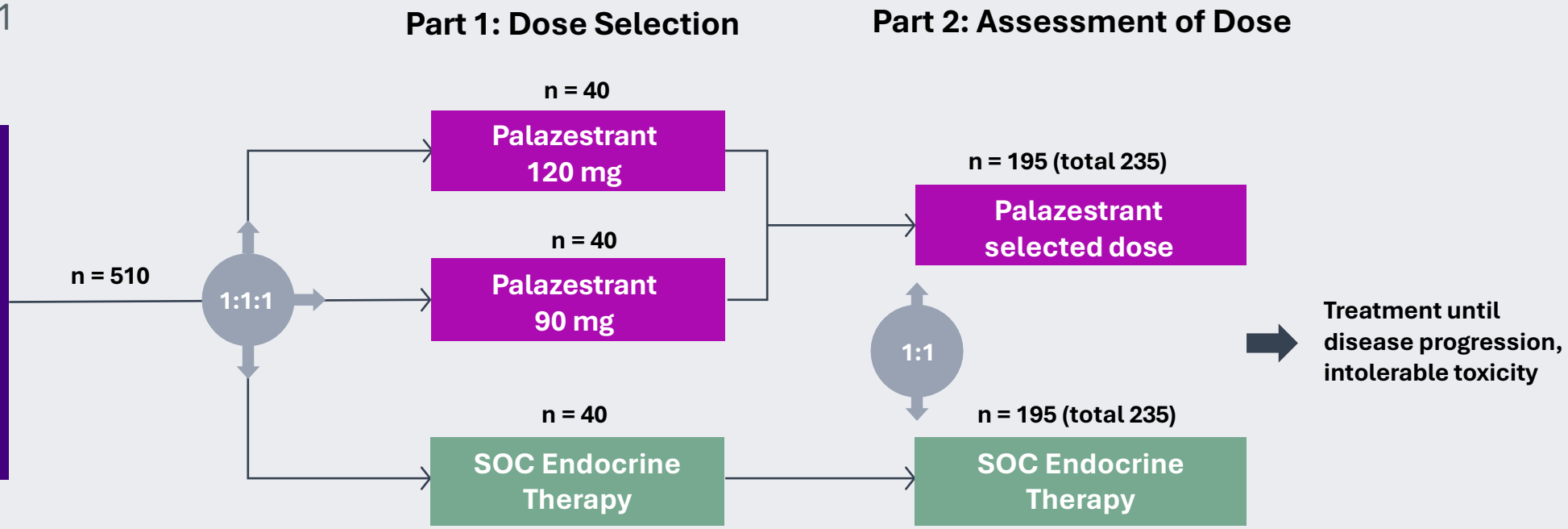
OPERA-01 Phase 3 monotherapy trial designed to show safety/efficacy

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

OPERA-01 Breast Cancer Study

Inclusion criteria:
- 1-2 prior lines of endocrine therapy
- Prior treatment with a CDK4/6 inhibitor
- No prior chemotherapy
- 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 4Q 2023. Results expected in 2026.

For more details on this trial, please visit www.opera01study.com.

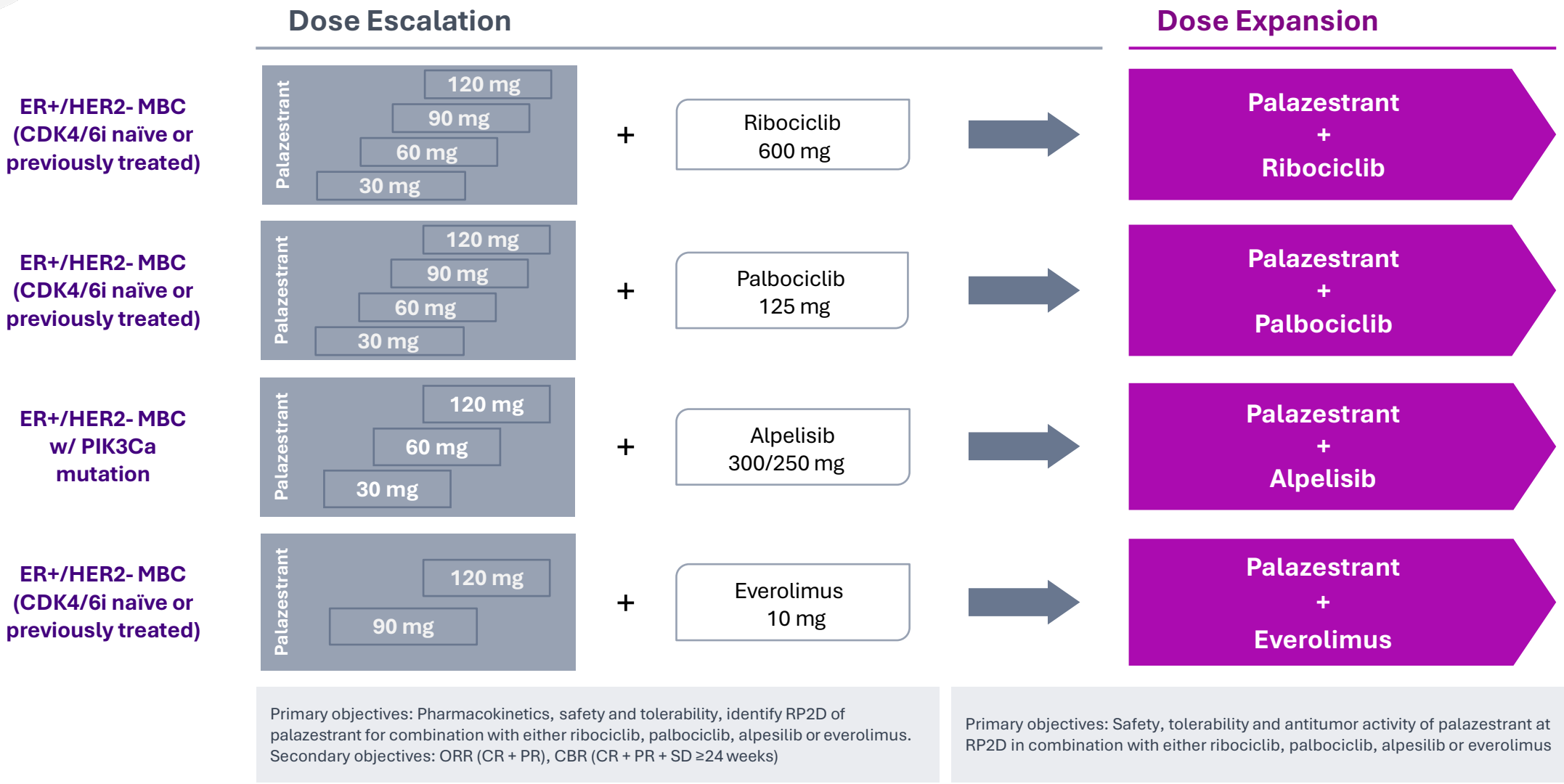
***CDK4/6i** = cyclin dependent kinase 4/6 inhibitor; **ESR1**=estrogen receptor 1 gene; **SOC** = standard of care; **ET** = endocrine therapy; **mut** = mutation; **mut-nd** = mutation not detected*

— “Patients with metastatic breast cancer urgently await therapeutic advances that can be used effectively either as monotherapies or in combination with today’s standard of care to not only extend survival rates, but also deliver a better quality of life. With the body of evidence to date and our continued experience in clinical studies, **palazestrant has strong potential to deliver on these persistent unmet needs**.”

Nancy Lin, M.D.
Associate Chief, Division of Breast Oncology
Dana-Farber Cancer Institute

Palazestrant demonstrates combinability with other targeted agents

Promising combinability for front-line use as well as in 2/3L setting



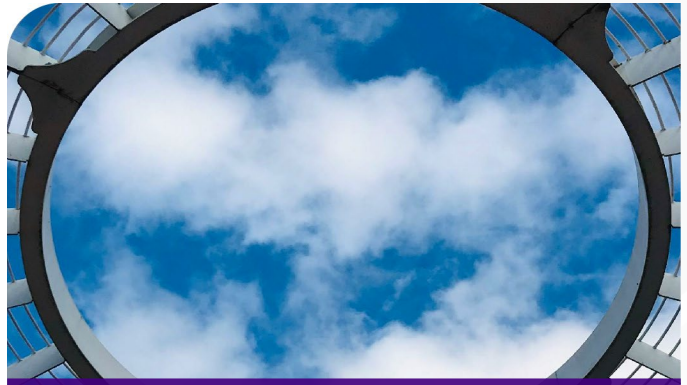
***CDK4/6i** = cyclin dependent kinase 4/6 inhibitor; **CBR** = clinical benefit rate; **CR** = complete response; **ER+** = estrogen receptor positive; **HER2-** = human epidermal growth factor receptor 2 negative; **MBC** = metastatic breast cancer; **PR** = partial response; **SD** = stable disease; **RP2D** = recommended Phase 2 dose; **ORR** = objective response rate*

Palazestrant + ribociclib Phase 2 data supports planned Phase 3 trial

Palazestrant + ribociclib combination demonstrated promising clinical activity, a safety profile consistent with ribociclib + ET, and favorable tolerability

Differentiated Efficacy Profile

- Six-month PFS rate of 73% in all patients
- Six-month PFS rate of 68% in patients with prior CDK4/6i
- Six-month PFS rate of 81% in ESR1-mutant patients
- Six-month PFS rate of 70% in ESR1 wild-type patients



Favorable Pharmacokinetics

- No drug-drug interaction; palazestrant did not affect ribociclib drug exposure
- All patients received the combination with the full and approved dose of 600mg of ribociclib

Summary Safety

- Overall safety profile was consistent with the established safety profile of ribociclib 600 mg + ET
- Most AEs were low grade (1/2)

Data cutoff date: November 11, 2024

***AEs** = adverse events; **ESR1** = estrogen receptor 1 gene; **ET** = endocrine therapy; **PFS** = progression free survival*

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.

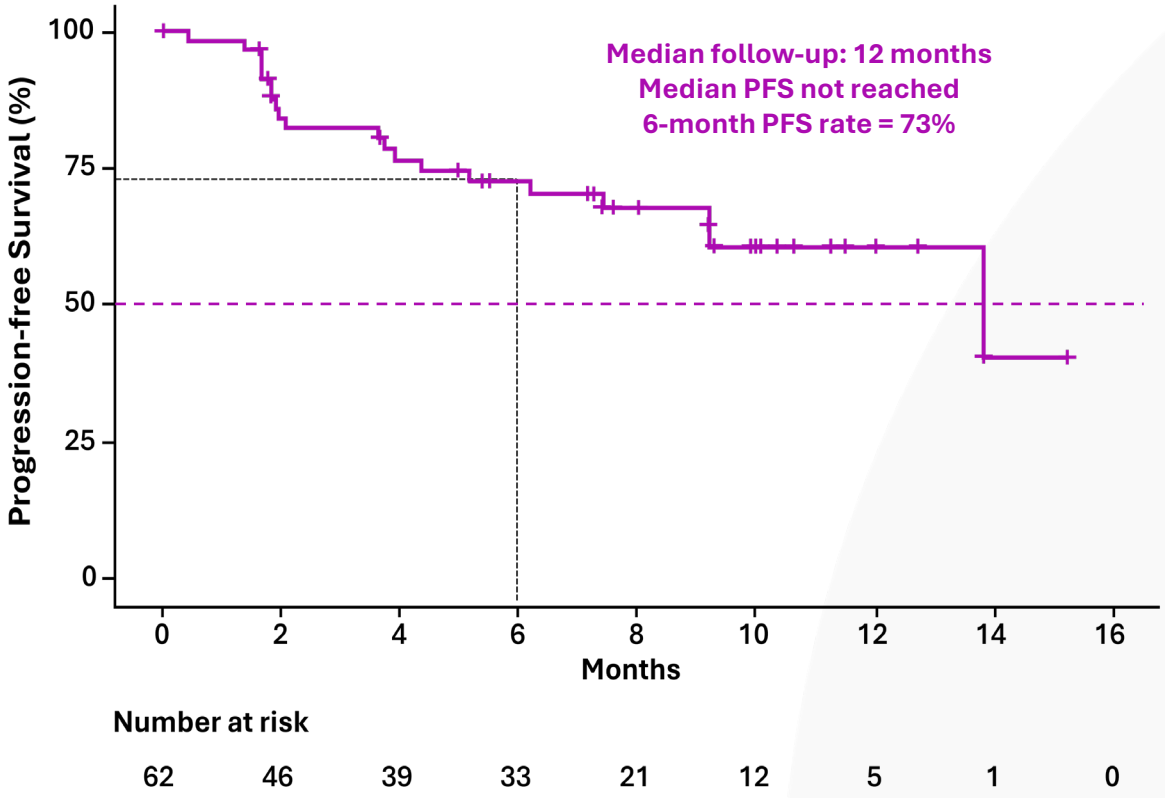
**Includes 3 patients at each of 30 mg and 60 mg palazestrant and 56 patients at 120 mg palazestrant in combination with 600 mg ribociclib. †Adverse reactions reported in ≥10% of patients who received ribociclib plus letrozole in the MONALEESA-2 study.(KISQALI (ribociclib). Prescribing information. Novartis; 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

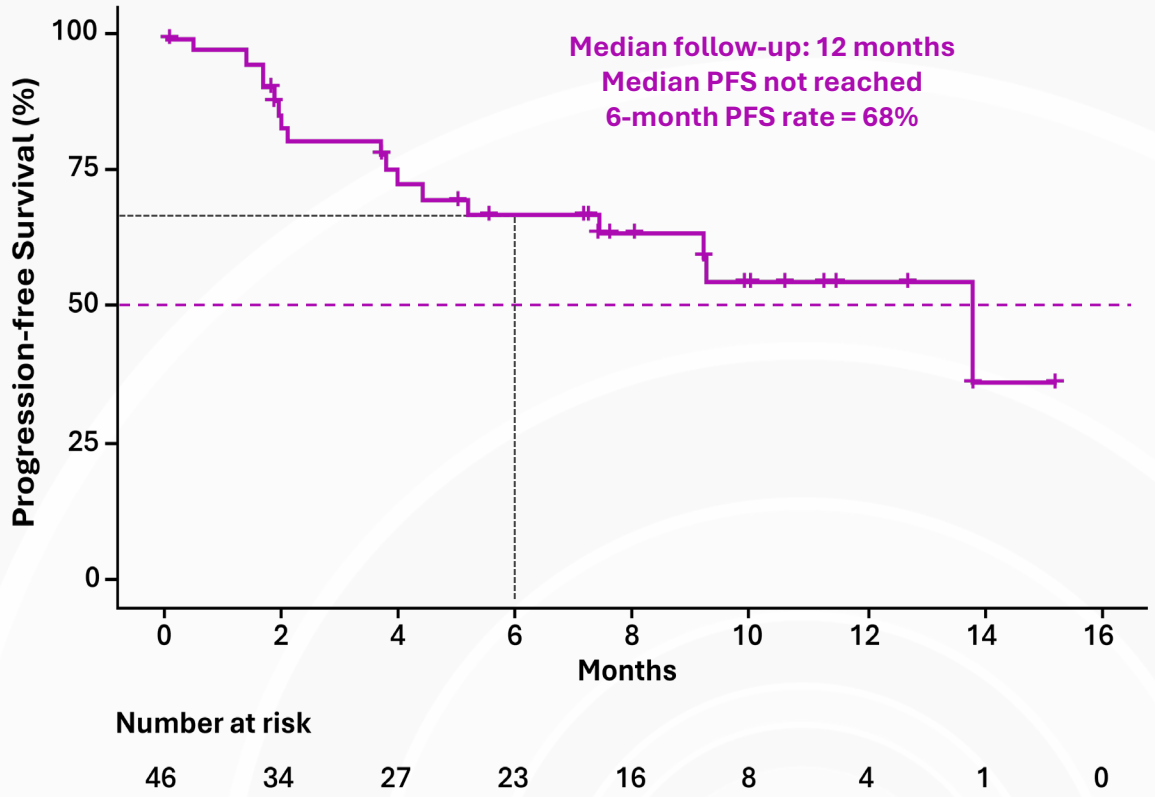
Six-month PFS rate of 73% in all patients, 68% in those with prior CDK4/6i

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

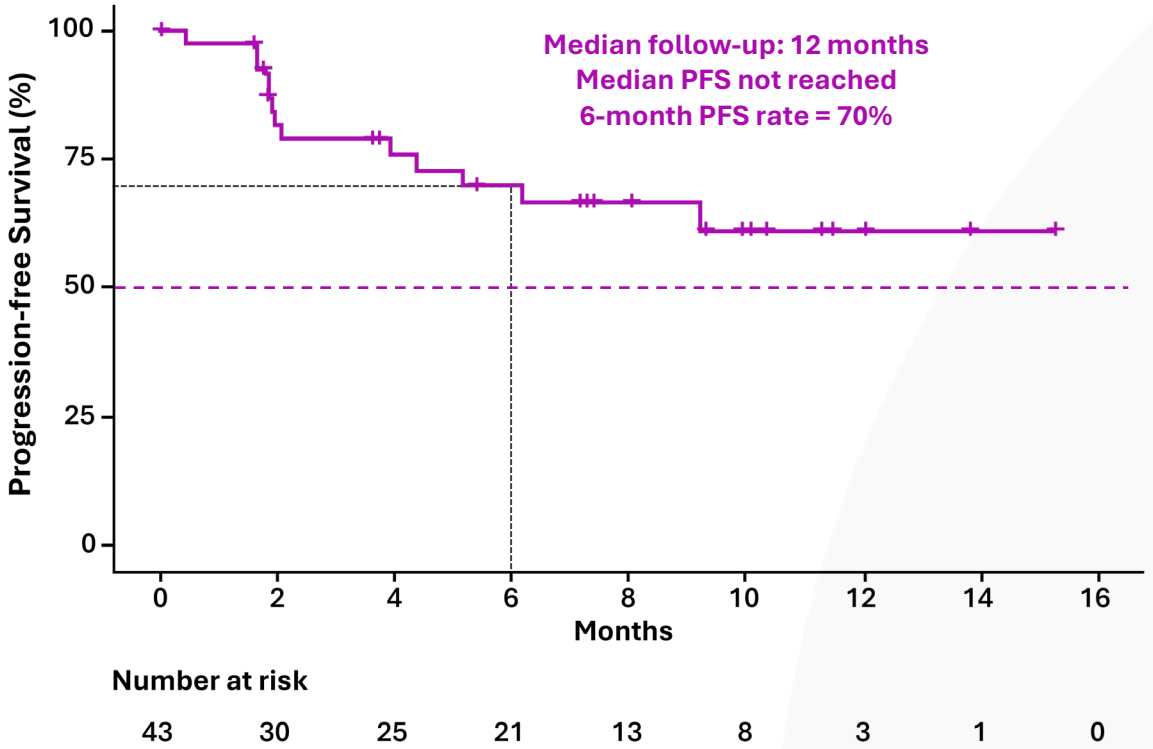
* Follow up was calculated from first dose date to data cutoff date regardless of disease progression status.

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

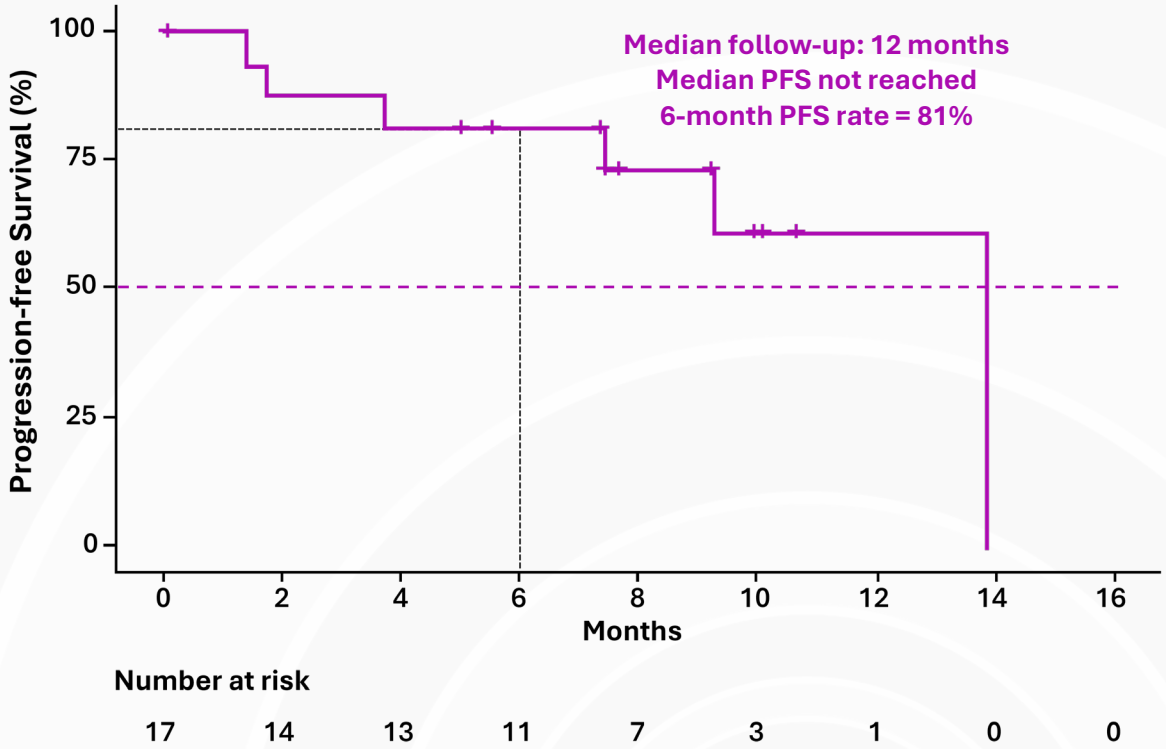
Six-month PFS rate of 81% in *ESR1*-mutant patients, 70% in *ESR1* wild-type

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.

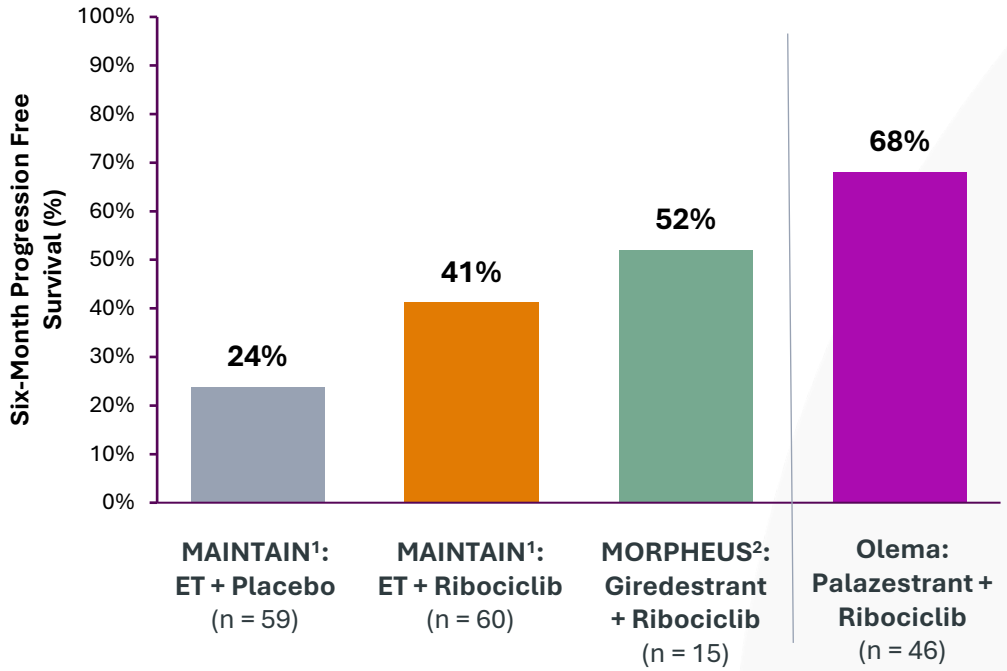
ESR1 = estrogen receptor 1 gene; **PFS** = progression-free survival

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

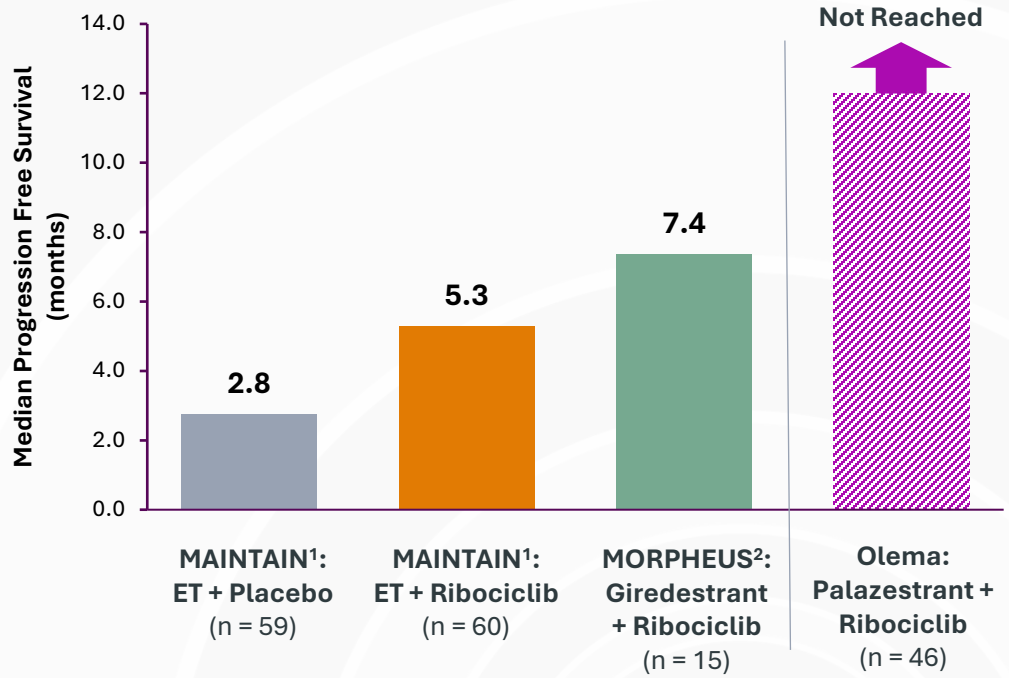
MAINTAIN study of ribociclib plus ET after CDK4/6i progression serves as best clinical benchmark*

Interim efficacy signals for palazestrant in combination with ribociclib

Six-Month PFS Rate* in CDK4/6i pre-treated patients



Median PFS (months)* in CDK4/6i pre-treated patients



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 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

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

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

~1,000-patient trial vs. standard of care 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)

n ≈ 1,000

1:1

Palazestrant + ribociclib

Letrozole + ribociclib

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

In collaboration with NOVARTIS

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

Building momentum for palazestrant as a potential backbone therapy

Registration-directed pivotal Phase 3 clinical trials underway and planned

Key factors driving palazestrant momentum

- Complete inhibition of key ER+ receptors
- Mono and combo potential
- Experience in 400+ patients and counting

OPERA-01 Breast Cancer Study

- 510-patient 2/3L Phase 3 monotherapy trial vs. standard of care
- Currently enrolling
- Visit opera01study.com for more information

OPERA-02 Breast Cancer Study

- ~1,000-patient 1L Phase 3 combination trial with ribociclib vs. standard of care
- Preparing for initiation in 2025

Planning for palazestrant U.S. commercial launch in 2027

Initial launch anticipated in 2/3L setting with potential 1L launch following positive OPERA-02 trial

Annual U.S. incidence estimated at **~40K** patients

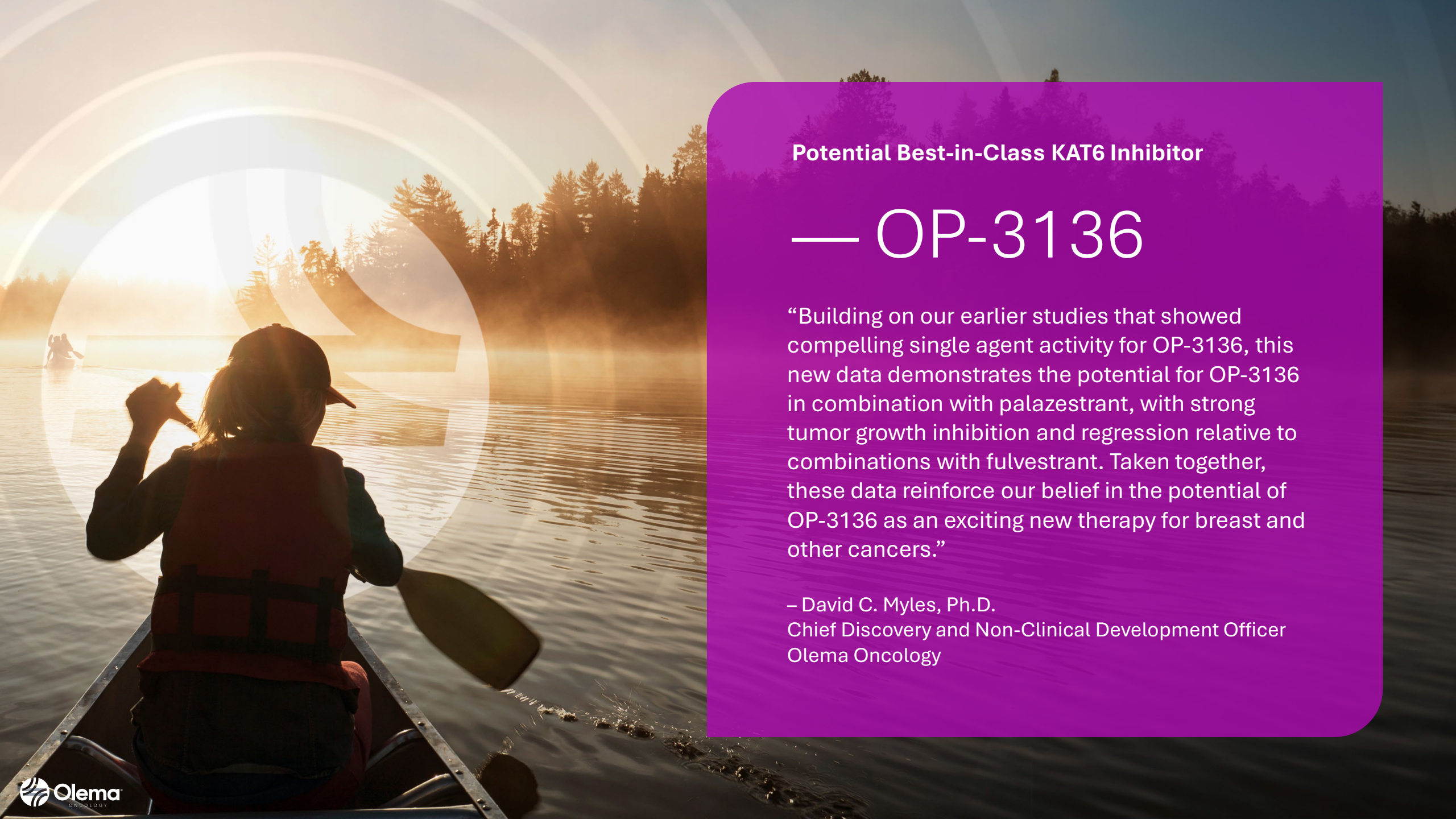
Commercial launch planning beginning in 2025

Early commercial leadership build in 2026

Establishing manufacturing supply and distribution for commercial use

Anticipated targeted field force of **~75–100 reps** to cover U.S. breast oncologists

U.S. market potential of **$3-5B** in 2/3L setting



Potential Best-in-Class KAT6 Inhibitor

— OP-3136

“Building on our earlier studies that showed compelling single agent activity for OP-3136, this new data demonstrates the potential for OP-3136 in combination with palazestrant, with strong tumor growth inhibition and regression relative to combinations with fulvestrant. Taken together, these data reinforce our belief in the potential of OP-3136 as an exciting new therapy for breast and other cancers.”

– David C. Myles, Ph.D.
Chief Discovery and Non-Clinical Development Officer
Olema Oncology

Olema ONCOLOGY

OP-3136: Olema's KAT6 inhibitor*

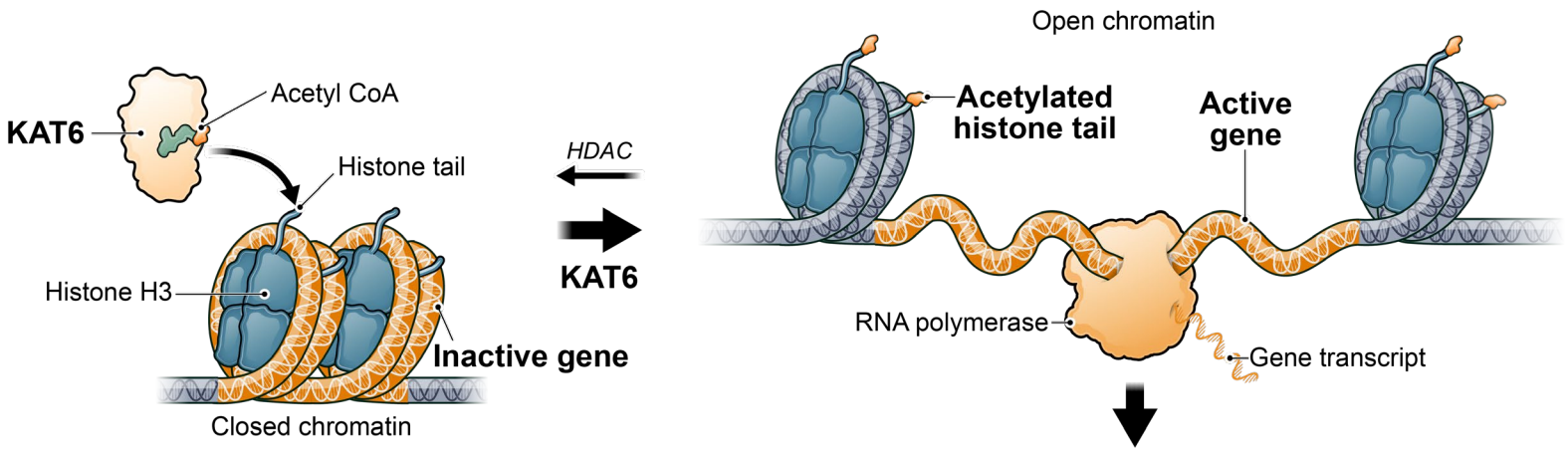
An exciting new and validated target^ for ER+/HER2- metastatic breast cancer

- Highly 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
- New data presented at the ENA ("Triple") meeting in October 2024
- IND cleared by FDA, expected to enter Phase 1 clinical trial in early 2025

*Discovered in collaboration with Aurigene ^*Mukohara T, et al. Inhibition of lysine acetyltransferase KAT6 in ER+ HER2- metastatic breast cancer: a phase 1 trial. Nat Med (2024)*
***KAT6i** = lysine acetyltransferase 6 inhibitor*

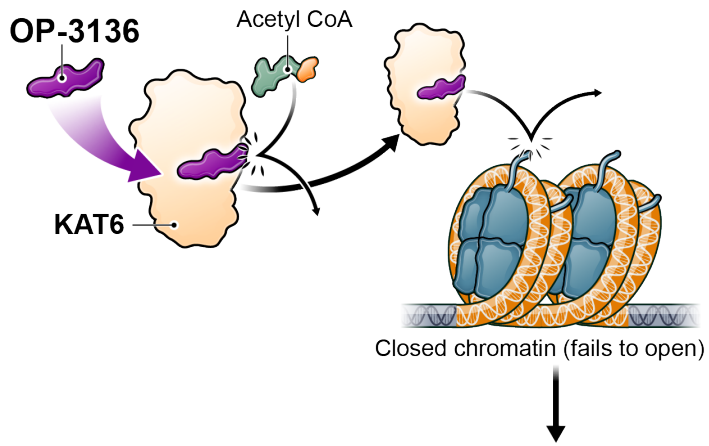
KAT6 inhibitor mechanism of action

KAT6 acetylates chromatin enabling transcription and proliferation



⬆Transcription of proliferation-associated genes
(ER, MYC, etc.)

KAT6 inhibitor prevents transcription



KAT6 inhibition by **OP-3136 stops acetylation** of histones and **blocks transcription of proliferation-associated genes** (ER, MYC, etc.)

- KAT6 is a clinically validated target[1] and overexpression correlated with worse clinical outcomes in ER+ breast cancer[2]
- KAT6 inhibition downregulates genes involved **in estrogen receptor signaling** and other signaling pathways[3]
- Inhibition regulated gene expression through blockade of acetylation of histones

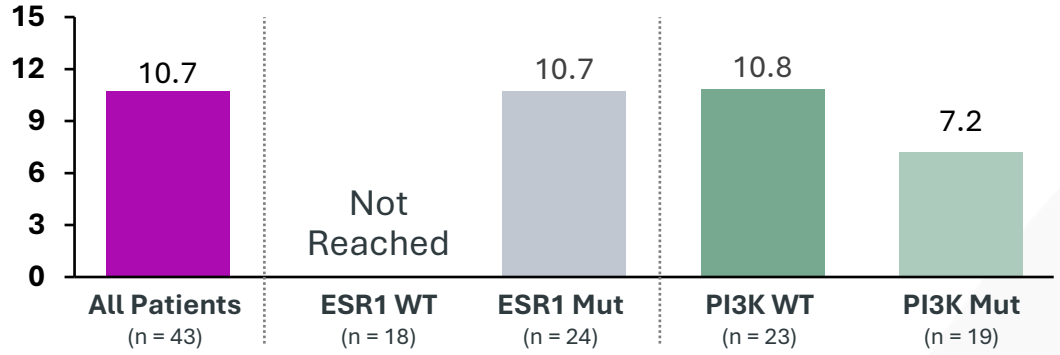
***AR** = androgen receptor; **ER** = estrogen receptor; **KAT6i** = lysine acetyltransferase 6 inhibitor*

[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*

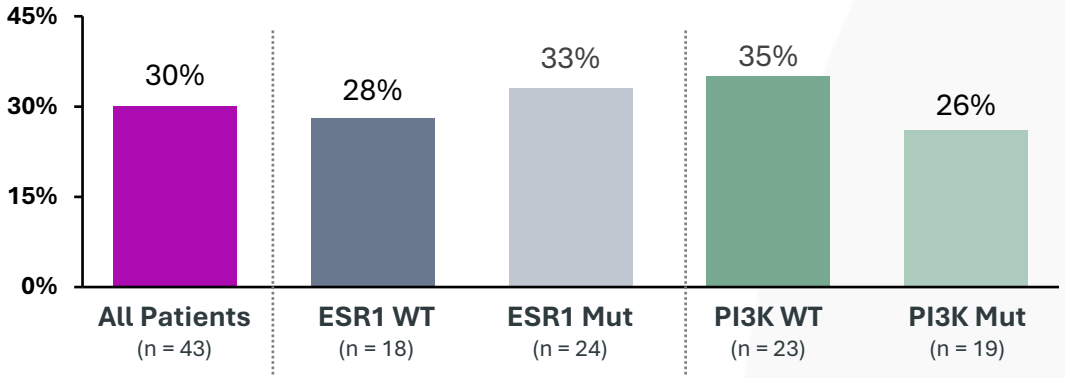
Note: Olema KAT6 inhibitors discovered in collaboration with Aurigene

Pfizer's KAT6i data demonstrated potential in metastatic breast cancer*

PF-8144 Median PFS with ET[1]



PF-8144 Overall Response Rate (ORR) with ET[1]



First-in-human clinical proof of concept for KAT6 inhibitor from Pfizer has important implications:

- **Validates KAT6 as an active new target for the treatment of metastatic breast cancer**
  - Activity demonstrated regardless of mutation status (ESR1 and PI3K/AKT/PTEN)
- **Demonstrates promising avenue to have a significant impact on future standard of care**
  - Combination of KAT6 inhibitor + ET demonstrated synergistic activity, consistent with preclinical observations
- **Highlights opportunity for potential best-in-class KAT6 inhibitor OP-3136 in combination with potential best-in-class CERAN palazestrant**

NOTE: Incorporates publicly-available third-party data that we have not independently verified. These results should be interpreted with caution. Such third-party data has been pulled by us from publicly-available sources for supplemental informational purposes, only. Refer to further disclaimers on slide 2.

ET = endocrine therapy; KAT6i = lysine acetyltransferase 6 inhibitor; PFS = progression free survival.

[1] Mukohara T, et al. Inhibition of lysine acetyltransferase KAT6 in ER+ HER2- metastatic breast cancer: a phase 1 trial. Nat Med (2024)

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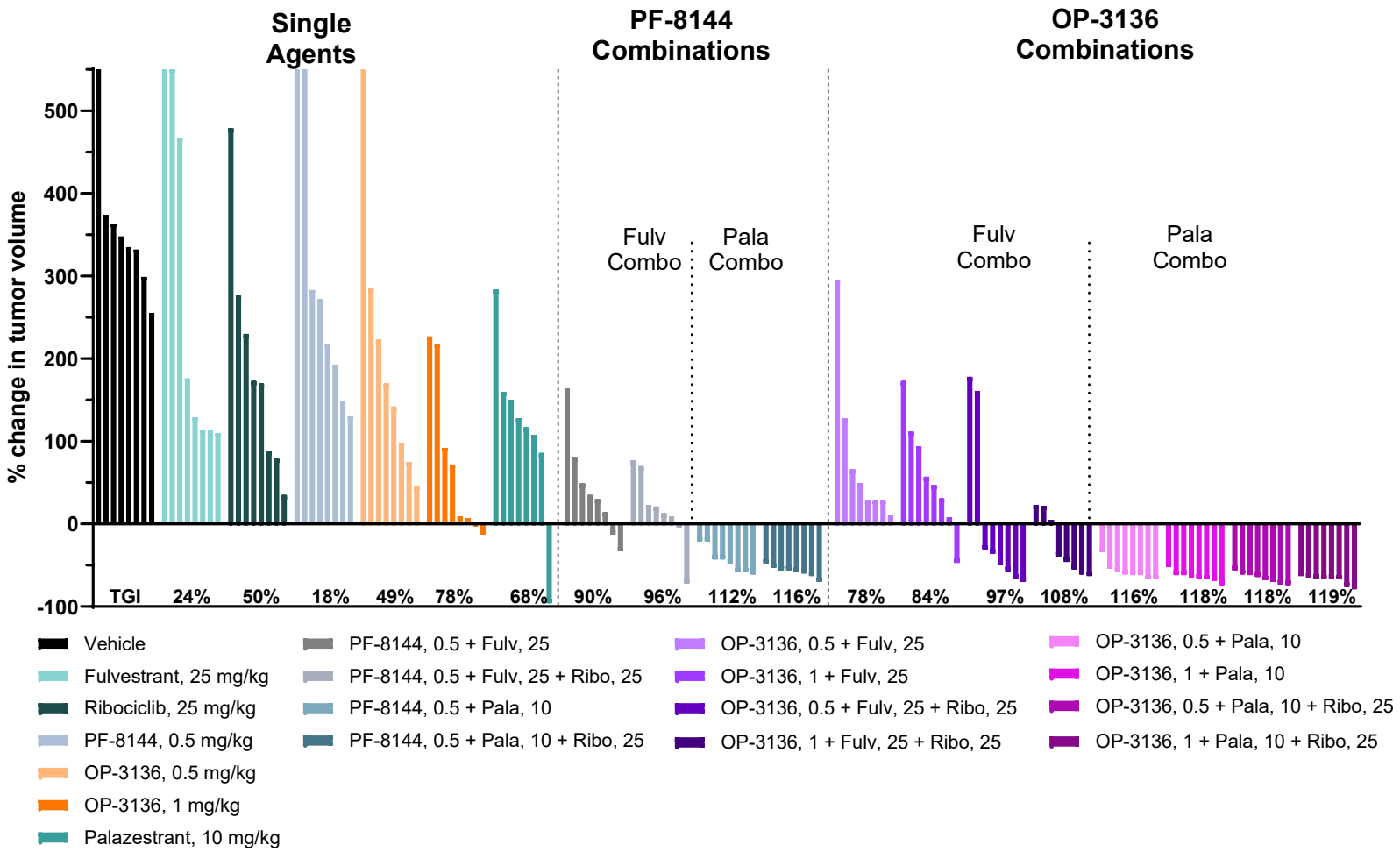
OP-3136 demonstrates synergistic activity in combination with palazestrant

OP-3136-palazestrant combinations appear superior to OP-3136–fulvestrant combinations

Waterfall Plot (T47D CDX model)



- Palazestrant in combination with either OP-3136 or PF-8144 resulted in strong tumor regression relative to fulvestrant combinations
- OP-3136 and palazestrant combinations showed significantly improved anti-tumor efficacy compared to PF-8144 in combination with fulvestrant
- All OP-3136 combinations were well tolerated, with no significant changes in body weight and no mortality

Source: 2024 EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics. Poster #230
** T47D model (ER+, HER2-, KAT6A overexpressing, ESR1 wild type, PIK3CA H1047R cell line); Abbreviations: **Fulv** = fulvestrant; **Pala** = palazestrant*

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