Olema ONCOLOGY

Pursuing Transformational Therapies for Women's Oncology

May 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. 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, 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. 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 – A Leading Women's Oncology Company

Focused mission to transform the standard of care for women's cancers

Palazestrant: **best-in-class potential** to become **the backbone therapy** for ER+/HER2- metastatic breast cancer

Emerging pipeline leveraging deep expertise in **endocrine-driven cancers and mechanisms of acquired resistance**

Well-positioned with experienced management team and $249M[1] in cash and cash equivalents

[1] Cash position as of March 31, 2024, includes the Company's cash, cash equivalents, and marketable securities.

Multiple 2024 Catalysts To Further Establish Olema Leadership Potential

Execute OPERA-01 pivotal Phase 3 2/3L **monotherapy** trial

Present **new palazestrant-ribociclib Phase 2 data** in May

Prepare for Phase 3 pivotal 1L combination trial with ribociclib

Initiate palazestrant-everolimus Phase 1b/2 clinical study

File IND for KAT6i OP-3136 in late 2024

Breast Cancer is the Second Most Common Diagnosed Cancer Worldwide

1 in 8 women in the U.S. will be diagnosed with invasive breast cancer in her lifetime

In 2024, it is estimated that

311K

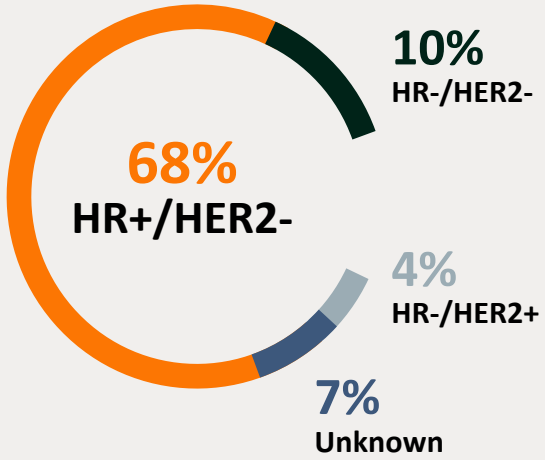
Women in the U.S. will be diagnosed with breast cancer

42,250

Women in the U.S. will die of metastatic breast cancer

Majority of all breast cancers

Express Estrogen Receptor (ER+)



Current endocrine therapies have considerable limitations

SERDs, SERMs, AIs

Incomplete ER antagonism

Sub-optimal PK profile

Limited CNS penetration

Tolerability issues

Better ER-Targeting Agents Are Needed

References: National Breast Cancer Foundation, World Health Organization; American Cancer Society. Facts and Figures 2024; SEER database

Significant Unmet Need in ER+/HER2- Breast Cancer Therapy

	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+

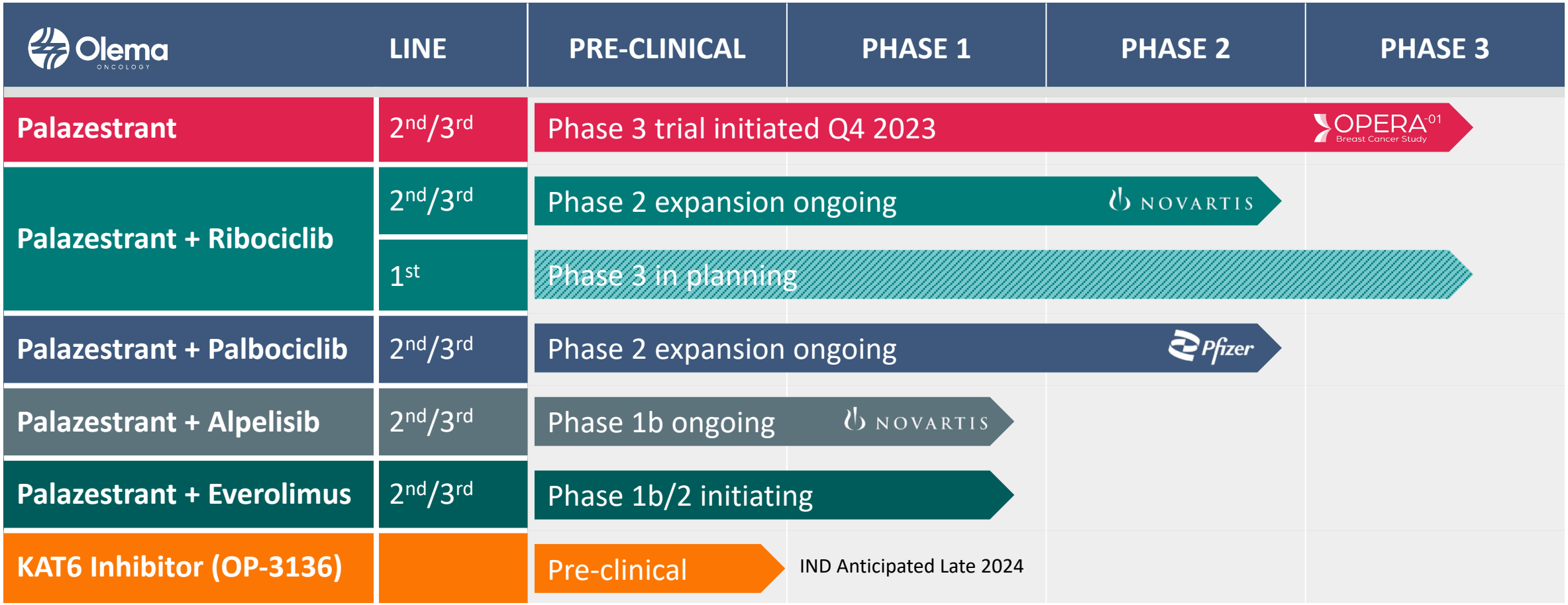
Estimated $20B+ market for endocrine therapies (ET) and targeted agents for ER+ breast cancer[4]

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

[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).
[3] Olema internal data. [4]2025 opportunity estimates for total endocrine therapy market (US and EU5). Olema internal data.

Olema's Expanding Pipeline Focused on Women's Oncology

Advancing Palazestrant in 2nd/3rd Line and in 1st Line Metastatic Breast Cancer

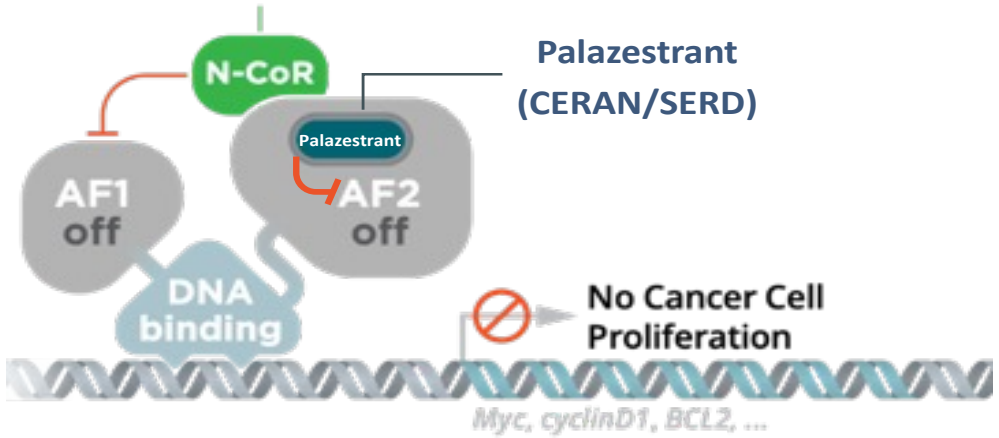


Our Phase 3 Asset – Palazestrant

Palazestrant: A Differentiated Next Generation Endocrine Therapy

Palazestrant has demonstrated ideal characteristics for a potential best-in-class endocrine therapy in approximately 300 women to date

Palazestrant, a complete ER antagonist (CERAN) and selective ER degrader (SERD)



CERANs turn off AF2 and recruit N-CoR to inactivate AF1

- **Complete ER Antagonism**
- **Attractive PK Profile**
- **Favorable Tolerability**
- **Robust Tumor Shrinkage**
- **Combinability**
- **CNS Penetration**

*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

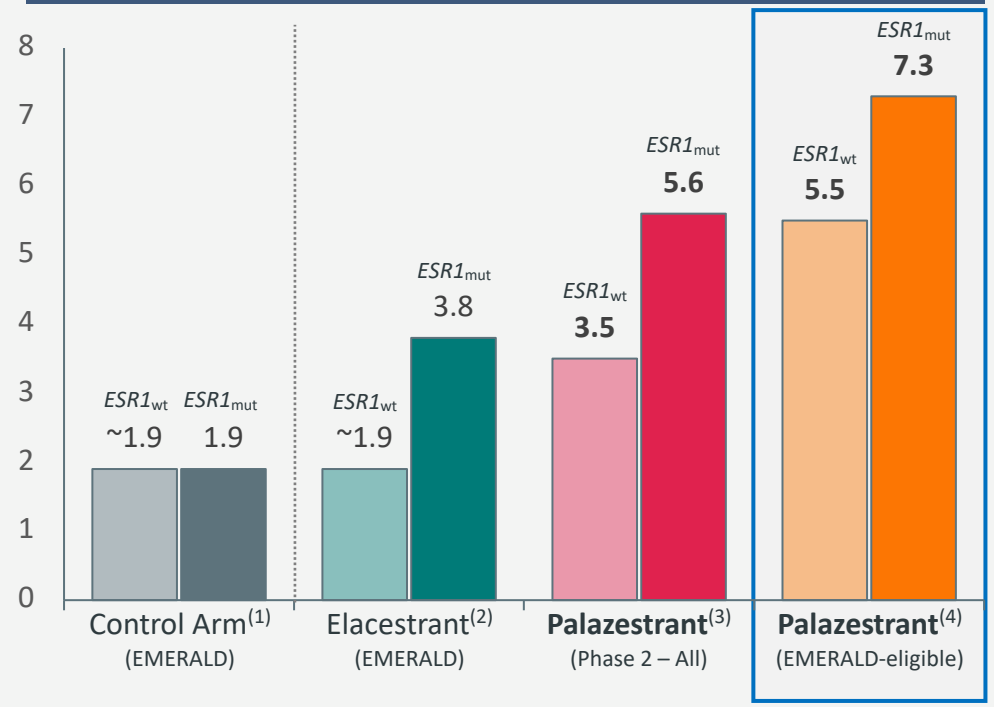
References: Shang and Brown, *Science*, 2002: Vol. 295, Issue 5564, pp. 2465-2468 ; Webb, Nguyen, and Kushner, *JBC*, 2003: Vol. 278, pp. 6912–6920

Demonstrated Activity Alone (Mutant and Wild-Type) and in Combination with CDK4/6i

Best-in-class Monotherapy PFS Potential and No DLTs/DDIs at Full Dose in Combination

Second-/Third-Line: Palazestrant Monotherapy

Median PFS (months) - *ESR1* Mut and WT Patients



First-Line: Attractive Combinability with CDK4/6i

- Combinable with CDK4/6 inhibitors ribociclib and palbociclib:
  - No significant drug-drug interaction
  - No dose-limiting toxicities
  - Tolerability profile consistent with the FDA-approved labels of ribociclib or palbociclib plus an endocrine therapy
- Full dose CDK4/6 inhibitor and palazestrant
- Efficacy continues to mature

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 and in elacestrant 400 mg dose. EMERALD Control Arm n=113 in ESR1 mutation detected at baseline and n=125 in ESR1 mutation not detected at baseline.
2. Source: 2022 JCO Bidard Supplemental EMERALD data. Median PFS in elacestrant 400 mg dose in ESR1 mutation detected n=115 and in ESR1 mutation not detected n=124.
3. Source: Palazestrant Phase 2 dataset with ESR1 mutations detected at baseline (n=36) and ESR1 mutation not detected at baseline (n=39).
4. Source: Emerald-eligible patient population from palazestrant Phase 2 dataset (2/3L +/-CT) with ESR1 mutations detected at baseline (n=23) and ESR1 mutations not detected at baseline (n=21).

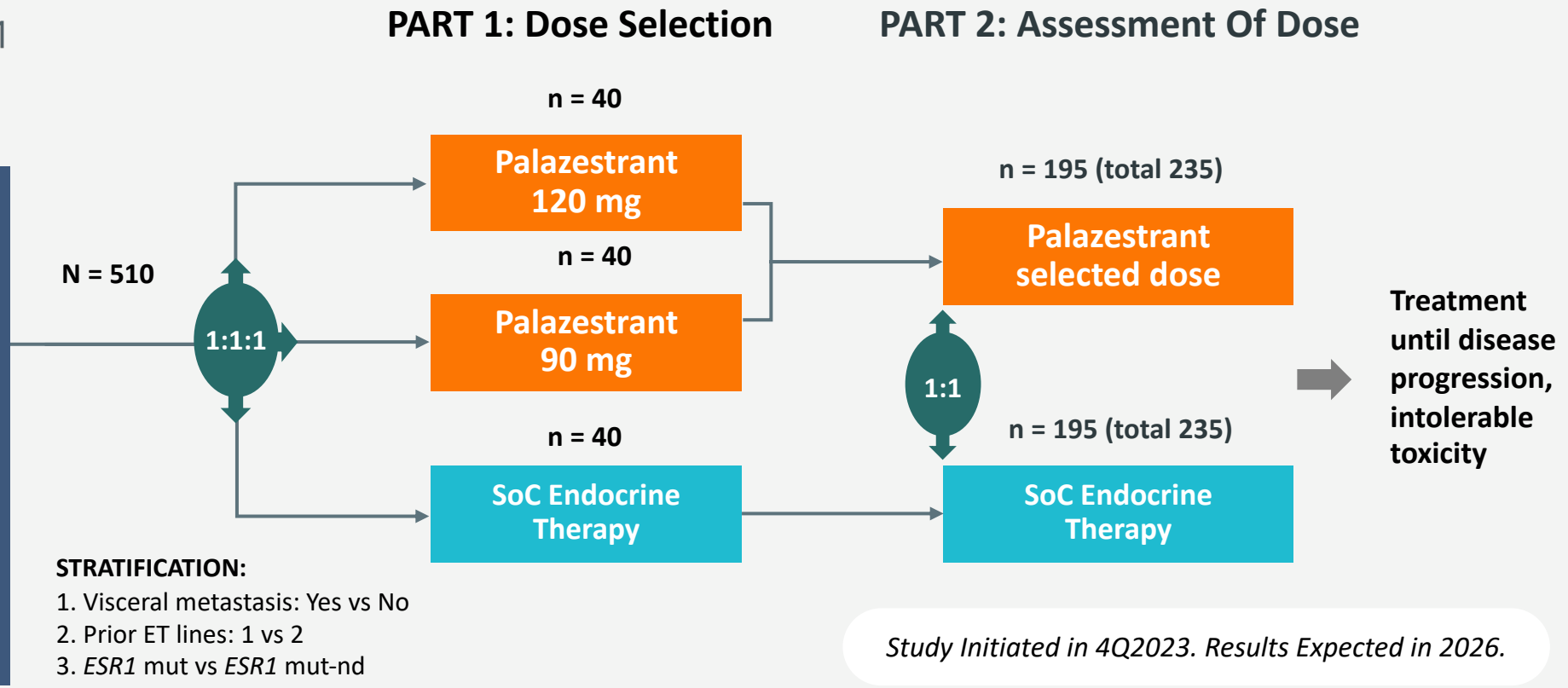
OPERA-01 Designed to Show Effectiveness over Standard of Care

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

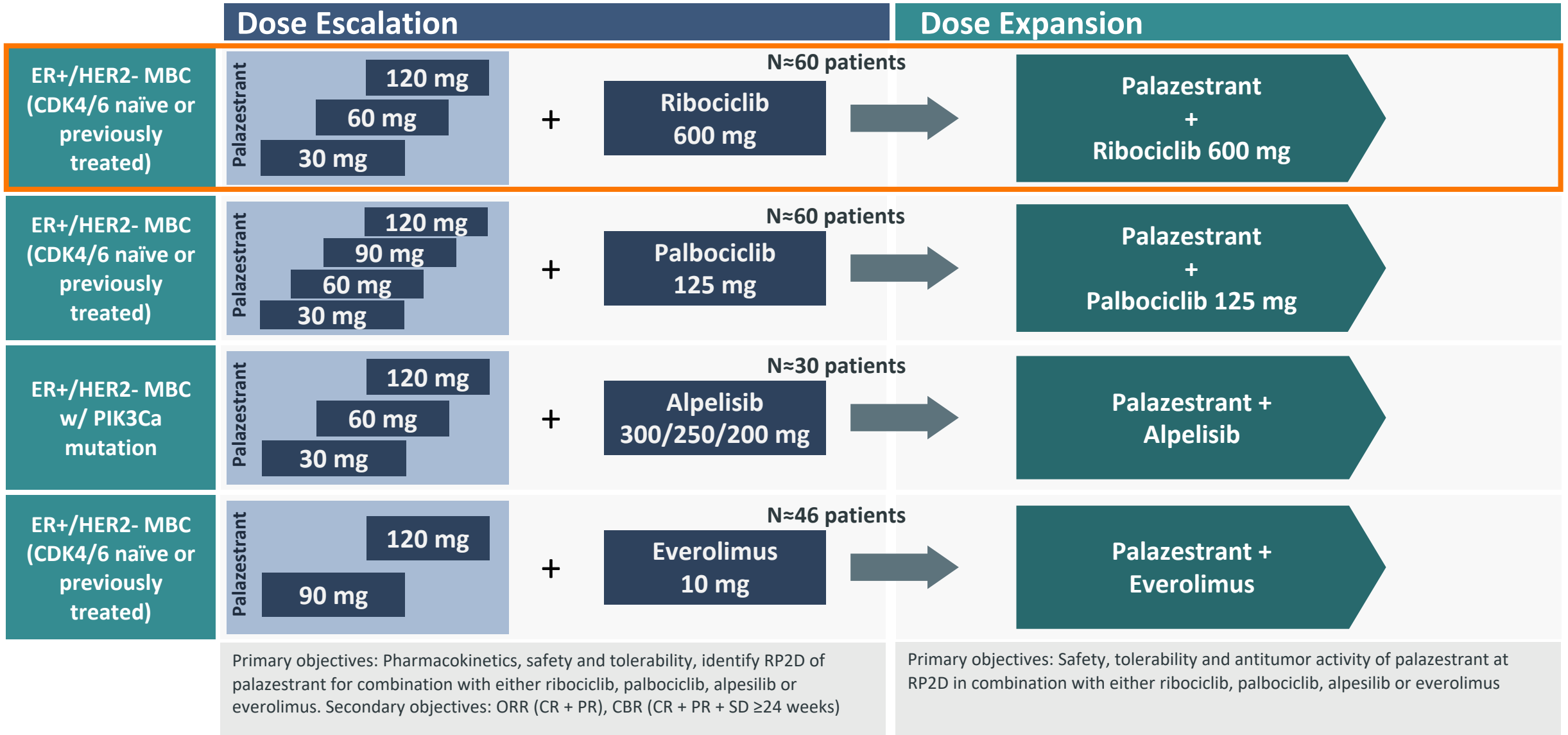


STRATIFICATION:
1. Visceral metastasis: Yes vs No
2. Prior ET lines: 1 vs 2
3. *ESR1* mut vs *ESR1* mut-nd

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

Demonstrating Palazestrant's Combinability with Other Targeted Agents



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

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/2 combination data, 60-patient enrollment complete

Demographics

- 19 heavily pretreated patients
- 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, MTD was not reached, and no dose-related increases in the incidence or severity of TEAEs was observed
- 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®

For more details on this data milestone, please refer to this presentation, slides 18-24, at this link.

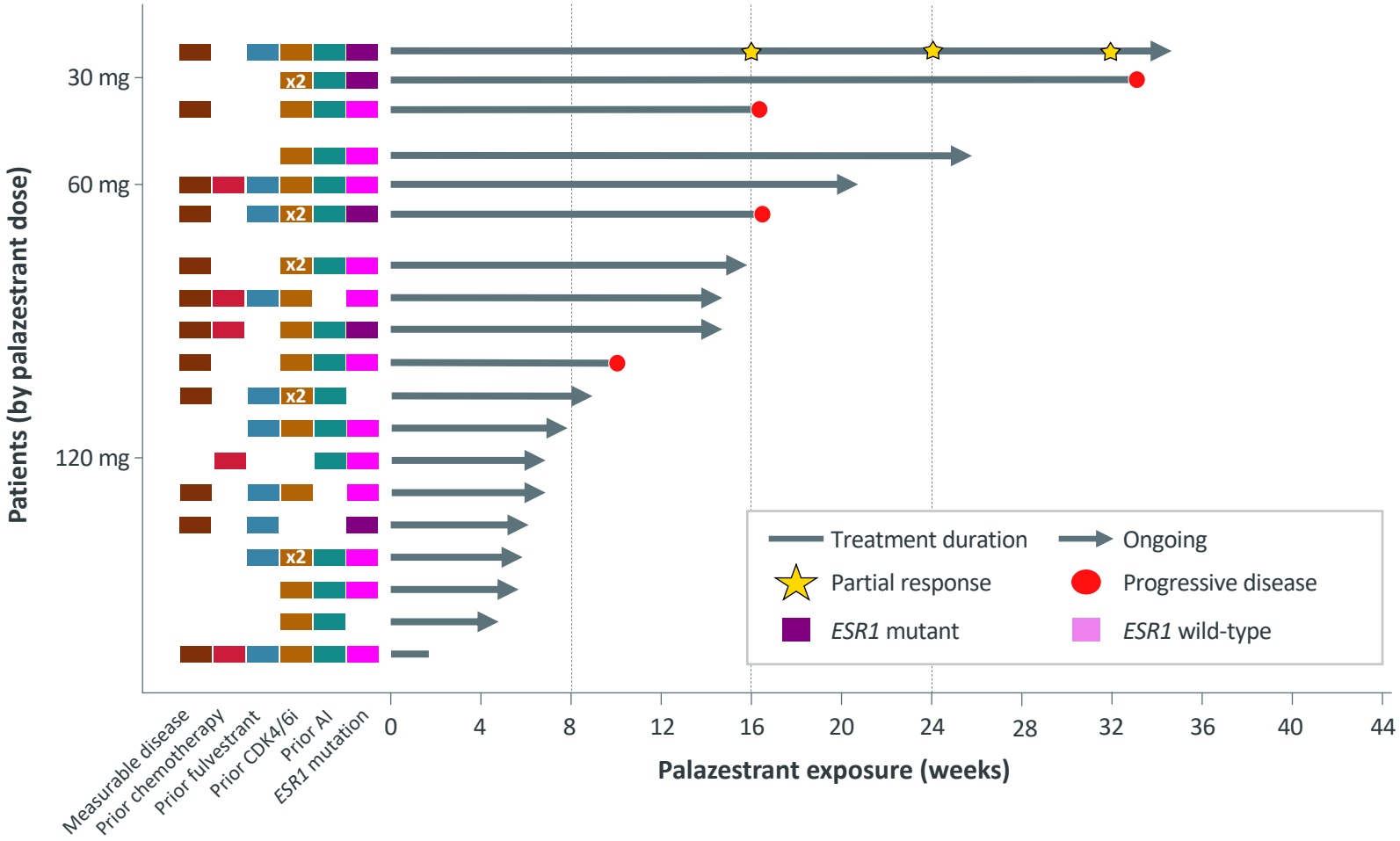
Abbreviations: **CDK4/6i**, cyclin dependent kinase 4/6 inhibitor; ***ESR1***, estrogen receptor 1 gene; **DLT**, dose-limiting toxicity; **MTD**, maximum tolerated dose; **TEAE,** treatment-emergent adverse event

Data Cut-off Date: November 1, 2023

Ribociclib Combination: Preliminary Efficacy

Promising efficacy data are maturing

Duration of Treatment as of November 1, 2023[a] (n=19)



- 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 Cut-off 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

Preclinical Program – OP-3136 KAT6 Inhibitor

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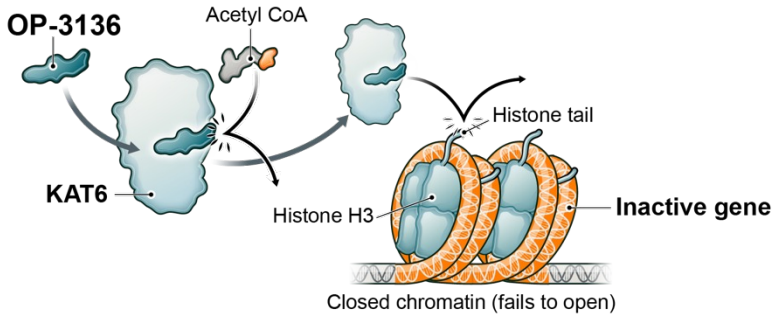
OP-3136 – Olema KAT6 Inhibitor Development Candidate

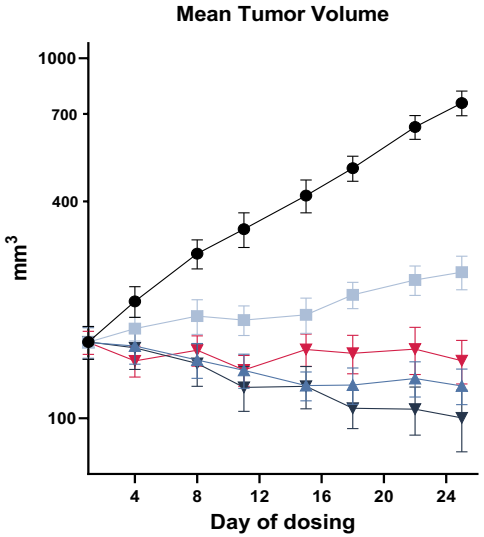
OP-3136 KAT6i Inhibitor Mechanism

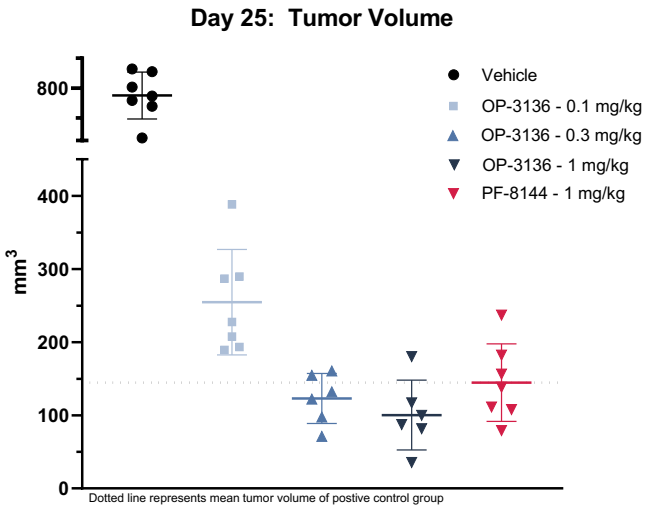


KAT6 inhibition by **OP-3136 stops acetylation** of histones and **blocks transcription of proliferation-associated genes** (ER, MYC, etc.)

- KAT6 is a clinically validated target[1] and its 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]

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

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.

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