Olema ONCOLOGY

Aspiring to Improve the Lives of Women with Breast Cancer

January 2023

January 11, 2023

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, expected manufacturing capabilities, strategy, regulatory matters, including the timing and likelihood of success of obtaining drug approvals, market size and opportunity and our ability to complete certain milestones. 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 Olema, including those described under the caption "Risk Factors" and elsewhere in Olema’s quarterly report on Form 10-Q filed on November 8, 2022, and future filings and reports of Olema 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.

Leading the Next Generation of Oral CERAN/SERDs for the Treatment of ER+/HER- Metastatic Breast Cancer (MBC)

OP-1250, Best-in-Class CERAN/SERD for ER+/HER2- MBC

- Completely shuts down estrogen receptor signaling pathways in women with ER+/HER- MBC
- Internally-discovered, wholly-owned IP with no royalty burden

Clinical Validation as a Monotherapy and in Combo w/ CDK4/6i

- Over 160 patients treated to date with OP-1250
- Highly encouraging Phase 1/2 clinical results in both monotherapy and combination studies

Initiating 1st Pivotal Phase 3 monotherapy study in mid-2023

- FDA Fast Track designation in 2L+ ER+/HER2- MBC
- Combination studies ongoing with Ibrance®, Kisqali® and Piqray®

Multi-Billion Dollar Commercial Market Opportunity

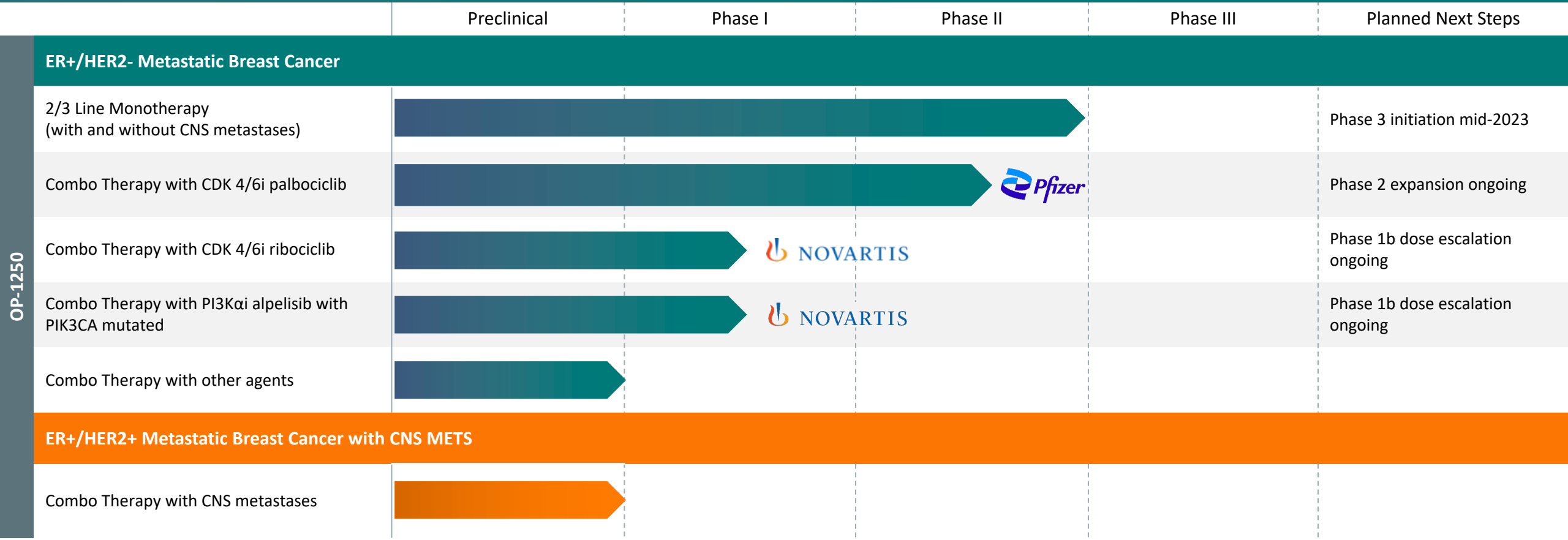
- 2L/3L+ MBC, represents a **$3-5B** commercial opportunity
- 1L MBC in combination with CDK 4/6i, represents a **$5-10B** commercial opportunity

Strong cash position of $222.6M(1) to support clinical development and operations into 2H 2024

(1) As of September 30, 2022.

Rapidly Advancing OP-1250 into Pivotal Studies Beginning in 2023

Evaluating OP-1250 across a range of ER cohorts in monotherapy and combination trials



MBC = metastatic breast cancer; PI3Kα = phosphatidylinositol 3-kinase alpha; CDK4/6i = CDK4/6 inhibitor
(1) Patient population may be studied as additional cohort(s) of current Phase 1/2 clinical trial or may be studied in a separate clinical trial.

Breast Cancer is the Second Most Common Diagnosed Cancer Worldwide

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

In 2022, approximately

288K

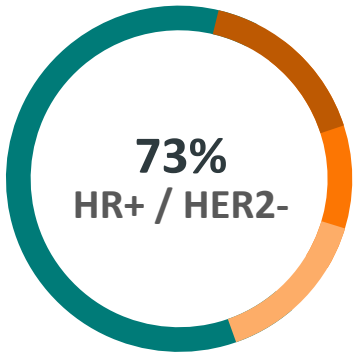
Women in the U.S. were diagnosed with breast cancer

43,250

Women in the U.S. will succumb to metastatic breast cancer

Majority of All Breast Cancers

express Estrogen Receptor (ER+)



12%
HR- / HER2-

4%
HR- / HER2+

11%
HR+ / HER2+

Current Endocrine Therapy Options

SERMs, AIs, SERDs

Limitations include:

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

Better ER targeting agents are needed

References: World Health Organization; American Cancer Society. Facts and Figures 2022; SEER database

Endocrine Therapy Remains the Backbone of ER+ Breast Cancer Treatment

OP-1250 has the potential to improve upon existing treatments to become the best-in-class ET

Illustrative Examples of ER+/HER2- Breast Cancer Treatment Options

Relapsed or Metastatic Breast Cancer: Patients eventually progress on therapy or discontinue due to toxicity

2nd/3rd LINE +: ~2-12+ months of therapy

Oral CERAN/SERDs (emerging) | Fulvestrant (CERAN/SERD) | AI[1] | Tam (SERM) | PI3Ki [3] +/- Fulv (CERAN/SERD) | AI + mTORi [4] | Chemo*

Physician choice of one of the above options based on patient characteristics, tumor biology, prior therapy and response to prior therapy and whether there is a need for chemo

1st Line: ~6-36+ months of therapy

Oral CERAN/SERDs + CDK4/6i[2] | AI + CDK4/6i[2] | Fulvestrant (CERAN/SERD) + CDK4/6i[2] | Chemo*

Physician choice of one of the above options based on patient characteristics, tumor biology, prior therapy and response to prior therapy and whether there is a need for chemo

Early Breast Cancer: Curative therapies are still needed

LOCAL: Up to 5 years of therapy

Lumpectomy/ Mastectomy **+/-** Radiation Therapy ▶

ADJUVANT: Up to 5 years of therapy

AI | AI + CDK4/6i | tam (SERM) **+/-** Chemo*

Physician choice of one of the options above based on patient characteristics and tumor biology

OP-1250

OP-1250 has the potential to be used across multiple lines of treatment

* Indications for Chemo include impending visceral crisis, endocrine resistance or other need for rapid debulking

Sources: American Cancer Society; UptoDate.com; Sammons et al. *Target Oncol.* (2019); industry knowledge
Tam: tamoxifen; Fulv: fulvestrant; DFS: Disease-Free Survival; mPFS: Median Progression-Free Survival; ORR: Objective Response Rate

(1) anastrozole, letrozole, exemestane; (2) abemaciclib, palbociclib, ribociclib; (3) copanlisib; (4) sirolimus, everolimus, temsirolimus

Segments of Therapy in ER+/HER2- Breast Cancer

First Pivotal Study will target 2L/3L therapy, followed by studies in 1L therapy setting

	ER+ / HER2-[1]				ER+ / HER2+[2]
LINE OF THERAPY	2L/3L+	1L	High-Risk Adjuvant	Early Breast Cancer	HER2+ w/ CNS Mets
PATIENTS	~150K	~115K	~75K	~285K+	~10K
DURATION OF THERAPY[3]	~2-12+ months	~6-36+ months	Up to 5 years	Up to 5 years	~12 months
MARKET POTENTIAL[4]	~$3-5B	$5-10B+	~$3-5B	$10B+	~$500M

[1]2025 incidence projection estimates. Olema internal data, Informa ER+ HER2- BC Prevalence Based Market Forecast. 26% of adjuvant eligible patients assumed to have Ki-67 ≥ 20%. Early breast cancer incidence includes high risk adjuvant segment. [2]2025 incidence projection estimates. Olema internal data, Informa HER2+ BC Prevalence Based Market Forecast. Forecast based on 2L+ ER+ HER2+ metastatic breast cancer projections. [3]Olema internal data. [4]2025 opportunity estimates for total endocrine therapy market (US and EU5). Olema internal data.

Significantly Fewer Competing Programs for 2/3L and 1L MBC Treatment

2L/3L ER+/HER2- MBC

10 Active Programs YE 2021

Olema Oncology
SANOFI
Roche
ARVINAS
AstraZeneca
Lilly
zentalis
G1 Therapeutics
Eisai
Menarini group

4 Active Programs YE 2022

Olema Oncology
Lilly
ARVINAS
Menarini group

1L ER+/HER2- MBC

6 Active Programs YE 2021

Olema Oncology
AstraZeneca
SANOFI
zentalis
ARVINAS
Roche

4 Active Programs YE 2022

Olema Oncology
AstraZeneca
ARVINAS
Roche

OP-1250: Best-in-Class Potential for ER+/HER2- Breast Cancer

Clinical dataset with over 160 patients treated with OP-1250 supports opportunity in both monotherapy and combination settings for patients with ER+/HER2- advanced metastatic breast cancer

Complete ER Antagonism

Dual activity as a next-generation CERAN / SERD 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 leading to steady-state plasma levels with minimal peak-to-trough variability

Favorable Tolerability

Favorable tolerability profile 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 w/ CDK4/6i

Combinable with Palbociclib – no DDI* and overall tolerability profile consistent with expected profile of palbociclib plus endocrine therapy

CNS Penetration

Demonstrated activity in nonclinical brain metastases studies

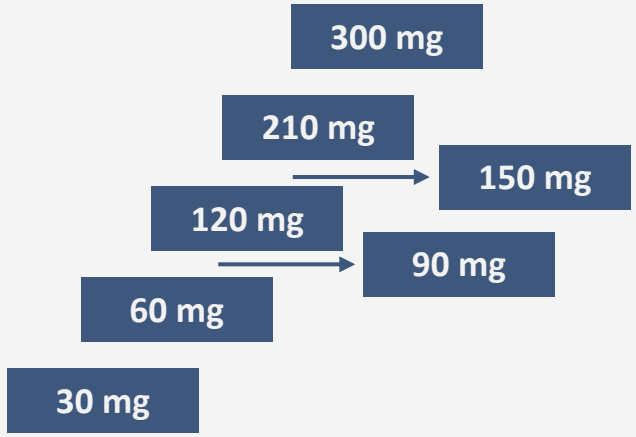
Data referenced above as of October 26, 2022.
*In completed dose escalation cohorts from Phase 1b combination study with palbociclib. DDI = Drug Drug Interaction.

Phase 1/2 Monotherapy Clinical Update from ENA 2022

Olema ONCOLOGY

OP-1250-001 First-in-Human Phase 1/2 Monotherapy Trial: Study Design

Phase 1a Dose Escalation



Phase 1b Dose Expansion

- 60 mg (n=25)
- 120 mg (n=25)

RP2D of 120 mg

Phase 2 Cohorts

Patients with measurable disease*	(n=50)
Patients with non-measurable disease*	(n=15)
Patients with CNS metastasis	(n=15)

Primary objectives: Pharmacokinetics, safety and tolerability, identify RP2D
Secondary objectives: ORR (CR + PR), CBR (CR + PR + SD ≥24 weeks)

Objectives: Anti-tumor activity in measurable disease cohort, safety and tolerability at RP2D

Key Inclusion Criteria:

Phase 1a:
- Tumor must be ER+/HER2 negative
- At least one prior hormone-based therapy for locally advanced, recurrent, or metastatic disease
- 0-2 prior chemotherapy regimens for locally advanced or metastatic disease
- Measurable and non-measurable disease (evaluable disease)

Phase 1b:
- Tumor must be ER+/HER2 negative
- 1-4 prior hormone-based therapy for locally advanced, recurrent, or metastatic disease
- 0-1 prior chemotherapy regimens for locally advanced or metastatic disease
- Measurable disease by RECIST 1.1 Criteria

*Fully-enrolled.
CBR: Includes patients who received at least one cycle of treatment and had at least 1 postbaseline tumor assessment were evaluable for a response, and enrolled ≥24 weeks prior to the data cut-off date. CBR, Clinical Benefit Rate; CR, Confirmed Response; ORR, Objective Response Rate; PR, Partial Response; RP2D, Recommended Phase 2 Dose; SD, Stable Disease

OP-1250 Phase 1/2 Dose Expansion

Patients Received Extensive Prior Therapies

Patient characteristics	60 mg (n=33)	120 mg (n=35)	Total[a] (N=68)
Age, median, years	61	61	61
Range	30–81	39–77	30–81
ECOG performance status, n (%)			
0	22 (67)	17 (49)	39 (57)
1	11 (33)	18 (51)	29 (43)
Measurable disease at baseline, n (%)	32 (97)	34 (97)	66 (97)
Visceral disease (liver, lung, peritoneum, pleura, ascites), n (%)	27 (82)	29 (83)	56 (82)
Prior lines of therapy in advanced setting, n (%)			
1	9 (27)	11 (31)	20 (29)
2	9 (27)	10 (29)	19 (28)
≥3	15 (46)	13 (37)	28 (41)
Missing	0	1 (3)	1 (2)
Prior lines of endocrine therapy in advanced setting, n (%)			
1	13 (39)	12 (34)	25 (36)
2	8 (24)	15 (43)	23 (34)
≥3	11 (33)	7 (20)	18 (27)
Missing	1 (3)	1 (3)	2 (3)
Types of prior therapy in advanced setting, n (%)			
Chemotherapy	14 (42)	8 (23)	22 (32)
AI	26 (79)	29 (83)	55 (81)
Fulvestrant	22 (67)	22 (63)	44 (65)
CDK4/6 inhibitor	32 (97)	33 (94)	65 (96)
ESR1 mutations at baseline (ctDNA), n/N (%)	15/20 (75)	12/26 (46)	27/46 (59)

- 69% of patients received 2 or more prior lines of therapy in the advanced setting; 82% visceral disease
- 96% received prior CDK 4/6i; 81% received prior AI; 65% received prior fulvestrant
- 59% had activating mutations in ESR1
- Up to 50% of patients expected to be endocrine resistant*

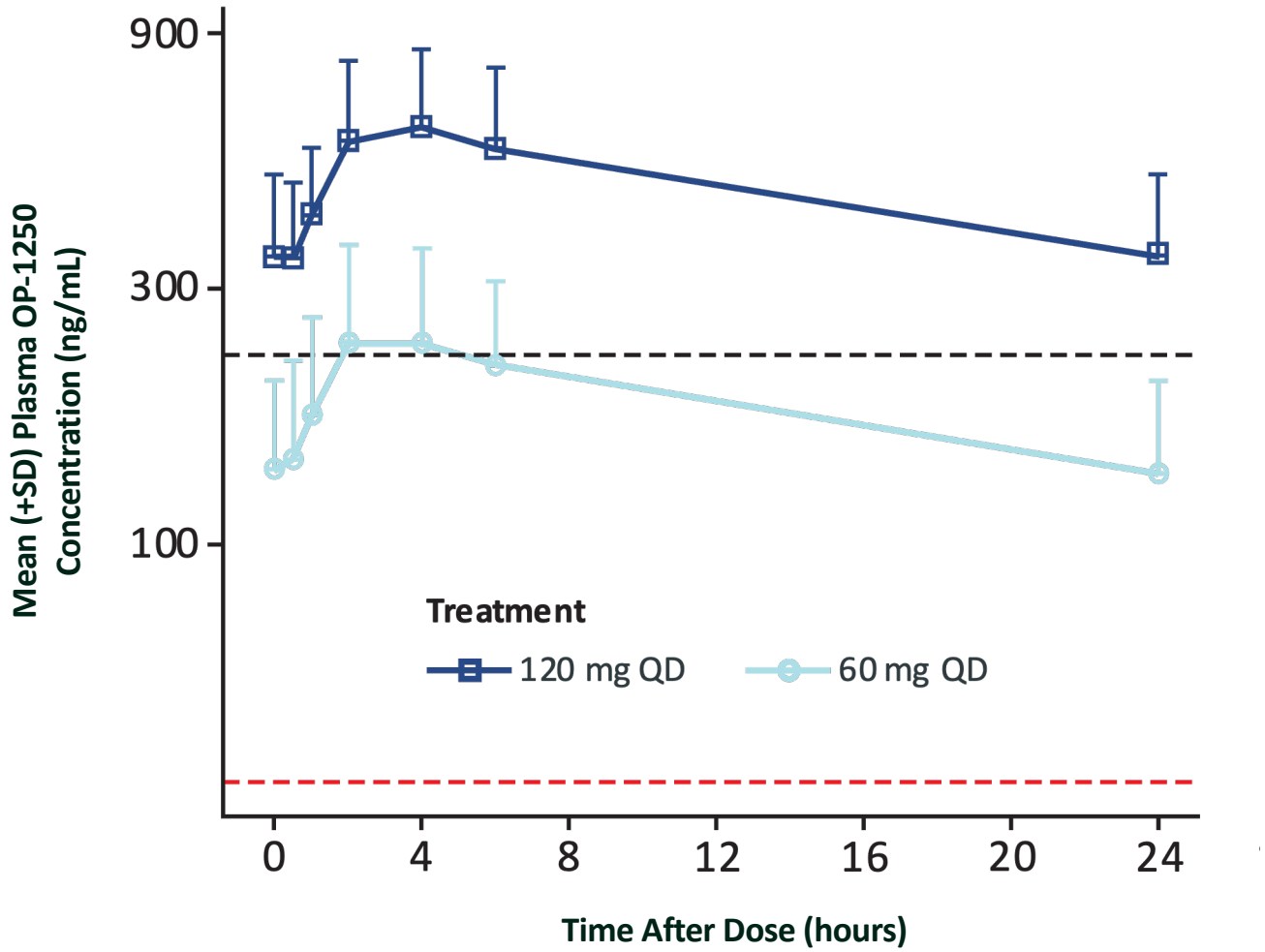
[a]Sums may not total to 100% due to rounding.

*Source: EMERALD Phase 3 trial in CDK 4/6 inhibitor-experienced 2/3L patients, Journal of Clinical Oncology.

AI, aromatase inhibitor; CDK4/6, cyclin-dependent kinase 4/6; ECOG, Eastern Cooperative Oncology Group.

Dose-Proportional PK with Optimal Steady-State Plasma Concentrations

OP-1250 Steady-state Plasma Concentration-time Profiles



Dashed black line=target efficacious exposure based on estradiol-supplemented preclinical models (C_{min}=226 ng/mL) (8 studies); dotted red line=fulvestrant C_{max}=28mg dosed at 500mg every 28 days QD, once daily.

- High oral bioavailability and steady-state plasma levels with minimal peak-to-trough variability allowing complete inhibition of the ER for the full dosing interval
- Dosing at the RP2D of 120 mg yields drug exposures that exceed the predicted efficacious threshold based on pre-clinical models
- Mean terminal half-life ($T_{1/2}$)= 8 days, supporting once-daily dosing

60 mg and 120 mg Doses Well Tolerated in Phase 1/2 Monotherapy Dose Expansion

TRAEs in ≥15% of Patients in Phase 1a/1b	60 mg (n=33)			120 mg (n=35)			Total (60 mg & 120 mg, n=68)	
	Grade 1	Grade 2	≥Grade 3	Grade 1	Grade 2	≥Grade 3	Grade 1/2	≥Grade 3
Any TRAE	9	7	1	18	3	6	**37 (54%)**	**7 (10%)**
Nausea	8	2	0	18	0	1	**28 (41%)**	**1 (1%)**
Fatigue	5	4	0	5	2	1	**16 (24%)**	**1 (1%)**
Vomiting	2	1	0	7	0	0	**10 (15%)**	**0**

Grade 3/4 Neutropenia

Four out of 68 patients had Grade 3/4 neutropenia, occurring ~4-6 weeks into therapy and have recovered

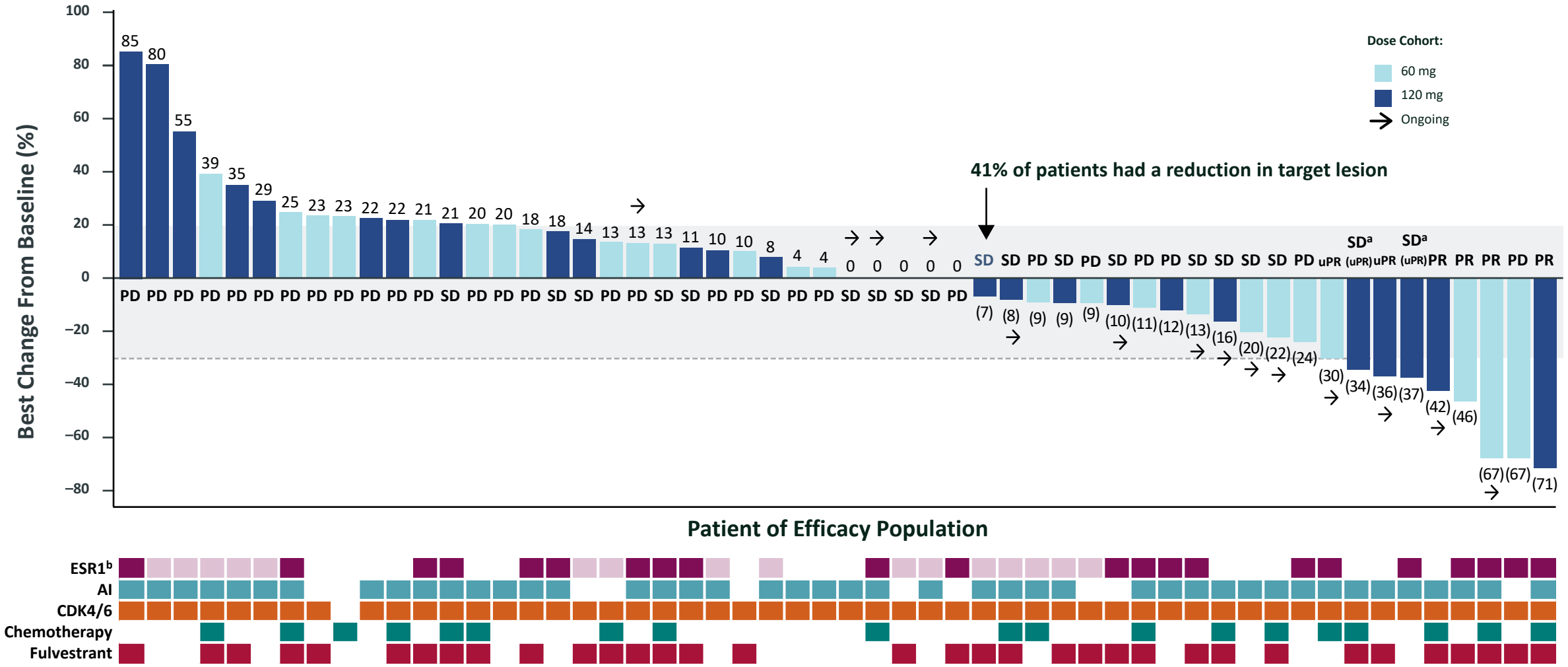
- 1 patient had Grade 3 neutropenia at 120 mg, discontinued due to concurrent disease progression; neutropenia recovered
- 3 patients had Grade 4 neutropenia at 120 mg:
  - 1 patient's dose was interrupted for 1 week and was restarted at a lower dose (60 mg) with a subsequent cPR and no further neutropenia
  - 1 patient had Grade 4 neutropenia concurrent with disease progression, discontinued, and recovered
  - 1 patient had febrile neutropenia with no evidence of infection, discontinued from treatment, and recovered
- Oncologists are comfortable monitoring for and managing neutropenia in breast cancer patients

Other Grade 3 Events

- Three additional grade 3 events assessed as potentially related to study drug:
  - Anemia (1 at 60 mg)
  - Nausea (1 at 120 mg)
  - Fatigue (1 at 120 mg)

TRAE, Treatment-Related Adverse Event
Data Cutoff Date: September 2, 2022

Meaningful Anti-Tumor Activity in OP-1250 Dose Expansion

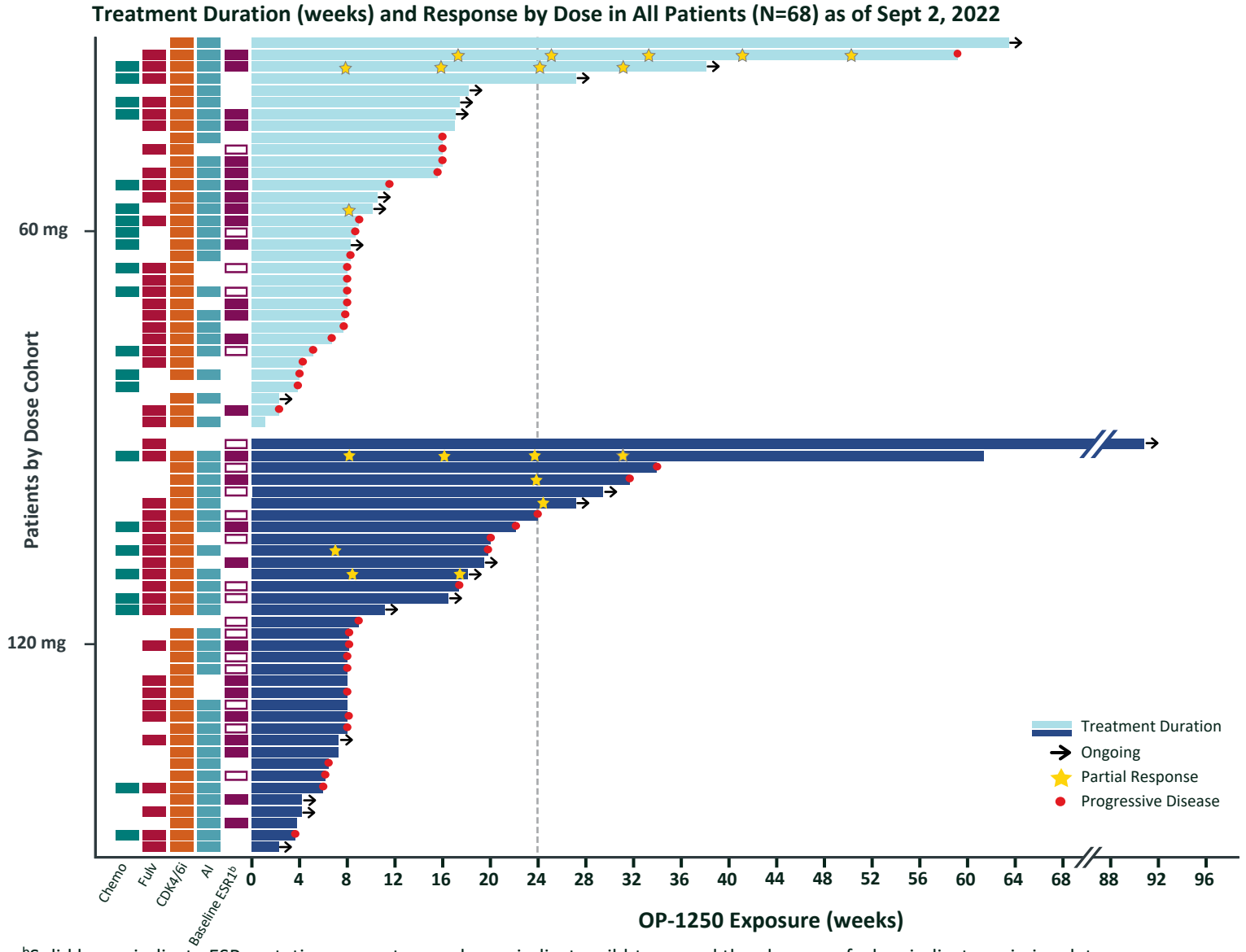


[a]Patient had an unconfirmed partial response and later progressed at a subsequent scan.

[b]Dark shaded boxes indicate ESR mutation present, light shaded boxes indicate wild-type, and the absence of a box indicates missing data.

AI, aromatase inhibitor; CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; Chemo, chemotherapy; Fulv, fulvestrant; PD, progressive disease; PR, partial response; QD, once daily; SD, stable disease; uPR, unconfirmed partial response.

Clear Efficacy and Durable Clinical Benefit in Heavily Pretreated Population



- Across all patients:
  6 PRs out of 57 response-evaluable patients (4 cPRs and 2 uPRs*)
- In ESR1 mutant patients:
  4 PRs out of 22 response-evaluable patients (3 cPRs and 1 uPR*)
- 39% CBR at RP2D of 120 mg (7/18)
- 32% CBR across both doses (11/34)
- Data maturing with 31% of patients remaining on treatment as of Sept 2, 2022

[b]Solid boxes indicate ESR mutation present, open boxes indicate wild-type, and the absence of a box indicates missing data.
*Unconfirmed partial responses awaiting confirmation at a subsequent scan.
AI, aromatase inhibitor; CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; Chemo, chemotherapy; Fulv, fulvestrant; PD, progressive disease; PR, partial response.

Phase 1/2 Dose Expansion Summary

OP-1250 is a Phase 3-ready asset with an emerging best-in-class profile

A complete ER-antagonist with attractive PK, high drug exposures and a long-half life

Heavily Pre-treated Patients	
82%	of patients had visceral disease at baseline
96%	of patients were CDK 4/6 inhibitor experienced
65%	of patients had prior fulvestrant
69%	2 or More Prior Lines in the Advance Setting

Best-in-Class Emerging Profile	
84%	of TRAEs were Grade 1 / 2 in severity with no MTD
41%	of target tumor lesions reduced in size
4 + 2	Confirmed / Unconfirmed partial responses*
39%	CBR at RP2D of 120 mg; 31% of patients still on therapy; efficacy maturing

Up to 50% of patients expected to be endocrine resistant**

Clinically meaningful durable responses in endocrine sensitive patients

*Unconfirmed partial responses awaiting confirmation at a subsequent scan.
**Source: EMERALD Phase 3 trial in CDK 4/6 inhibitor-experienced 2/3L patients, Journal of Clinical Oncology.
Data cut as of September 2, 2022.

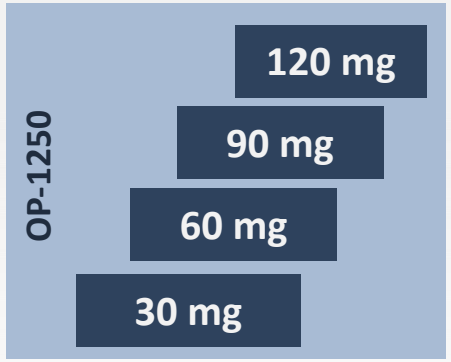
Olema ONCOLOGY

Phase 1b Combination Study Update from SABCS 2022

Phase 1b Combination Study with Palbociclib: Study Design

Initiated January 2022

Dose Escalation



\+

Palbociclib 125 mg

- 3+3 design
- N=12 patients

Primary objectives: Pharmacokinetics, safety and tolerability, identify RP2D of OP-1250 for combination with palbociclib
Secondary objectives: ORR (CR + PR), CBR (CR + PR + SD ≥24 weeks)

Dose Expansion

OP-1250 120 mg + Palbociclib 125 mg

- N=30 - 40 patients

Objectives: Safety, tolerability and antitumor activity of OP-1250 at RP2D in combination with palbociclib

Key Inclusion Criteria:

- ER+/HER2- advanced breast cancer
- Evaluable disease (measurable and non-measurable)
- ≤ 1 prior hormonal regimen for locally advanced or metastatic disease
- Can be CDK4/6i naïve or pre-treated

CBR, clinical benefit rate; ORR, objective response rate; CR, complete response; PR, partial response; SD, stable disease; RP2D, recommended phase 2 dose

OP-1250 Phase 1b Dose Escalation in Combination with Palbociclib

Of 12 Patients, 8 had prior CDK 4/6i treatment, 4 patients with baseline ESR1 mutations

Patient characteristics	Total[a] (N=12)
Median age (years)	62
Range	49–76
ECOG performance status, n (%)	
0	9 (75)
1	3 (25)
Measurable disease at baseline, n (%)	11 (92)
Visceral disease (liver, lung, peritoneum, pleura, ascites), n (%)	6 (50)
Prior lines of therapy in advanced setting, n (%)	
0	2 (17)
1	7 (58)
2	2 (17)
3	1 (8)
Prior lines of endocrine therapy in advanced setting, n (%)	
0	3 (25)
1	9 (75)
Types of prior therapy in advanced setting, n (%)	
Chemotherapy	3 (25)
Aromatase inhibitor (AI)	8 (67)
Fulvestrant	1 (8)
CDK4/6 inhibitor	8 (67)
ESR1 mutations at baseline (ctDNA), n/N (%)	4 (36); N=11 evaluated

[a]Sums may not total to 100% due to rounding.
AI, aromatase inhibitor; CDK4/6, cyclin-dependent kinase 4/6; ECOG, Eastern Cooperative Oncology Group.

OP-1250 Phase 1b Dose Escalation in Combination with Palbociclib
Well Tolerated with No DLTs

TEAEs in ≥15% of Patients	Total (N=12)			
	Grade 1	Grade 2	Grade 3	Grade 4
Neutropenia[a]	1	2	8	0
Nausea	3	3	0	0
Vomiting	5	0	0	0
Anemia	2	2	0	0
GERD	2	2	0	0
Constipation	2	1	0	0
Fatigue	2	0	1	0
Thrombocytopenia	3	0	0	0
COVID-19	0	2	0	0
Decreased appetite	1	1	0	0
Diarrhea	0	2	0	0
Headache	2	0	0	0
Sinus bradycardia	1	1	0	0
UTI	0	2	0	0
WBC count decreased	0	1	1	0

[a] Includes adverse events reported as either "Neutropenia" or "Neutrophil count decreased."

TEAE, Treatment-Emergent Adverse Event. UTI, urinary tract infection, WBC, white blood cell

Data Cutoff Date: September 12, 2022

Safety

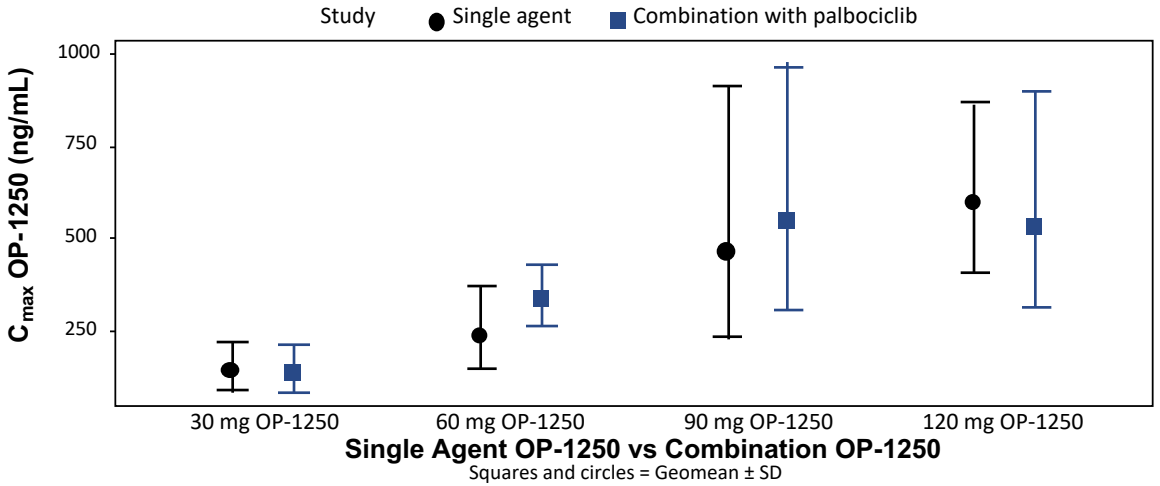
- No DLTs were observed during dose escalation and MTD was not reached
- No dose-related increase in the incidence or severity of adverse events was observed
- Majority of TEAEs were grade 1 or 2
  - Increasing dose did not show increase in frequency
  - Frequently reported TEAEs included neutropenia, nausea, vomiting, anemia, and gastroesophageal reflux disease
- No patients discontinued treatment due to adverse event, including neutropenia
- OP-1250 was not dose reduced in any patient
- Grade 3 neutropenia was reported in 8 patients (67%)
  - Time of onset was approximately 2-4 weeks on treatment
  - Rate of neutropenia consistent with the FDA-approved label for palbociclib plus an endocrine therapy (PALOMA 2[1] – overall incidence of neutropenia was 80% with 56% grade 3 and 10% grade 4)
- **No Grade 4 neutropenia was reported**

[1] Ibrance (palbociclib) prescribing information. Pfizer Inc. 2019.

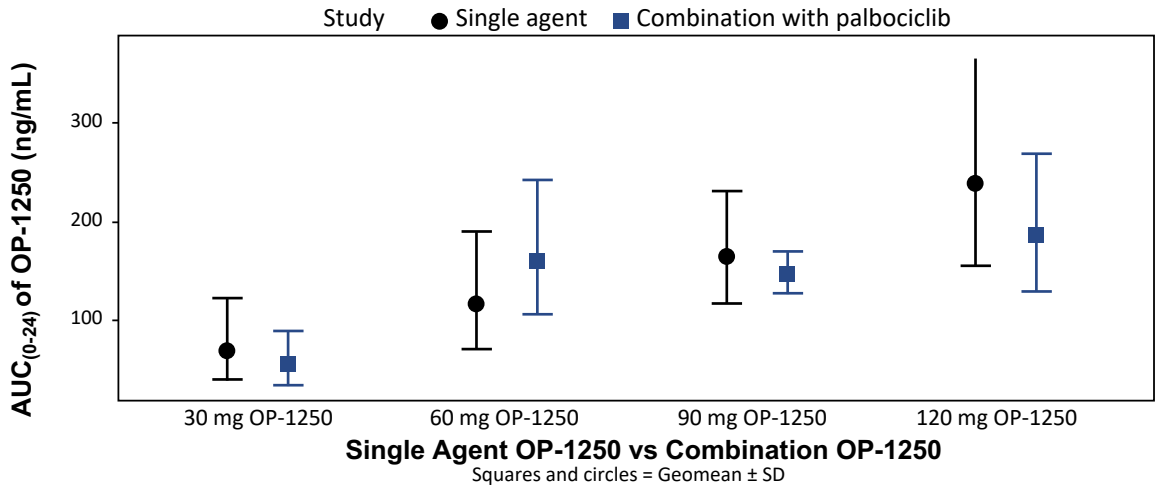
OP-1250 Phase 1b Dose Escalation in Combination with Palbociclib

No drug-drug interaction observed between OP-1250 and Palbociclib

Steady State C_{max} of OP–1250 Combination vs. Single Agent



Steady State $AUC_{(0-24)}$ of OP-1250 Combination vs. Single Agent



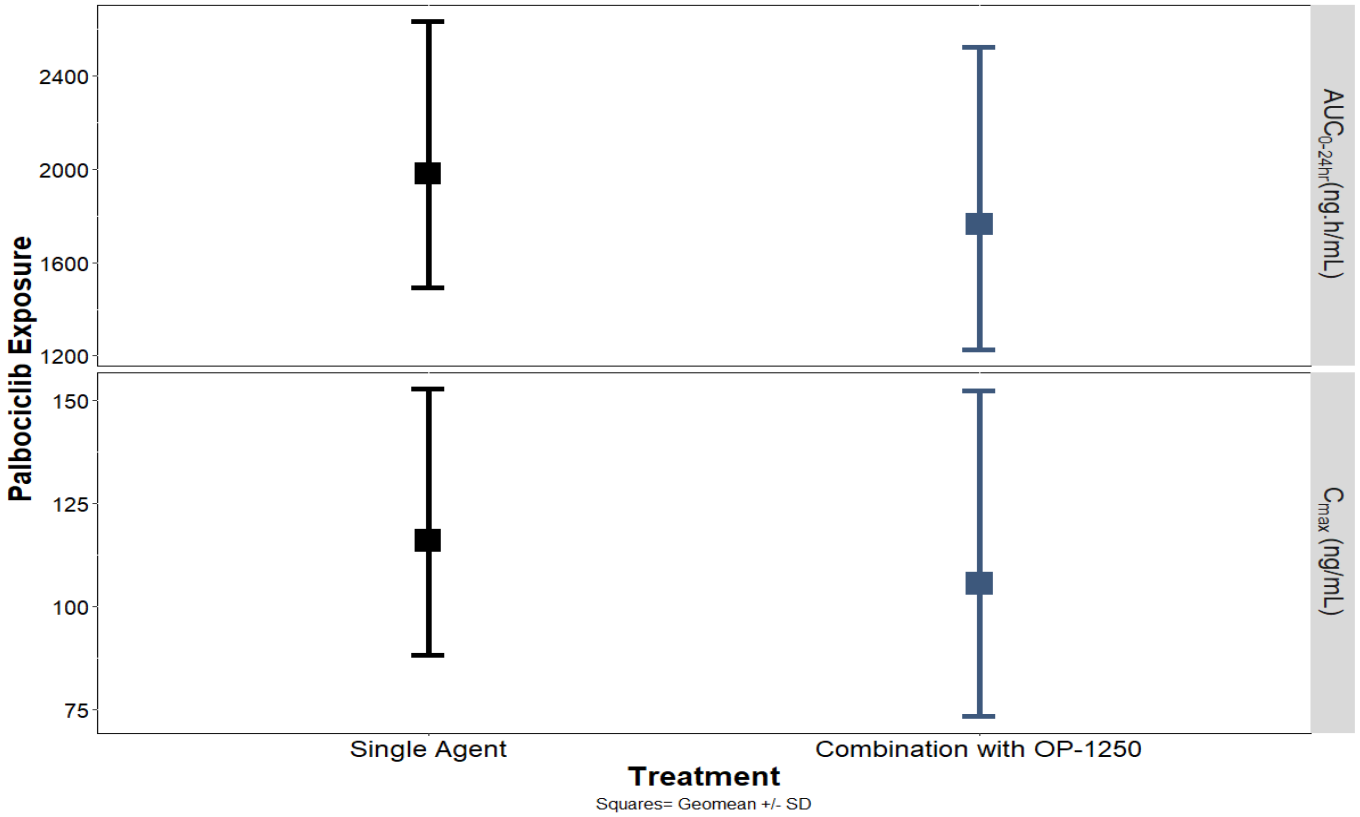
Pharmacokinetics

- No drug-drug interaction between palbociclib and OP-1250 in the dose range of 30 to 120 mg
  - Palbociclib did not affect OP-1250 exposures compared to OP-1250 monotherapy
- OP-1250 was readily bioavailable and demonstrated dose-proportional exposures and a long half-life
- Steady-state plasma levels show minimal peak-to-trough variability, enabling consistent inhibition of ER for the full dosing interval

OP-1250 Phase 1b Dose Escalation in Combination with Palbociclib

No drug-drug interaction observed between OP-1250 and Palbociclib

Steady State AUC_{0-24} and C_{max} of Palbociclib vs. Published Concentrations[a]



Pharmacokinetics

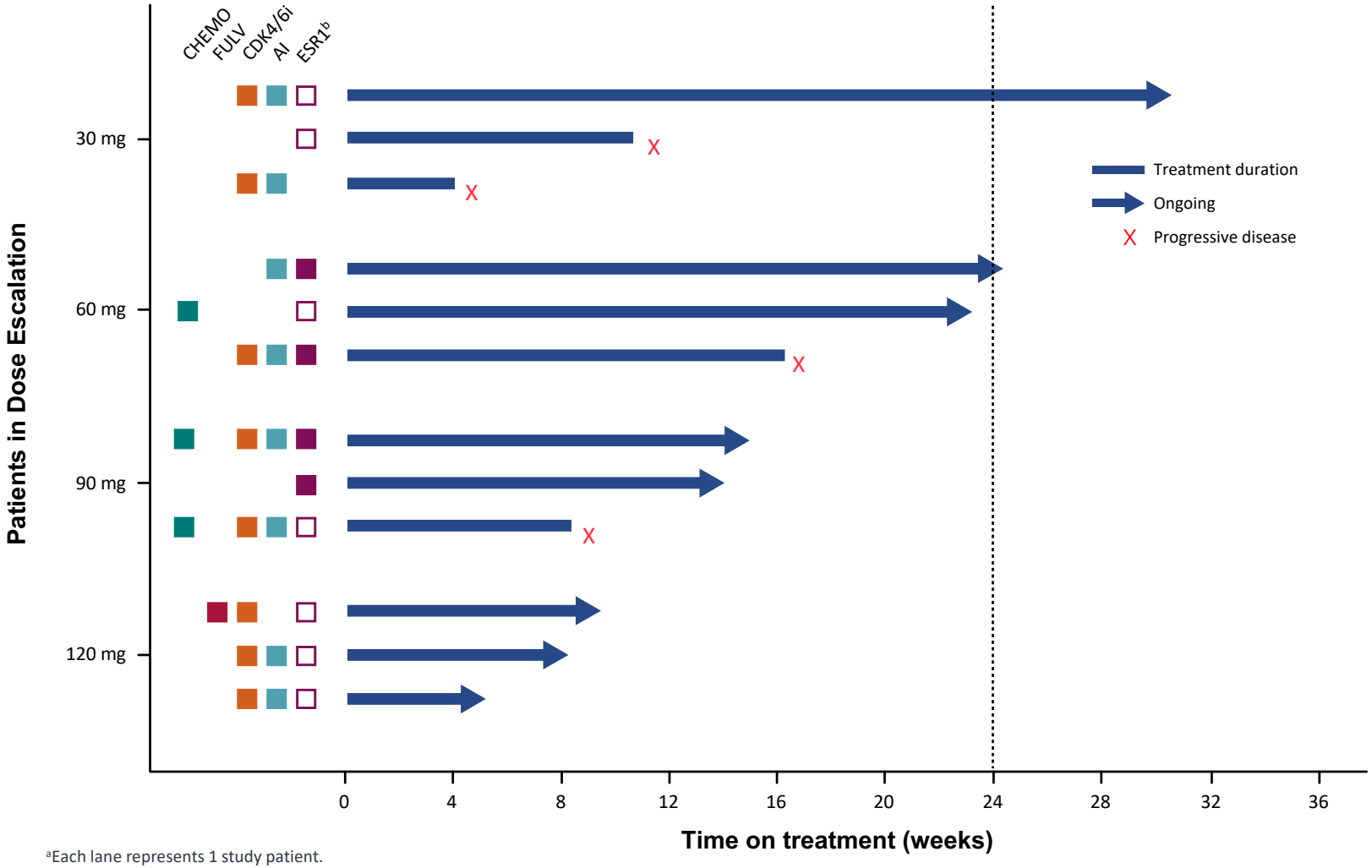
- No drug-drug interaction between palbociclib and OP-1250 in the dose range of 30 to 120 mg
- OP-1250 did not affect palbociclib 125 mg exposures when compared to published concentrations
- Exposure of palbociclib was within 90% of reported geometric means values for palbociclib

[a]Figure includes all doses of OP-1250. N=12 patients.

OP-1250 Phase 1b Dose Escalation in Combination with Palbociclib

Preliminary Duration on Treatment

Duration of Treatment as of September 15, 2022[a]

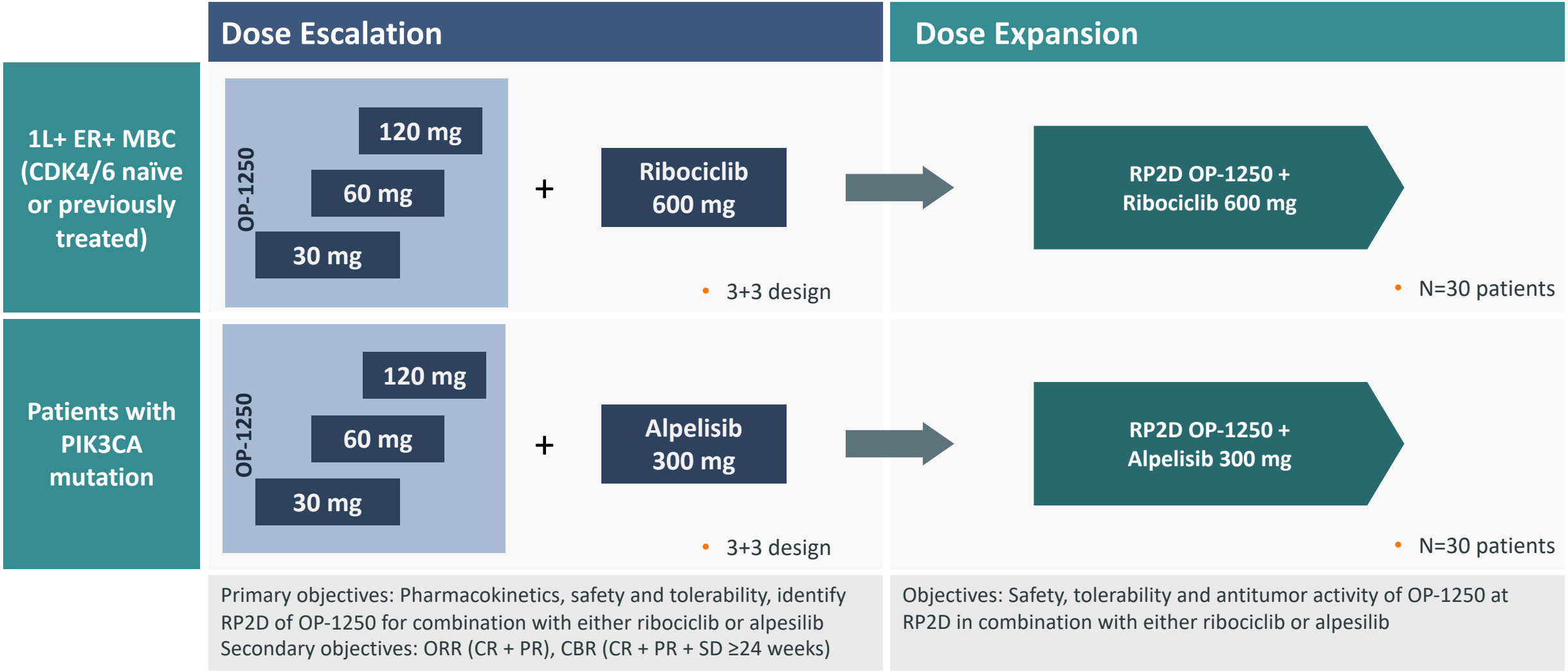


- 8 of 12 patients remain on treatment as of data cutoff Sept. 12, 2022
- Data continues to mature with stable disease lasting ≥24 weeks and ongoing for 2 patients; longest duration of treatment in the study is 31 weeks
- 4 patients have discontinued treatment due to disease progression
- Phase 2 dose expansion in up to 30 additional patients at 120mg OP-1250 in combination with palbociclib ongoing

[a]Each lane represents 1 study patient.
[b]Solid boxes indicate ESR mutation present, open boxes indicate wild-type, and the absence of a box indicates missing data.
AI, aromatase inhibitor; CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; CHEMO, chemotherapy; ESR1, estrogen receptor 1; FULV, fulvestrant.

Phase 1b Combination Study with Ribociclib and Alpelisib

Initiated Q3 2022

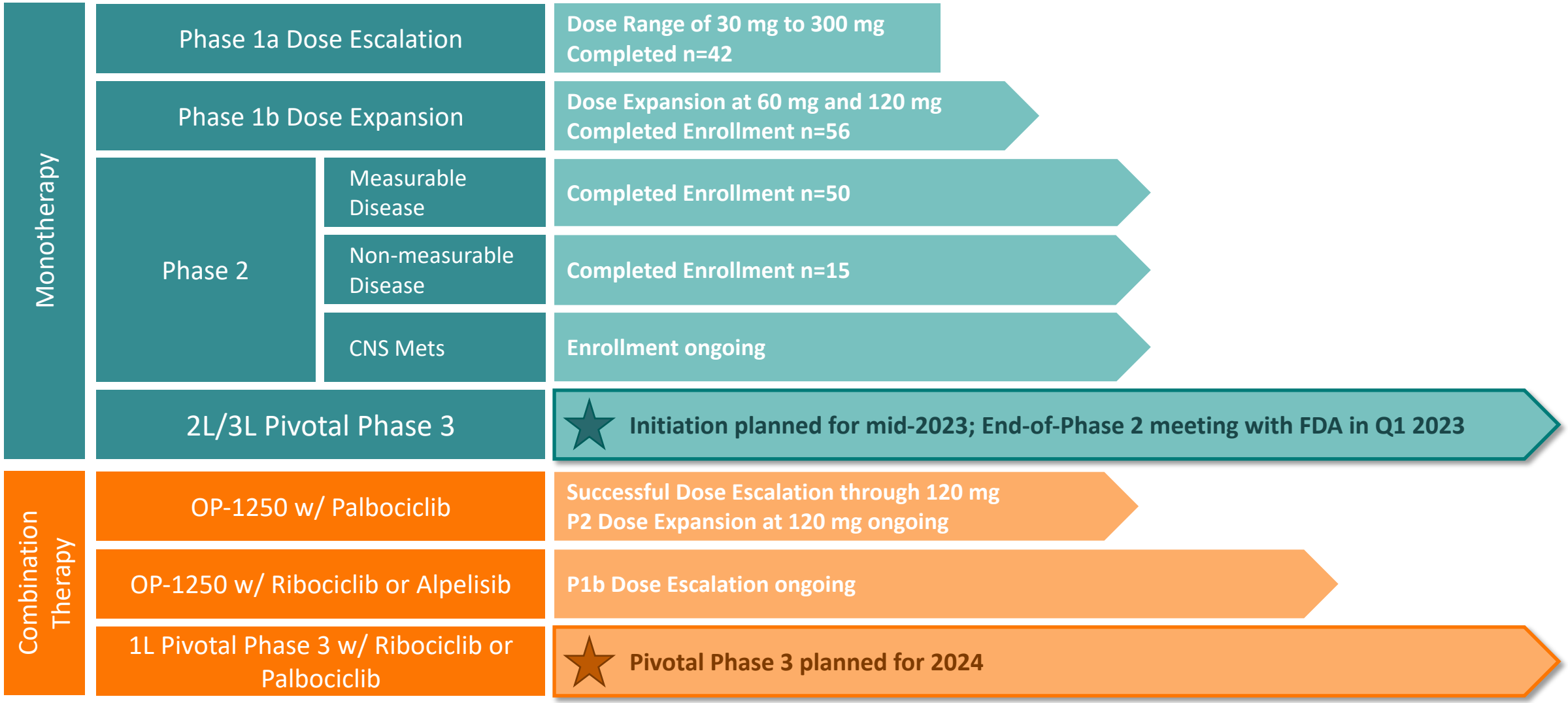


Primary objectives: Pharmacokinetics, safety and tolerability, identify RP2D of OP-1250 for combination with either ribociclib or alpesilib
Secondary objectives: ORR (CR + PR), CBR (CR + PR + SD ≥24 weeks)

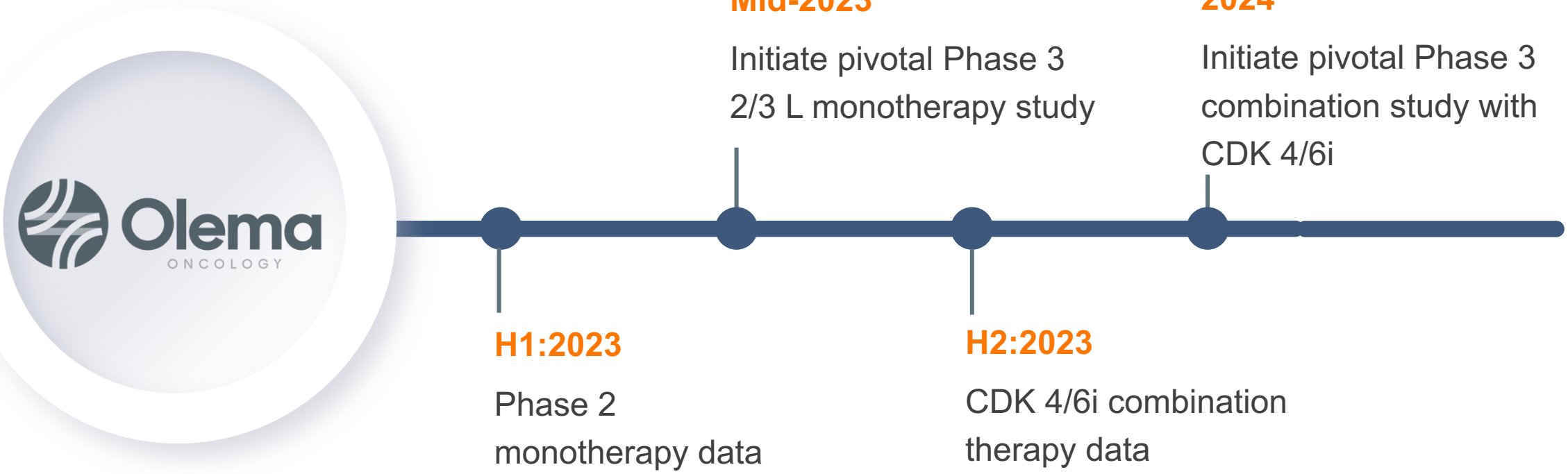
Objectives: Safety, tolerability and antitumor activity of OP-1250 at RP2D in combination with either ribociclib or alpesilib


Rapidly Advancing
Toward Phase 3
Olema
ONCOLOGY

Rapidly Advancing OP-1250 Toward Pivotal Phase 3 Studies



Delivering on Value Creating Milestones



Strong cash position of $222.6M[(1)] to support clinical development and operations into 2H 2024

(1) As of September 30, 2022.

Leading the Next Generation of Oral CERAN/SERDs for the Treatment of ER+/HER- Metastatic Breast Cancer (MBC)

OP-1250, Best-in-Class CERAN/SERD for ER+/HER2- MBC

- Completely shuts down estrogen receptor signaling pathways in women with ER+/HER- MBC
- Internally-discovered, wholly-owned IP with no royalty burden

Clinical Validation as a Monotherapy and in Combo w/ CDK4/6i

- Over 160 patients treated to date with OP-1250
- Highly encouraging Phase 1/2 clinical results in both monotherapy and combination studies

Initiating 1st Pivotal Phase 3 monotherapy study in mid-2023

- FDA Fast Track designation in 2L+ ER+/HER2- MBC
- Combination studies ongoing with Ibrance®, Kisqali® and Piqray®

Multi-Billion Dollar Commercial Market Opportunity

- 2L/3L+ MBC, represents a **$3-5B** commercial opportunity
- 1L MBC in combination with CDK 4/6i, represents a **$5-10B** commercial opportunity

Strong cash position of $222.6M(1) to support clinical development and operations into 2H 2024

(1) As of September 30, 2022.

Olema ONCOLOGY

Investor Relations
ir@olema.com

Media
media@olema.com

Business Development
partnering@olema.com

Careers
careers@olema.com

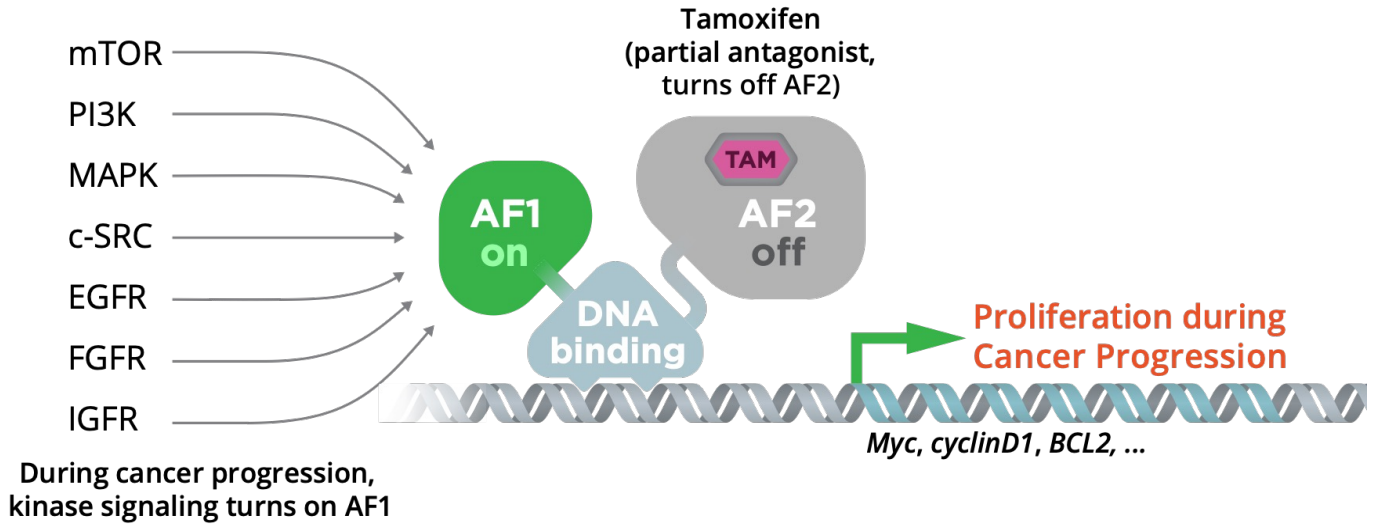
Understanding OP-1250's Mechanism of Action

Olema ONCOLOGY

OP-1250: a Complete Estrogen Receptor ANtagonist (CERAN)

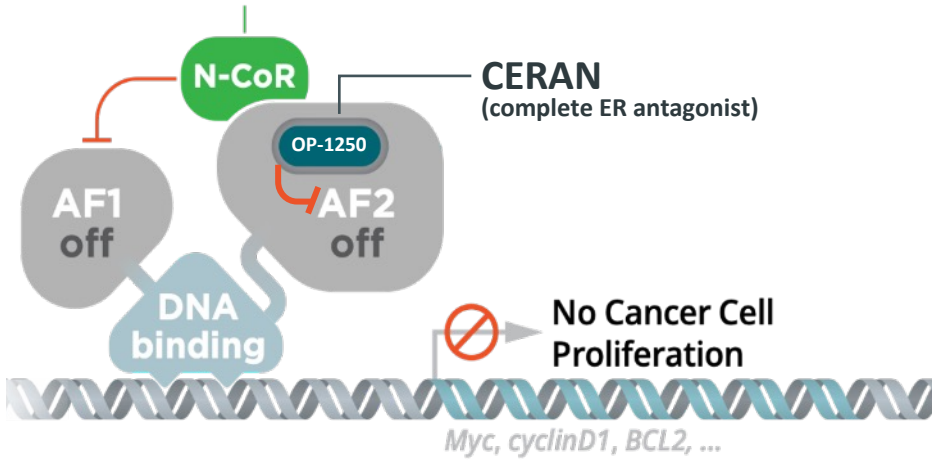
OP-1250 potently and completely inactivates the Estrogen Receptor (ER), blocks ER-driven transcriptional activity, inhibits ER-driven breast cancer cell growth, and strongly induces degradation of ER

Partial Antagonists Have a Short Duration of Response for Treatment of Metastatic Breast Cancer



SERM/SERDs block AF2 activity, but enable AF1 activation

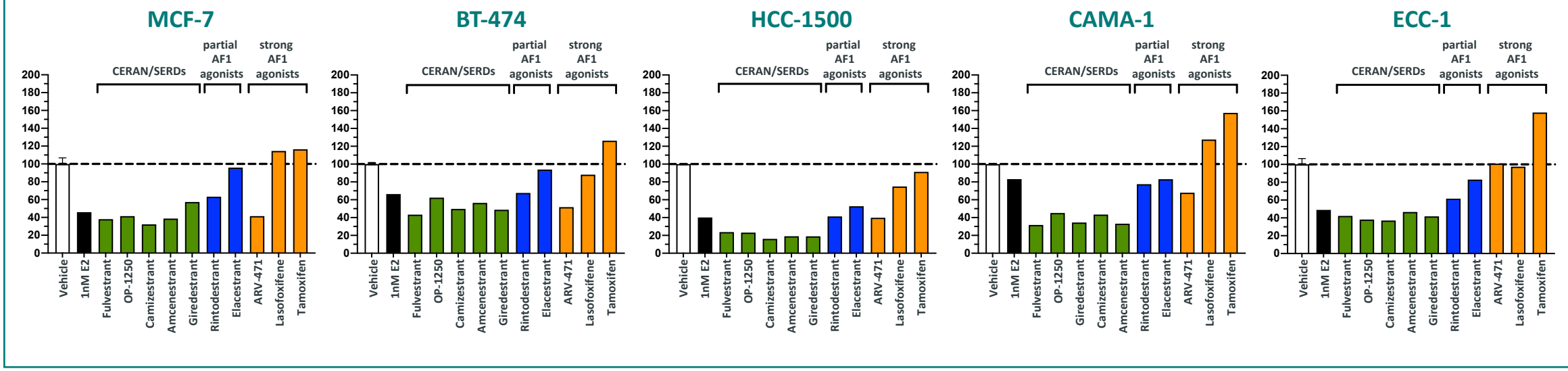
Complete antagonists turn off AF2 and recruit N-CoR to inactivate AF1



AF1: activation factor 1
AF2: activation factor 2

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

Both CERAN/SERDs and SERM/SERDs Are Strong Degraders of ERα



OP-1250 and CERAN/SERDs strongly degraded the estrogen receptor (ER) in five ER+ cell lines

Partial and strong agonists demonstrated variable and inconsistent ER degradation

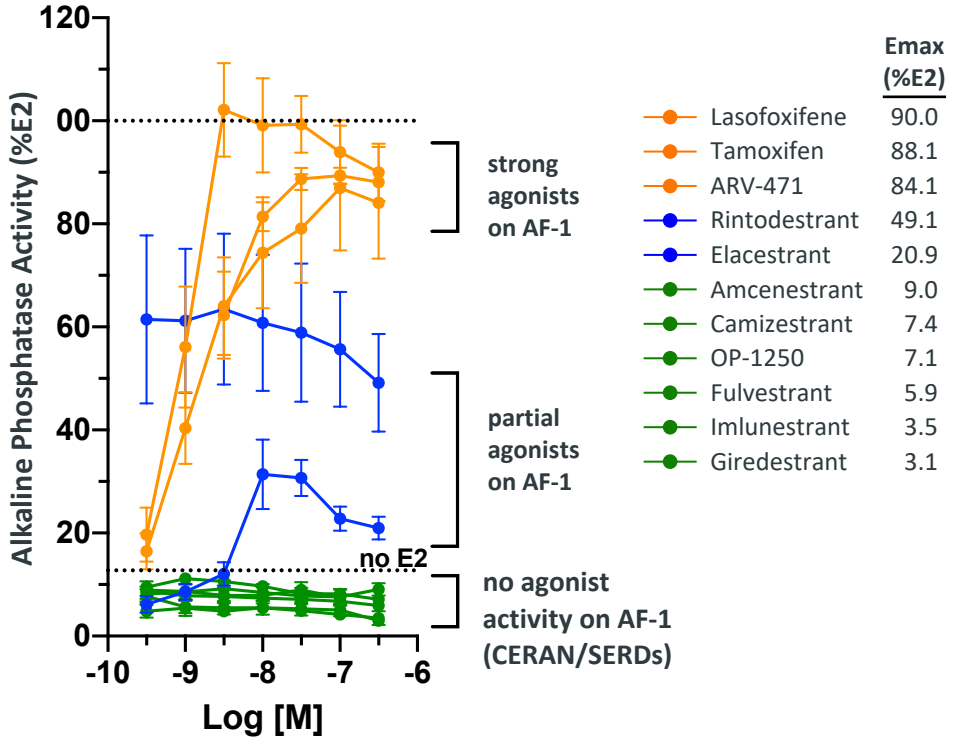
Estradiol (E2), the prototypical agonist of ERα, degraded ERα in all five ER+ cell lines

In all cases, none of the compounds achieved full ER degradation; complete ER antagonism is independent from degradation and key to inactivating remaining ER receptor

Reference: Sun et al, Proceedings: 2021 JCA-AACR Precision Cancer Medicine International Conference; September 10-12, 2021.

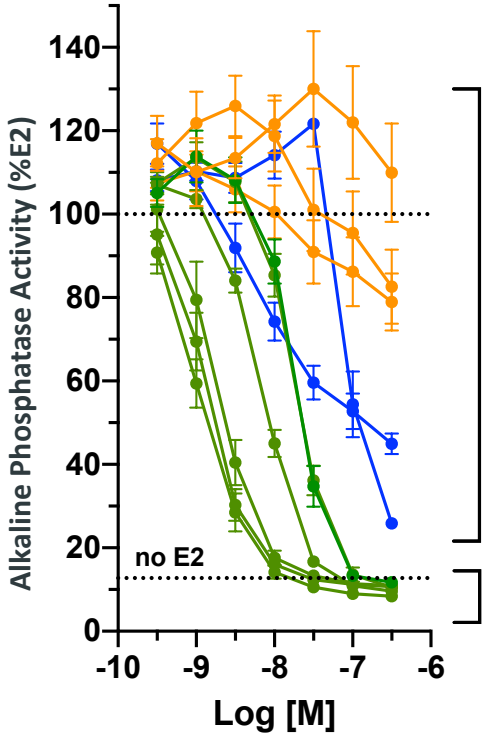
CERAN/SERDs Inactivate Both AF1 & AF2 Activity, While SERM/SERDs Only Inactivate AF2

Agonist Mode (No Estrogen)



	Emax (%E2)
Lasofoxifene	90.0
Tamoxifen	88.1
ARV-471	84.1
Rintodestrant	49.1
Elacestrant	20.9
Amcenestrant	9.0
Camizestrant	7.4
OP-1250	7.1
Fulvestrant	5.9
Imlunestrant	3.5
Giredestrant	3.1

Agonist Mode (+ Estrogen)



	pIC50	Emax (%E2)
Tamoxifen	NA	109.9
Lasofoxifene	NA	82.6
ARV-471	NA	78.9
Elacestrant	6.71	25.9
Rintodestrant	7.00	44.9
Imlunestrant	7.53	11.7
Giredestrant	8.71	10.7
Amcenestrant	7.54	10.5
Camizestrant	8.54	10.5
OP-1250	7.98	9.6
Fulvestrant	8.80	8.4

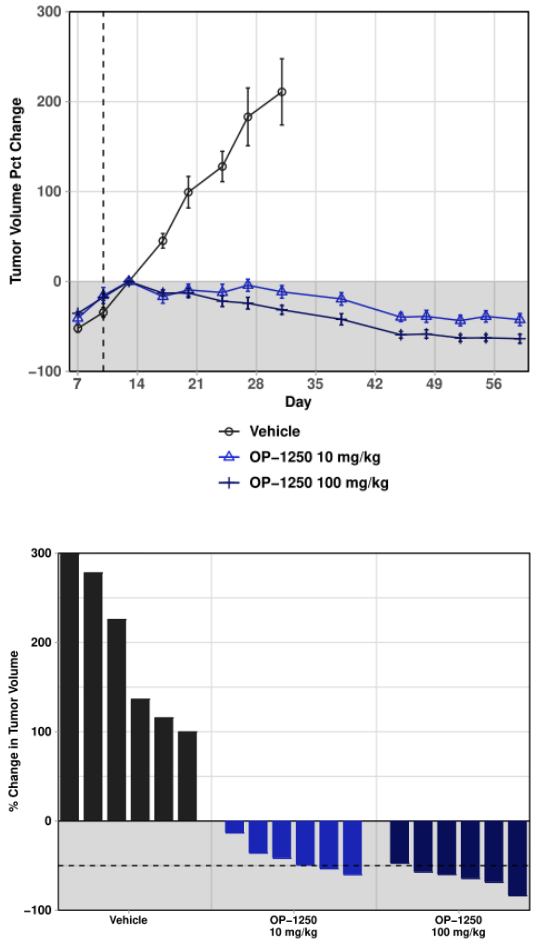
CERAN/SERDs completely inactivate AF1 activity of the estrogen receptor, while partial and strong agonists (SERM/SERDs) do not fully inhibit AF1 activity.

Reference: Sun et al, Proceedings: 2021 JCA-AACR Precision Cancer Medicine International Conference; September 10-12, 2021.

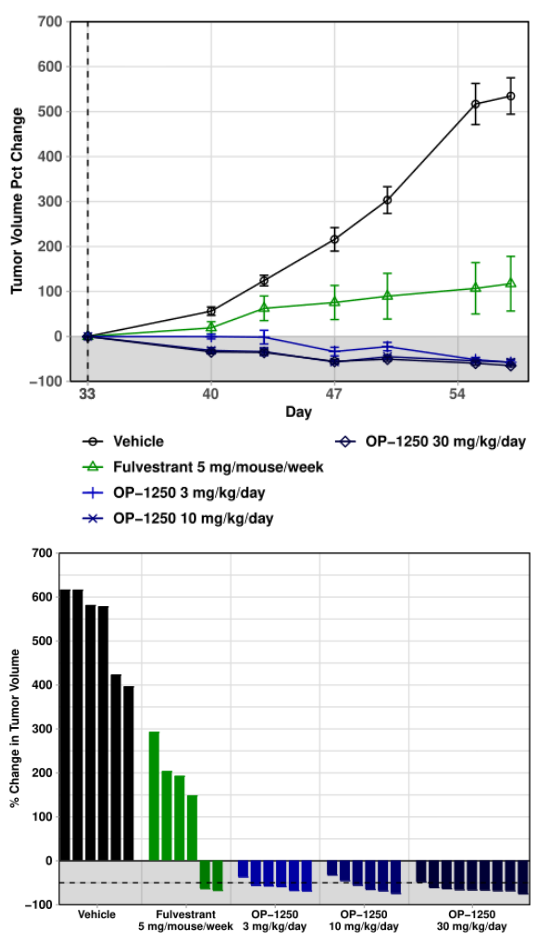
Xenograft Efficacy Studies: OP-1250 vs. Fulvestrant

OP-1250 Demonstrates Tumor Shrinkage Across Multiple Xenograft Models

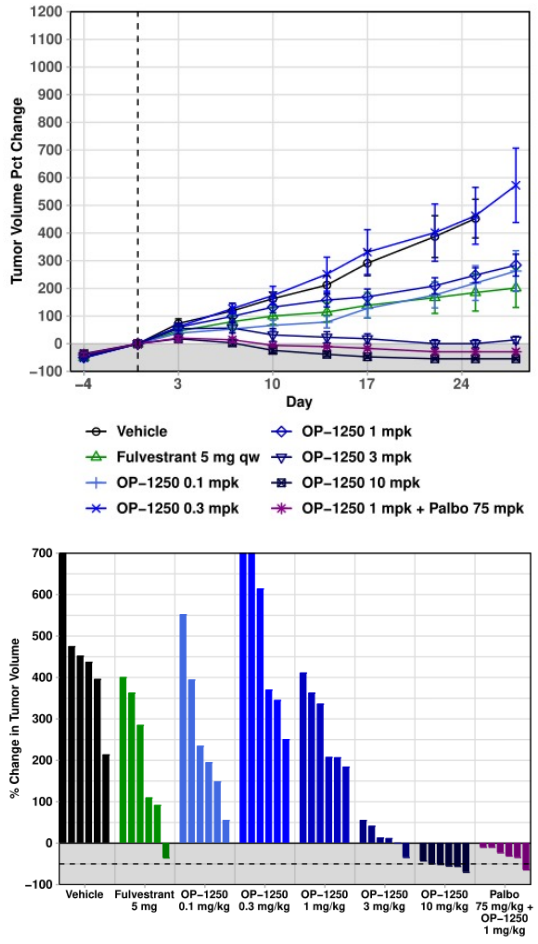
MCF-7 (HER2/neu)



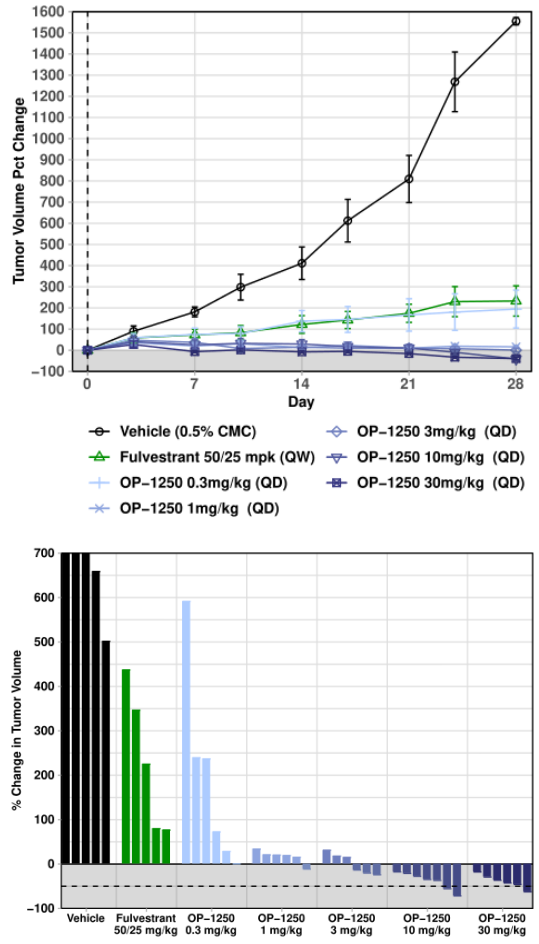
HCC1500



ST941



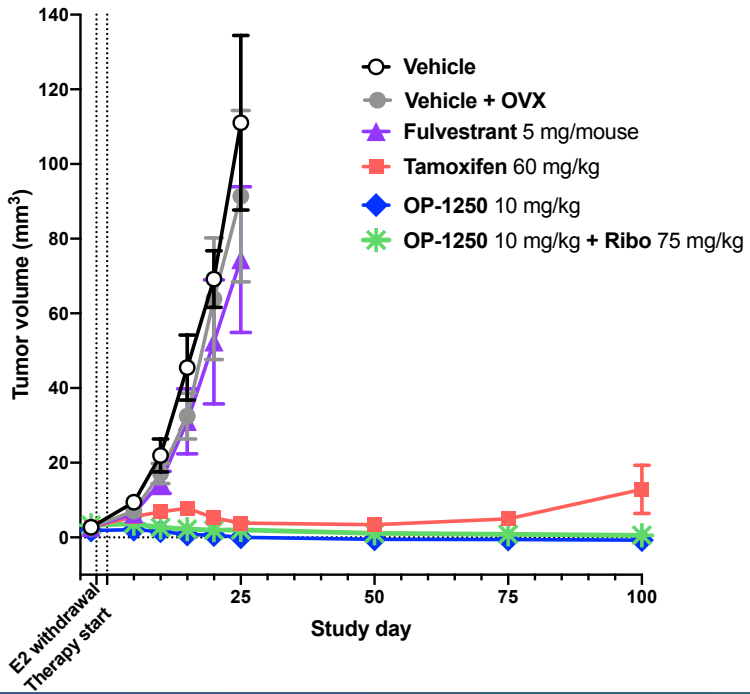
HCI-013

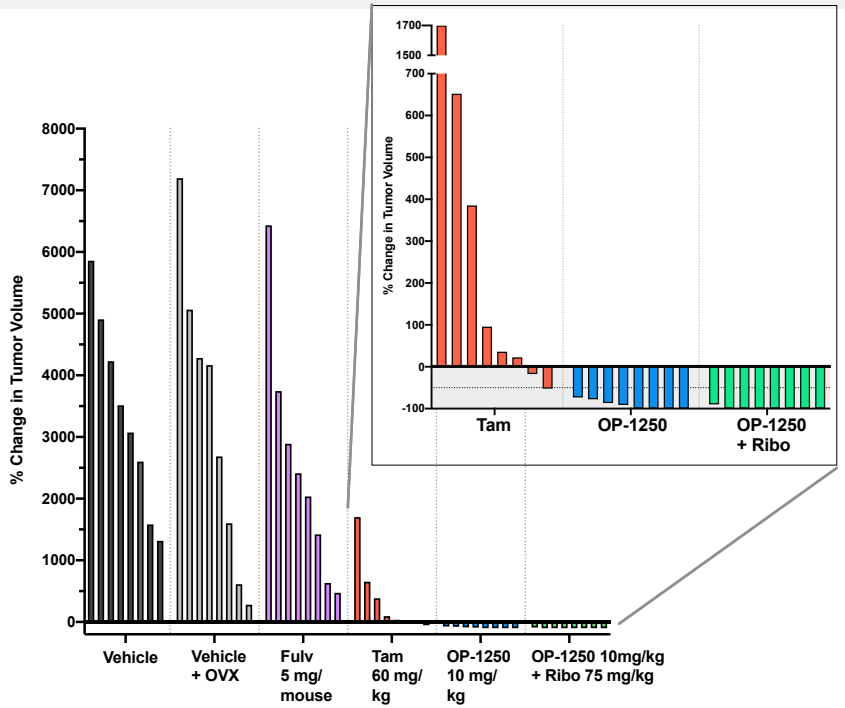


OP-1250 Has Demonstrated Activity in CNS Metastases Models

AACR 2021: Intracranial Breast Cancer Brain Metastases Xenograft Study

10 mg/kg OP-1250 is superior to tamoxifen, fulvestrant and ovariectomy in shrinking mutant ESR1-Y537S tumors in an intracranial model of ER+ breast cancer brain metastasis





Treatment	Endpoint	n
Vehicle PO, QD	PD	8
	SD	0
	PR	0
	CR	0
Vehicle + OVX PO, QD	PD	7
	SD	1
	PR	0
	CR	0
5 mg Fulvestrant SC, QW	PD	8
	SD	0
	PR	0
	CR	0
60 mg/kg Tamoxifen PO, QD	PD	6
	SD	1
	PR	1
	CR	0
10 mg/kg OP-1250 PO, QD	PD	0
	SD	0
	PR	4
	CR	4
10 mg/kg OP-1250 + 75 mg/kg Ribociclib PO, QD	PD	0
	SD	0
	PR	1
	CR	7

Endpoint criteria: PD (progressed disease) >20% increase tumor size; PR (partial response) >30% decrease in tumor size; CR (complete response): no tumor observed; SD (stable disease): does not meet above criteria.

After 100 days, tumors in mice treated with OP-1250 remain small or undetectable while tumors in mice treated with fulvestrant and tamoxifen have started to grow.

Reference: Hodges-Gallagher et al., Proceedings: AACR Annual Meeting 2021; April 9-14, 2021