Investor Event

Zotatifin in ER+ Metastatic Breast Cancer

June 4, 2023

eFFECTOR

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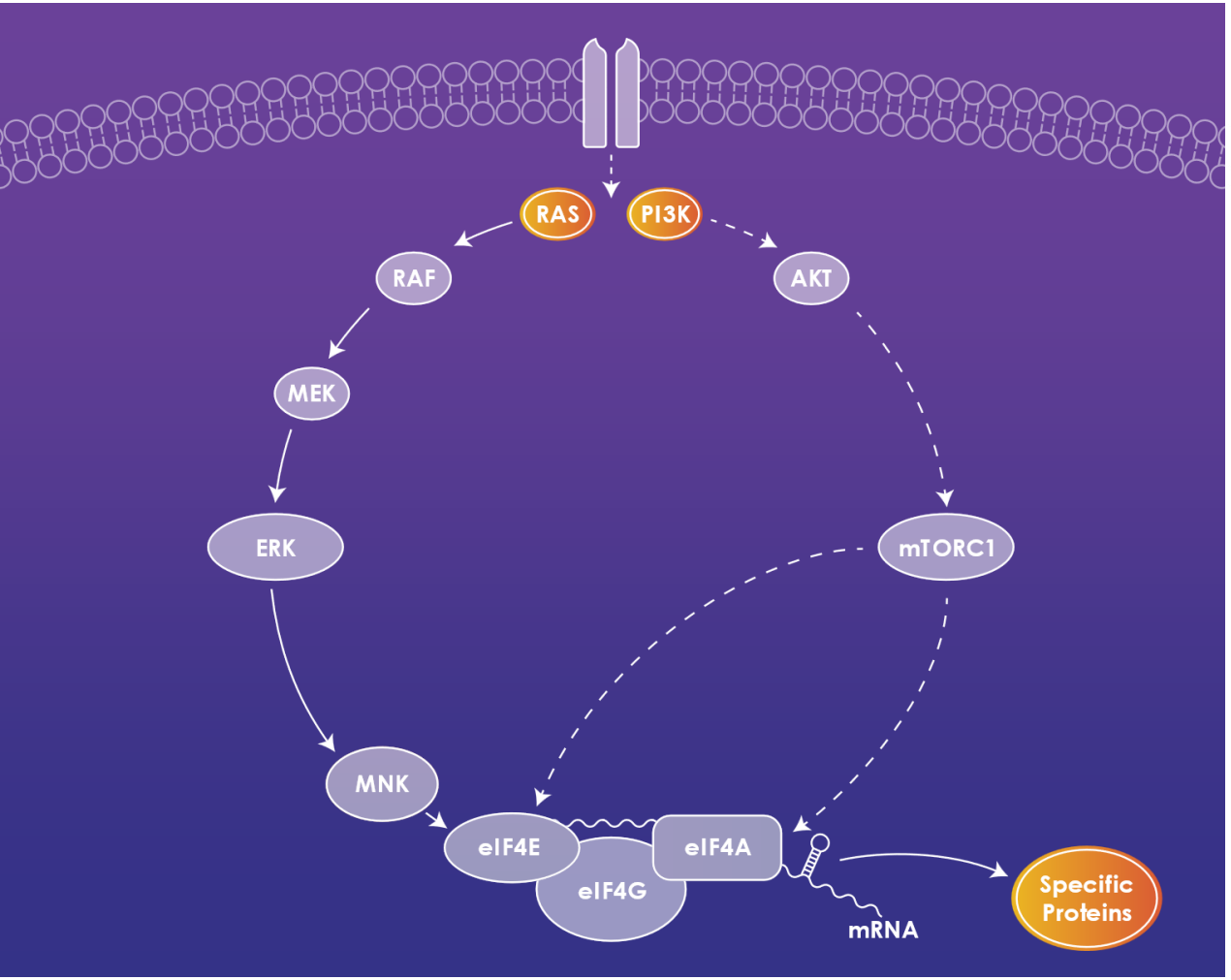
Agenda

Company introduction	Steve Worland, Ph.D. eFFECTOR President and CEO
Treatment landscape for 2nd line plus ER+ BC	Sarat Chandarlapaty, M.D., Ph.D. Patricia and James Cayne Chair for Junior Faculty, Memorial Sloan Kettering
Zotatifin data presented at ASCO	Doug Warner, M.D. eFFECTOR Chief Medical Officer
Zotatifin product development strategy and closing remarks	Steve Worland, Ph.D.

Company Overview

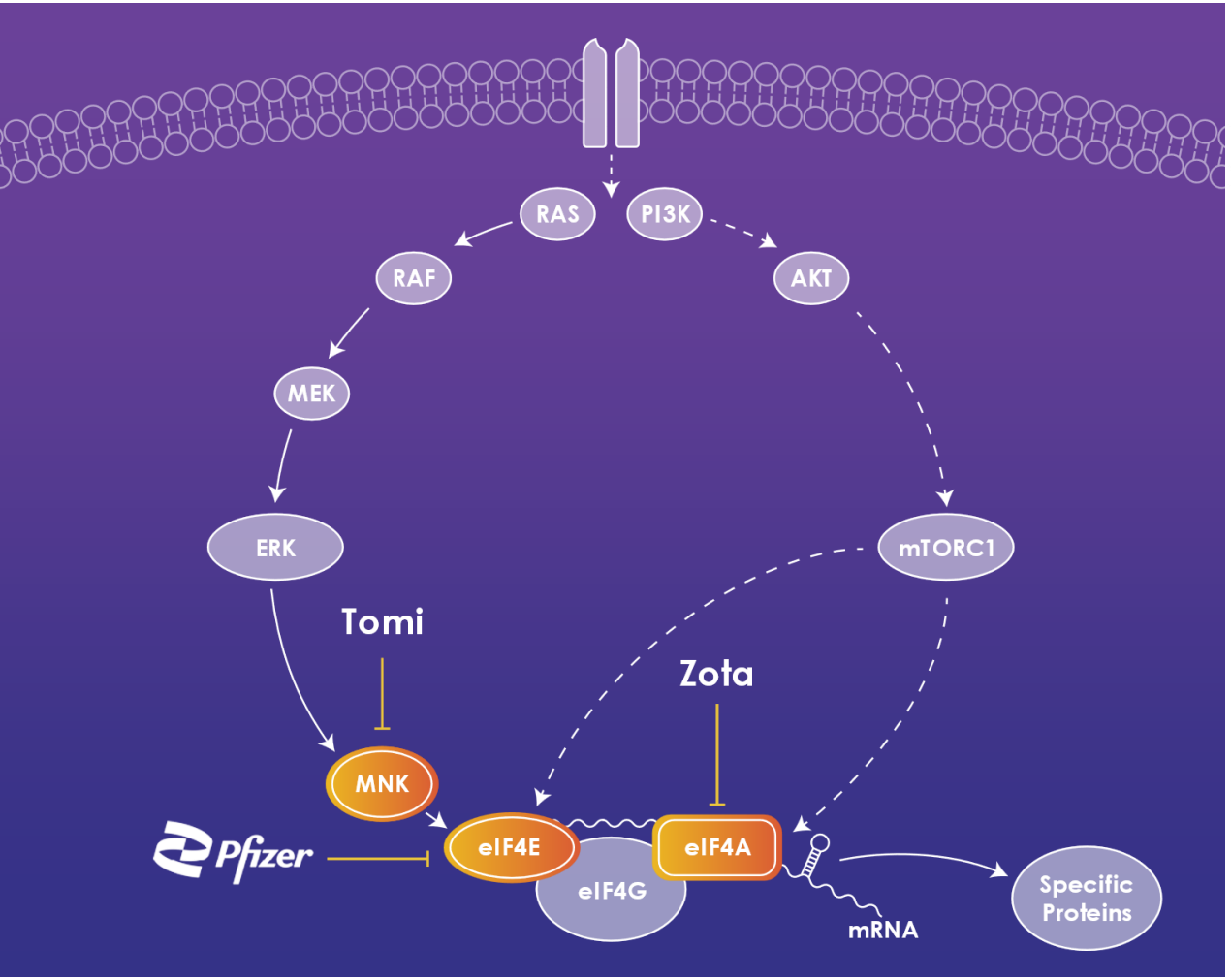
- Novel platform designed to **block upregulated production of specific oncoproteins** driven by oncogenic signaling
  - Next-generation targeted approach designed to broaden impact beyond addressing mutated oncogenes
  - Underlying technology licensed from UCSF, labs of Drs. Kevan Shokat and Davide Ruggero
  - Product candidates referred to as Selective Translation Regulator Inhibitors (STRIs)
- **Two wholly owned novel clinical assets**
  - Tomivosertib: MNK inhibitor in a **randomized P2b trial in NSCLC combined with pembrolizumab** with **data anticipated H2 2023**
  - Zotatifin: eIF4A inhibitor in escalation and expansion cohorts in **ER+ BC** with data presented today at ASCO and **further data anticipated in H2 2023**
- Validating **partnership with Pfizer**
  - $507M partnership on third STRI product candidate targeting eIF4E
  - Retained option to co-promote and profit share in U.S.

Oncogenic Signaling Selectively Activates Translation to Drive Production of Specific Tumor-Promoting Proteins



- Multiple signaling pathways, including **RAS** and **PI3K**, activate mRNA translation to drive production of **specific proteins**
- Tumors are dependent on upregulated protein production for growth, avoidance of apoptosis, and immune evasion
- eFFECTOR is taking the novel approach to block oncogenic signaling at the point of mRNA translation
- Potential **benefits** to targeting translation
  - Certain tumors are **acutely dependent** on upregulated protein production
  - Numerous **opportunities to combine** with agents acting elsewhere in these pathways or in complementary pathways

Selective Translation Regulator Inhibitor (STRI) Platform: Controlling the Outputs of Tumor-Driving Pathways

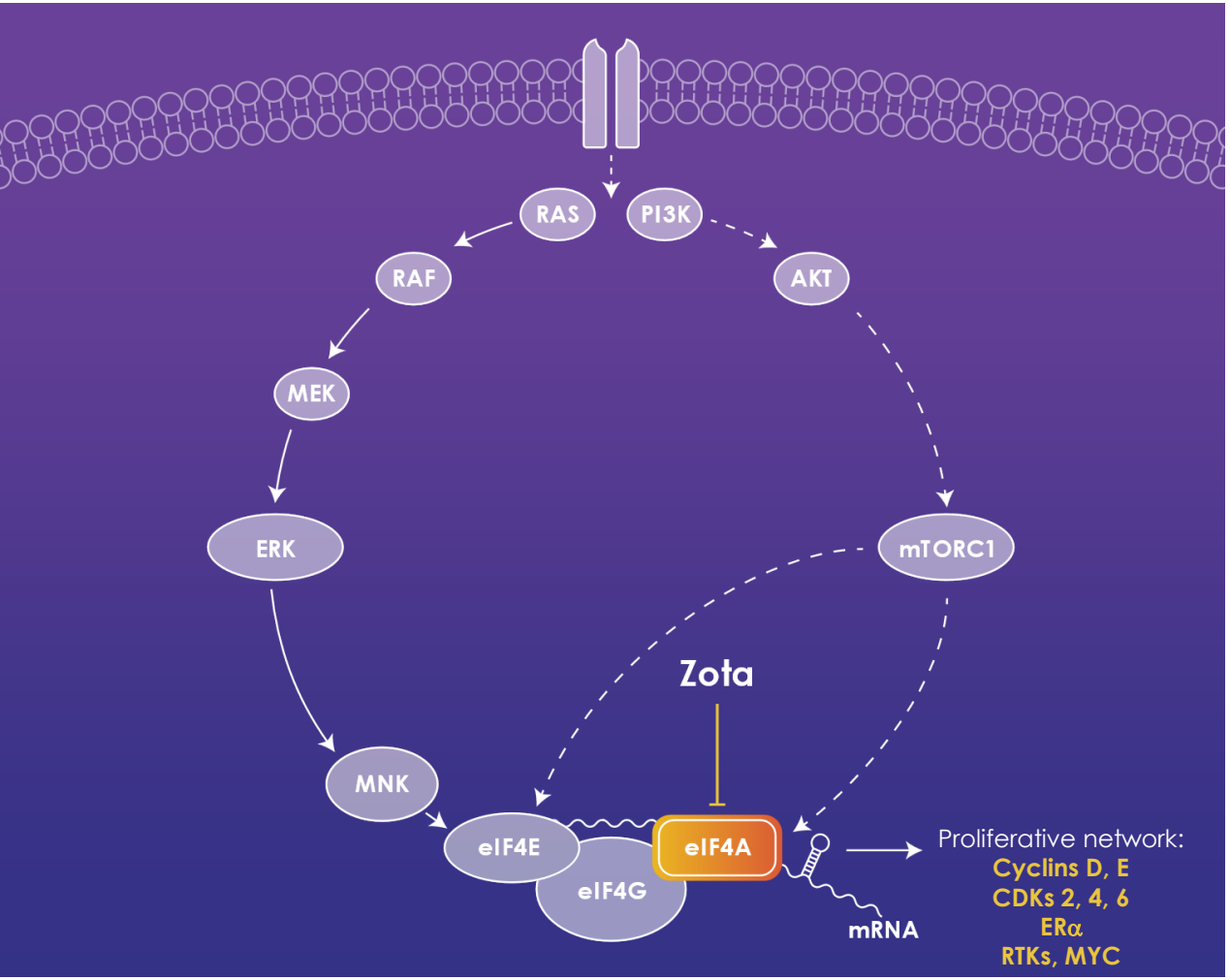


- Focused on three targets that drive translation:
  - **MNK:** kinase phosphorylates RNA-binding proteins
  - **eIF4A:** helicase unwinds RNA secondary structures
  - **eIF4E:** binds 5'-cap of mRNA
- Each target controls production of a distinct set of proteins
  - STRI platform enabled identification of regulated proteins and vulnerable tumor types
- eFFECTOR invented novel product candidates with strong intellectual property to address each of the three targets

Robust Pipeline: Multiple STRIs in Development

Program (Target)	Discovery	Preclinical	Phase 1	Phase 2a	Phase 2b	Phase 3	Global Rights	Anticipated Milestones
Tomivosertib (MNKi)	1L NSCLC PD-L1 ≥50% - 1L in combo with pembro						eFFECTOR	H2 2023 Topline data readout
Zotatifin Oncology (eIF4Ai)	Solid Tumors ER+ BC and KRAS NSCLC						eFFECTOR	ASCO 2023 Topline data from fully enrolled ZFA triplet H2 2023 Data from resumed dose escalation Q2W and QW
eIF4Ei	Solid Tumors						Pfizer *eFFECTOR Option to Co-Promote/ Profit Share in US*	

Zotatifin Designed to Suppress a Network of Important Tumor-Driving Proteins by Inhibiting eIF4A



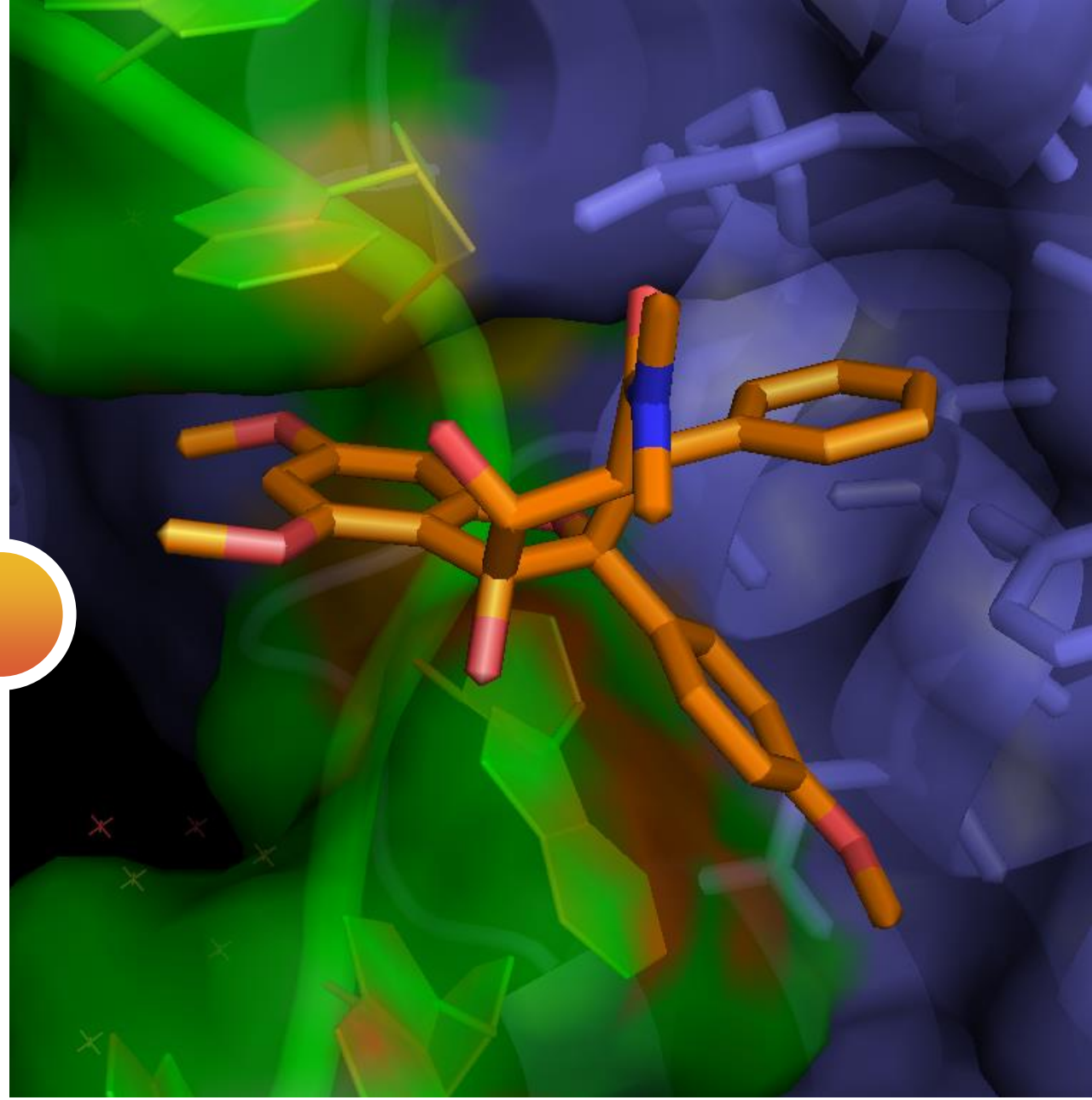
- Cancer signaling **activates eIF4A** to upregulate a network of tumor promoting proteins
- Zotatifin designed to **suppress the network** in a single product
- In preclinical studies, zotatifin downregulated a network of cell-cycle proteins and oncoproteins including:
  - **Cyclins D, E** and **CDKs 2, 4, 6**
  - Estrogen receptor (**ERα**)
  - **RTKs** and **MYC**

Zotatifin Executive Summary

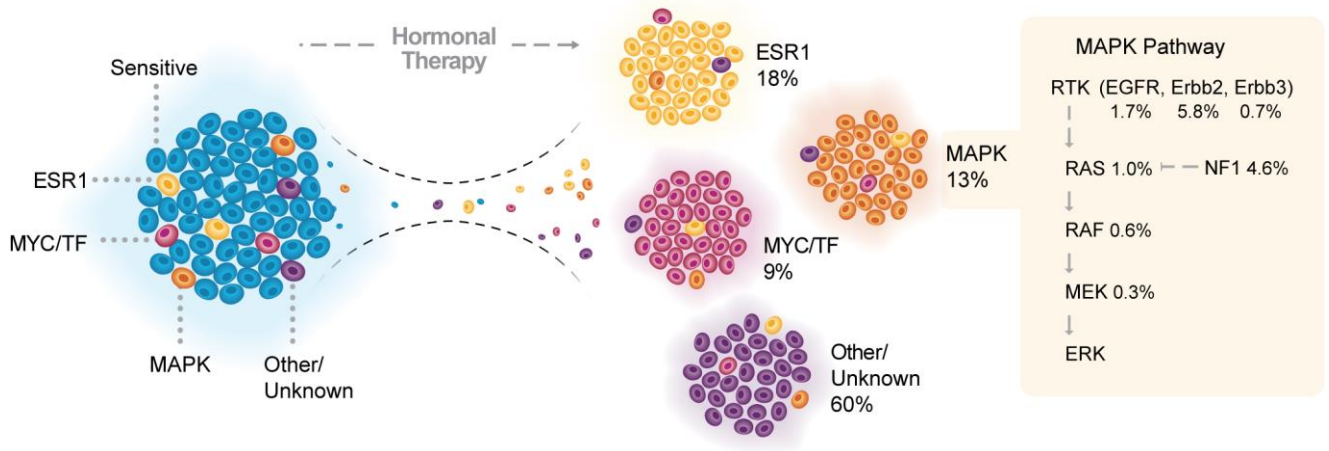
- Zotatifin, a first-in-class clinical stage asset with a **novel mechanism of action** (eIF4Ai) which is complementary to existing/emerging therapies for **ER+ metastatic breast cancer** (mBC)
  - Options for **rational combinations** with CDK4/6i, endocrine therapy and PI3K/AKT inhibitors
- Initial dose escalation completed as monotherapy
  - RP2D selected to be 0.07 mg/kg dosed on Days 1 and 8 of a 21-day cycle
  - Expansion cohorts opened in ER+ breast cancer with early signals of activity
- **New interim data for ZFA triplet presented at ASCO 2023**
  - 5 of 19 (26%) RECIST-evaluable patients had partial responses (PR)
    - 4 confirmed
    - 1 unconfirmed
  - **Efficacy results exceed our expectations** for fulvestrant + abemaciclib (FA doublet) in such heavily pre-treated patients after CDK4/6, endocrine and/or chemo therapies
- Based on safety and tolerability results observed at initial RP2D, in addition to phamacodynamic data, resumed dose escalation
  - 1 of 3 (33%) patients in first fully enrolled escalation cohort had a confirmed PR

Sarat Chandarlapaty, M.D., Ph.D.

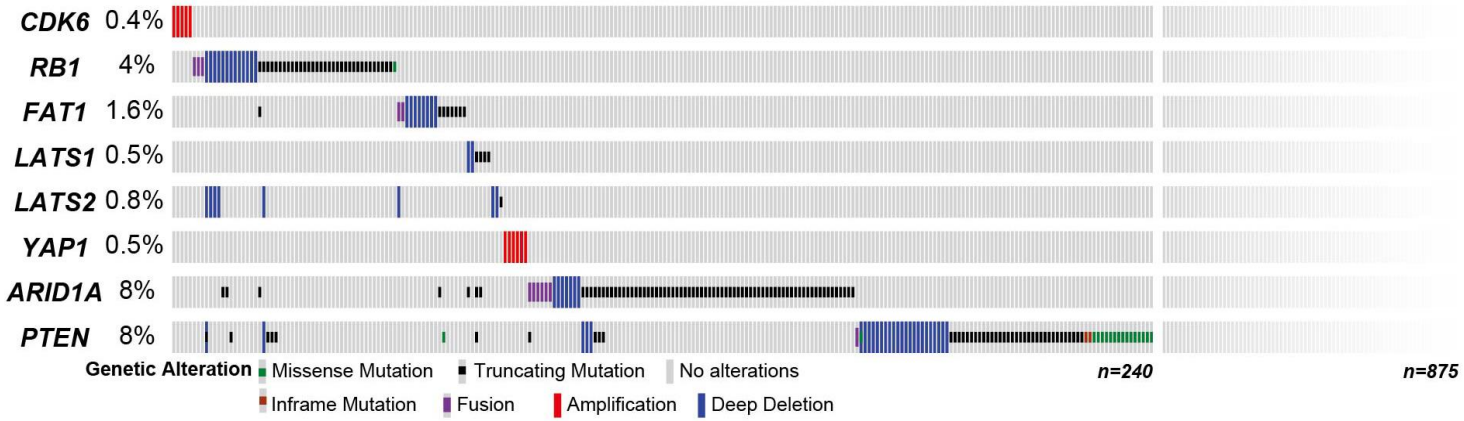
Patricia and James Cayne Chair for Junior Faculty, Memorial Sloan Kettering



Acquired Genetic Alterations => Resistance By Reactivating ER and CDK4/6

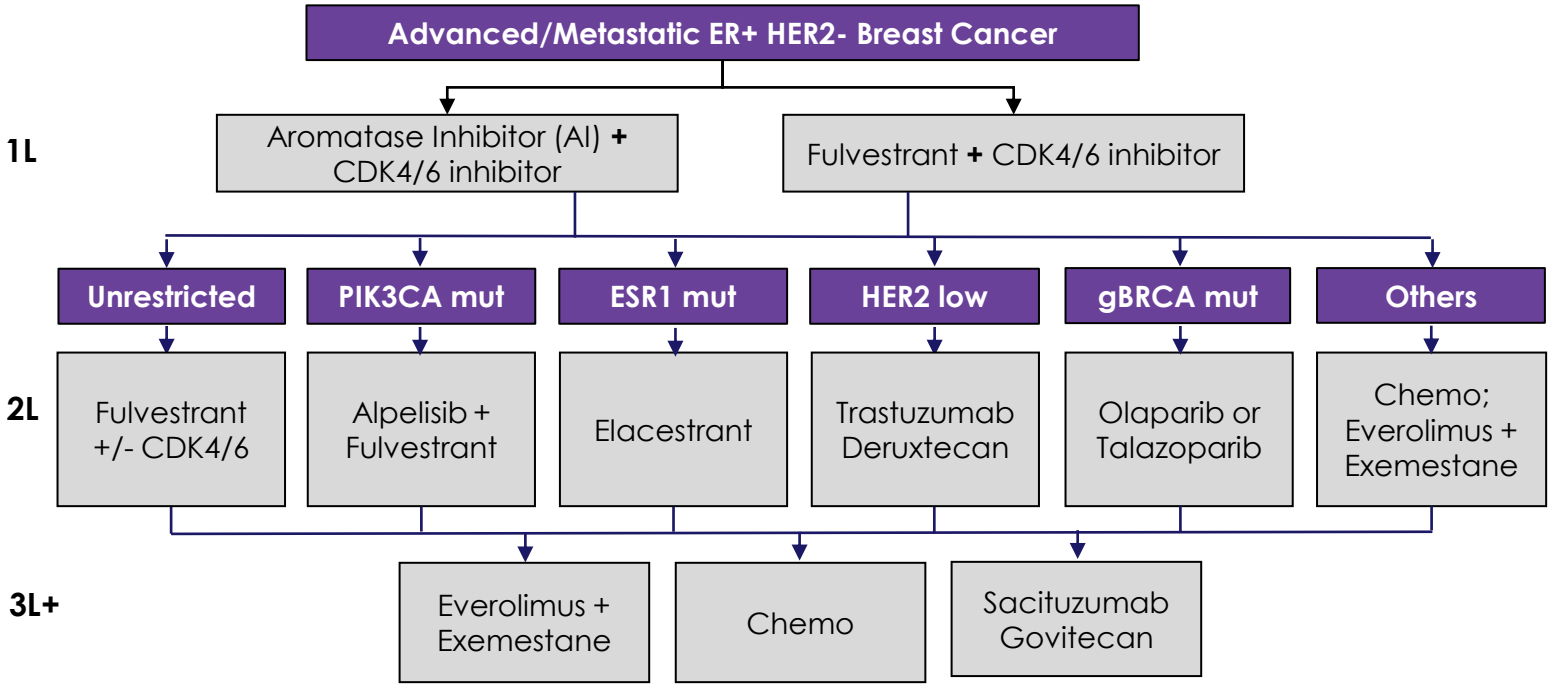


Razavi et al., Cancer Cell 2018



Li et al., Cancer Discovery 2021

Treatment Algorithm in HR+, HER2- mBC



- Additional agents in development include:
  - AKT inhibitors
  - Oral SERDS
  - Mutant-selective PI3K inhibitors

Significant Unmet Need Exists in HR+/HER2- mBC Patients Who Progress on 1L CDK4/6i-based Treatment (mPFS of 2-7 months)

		CDK-naïve		2L (post-CDK)	
Treatment/s	**Patient population**	**ORR**	**mPFS**	**ORR**	**mPFS**
Fulvestrant [1, 2]	Unrestricted	11-29%	4.6-12.8 mos	4%	1.9 mos
Elacestrant [2]	ESR1 mut	N/A	N/A	7%	3.8 mos
CDK4/6 + Fulvestrant [1, 3]	Unrestricted	25-48%	9.5-20.5 mos	14-20%	4.6-5.3 mos
Alpelisib + Fulvestrant [4]	PIK3CA mut	36%	11 mos	17%	7.3 mos
Capivasertib + Fulvestrant [5]	Unrestricted	N/A	10.9 mos	N/A	5.5 mos
Everolimus + Exemestane [6]	Unrestricted	10%	6.9 mos	Unknown (no prospective data)	

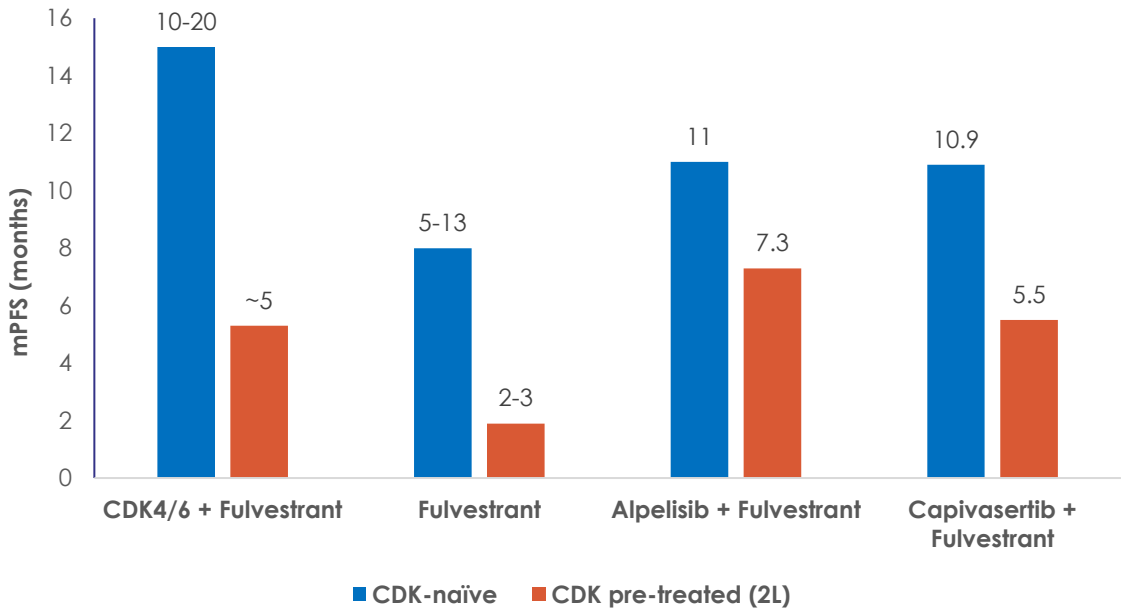
CDK-naive trials: [1]PALOMA-3, MONALEESA-3, MONARCH-2; [4]SOLAR-1; [5]CAPItello-291; [6]BOLERO-2

Post-CDK trials: [2]EMERALD, VERONICA; [3]MAINTAIN, PACE; [4]BYLieve; [5]CAPItello-291

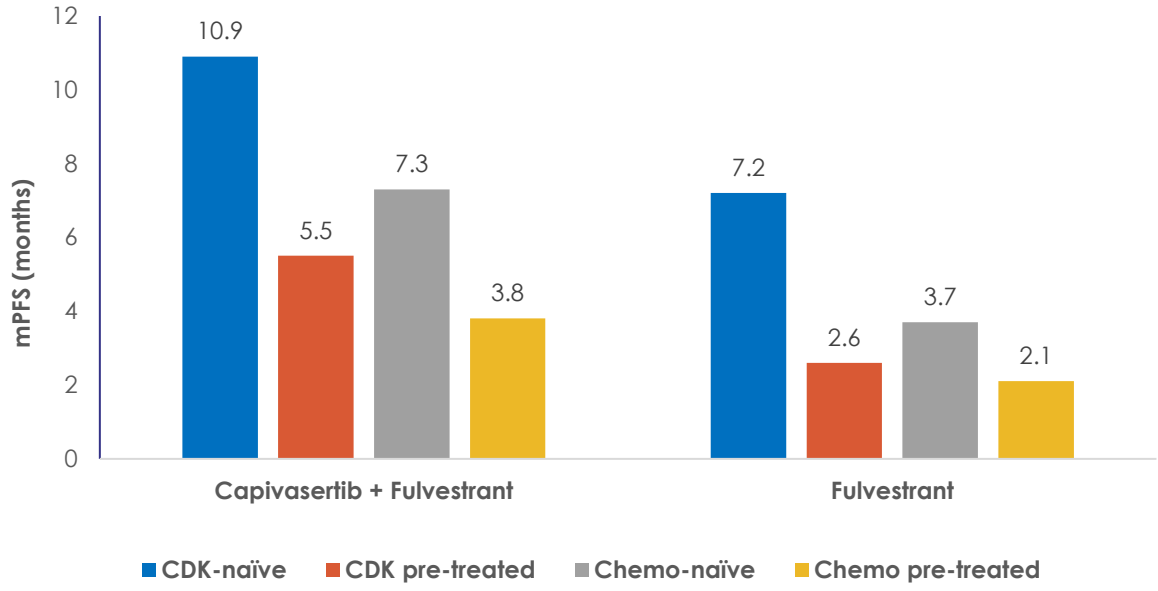
Note, table is not based on head-to-head comparisons and caution should be exercised when comparing data across studies

One Additional Prior Line of Treatment Decreases mPFS ~50% in mBC

Comparison of mPFS of SoC regimens based on prior CDK4/6 exposure



Comparison of mPFS of Fulvestrant +/- Capivasertib based on prior CDK4/6 or chemo exposure



Data from trials presented on previous slide

Expectation of ~10% ORR for Abemaciclib + Fulvestrant in Heavily Pre-treated Patients Post CDK/ET/Chemo*

		EFTR	MAINTAIN[1]		EMERALD[2]	MONARCH-1[3]
		ZFA triplet CDK/F exposed n=19	Switch ET mono CDK exposed n=59	R + Switch ET CDK exposed n=60	F mono CDK exposed n=165	A mono CDK naïve n=132
Response		**26%**	**11%**	**20%**	**4%**	**20%**
Prior therapies in metastatic setting	CDK4/6	95%	100%	100%	100%	0%
	Fulvestrant	65%	0%	0%	30%	51%
	Chemo	75%	10%	10%	22%	100%

Z = zotatifin, F = fulvestrant, A = abemaciclib, R = ribociclib, [1]Kalinsky et al., ASCO 2022; [2]Bidard et al., JCO 2022; [3]Dickler et al., Clin Cancer Res 2017
MAINTAIN Trial Design: All patients switched ET (83% switched from F) and of patients randomized to also receive R, it was a CDKi switch for 87% of patients

- MAINTAIN – ORR was 20% when patients switched endocrine therapy (ET) and CDKi, whereas ORR was 11% when patients only switched ET and received no CDKi, suggesting the difference in ORR was due, in part, to switching ET
  - In contrast, majority of patients in EFTR trial and all responders did not switch ET (i.e. they were retreated with fulvestrant)
- EMERALD and other studies – ORR was ~ 5-10% on fulvestrant in patients who received prior CDK4/6 treatment
- MONARCH-1 – ORR was 20% on abemaciclib in CDK-naïve patients
  - ORR for abemaciclib after progression on another CDK4/6 inhibitor expected to be substantially lower than 20%, given common mechanisms of resistance to CDK4/6 inhibitors

*Company estimate based on review of historical data for fulvestrant and abemaciclib.
DISCLAIMER: Differences exist between trial designs and subject characteristics, and caution should be exercised when comparing data across trials. No head-to-head clinical study has been conducted comparing Zotatifin to any other product or candidate.
Zotatifin interim data as of May 3, 2023 cut-off. Prior therapies presented for enrolled patients (n=20), responses for RECIST-evaluable patients (n=19).

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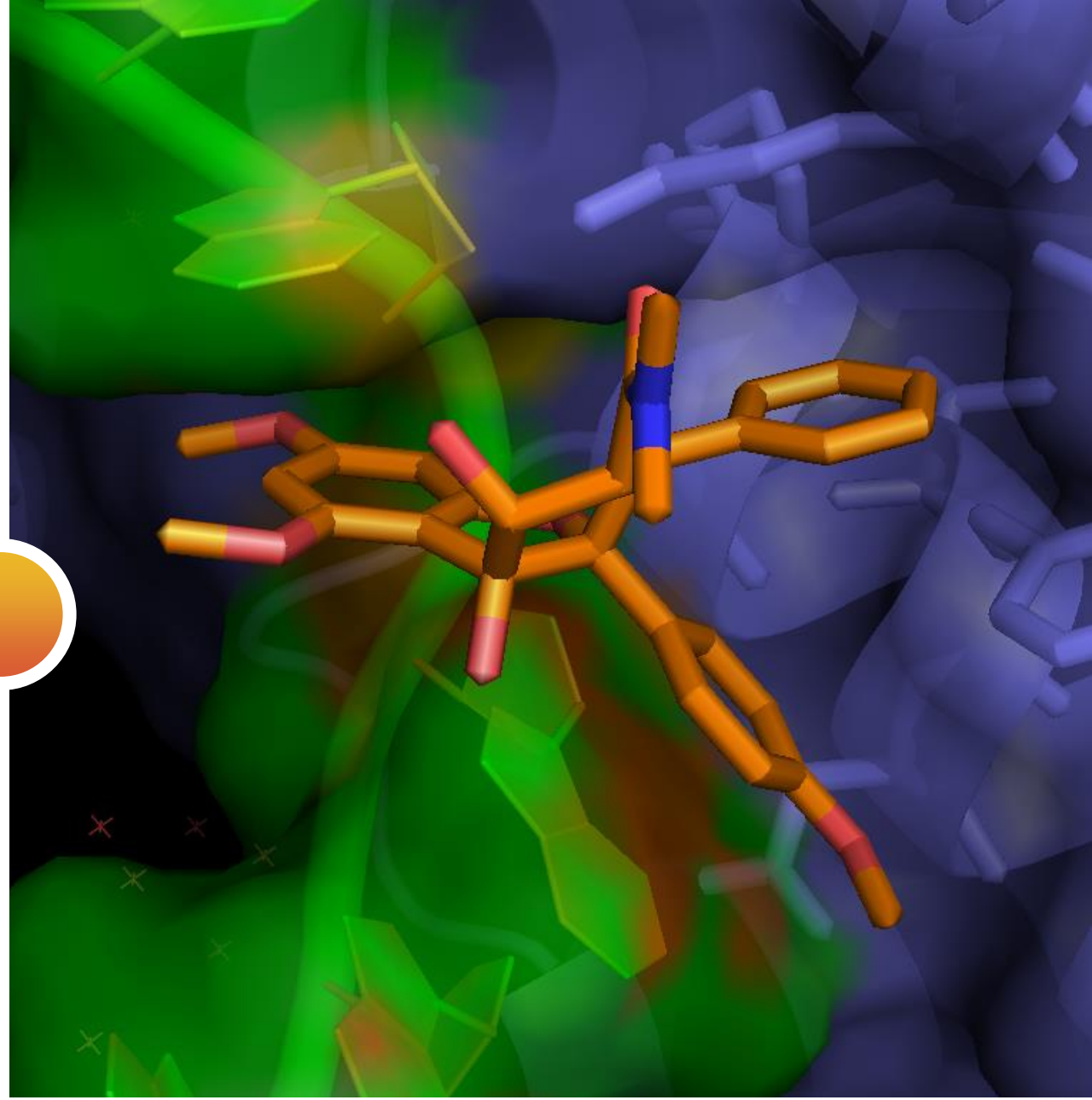
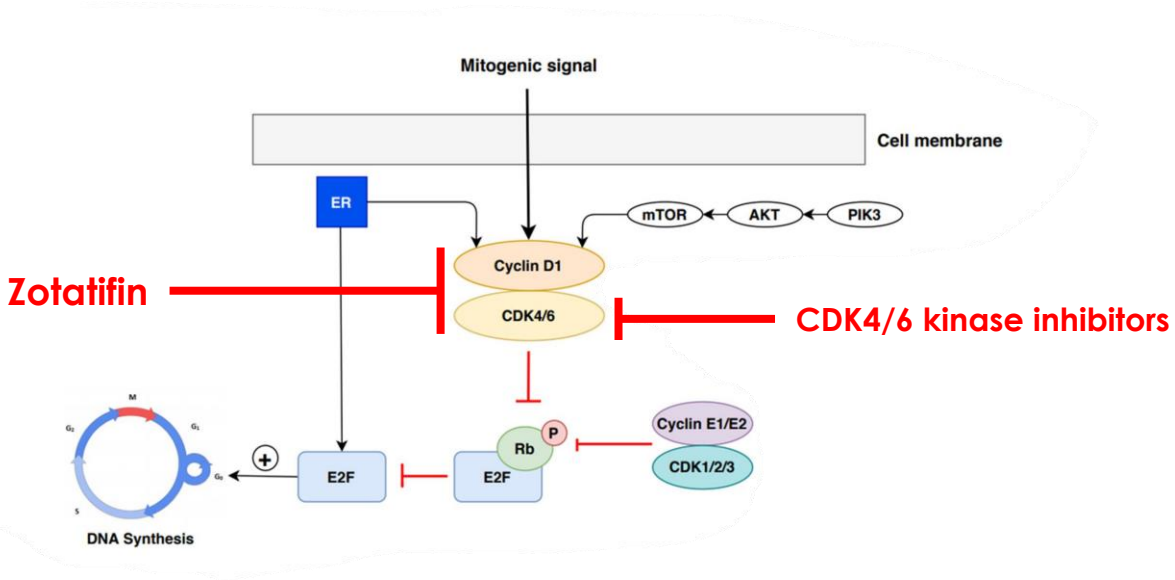
Doug Warner, M.D.

eFFECTOR CMO

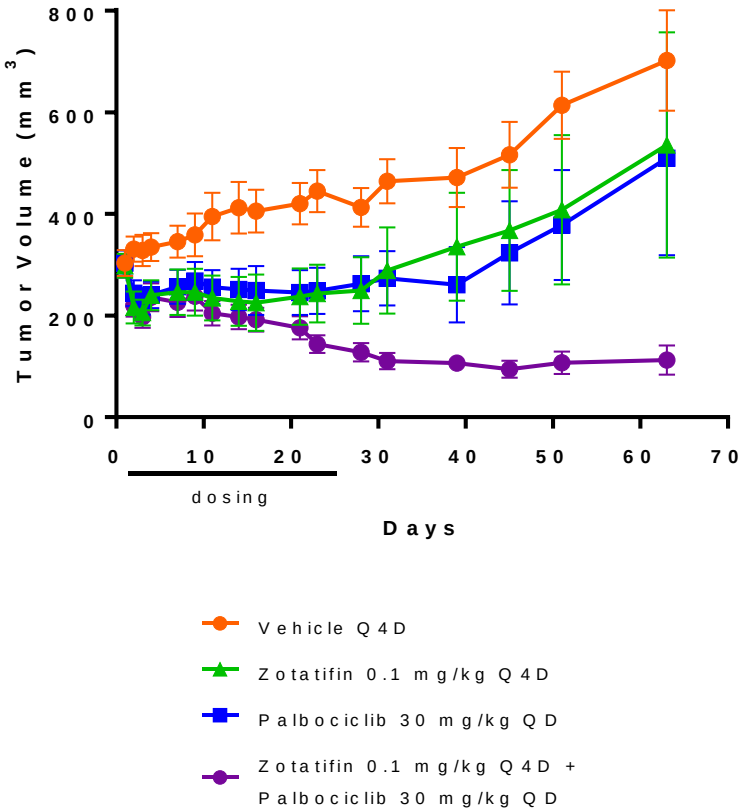


Zotatifin Downregulation of Cyclin D1 and CDK4/6 Designed To Complement CDK4/6 Inhibitors That Target Kinase Subunit

Zotatifin downregulated both Cyclin D1 and CDK 4/6 subunits In contrast to kinase inhibitors



Zotatifin was active in preclinical models of ER+ BC and showed strong combination benefit with palbociclib



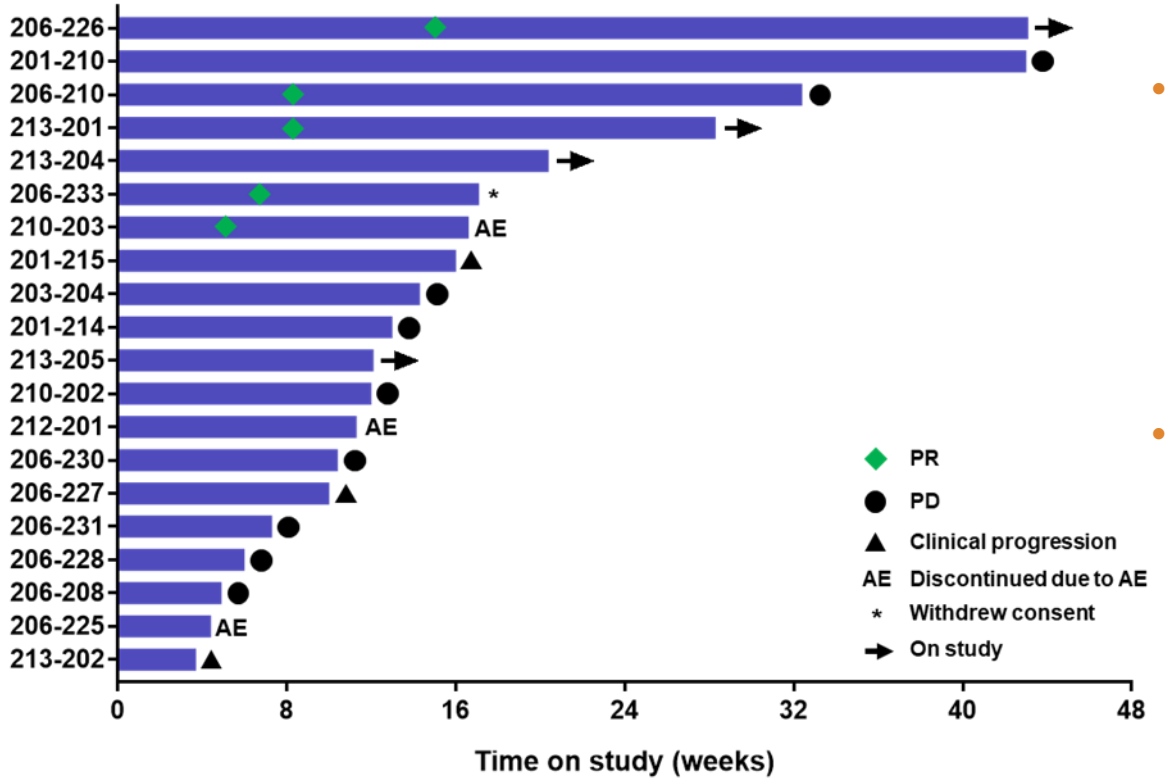
Zotatifin + Fulvestrant + Abemaciclib (ZFA) Triplet Expansion Cohort Trial Description

- Phase 2a expansion cohort in ER+ BC in a Simon 2-stage design
- Key eligibility criteria
  - Metastatic disease or locoregionally recurrent ER+ breast cancer
  - Minimum of one prior line of therapy for advanced/metastatic disease
  - Recurrence or progression on at least one line of endocrine therapy in the advanced/metastatic disease setting
- Patients received zotatifin at 0.07 mg/kg on Days 1 and 8 of 21-day cycles combined with fulvestrant and abemaciclib
- Primary endpoint is objective response rate per RECIST v1.1

ZFA Triplet Expansion Cohort
Patient Characteristics and Prior Treatment

Characteristic	Total (N=20)
Median age, years (range)	57 (38-82)
ECOG PS, no. (%)	
0	10 (50)
1	10 (50)
Visceral metastases, no. (%)	15 (75)
Median no. prior regimens for MBC (range)	4 (1-11)
≥ 2 prior ET for metastatic disease, no. (%)	12 (60)
Type of prior therapy for MBC, no. (%)	
CDK 4/6 inhibitor	19 (95)
Fulvestrant	13 (65)
Chemotherapy	15 (75)
≥ 2 prior chemo regimens for MBC	10 (50)

ZFA Triplet Expansion Cohort Swimmers Plot

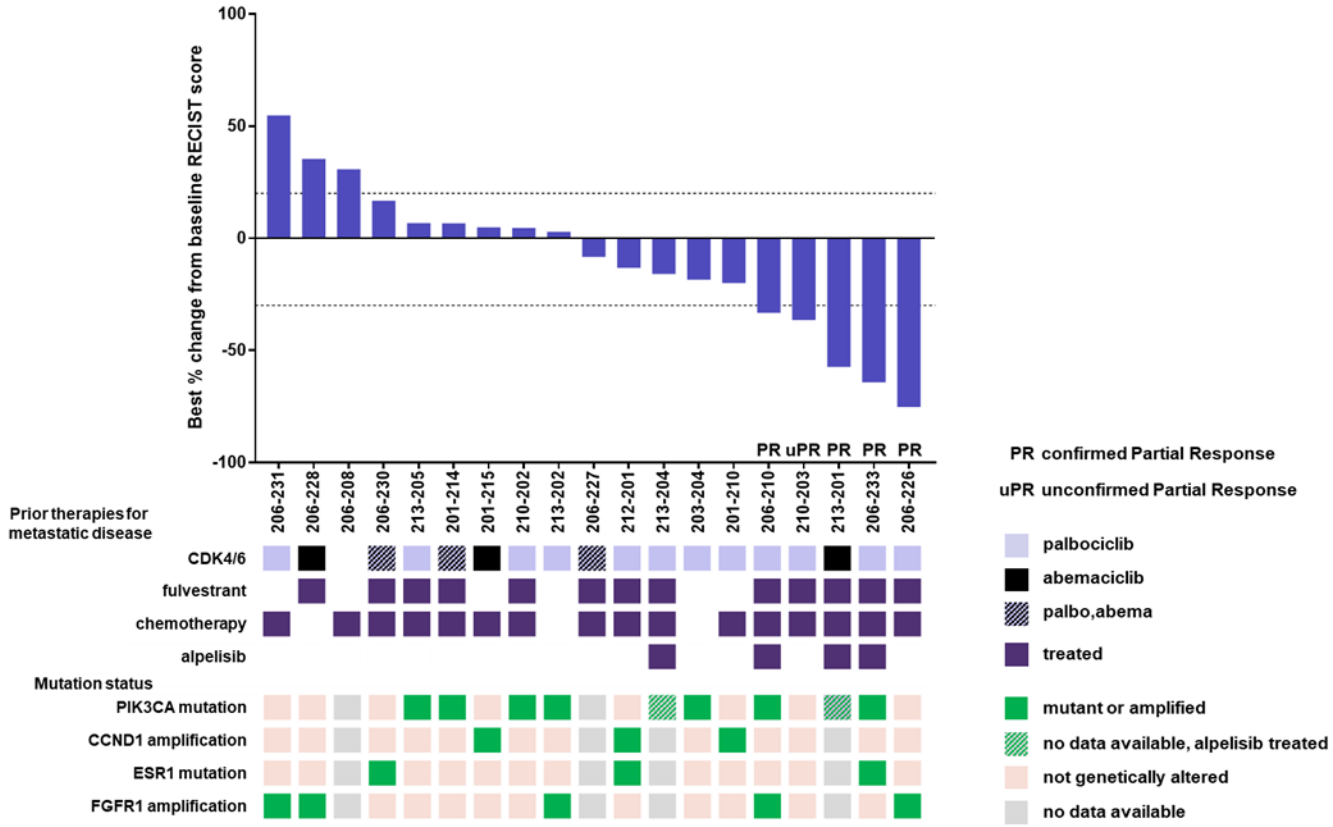


- 5 of 19 (26%) RECIST-evaluable patients experienced a PR
  - 4 confirmed PRs
  - 1 unconfirmed PR, patient discontinued due to AE before confirmatory scan
  - All patients with PRs had previously progressed on prior CDK4/6 and fulvestrant treatments
- Data continues to mature
  - 4 patients remained on treatment
  - Longest duration of treatment ~43 weeks

Interim Data as of 5/03/2023 Cut-Off

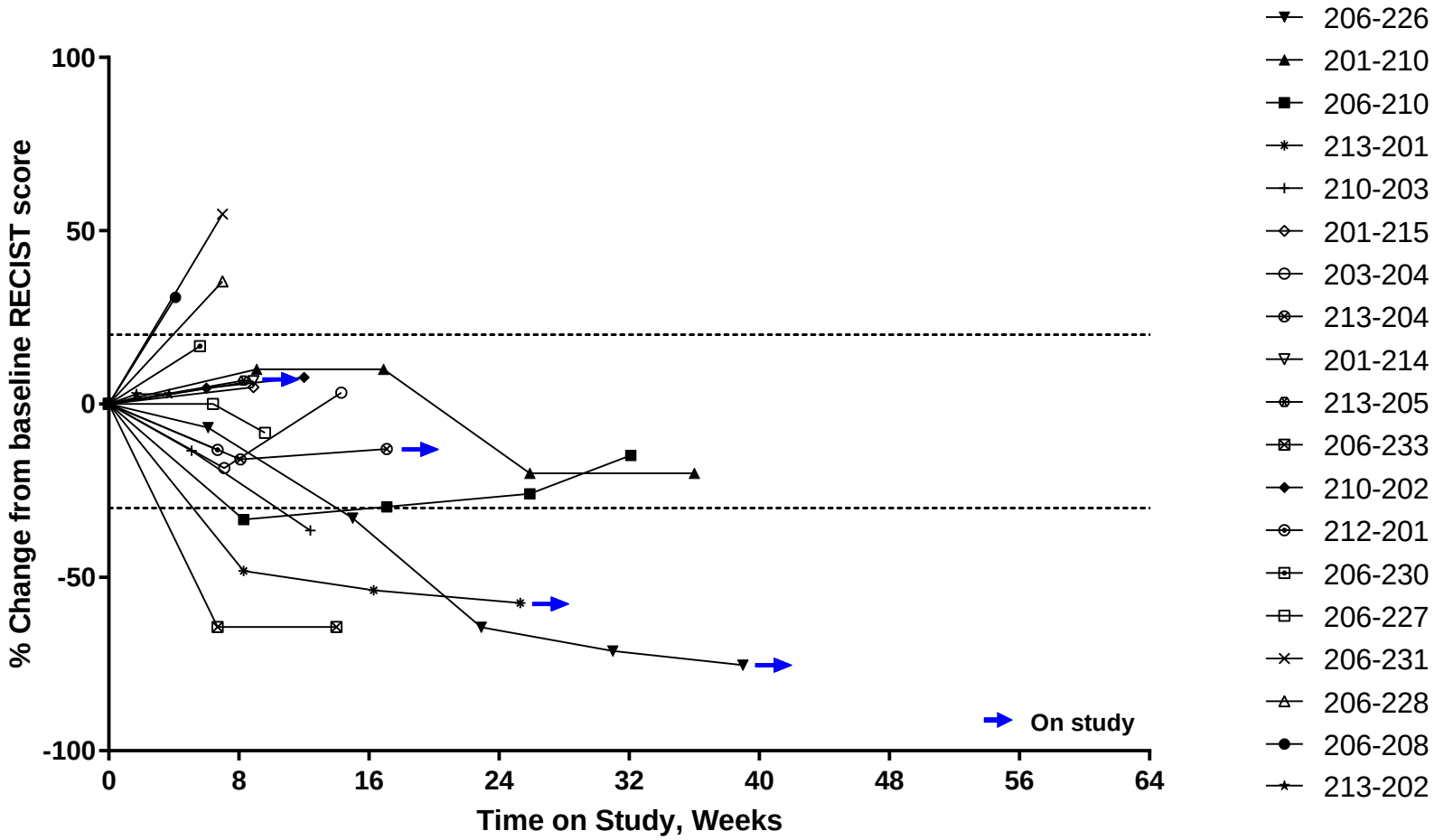
ZFA Triplet Expansion Cohort Waterfall Plot

Confirmed PRs seen in patients with and without mutations in PIK3CA or ESR1



Interim Data as of 5/03/2023 Cut-Off

ZFA Triplet Spider Plot
RECIST-Evaluable Patients (n=19)



Individual Vignettes for Patients with Confirmed PRs

- 206-226
  - $FGFR^{amp}$, ctDNA showed ESR1 rearrangement
  - 3 prior lines in metastatic setting, including palbociclib, fulvestrant, chemo
  - Ongoing confirmed PR, DoR ≥ 28 weeks
- 213-201
  - Her2 2+ by IHC, ctDNA showed $ESR1^{mut}$, $PIK3CA^{mut}$, $ERBB2^{mut}$
  - 4 prior lines in metastatic setting, including chemo, alpelisib, abemaciclib and fulvestrant immediately prior to study entry
  - Ongoing confirmed PR, DoR ≥ 20 weeks
- 206-210
  - $PIK3CA^{mut}$, ctDNA not available
  - 3 prior lines in metastatic setting, including palbociclib, fulvestrant, oral SERD, alpelisib, chemo
  - Confirmed PR, DoR of 24 weeks
- 206-233
  - $PIK3CA^{mut}$, also observed in ctDNA
  - 5 prior lines in metastatic setting, including palbociclib, fulvestrant, alpelisib, chemo
  - Confirmed PR, DoR of 7 weeks prior to withdrawing consent

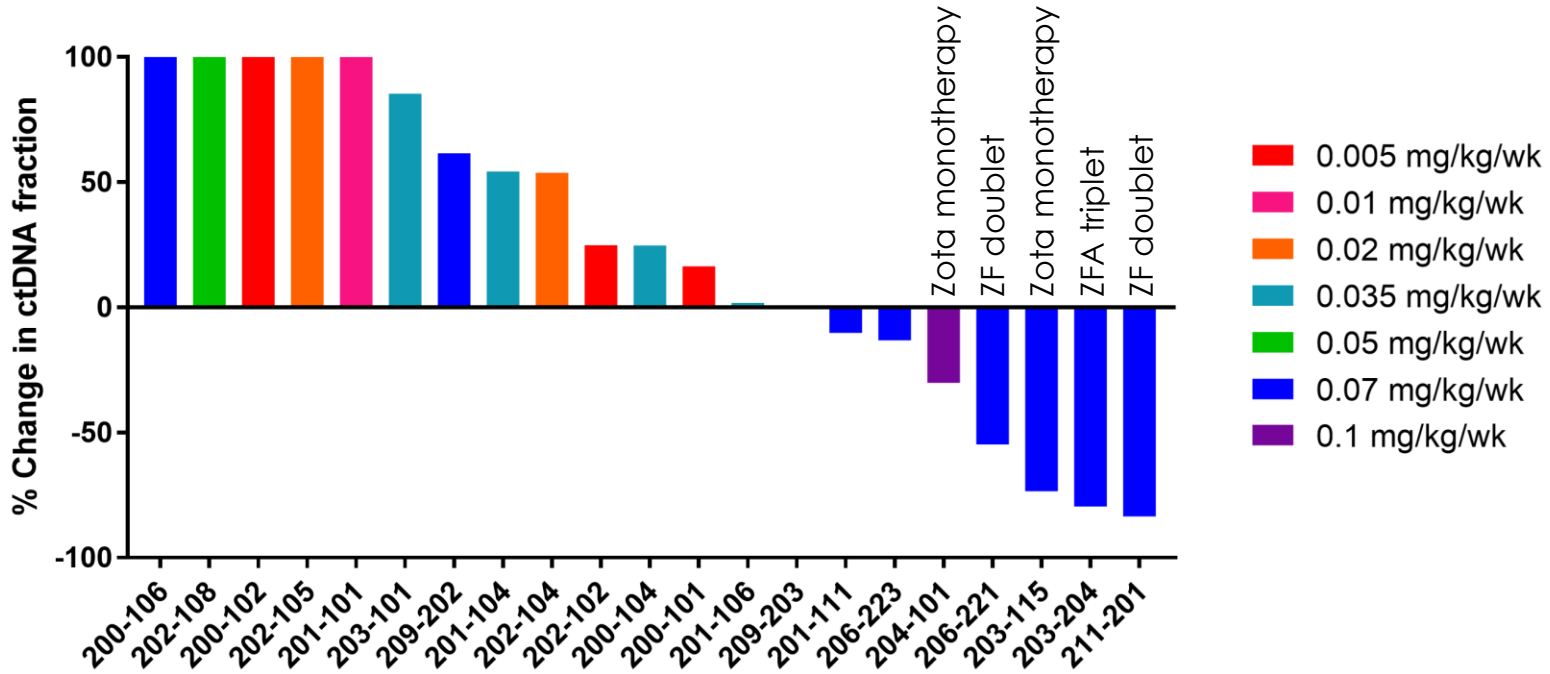
ZFA triplet: Summary of Treatment-Emergent Adverse Events

TEAE Preferred Term, N=20	TEAEs (All Grades) N (%)	Grade 3 or Higher N (%)
Diarrhea	16 (80%)	3 (15%)
Nausea	15 (75%)	0 (%)
Vomiting	11 (55%)	0 (%)
Fatigue	11 (55%)	0 (%)
Dysgeusia	8 (40%)	0 (%)
Dry mouth	7 (35%)	0 (%)
Abdominal pain	6 (30%)	0 (%)
Anemia	6 (30%)	0 (%)
Dyspnea	6 (30%)	2 (10%)
Peripheral neuropathy	6 (30%)	0 (%)
Epistaxis	5 (25%)	0 (%)
Dehydration	4 (20%)	0 (%)
Muscle spasms	4 (20%)	0 (%)
Back pain	4 (20%)	0 (%)
Constipation	3 (15%)	0 (%)
Platelet count decreased	3 (15%)	1 (5%)
Blood creatine phosphokinase increased	3 (15%)	1 (5%)
Gastroesophageal reflux disease	3 (15%)	0 (%)
Pruritus	3 (15%)	0 (%)
Myalgia	3 (15%)	0 (%)

Treatment-emergent adverse events (TEAEs) are defined as AEs that start during or after initiating study therapy, or AEs with an onset prior to initiating study therapy that worsen after study therapy initiation. TEAEs >10% Incidence are reported by Preferred Term. Percentage is calculated using the number of treated subjects as the denominator. Preliminary results with data cutoff of May 3, 2023

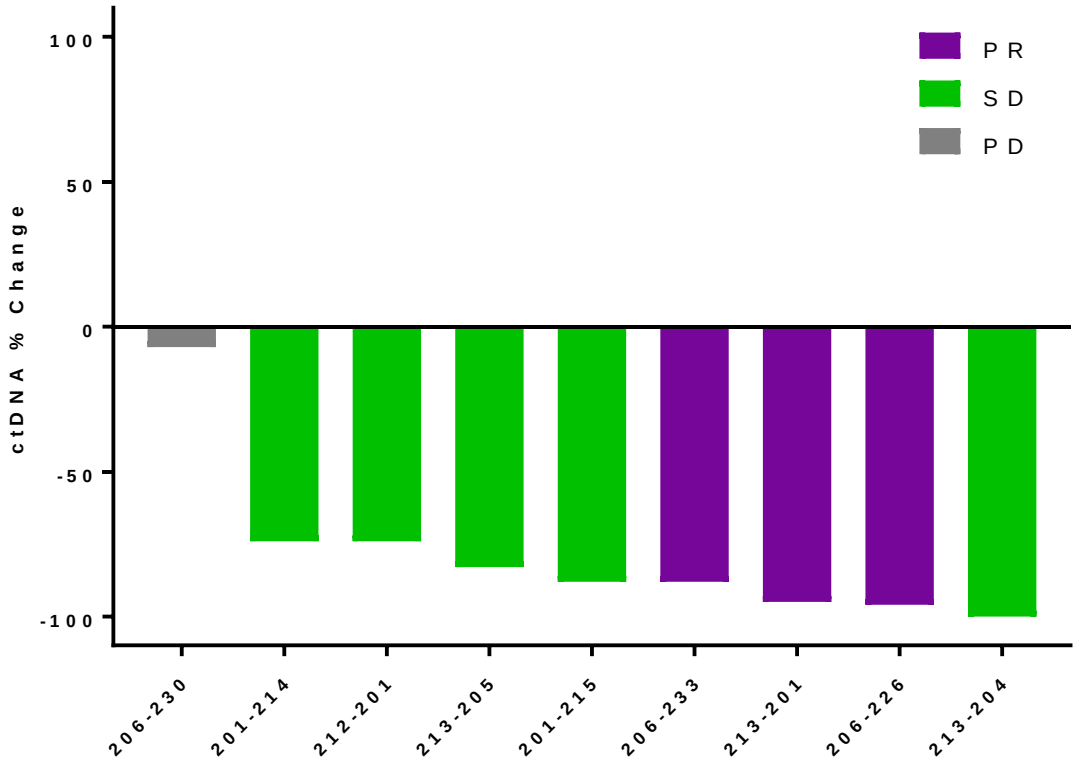
eIF4A Target Engagement was Assessed by Changes in Fraction of Circulating Tumor DNA (ctDNA)

Decreases in ctDNA fraction were seen once dose escalation reached 0.07 mg/kg and higher



Fraction of ctDNA relative to total DNA was measured at baseline and after treatment with zotatifin. % change in ctDNA fraction after treatment relative to baseline is plotted for all patients with available data from dose escalation and early expansion cohort. Preliminary results with a data cutoff of December 15, 2022

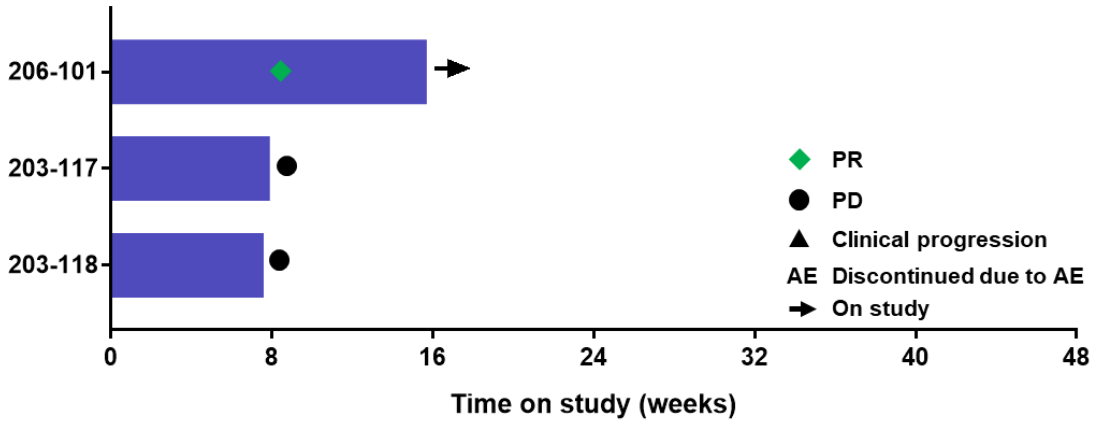
Majority of Assessable Patients Treated in ZFA Triplet Expansion Cohort Had ctDNA Decreases >50%

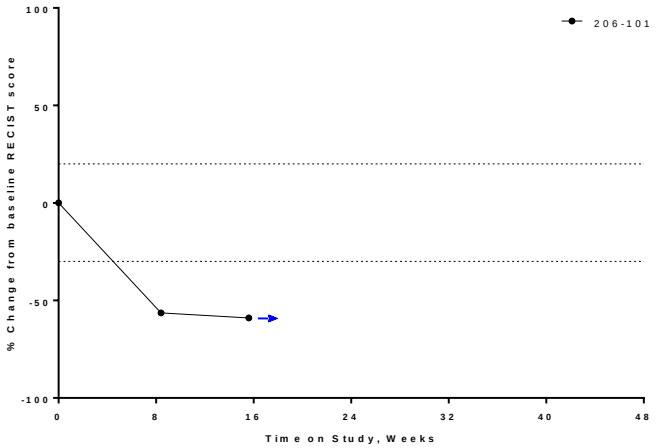


- All patients received zotatifin 0.07 mg/kg on Days 1 and 8 of a 21-day cycle
- Decreases in ctDNA correlated with PR and SD RECIST outcomes
- Mutant alleles that were reduced or eliminated are consistent with sensitivity to zotatifin mechanism, including known activating mutations in
  - ESR1
  - PIK3CA
  - ERBB2

Resumed Dose Escalation with Zotatifin + Fulvestrant (ZF) Doublet

- Based on favorable safety and tolerability results to date, and data that showed 0.07 mg/kg was the first dose from prior escalation cohort that demonstrated decreased ctDNA, we resumed dose escalation
- Utilizing every other week (Q2W) and weekly (QW) schedules for zotatifin
- 0.1 mg/kg zotatifin Q2W was first cohort to fully enroll
  - Confirmed PR observed in 1 of 3 patients at this dose and schedule



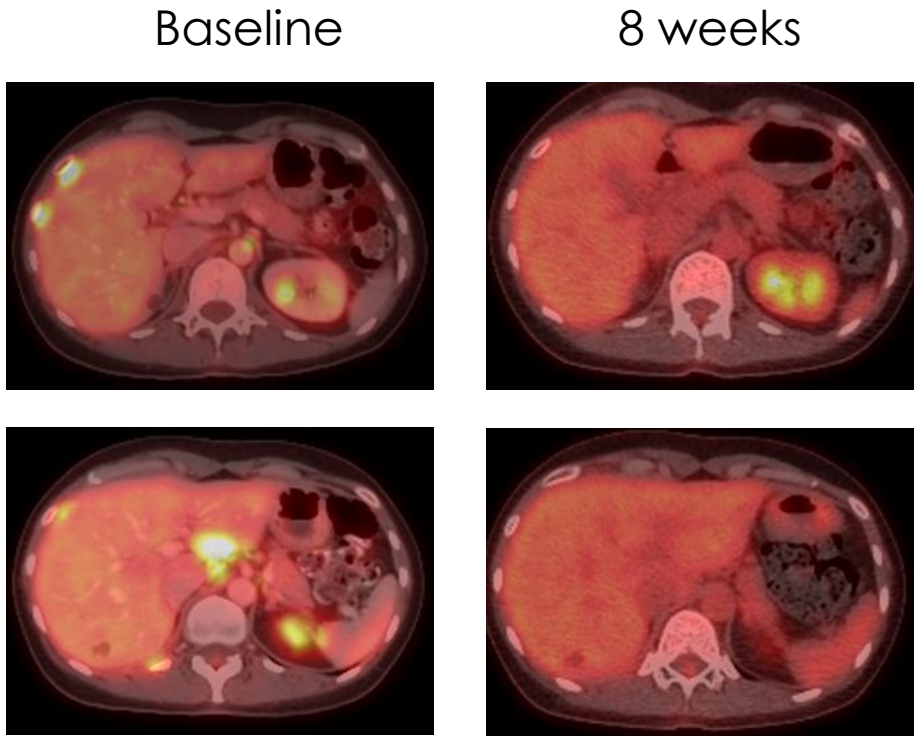


Data as of 5/03/2023 except confirmatory scan for patient 206-101

Early Response in ZF Dose Escalation at 0.1 mg/kg Q2W Patient 206-101

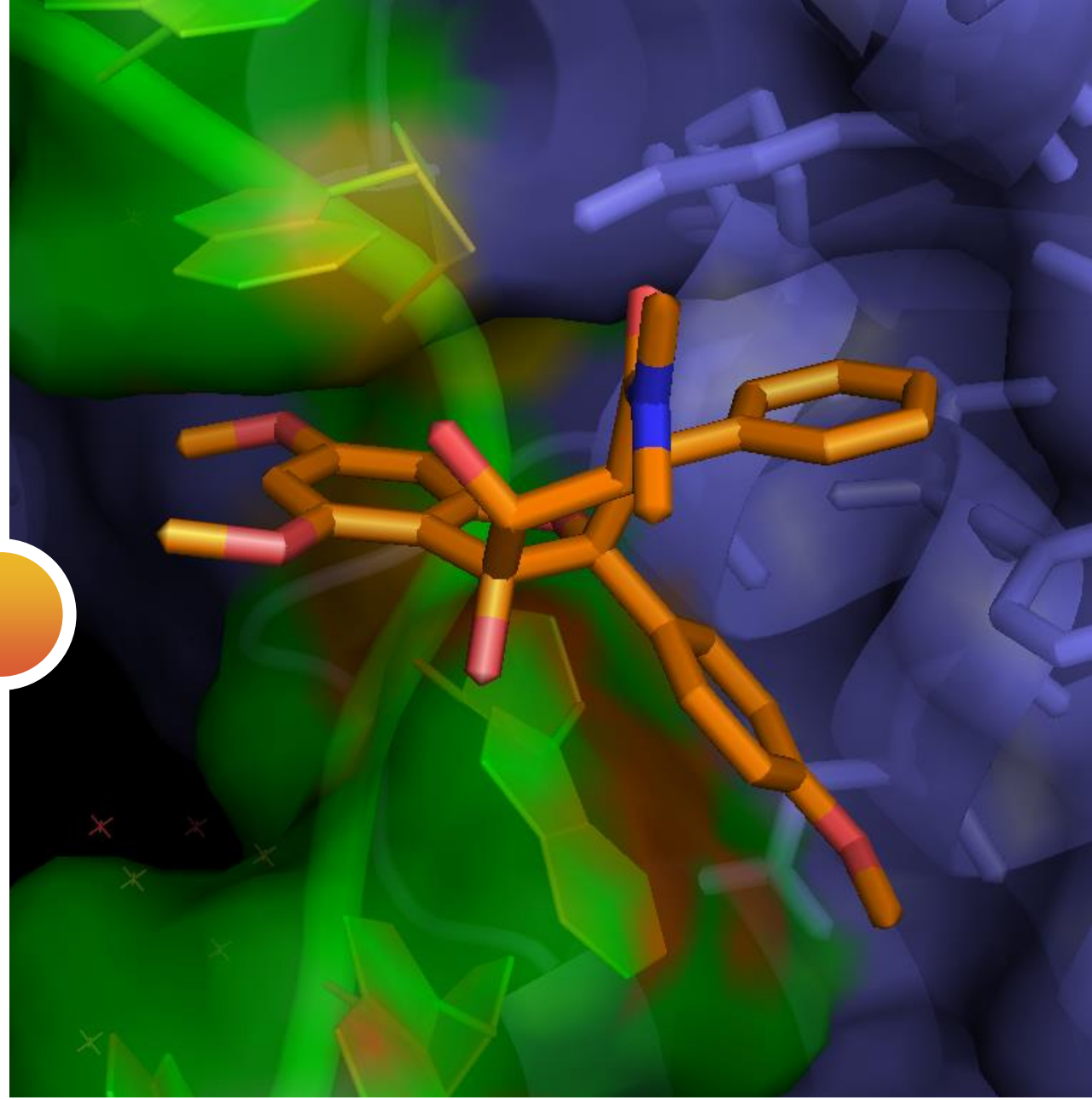
- BRCA2^{mut}
- Elimination of detectable ctDNA at Day 32
  - ESR1^{mut}, ERBB2^{mut}, BRCA2 reversions
- Achieved a PR on first scan which was confirmed on second scan
  - 56% reduction in RECIST score on first scan
  - Such a rapid, deep regression is uncharacteristic of fulvestrant
- 4 lines of prior treatment for mBC
  - palbociclib + anastrozole
  - trastuzumab deruxtecan
  - abemaciclib + anastrozole
  - olaparib
- Progressive disease was best response to four prior therapies

PET SCAN



Steve Worland, Ph.D.

eFFECTOR President and CEO

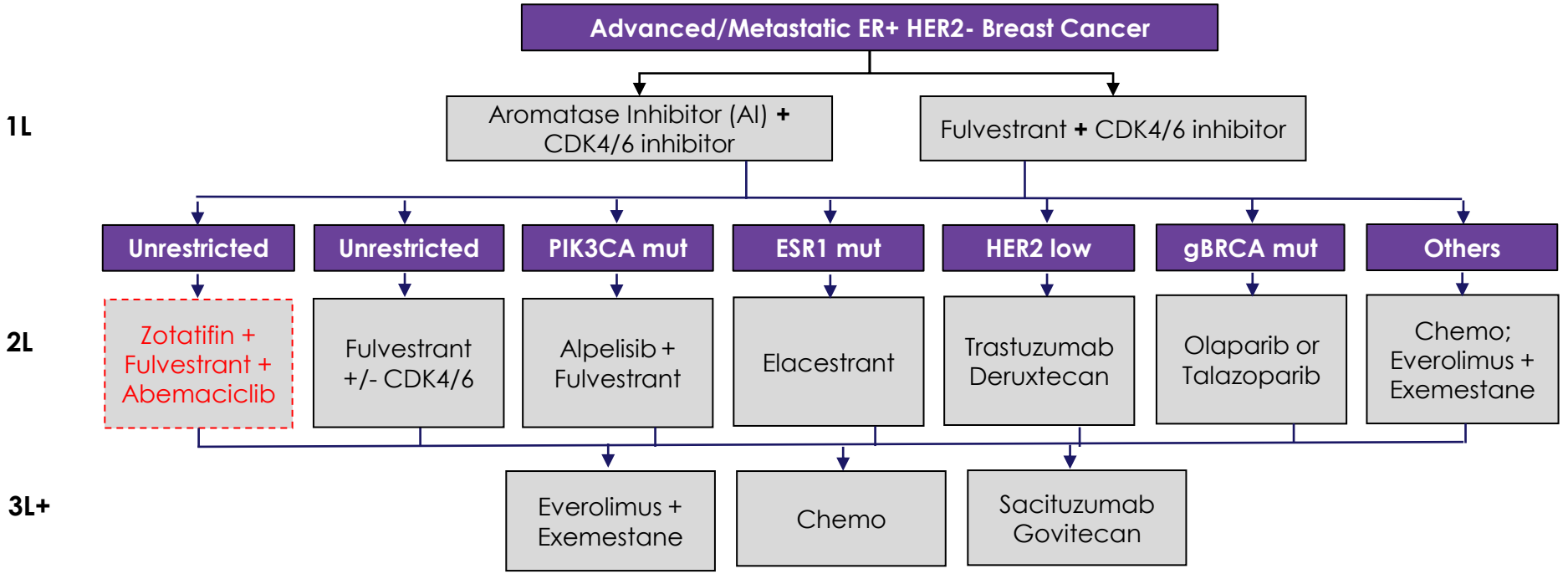


Zotatifin Product Development Strategy in ER+ Breast Cancer

- **2nd line plus opportunity** after progression on 1st line CDK4/6 + endocrine therapy
  - ZFA triplet therapy intended to capitalize on mechanistic synergy with CDK4/6i
  - Clinical activity of triplet already observed in ZFA expansion cohort
  - Current options for these patients include another endocrine therapy or chemotherapy, with limited benefit in most cases

- Development activities in next ~18 months intended to optimize dose/schedule prior to potential initiation of one or more **registration trials in early 2025**
  - Potential registration trial design: **ZFA triplet *vs* FA+placebo**

Zotatifin's Initial Positioning in HR+, HER2- mBC with Potential to Treat Majority of 2L+ ER+ BC



HR+/HER2- Metastatic Breast Cancer (mBC) Is a Large, Growing Market

- HR+/HER2- is the largest segment of BC, making up 65-70% of all patients (~200K annual incidence in the US)
- 1L mBC represents ~50K new patients annually in the US, with a majority of patients treated with CDK4/6i combinations (2-2.5yr PFS)
  - 2022A sales of ~$8.8B (+13% y/y) for CDK4/6 class propelled by a large treatable population and long duration of treatment
- 1L mBC patients eventually progress, and significant proportion of patients cycle through multiple lines of treatments and combinations thereafter (2-10mos PFS)
- New therapeutic options (ADCs, AKTi/PI3Ki, oral SERDs) will further expand the market opportunity

Company estimates of sales potential based on analyst reports and reported annual sales of approved agents

Multiple Upcoming Clinical Milestones

Anticipated Milestones		2023		2024
		1H	2H	
Tomivosertib	Top line data from P2b NSCLC frontline with pembro		●	
	Initiate P3 in NSCLC			●
Zotatifin Oncology	Initial ORR data from fully enrolled ZFA expansion cohort	✓		
	Data from ZF dose escalation cohorts		●	
	Complete activities to enable registration trial(s)			●

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