Next Generation Targeted Therapy for Cancer

Corporate Presentation | May 2024

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eFFECTOR

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This presentation contains forward-looking statements. All statements other than statements of historical facts contained in this presentation, including statements regarding the future clinical development of eFFECTOR Therapeutics, Inc.'s (eFFECTOR or the Company) product candidates, including expectations on enrollment and the timing of reporting data from ongoing clinical trials; the planned expanded development of zotatifin and tomivosertib, and the timing thereof; and the potential therapeutic benefits of such product candidates are forward-looking statements. In some cases, you can identify forward-looking statements by such terms as "may", "believe", "anticipate", "could", "should", "estimate", "expect", "intend", "plan", "project", "will", "forecast" and similar terms. These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including, but not limited to the risk that interim results of a clinical trial are not necessarily indicative of final results and one or more of the clinical outcomes may materially change as patient enrollment continues, following more comprehensive reviews of the data and more patient data become available; potential delays in the commencement, enrollment and completion of clinical trials; our dependence on third parties in connection with product manufacturing, research and preclinical and clinical testing; the results of preclinical studies and early clinical trials are not necessarily predictive of future results; the success of our clinical trials and preclinical studies for our product candidates is uncertain; our operations, stock price and ability to raise capital may be adversely affected by unstable market and economic conditions, financial institution instability, inflationary pressures, epidemic diseases and geopolitical events; we may use our capital resources sooner than expected and they may be insufficient to allow clinical trial readouts; unexpected adverse side effects or inadequate efficacy of our product candidates that may limit their development, regulatory approval and/or commercialization, or may result in recalls or product liability claims; our ability to obtain and maintain intellectual property protection for our product candidates; our failure to meeting the continued listing requirements of the Nasdaq Capital Market could result in a delisting of our securities; and other risks described in the Company's prior press releases and filings with the Securities and Exchange Commission (SEC), including under the heading "Risk Factors" in the Company's annual report on Form 10-K and any subsequent filings with the SEC. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond the Company's control, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in these forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements in this presentation, which speak only as of the date made. Except as required by applicable law, the Company does not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise. All forward-looking statements are qualified in their entirety by this cautionary statement, which is made under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995.

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This presentation concerns product candidates that are under clinical investigation and which have not yet been approved for marketing by the U.S. Food and Drug Administration (FDA). They are currently limited by Federal law to investigational use, and no representation is made as to their safety or effectiveness for the purposes for which they are being investigated.

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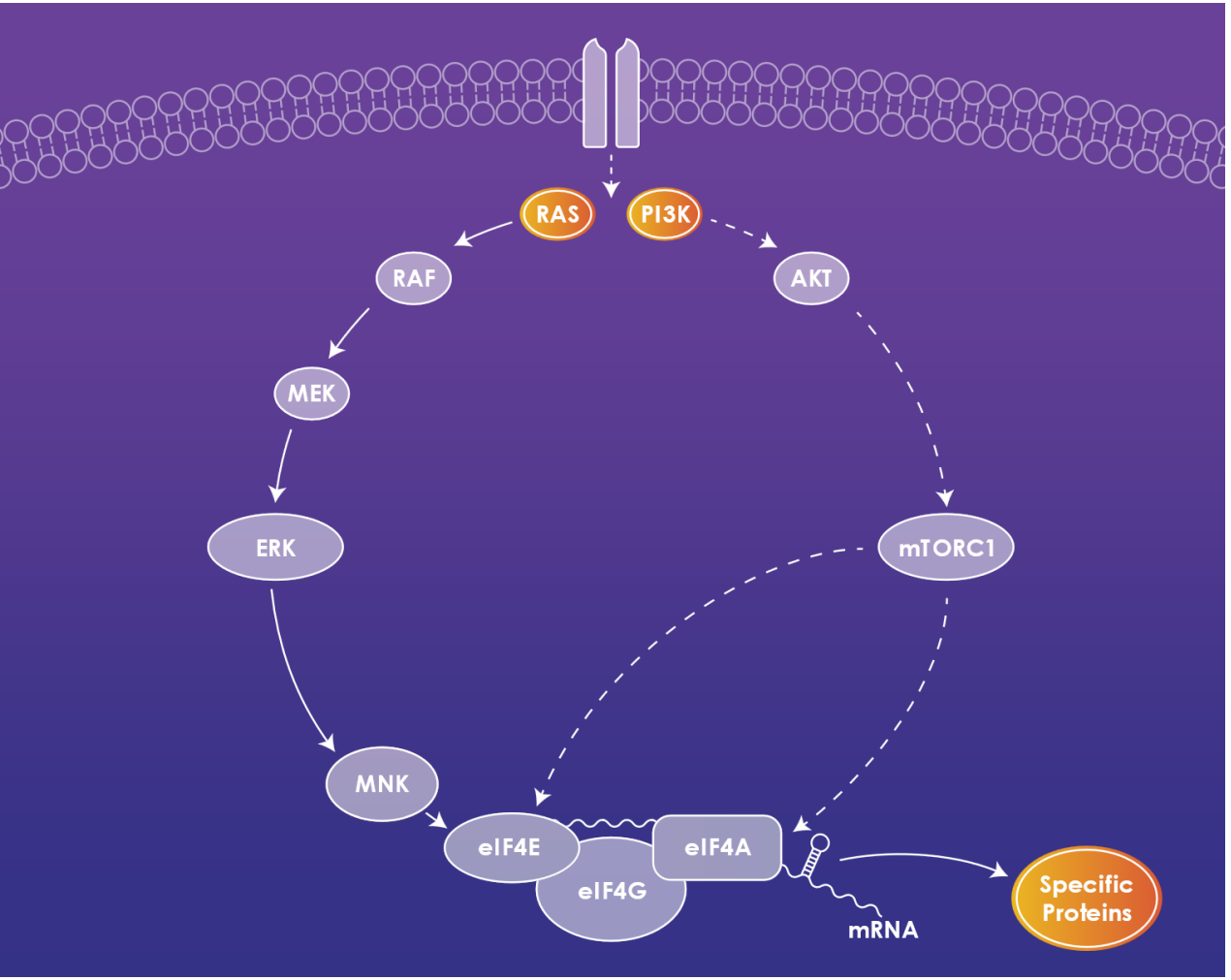
Company Overview

- Novel therapeutic strategy designed to **block overproduction of specific oncoproteins** driven by RAS and PI3K signaling
  - Next-generation targeted approach designed to treat tumors not well addressed by drugs that inhibit a single oncogene
  - Underlying technology licensed from UCSF, labs of Drs. Kevan Shokat and Davide Ruggero
- **Two wholly owned novel clinical assets**
  - Zotatifin: eIF4A inhibitor focused on **ER+ BC** with positive data presented in 2023 at ASCO and SABCS; **finalization of RP2D anticipated in second half of 2024 to enable late-stage development**
  - Tomivosertib: MNK inhibitor in an investigator-initiated Phase 1 dose escalation trial evaluating tomivosertib in patients with **relapsed/refractory Acute Myeloid Leukemia (AML)**
- Validating **partnership with Pfizer**
  - $507M* partnership on third product candidate, targeting eIF4E
  - Retained option to co-promote and profit share in U.S.
- Cash runway into **Q1 2025**

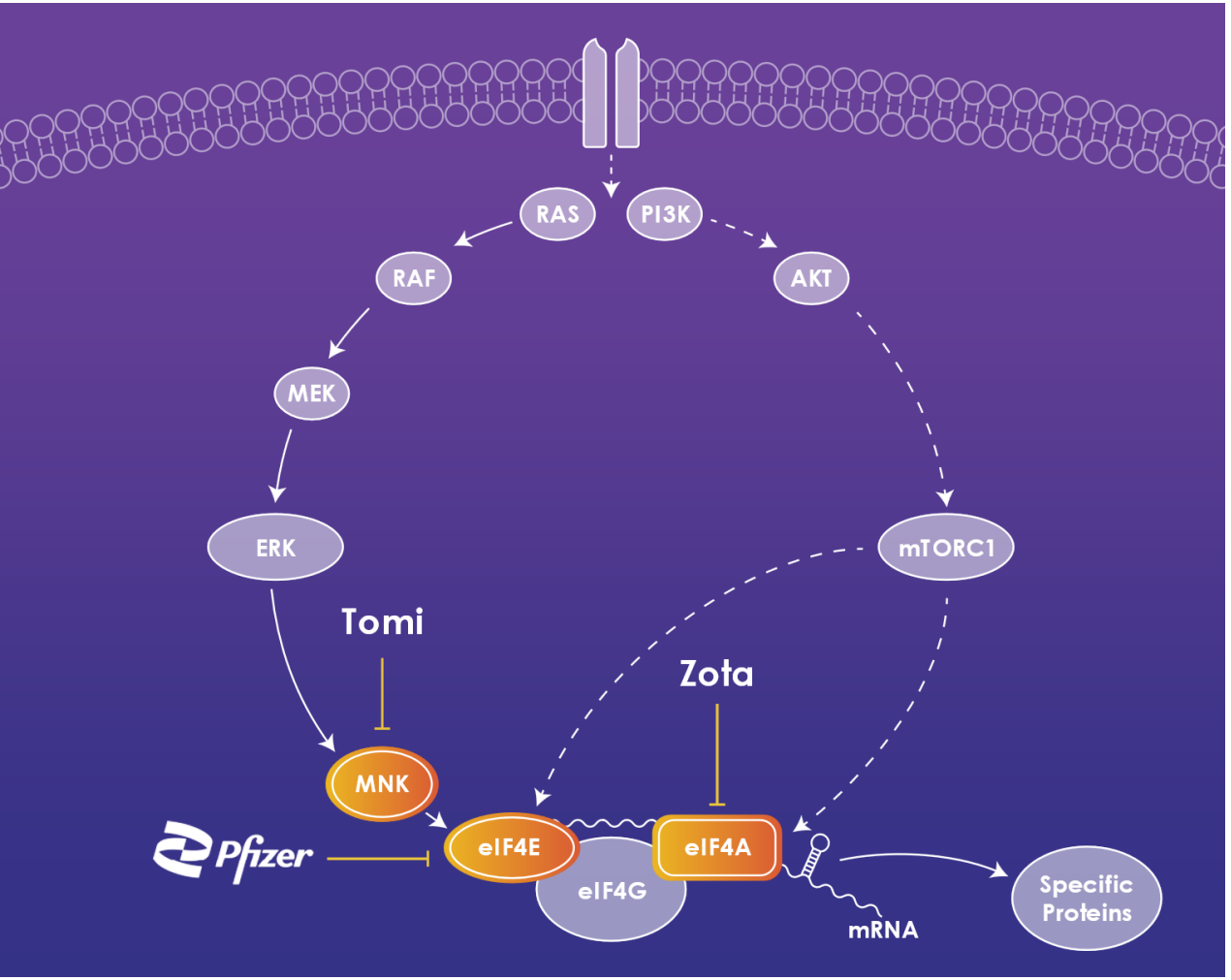
*Consists of $42 million received to date and potential to receive up to an additional $465 million in milestone payments. eFFECTOR is also eligible for potential royalties on sales.

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



- Oncogenic signaling pathways, including **RAS** and **PI3K**, activate mRNA translation to drive production of **specific proteins**
- Tumors depend on **overproduction** of specific proteins for growth, avoidance of apoptosis, and immune evasion
- eFFECTOR is taking the novel approach to block protein overproduction, a key **effector function** downstream of oncogenic signaling
- Potential **benefits** to targeting overproduction
  - Certain tumors are **acutely dependent** on ongoing overproduction of specific proteins
  - 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:
  - **eIF4A:** helicase unwinds RNA secondary structures
  - **MNK:** kinase phosphorylates RNA-binding proteins
  - **eIF4E:** binds 5'-cap of mRNA
- Each target controls production of a distinct set of proteins
- eFFECTOR invented novel product candidates with strong intellectual property to address each of the three targets
- STRI platform enabled identification of overproduced proteins and tumor vulnerabilities associated with each product candidate

Robust Pipeline: Multiple STRIs in Development

Program (Target)	Discovery	Preclinical	Phase 1	Phase 2a	Phase 2b	Phase 3	Global Rights	Anticipated Milestones
Zotatifin (eIF4Ai)	Solid Tumors ER+ BC and KRAS NSCLC						eFFECTOR	H2 2024 RP2D for ZFA Triplet
External Collaborations								
eIF4Ei	Solid Tumors						Pfizer	$507M deal value with option to co-promote and profit share
Tomivosertib (MNKi)	Investigator-initiated trial at Northwestern in r/r AML						eFFECTOR	2024 Initial safety and tolerability data from dose-escalation
Zotatifin (eIF4Ai)	Investigator-initiated trial at Stanford in ER+ HER2- breast cancer in pre-operative setting						eFFECTOR	

Experienced Leadership Team

Steve Worland, PhD
Founder, President, CEO and Director

Doug Warner, MD, MBA
Chief Medical Officer

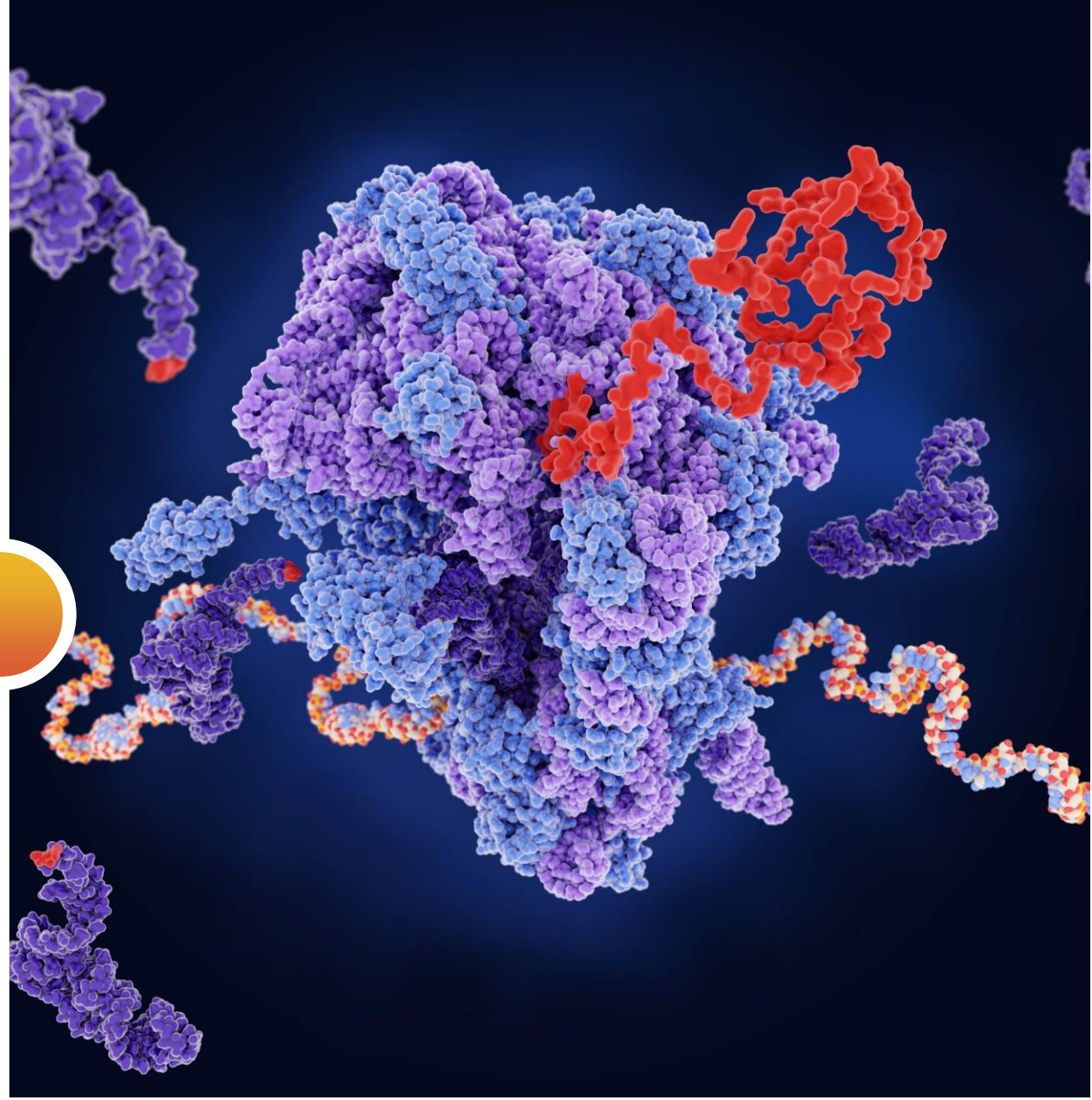
Mike Byrnes, MBA
Chief Financial Officer

Scientific Advisors	*Institution*	*Expertise*	*Clinical Advisors/ Key Investigators*	*Institution*	*Expertise*
Kevan Shokat, PhD	UCSF, EFTR Co-founder	Translation & KRAS	**Kapil Dhingra, MD**	Former Roche Oncology	Oncology Development
Davide Ruggero, PhD	UCSF, EFTR Co-founder	Translation	**Sarat Chandarlapaty, MD, PhD**	Memorial Sloan Kettering	Oncology Development
Jennifer Doudna, PhD	UC Berkeley	RNA, CRISPR Co-Inventor	**Funda Meric-Bernstam, MD**	MD Anderson	Oncology Development
Joan Brugge, PhD	Harvard	Oncogenic Signaling	**Ezra Rosen, MD, PhD**	Memorial Sloan Kettering	Oncology Development
Neal Rosen, MD, PhD	Memorial Sloan Kettering	Oncogenic Signaling	**Jennifer Caswell-Jin, MD**	Stanford Medicine	Oncology Development

Zotatifin

eIF4A Helicase Inhibitor

Designed to suppress a network of key cell cycle proteins and oncoproteins



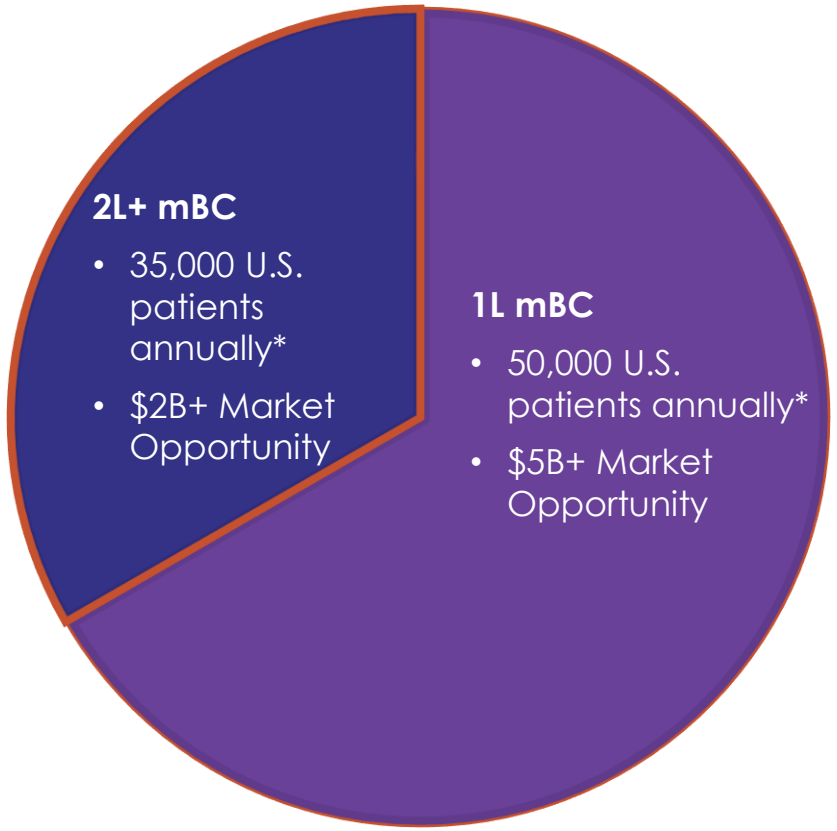
Executive Summary of Zotatifin Profile

- Zotatifin, a potentially 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
- **Promising efficacy results in ZFA triplet presented at ASCO 2023 and SABCS 2023**
  - 5 of 19 (**26%**) RECIST-evaluable patients had partial responses (PR)
    - 4 confirmed, 1 unconfirmed
  - Median progression-free survival (mPFS) of **7.4 months**
  - **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 favorable safety, tolerability and pharmacodynamic data at initial RP2D*, resumed dose escalation with more convenient schedule, dosing every other week (Q2W)

*Initial RP2D was 0.07 mg/kg dosed on Days 1 and 8 of 21-day cycle
Data presented as of November 17, 2023 cut-off

Potential Multi-Billion Dollar Indications

Zotatifin (ER+Breast Cancer)

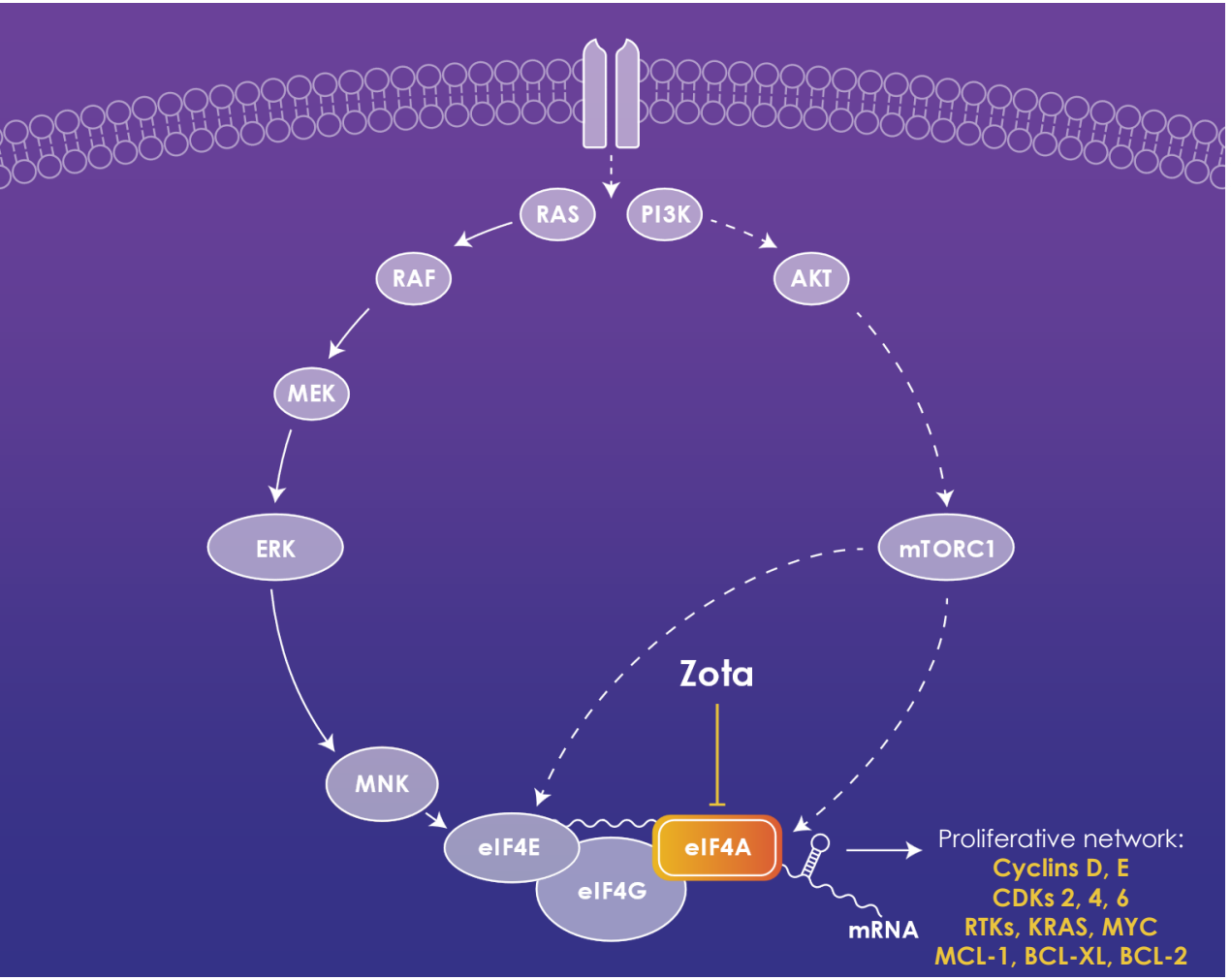


Key: Lead indication

mBC: Metastatic Breast Cancer

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

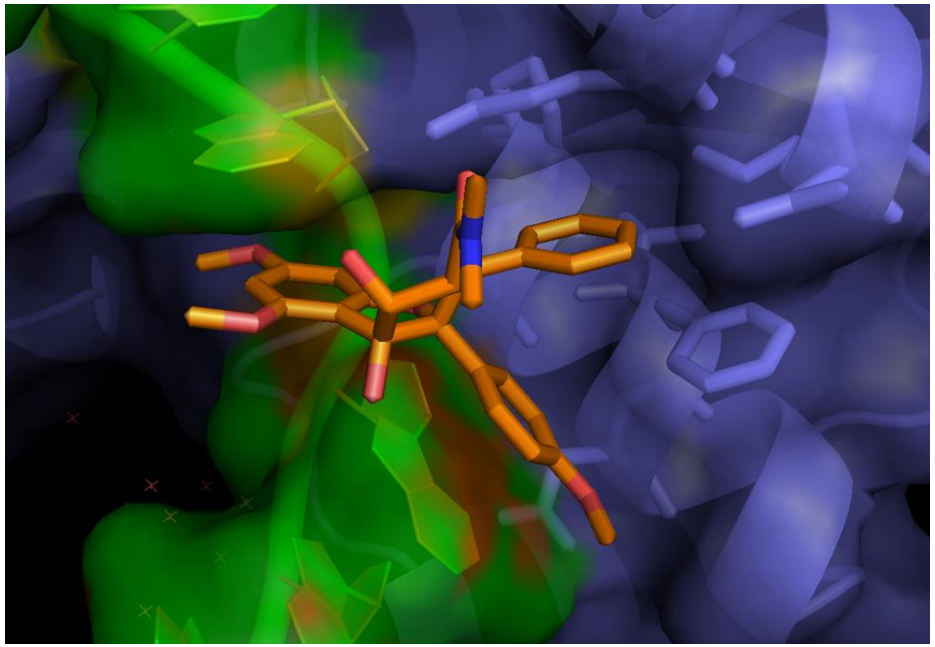
Zotatifin Designed to Suppress a Network of Important Tumor-Driving Proteins by Inhibiting eIF4A



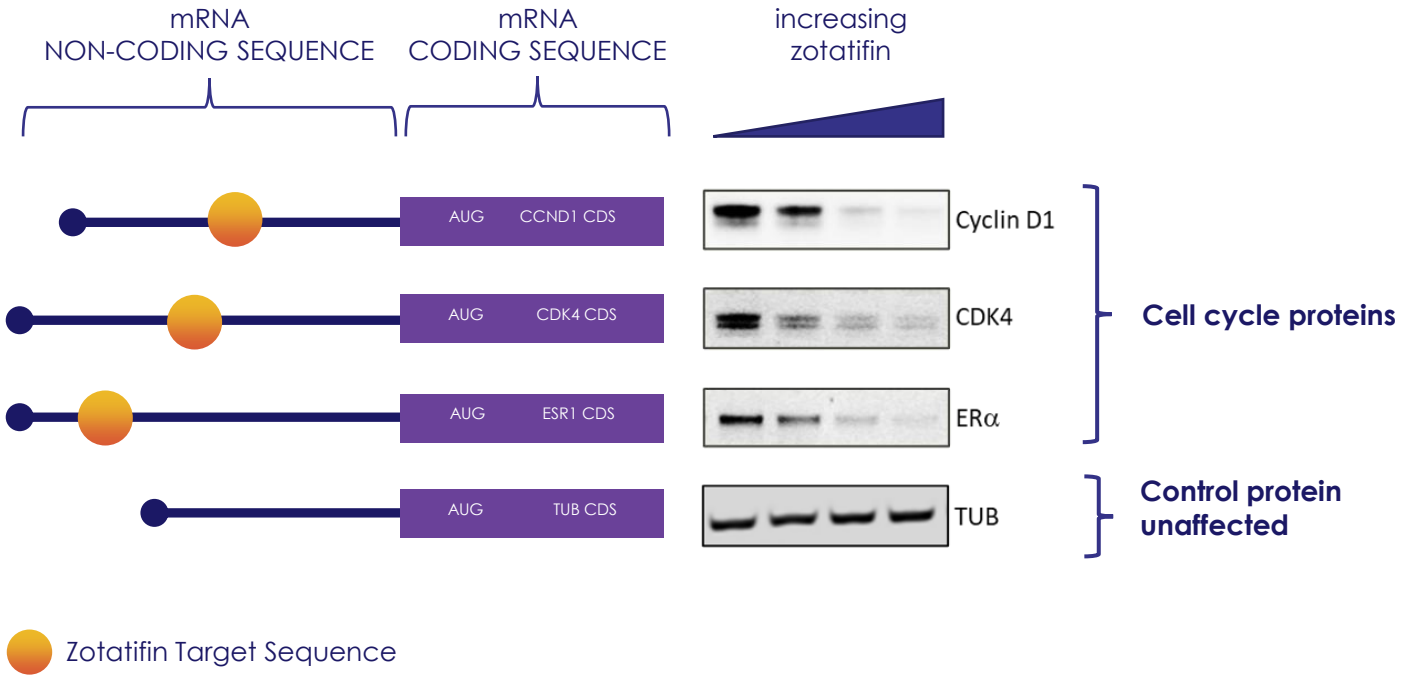
- Cancer signaling **activates eIF4A** to overproduce a network of tumor promoting proteins
- Zotatifin designed to **suppress the network** in a single product
- In preclinical studies, zotatifin downregulated a network of cell-cycle proteins and oncoproteins including:
  - **Cyclins D, E** and **CDKs 2, 4, 6**
  - Estrogen receptor (**ERa**)
  - **RTKs, KRAS** and **MYC**
  - **MCL-1, BCL-XL,** and **BCL-2**

Preclinical Regulation of Translation by Zotatifin Selectively Suppressed a Specific Set of Cancer Driving Proteins

Zotatifin selectively bound specific sequences found in the 5' non-coding region of mRNAs encoding certain cancer-driving proteins



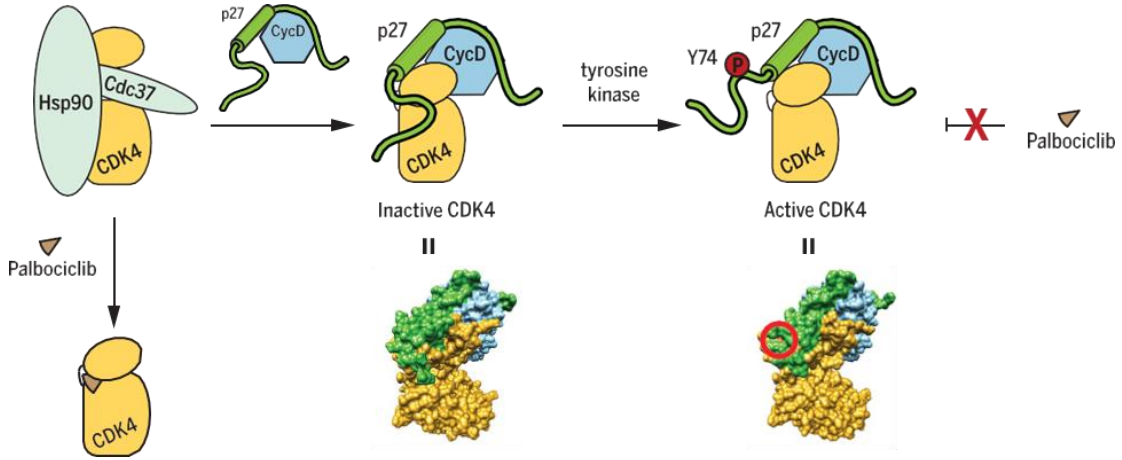
Experimental structure of natural product RocA bound to eIF4A and zotatifin RNA target sequence[1]



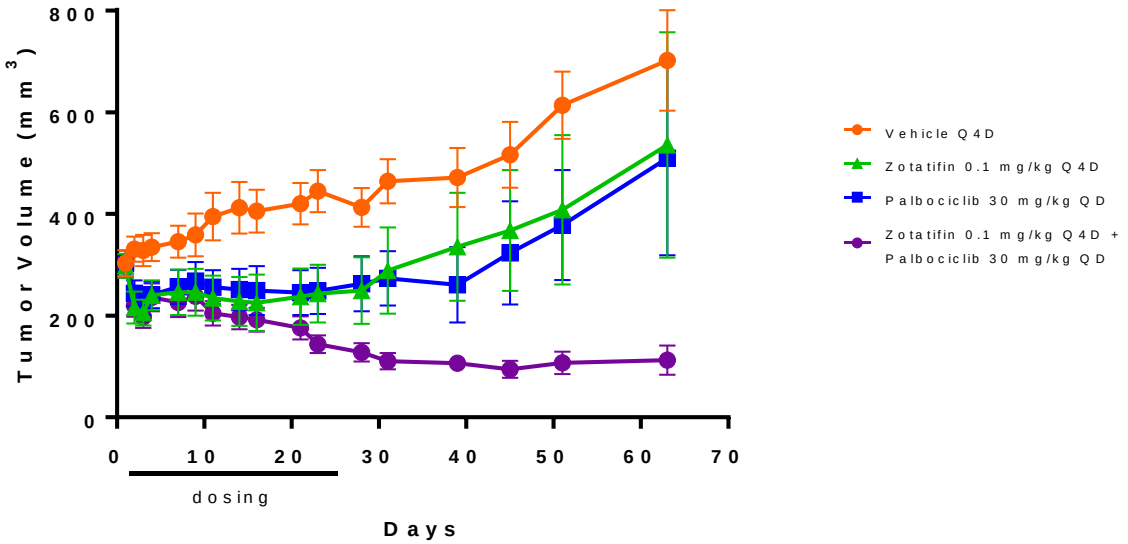
[1]Iwaski et al. 2019 Mol Cell (73) 738-748

Zotatifin Downregulation of Cyclin D1 and CDK4/6 Complements CDK4/6 Inhibitors That Target Kinase Subunit

Zotatifin downregulation of Cyclin D1 expected to inhibit formation of Active CDK4



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



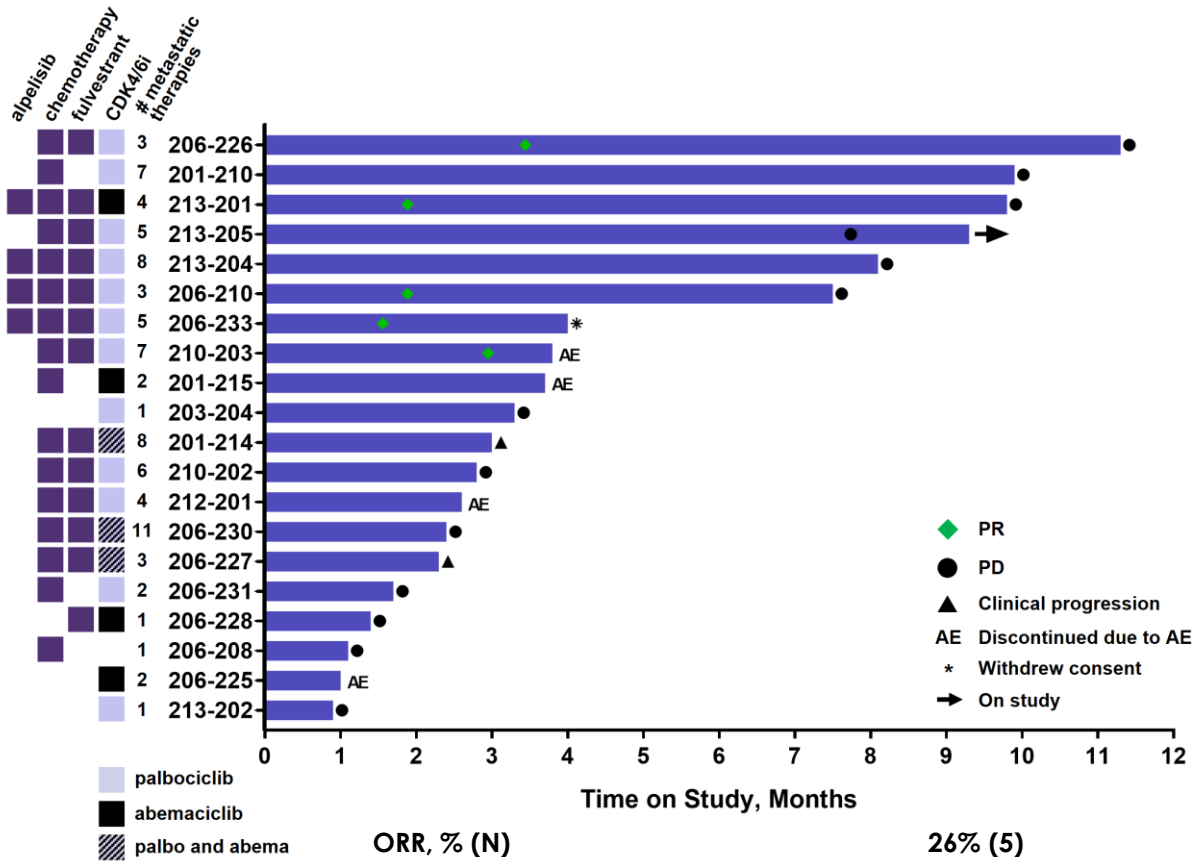
Palbociclib, abemaciclib and ribociclib were found to be inactive against the active, phosphorylated trimeric form of p27/D1/CDK4

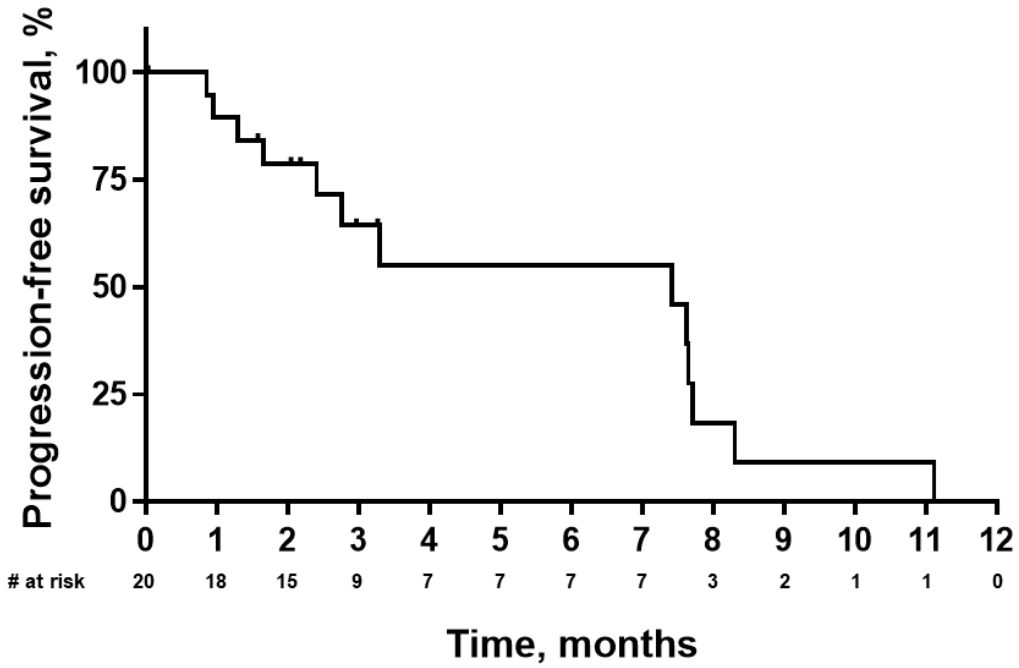
Guilley, et al Science 2019

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

- Phase 2a expansion cohort in ER+ BC in a Simon 2-stage design enrolled 20 patients
- 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 a 21-day cycle combined with fulvestrant and abemaciclib
- Primary endpoint is objective response rate per RECIST v1.1
- Heavily pretreated patients with a **median of 4 prior regimens** for metastatic disease
  - 95% received prior CDK4/6 inhibitor
  - 65% received prior fulvestrant
  - 75% received prior chemotherapy including 50% with ≥ 2 prior chemo regimens

Positive Data from ZFA Triplet Expansion Cohort (n=20) Exceeded our Expectations





ORR, % (N)	**26% (5)**
DCR, % (N)	**79% (15)**
CBR24, % (N)	**32% (6)**
Median TTR, mo (range)	**1.9 (1.6-3.5)**
Median DOR, mo (range)	**6.6 (1.7-7.7)**

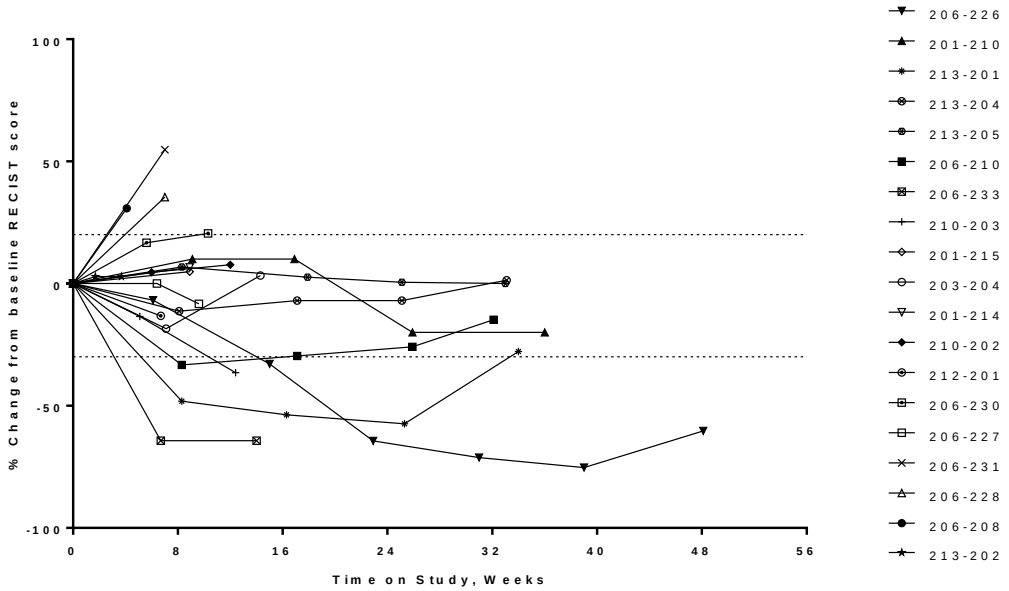
Longest duration of treatment ~48 weeks

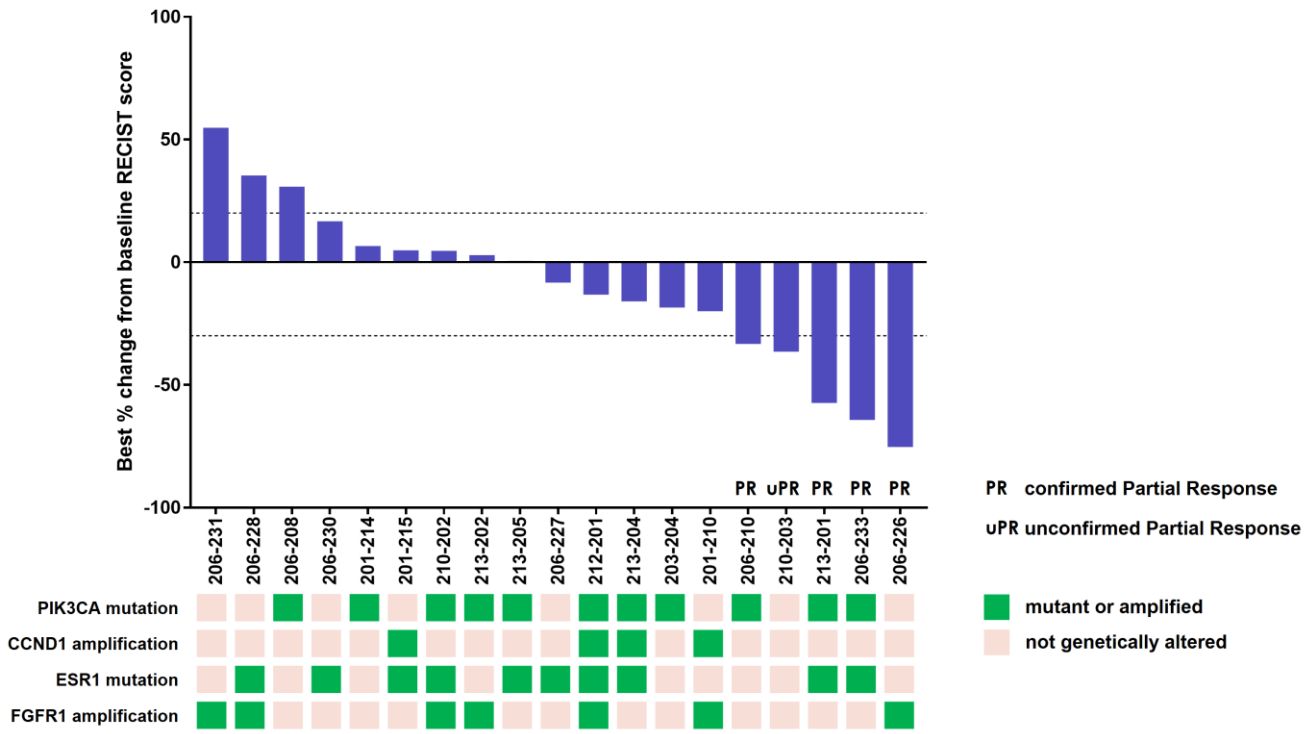
19 efficacy evaluable patients

Median PFS, months	**7.4**
95% CI	**2.8 – N.E**

N.E., non-estimable

Early Responses Observed in ZFA Triplet Expansion Cohort





- PRs seen in patients with and without mutations in PI3K and ESR1, enabling development path in potentially **unrestricted** patient population

ZFA Triplet: Summary of Zotatifin-Related Treatment-Emergent Adverse Events (N=20)

Preferred term	All Grades, N (%)	Grade 3 or 4, N (%)
Nausea	14 (70)	0 (0)
Vomiting	11 (55)	0 (0)
Fatigue	10 (50)	0 (0)
Diarrhea	9 (45)	1 (5)
Anemia	6 (30)	2 (10)
Dry mouth	6 (30)	0 (0)
Peripheral sensory neuropathy	6 (30)	0 (0)
Dehydration	4 (20)	0 (0)
Muscle spasms	4 (20)	0 (0)
Blood creatine phosphokinase increased	4 (20)	2 (10)
Dysgeusia	4 (20)	0 (0)
Stomatitis	4 (20)	0 (0)
Platelet count decreased	3 (15)	1 (5)
Abdominal pain	3 (15)	0 (0)
Hypertriglyceridemia	3 (15)	0 (0)

Zotatifin-related 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 that are considered by the investigator to be potentially related to zotatifin. TEAEs ≥ 15% Incidence are reported by Preferred Term and Maximum Reported CTCAE Grade for Subjects. Percentage is calculated using the number of treated subjects as the denominator.

Q2W Dose Escalation Cohorts

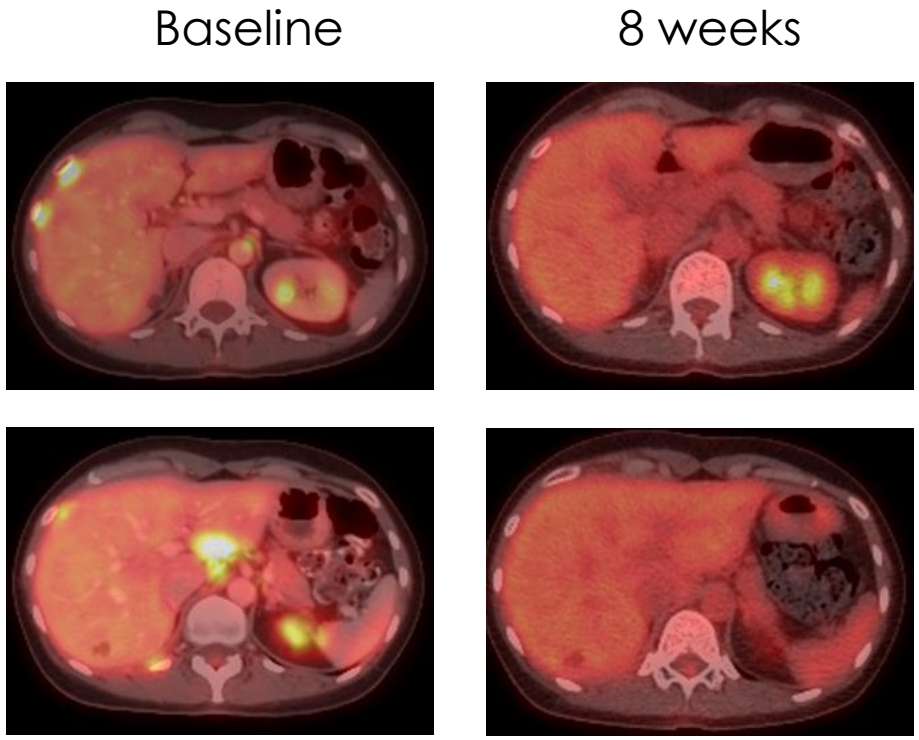
- Based on favorable safety and tolerability data at initial RP2D*, resumed dose escalation with more convenient schedule, dosing every other week (Q2W)
- ZF doublet RP2D declared as 0.2 mg/kg Q2W
  - Confirmed PR in one patient at 0.1 mg/kg Q2W dose
- ZFA triplet initiated at 0.1 mg/kg Q2W

*initial RP2D was 0.07 mg/kg dosed on Days 1 and 8 of a 21-day cycle

Early Response in ZF Dose Escalation at 0.1 mg/kg Q2W

- 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



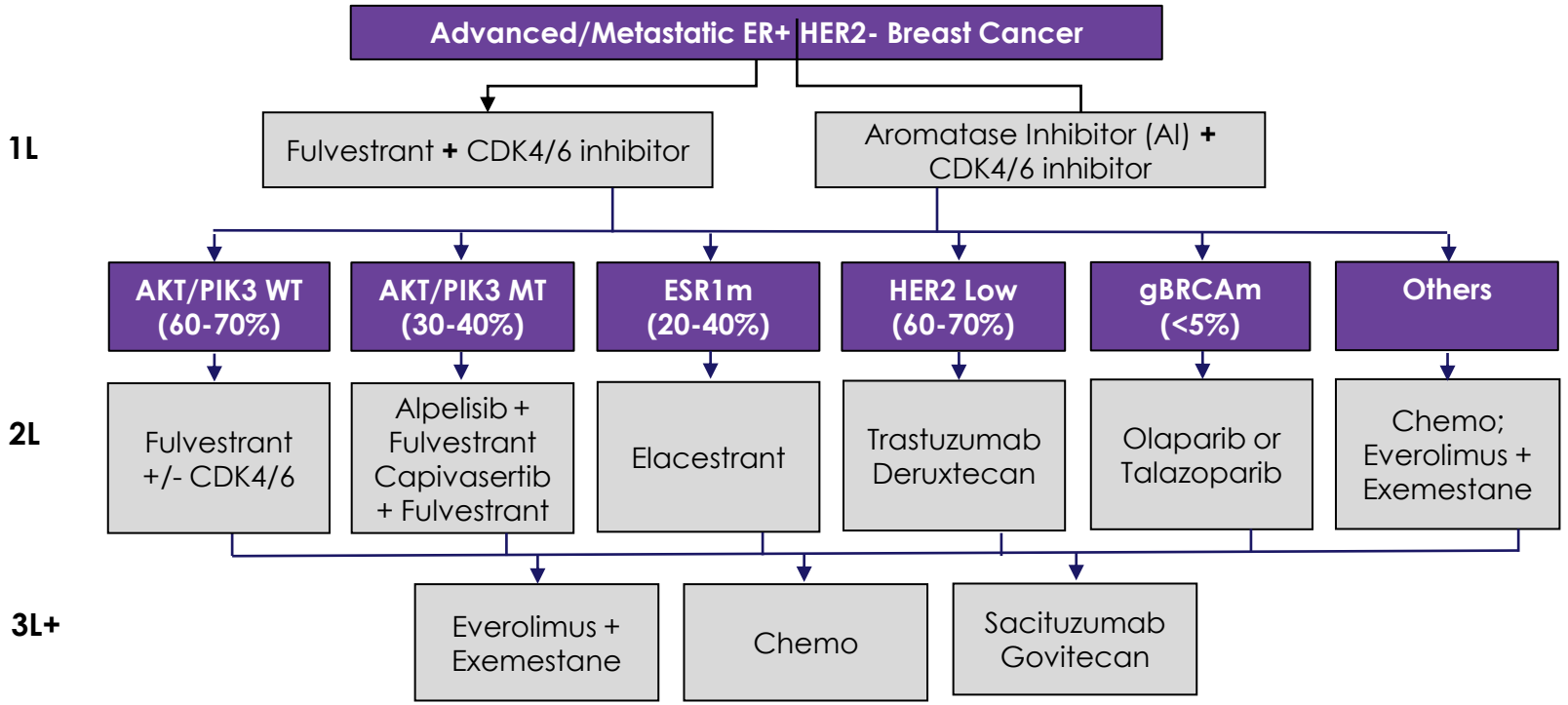
Zotatifin Clinical Summary and Development Plan

- Zotatifin has shown compelling efficacy in highly refractory ER+ metastatic breast cancer population (median 4 prior lines of tx) in ZFA triplet
- Robust clinical safety seen across multiple cohorts
- Strong KOL feedback on high unmet need following first line CDK 4/6i and desire to retreat with CDK 4/6i
- Development plans include:
  - Finalization of dose and schedule, with RP2D of ZFA anticipated in H2 2024
  - Evaluate ZFA triplet in randomized trial
    - Use FTD mechanism to align development strategy with FDA
    - Results from Lilly's postMONARCH* trial, expected at ASCO 2024, will help inform size of potential registration trial

*postMONARCH is a Phase 3 clinical trial sponsored by Eli Lilly and Company to compare the efficacy of abemaciclib plus fulvestrant to placebo plus fulvestrant in participants with HR+, HER2-, advanced or metastatic breast cancer following progression on a CDK4/6 inhibitor and endocrine therapy

Zotatifin Product Development Strategy in ER+ Breast Cancer

- Seeking to establish zotatifin as a backbone of therapy in 2nd line plus ER+ BC
- **ZFA triplet**, intended to capitalize on synergy with CDK 4/6i, could treat a **broad, unrestricted population**
- Alternative regimens, e.g. combined with a SERD, PI3Ki or AKTi, could address specific resistant populations

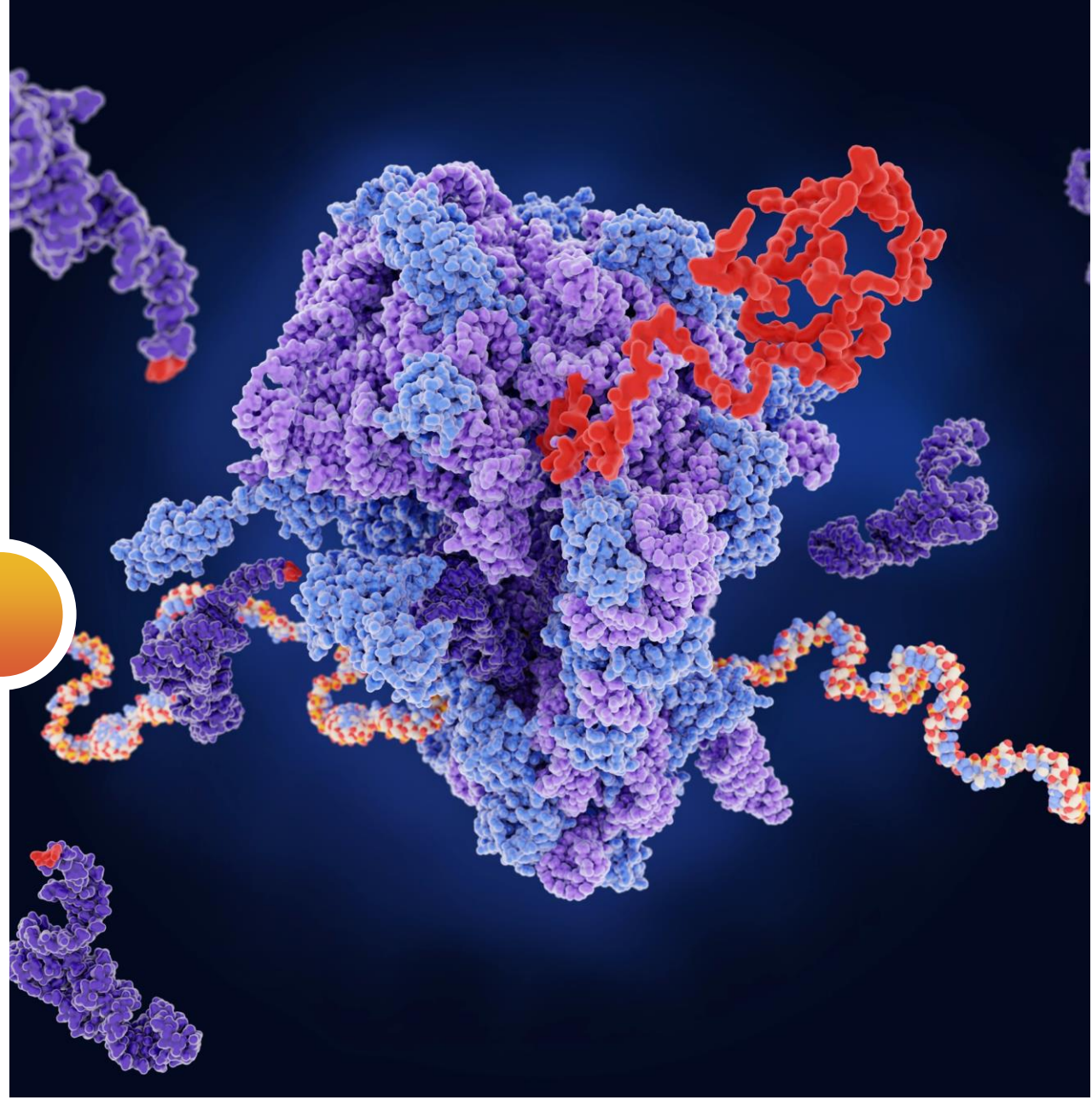


HER2-low defined as HER2 IHC 1+ or IHC 2+/ISH-; gBRCAm = germline BRCA mutant, SERM = selective estrogen receptor modulators, SERD = selective estrogen receptor degrader

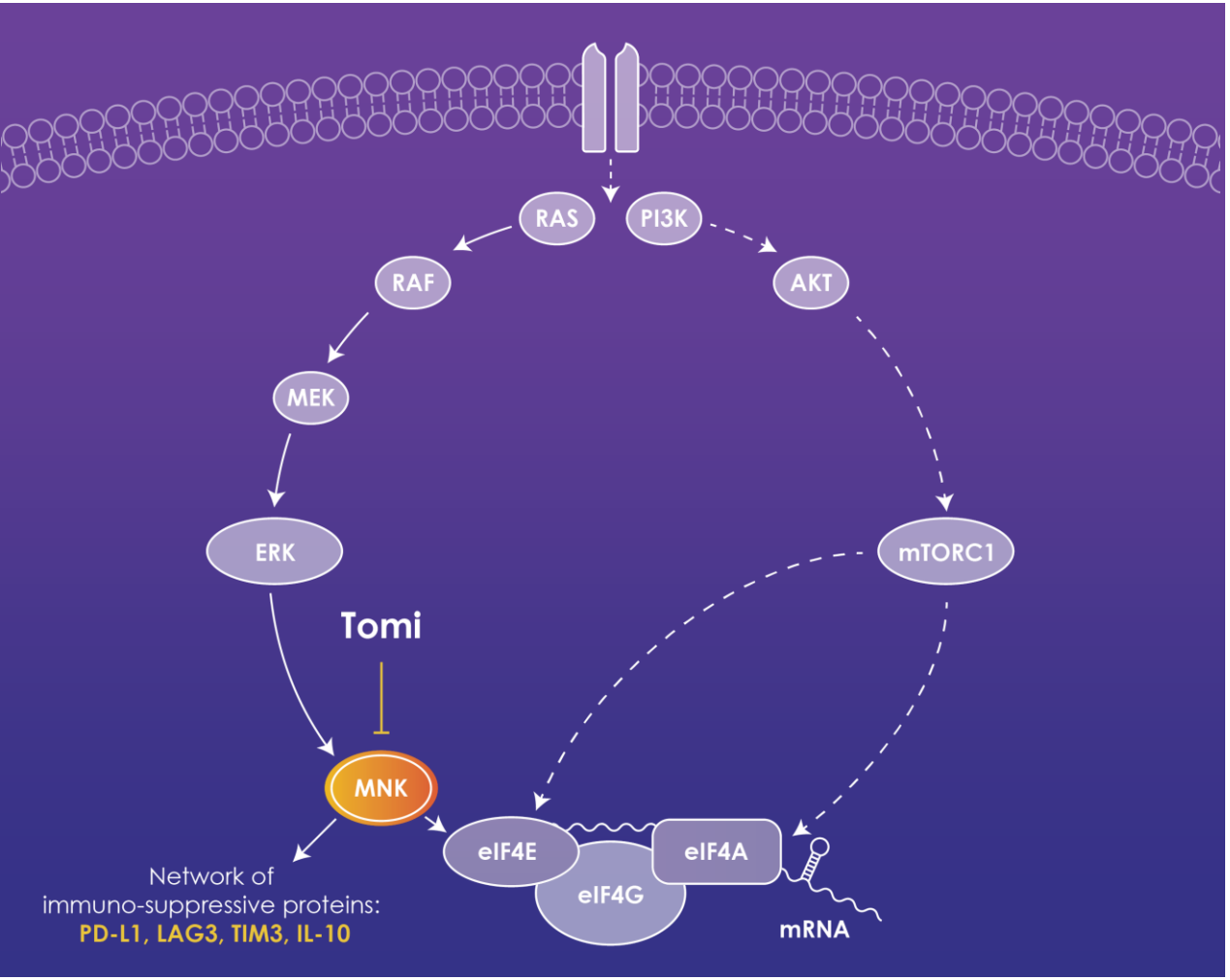
Tomivosertib

MNK Inhibitor

Designed to activate and prevent exhaustion of T cells, and block pro-survival signals in AML



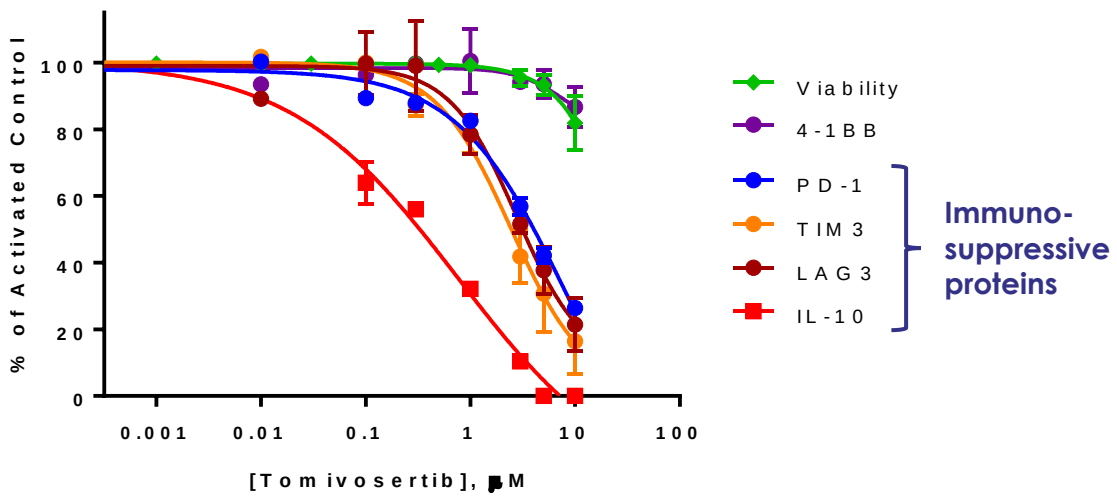
Tomivosertib Designed to Reprogram T Cells to Enhance Anti-tumor Activity in One Pill



- Tomi designed to **invigorate the immune response to cancer** by inhibiting tumor-driven T cell exhaustion
- Tomi inhibits MNK-dependent overproduction of multiple immunosuppressive proteins
  - **PD-1, LAG3, TIM3, IL-10**
- Tomi increases **target cell killing** by T cells
- Tomi increases **T cell memory pool**
- Tomi increases **response to checkpoint inhibitors** in pre-clinical models

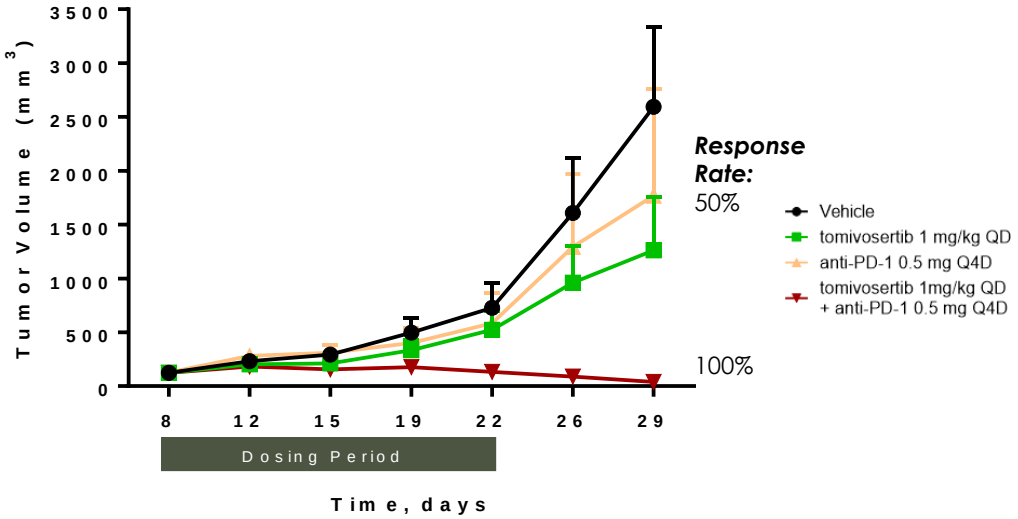
Tomivosertib Designed to Downregulate Network of Immunosuppressive Proteins in One Pill

Tomivosertib downregulated network of immunosuppressive proteins



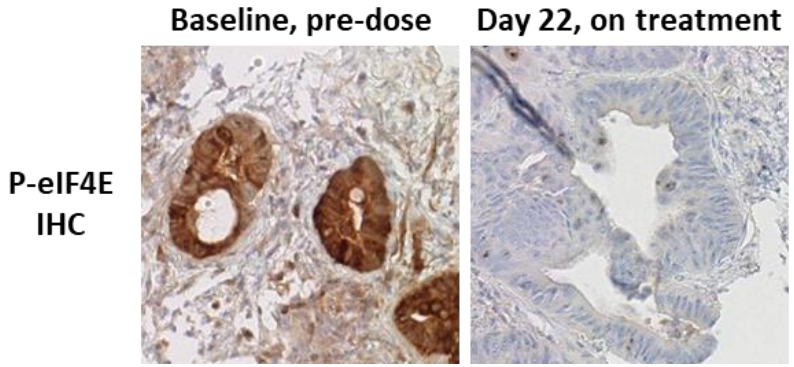
Tomivosertib Anti-tumor Activity Observed in CT26 Tumors

Single Agent and in Combination with Anti-PD-1

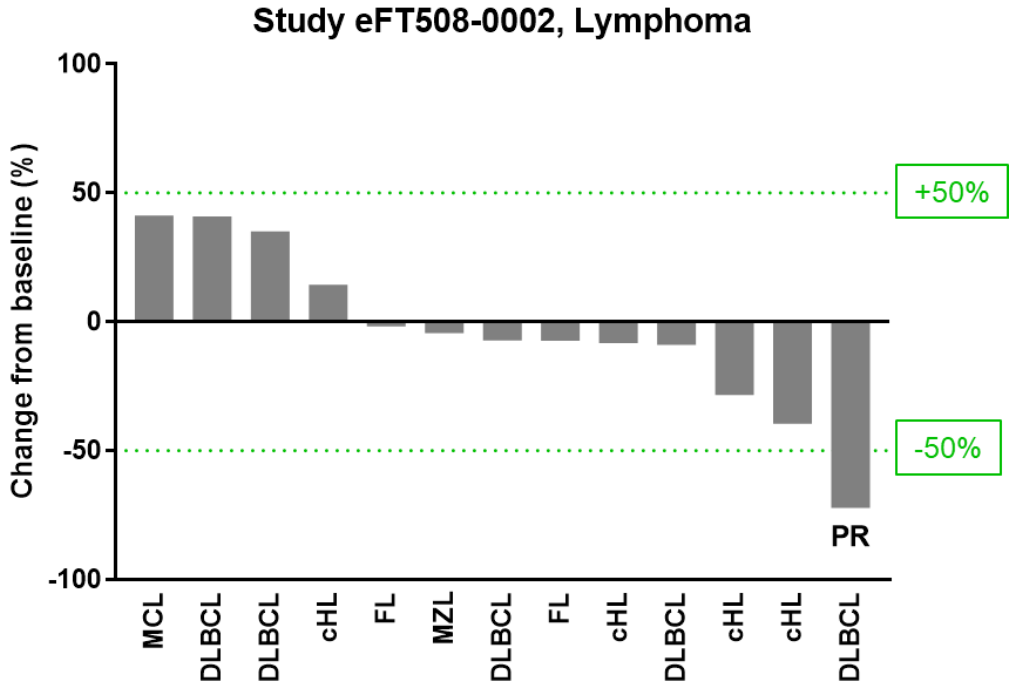


Tomivosertib: Generally Well Tolerated with Single-Agent Activity*

- Tomivosertib was generally well tolerated at the recommended Phase 2 dose (RP2D)
  - Low grade nausea, vomiting and tremors were most common treatment-emergent adverse events (TEAEs)
- MNK target was 90-100% inhibited at RP2D



- Single agent activity was observed in lymphoma patients



*Data from completed studies as of September 2020. Lymphoma waterfall plot represents all patients with evaluable disease (n=13) out of 19 patients total enrolled.

Tomivosertib Prolonged PFS When Combined with Anti-PD-(L)1 Agents

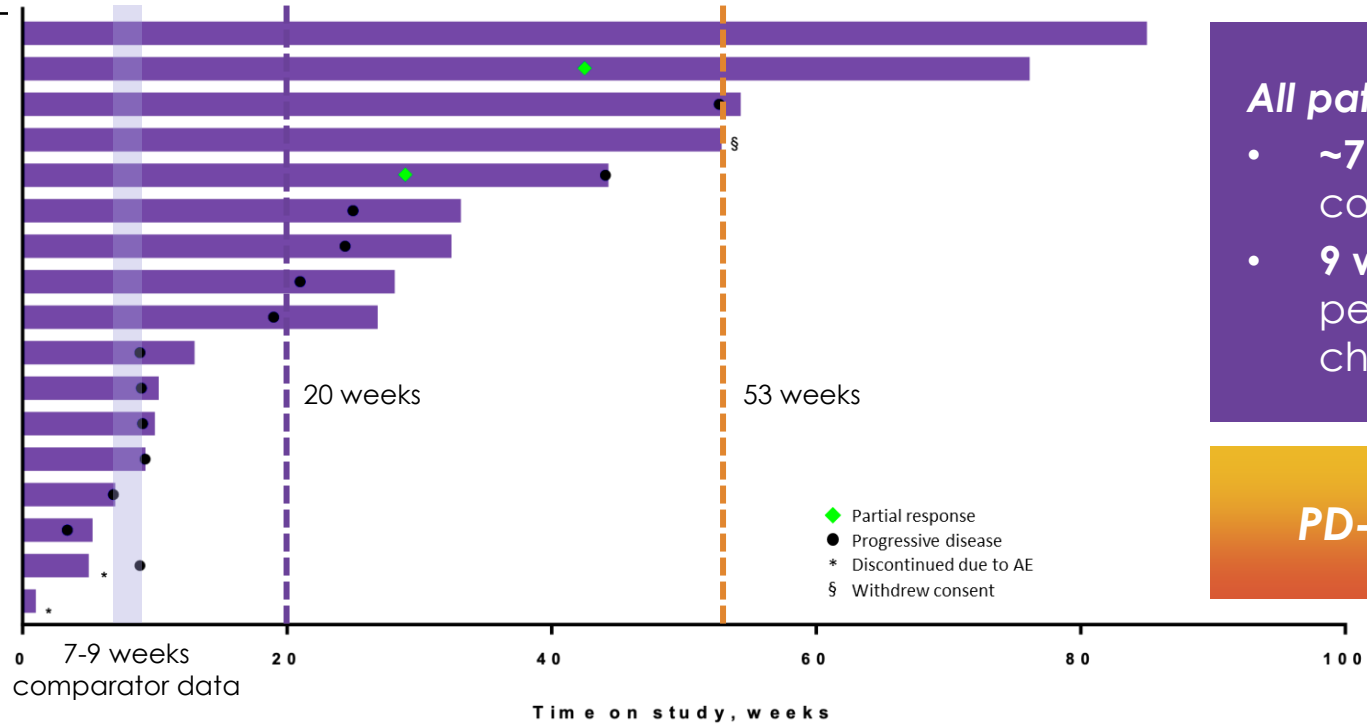
- Phase 2a trial (N=39)
  - Tomivosertib added on to patients not responding to anti-PD-(L)1 therapy, with no change or break in anti-PD-(L)1 regimen
  - Safety profile when combined with anti-PD-(L)1 agents comparable to anti-PD-L(1) agents alone
- Clinical benefit was most prominent in NSCLC patients (N=17)*
  - All patients had increasing metastatic disease on anti-PD-(L)1 therapy prior to adding tomivosertib
    - 16 of 17 met RECIST threshold for Progressive Disease
  - 12% ORR compares favorably to 3% for vibostolimab+pembrolizumab in PD-1 refractory setting**
  - **Adding tomivosertib substantially improved PFS, particularly in PD-L1+ patients**

**Data through study completion in September 2020; initial data presented at ASCO 2020; PR, CR and SLD (Sum of Long dimensions) as determined by RECIST 1.1 criteria.*

*FOR ILLUSTRATIVE PURPOSES ONLY: **Data for vibostolimab+pembrolizumab from trial NCT02964013. Differences exist between trial designs and subject characteristics, and caution should be exercised when comparing data across trials.*

Phase 2A: Demonstrated Extended PFS in NSCLC Patients Particularly Enriched in PD-L1+ Patients

Patient	CPI	PD-L1
115-103	Pembro	≥ 1%
120-103	Pembro	≥ 1%
113-102	Nivo	≥ 1%
113-103	Nivo	≥ 1%
104-101	Pembro	N.D.
106-103	Nivo	0
115-105	Durva	N.D.
111-101	Atezo	N.D.
106-104	Pembro	≥ 1%
106-107	Durva	≥ 1%
123-103	Pembro	0
105-102	Pembro	0
116-104	Nivo	0
108-106	Pembro	≥ 1%
123-101	Pembro	0
114-101	Nivo	0
112-104	Nivo	0



All patients: mPFS of **20 weeks** compared to

- **~7 weeks** for atezolizumab alone continued after progression and
- **9 weeks** for vibostolimab + pembrolizumab after progression on checkpoint inhibitor*

PD-L1+ patients: mPFS of 53 weeks

**FOR ILLUSTRATIVE PURPOSES ONLY: Data for atezolizumab from Treatment Beyond Progression (TBP) cohort in OAK trial. Data for vibostolimab+pembrolizumab from trial NCT02964013; Differences exist between trial designs and subject characteristics, and caution should be exercised when comparing data across trials.*

Data through study completion in September 2020
Patients 115-103 and 120-103 continued treatment past study completion on Single Patient Expanded Access INDs.

KICKSTART: Randomized, Double-blind, Phase 2b Trial In Treatment-Naïve NSCLC Patients w/ PD-L1 ≥50%

Topline data results:

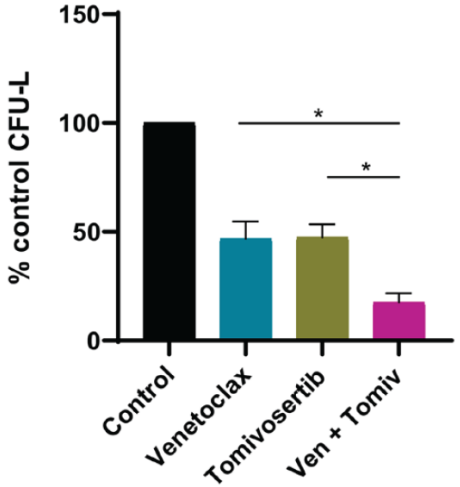
- Hazard ratio for PFS*: 0.62 (95% confidence intervals 0.3 to 1.3)
- Two-sided p value for PFS*: 0.21, which missed the pre-specified threshold of p≤ 0.2
- Median PFS: 13 weeks in experimental arm vs. 11.7 weeks in control arm
- OS: immature at data cutoff, no trend favoring tomivosertib observed

Additional data analysis and PD response assessment ongoing

*PFS hazard ration calculated using a stratified Cox proportional hazard model
*p value calculated using stratified log rank test

Tomivosertib in Acute Myeloid Leukemia (AML)

- MNK activity is associated with AML proliferation and resistance to chemotherapy
- Tomivosertib inhibited colony formation from AML-derived leukemic progenitor cells
- Tomivosertib was synergistic when combined with venetoclax
  - Similar effects seen with other MNK inhibitors combined with azacytidine



Colony formation assay with KG-1 cells
100 nM tomivosertib/100 nM venetoclax

- Investigator-sponsored trial of tomivosertib in AML is being conducted at the Lurie Comprehensive Cancer Center at Northwestern University
  - Part 1 is single agent dose escalation of tomivosertib from 100 mg QD to 100 mg BID in patients with relapsed/refractory AML
  - Part 2 is intended to combine tomivosertib with azacytidine and venetoclax in newly diagnosed patients after dose from Part 1 has been determined

Additional Program Opportunities

Zotatifin

- Additional combinations in ER+ breast cancer and expansion into other tumor types
- Investigator-initiated clinical trial at Stanford in ER+ HER2- breast cancer in pre-operative setting enrolling

eIF4E

- Worldwide partnership with Pfizer, up to $465M in additional milestones to be received plus royalties on sales
- eFFECTOR retained option to co-promote and profit share in the U.S.

Financial Summary

- Q1 2024 ending cash of **$25.4M** expected to fund operations into **Q1 2025**
- Approximately 4.7M shares outstanding as of April 30, 2024

Multiple Upcoming Clinical Milestones

Anticipated Milestones		2024		2025	
		1H	2H	1H	2H
Zotatifin	RP2D in ZFA triplet		●		
	Initiation of randomized trial(s) with ZFA triplet		●		
Tomivosertib	Initial data from investigator-sponsored trial in AML		●		

Next Generation Targeted Therapy for Cancer

Corporate Presentation | May 2024

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