Next Generation Targeted Therapy for Cancer

Corporate Presentation | April 2023

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eFFECTOR

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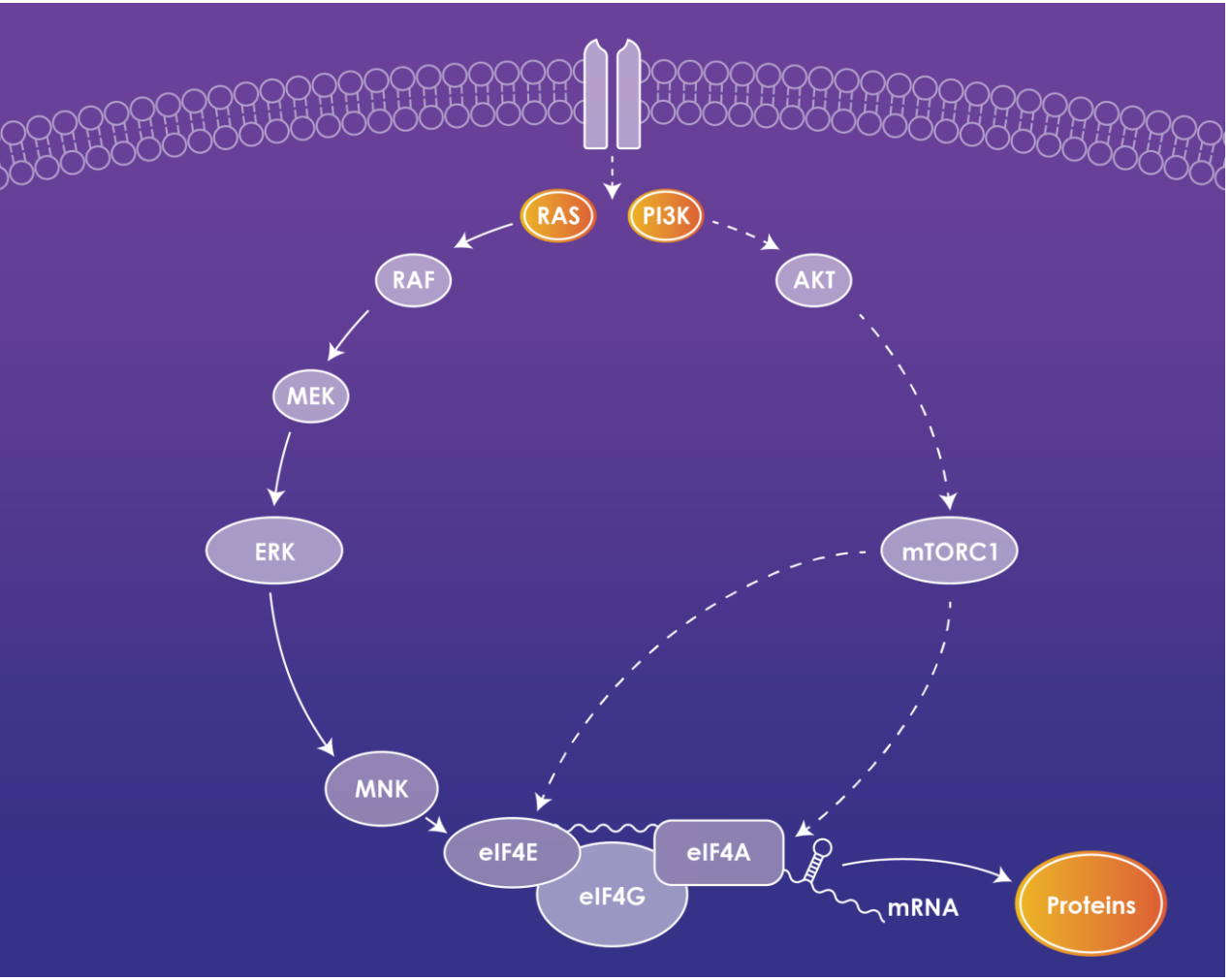
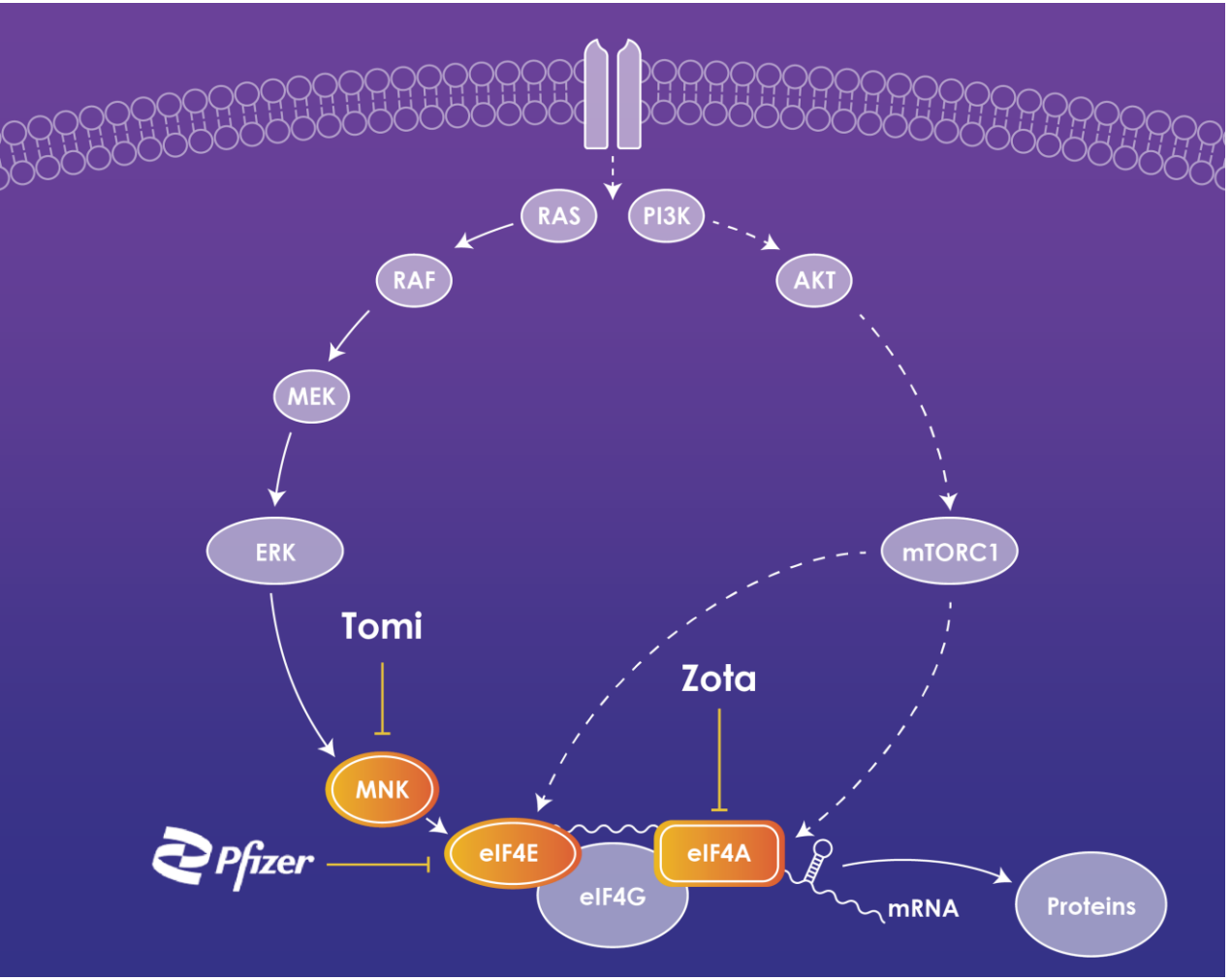
Oncogenic Signaling Selectively Activates Translation to Drive Production of Specific Tumor-Promoting Proteins



- 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

Investment Highlights

- **Novel platform designed to block one specific output of oncogenic signaling**
  - Selective Translation Regulator Inhibitors (STRIs)
- **Validating partnership with Pfizer**
  - $507M partnership on third STRI product candidate
  - Retained option to co-promote and profit share in U.S.
- **Current cash expected to fund operations into Q1-24**
- **Robust clinical pipeline with upcoming value inflection points**

Tomivosertib: Phase 2b in frontline non-small cell lung cancer (NSCLC) in combination with pembrolizumab

- Topline results – H2 2023
- Additional clinical initiations and indication expansions

Zotatifin: Phase 2a expansion cohorts including ER^+ breast cancer and $KRAS^{mut}$ NSCLC

- Multiple Phase 2a readouts – H1 2023 and H2 2023
- Additional clinical initiations and indication expansions

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	H1 2023 Topline data from remaining 11 patients in ECBF+A P2a (n=18) expansion cohort H2 2023 Data from P1b dose escalation cohorts
eIF4Ei	Solid Tumors						Pfizer *eFFECTOR Option to Co-Promote/ Profit Share in US*	

Experienced Leadership Team

Steve Worland, PhD
Founder, President, CEO and Director

Doug Warner, MD, MBA
Chief Medical Officer

Mike Byrnes, MBA
Chief Financial Officer

Mayank Gandhi, MD
Chief Business Officer

Scientific Advisors	*Institution*	*Expertise*
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Davide Ruggero, PhD	UCSF, EFTR Co-founder	Translation
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Joan Brugge, PhD	Harvard	Oncogenic Signaling
Neal Rosen, MD, PhD	Memorial Sloan Kettering	Oncogenic Signaling

Clinical Advisors/ Key Investigators	*Institution*	*Expertise*
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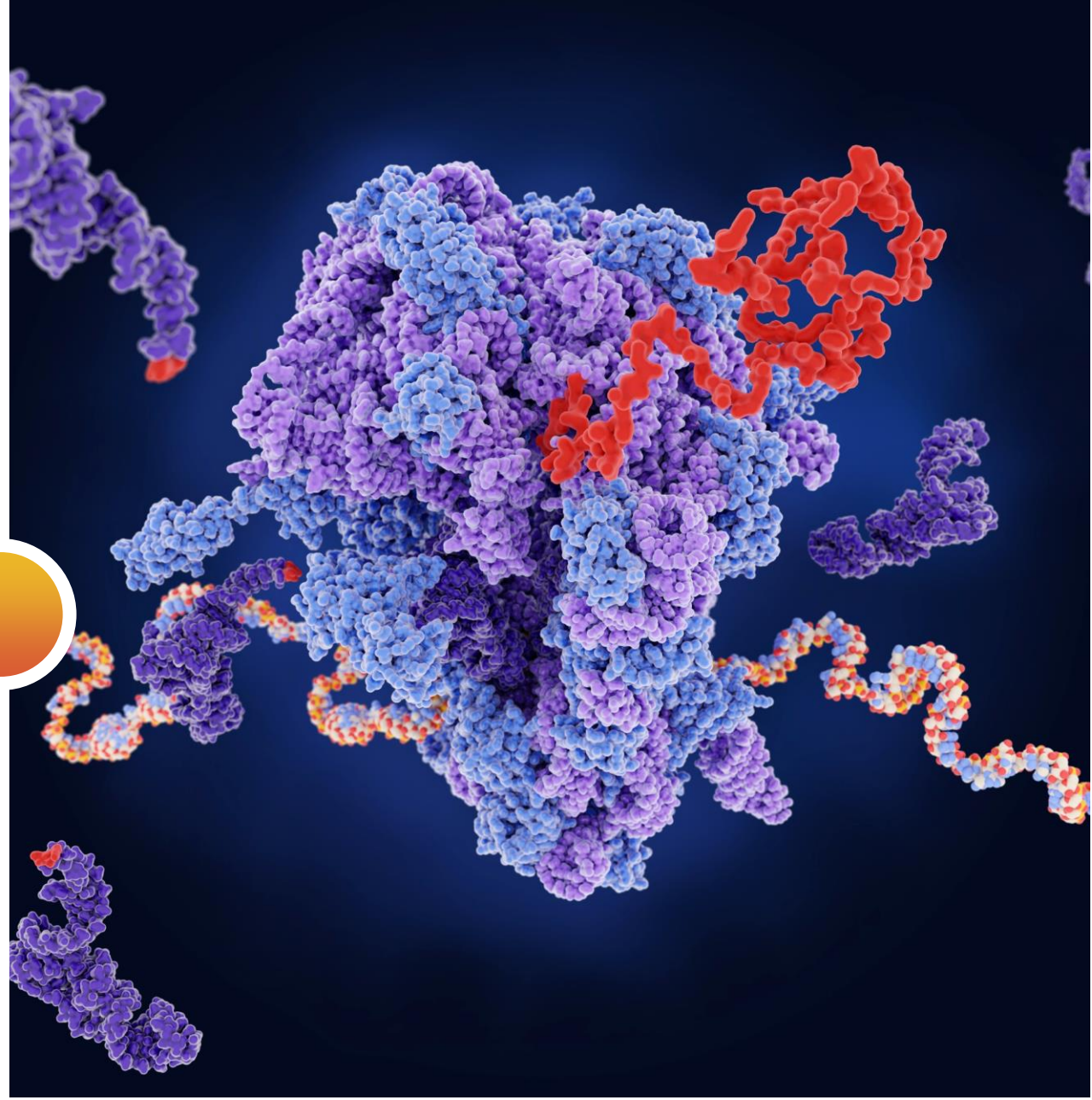
Robert Sikorski, MD, PhD	Former CMO, Five Prime	Oncology Development
Funda Meric-Bernstam, MD	MD Anderson	Oncology Development
Ezra Rosen, MD, PhD	Memorial Sloan Kettering	Oncology Development
Jennifer Caswell-Jin, MD	Stanford Medicine	Oncology Development

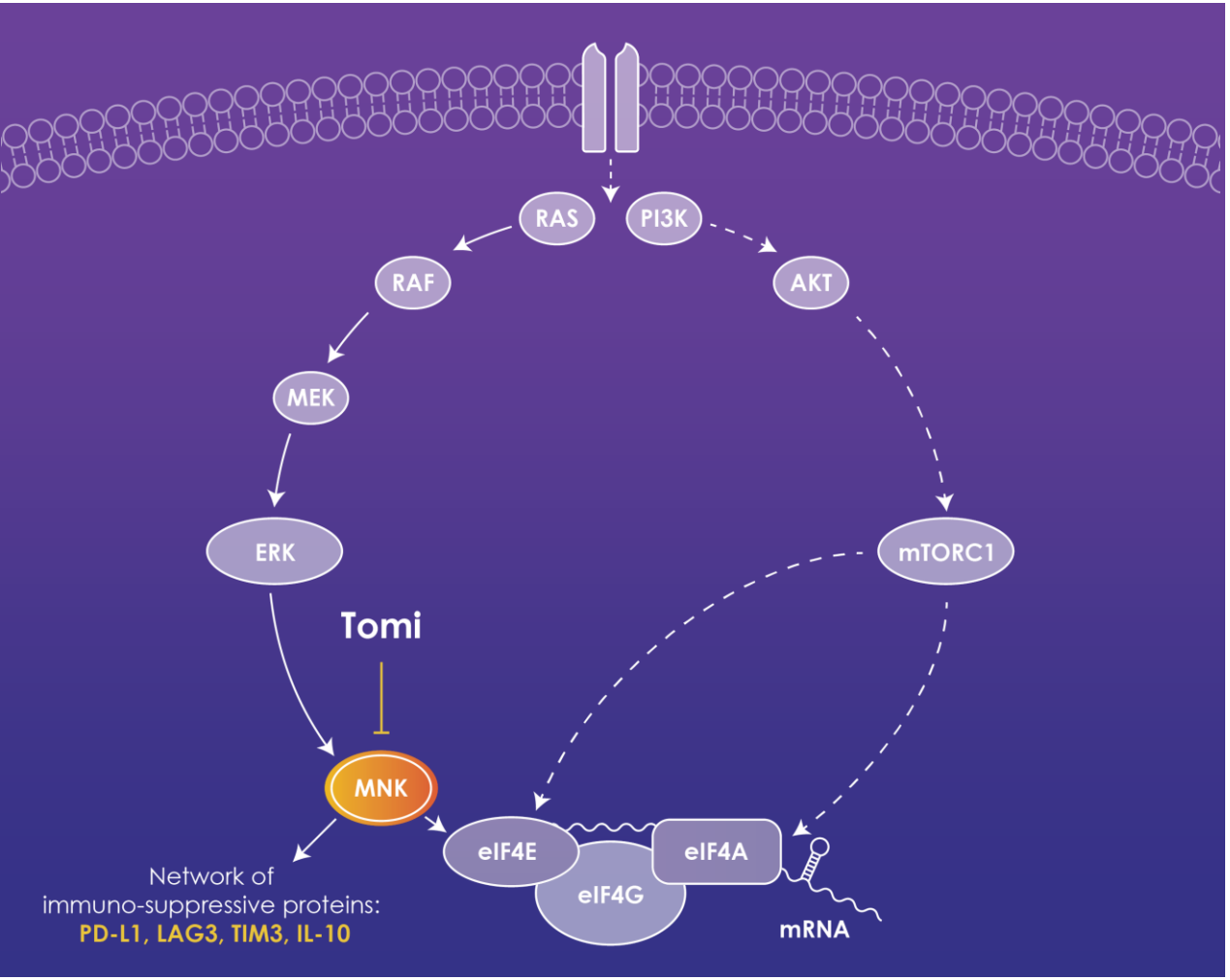
Tomivosertib

MNK Inhibitor

Designed to stimulate activation, prevent exhaustion and prolong memory of T cells



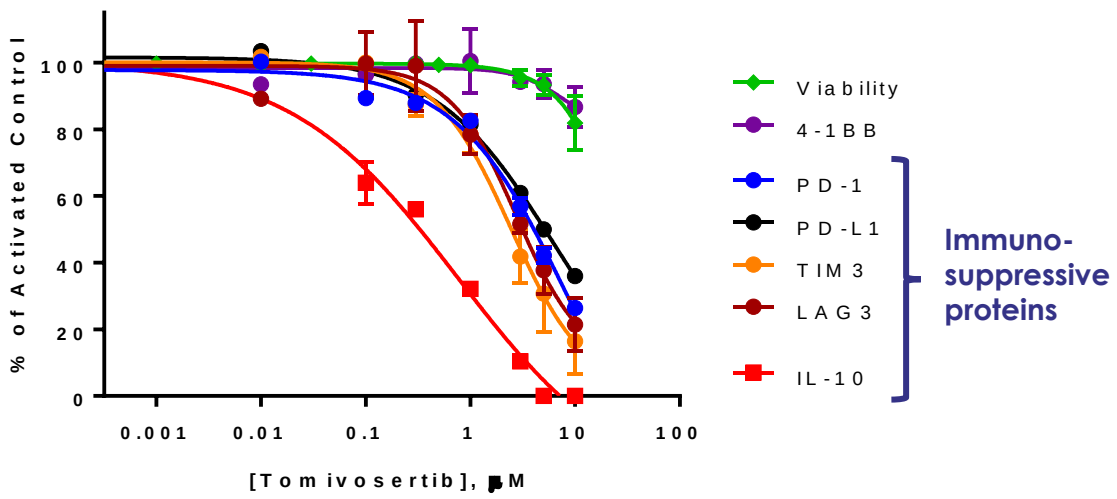
Tomivosertib Designed to Reprogram T Cells to Enhance Anti-tumor Activity in One Pill



- Tomi designed to **invigorate the immune response to cancer** by inhibiting tumor-driven T cell exhaustion
- Tomi inhibits MNK-dependent up-regulation 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

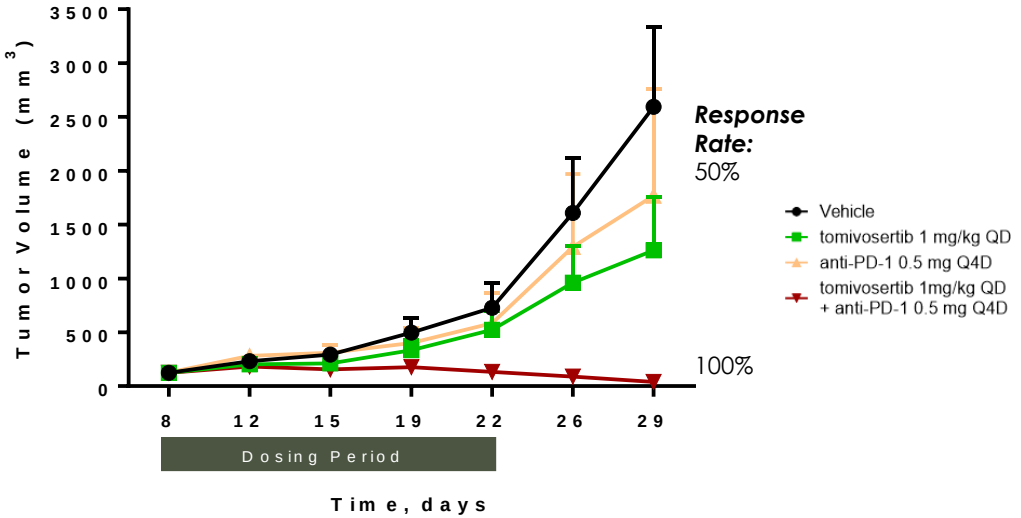
Tomivosertib Designed to Downregulate Network of Immunosuppressive Proteins in One Pill

Tomivosertib downregulated network of immunosuppressive proteins



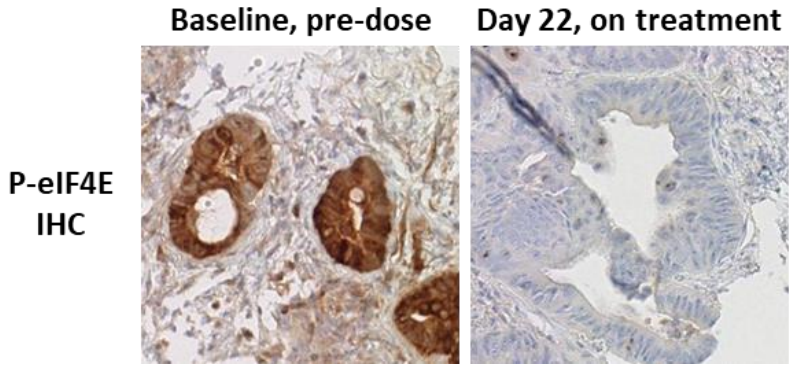
Tomivosertib Anti-tumor Activity Observed in CT26 Tumors

Single Agent and in Combination with Anti-PD-1

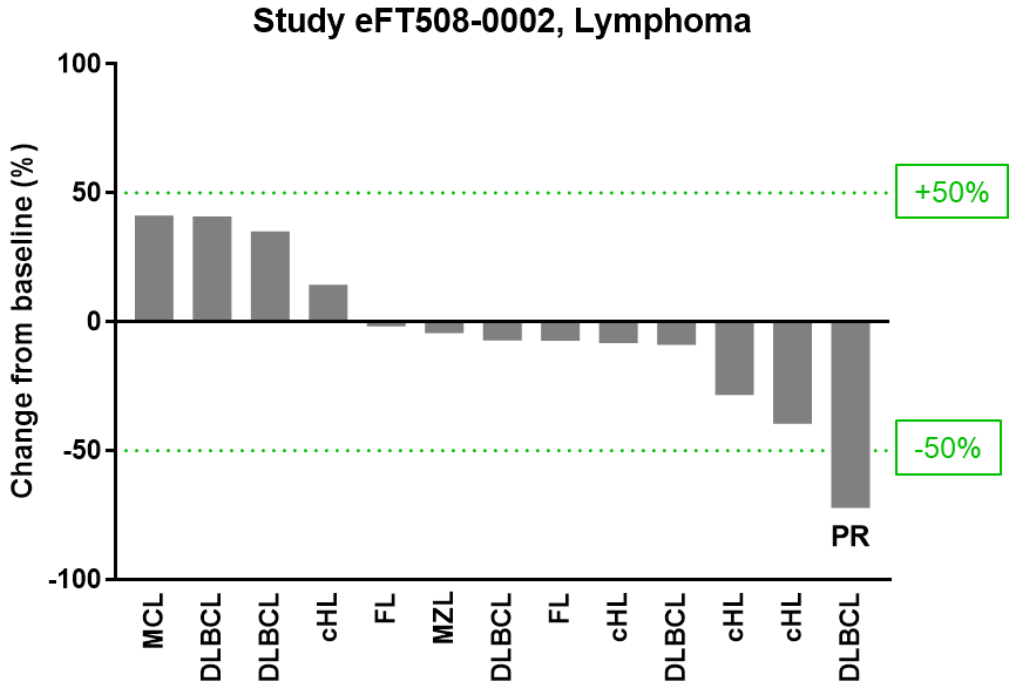


Tomivosertib: Generally Well Tolerated with Single-Agent Activity*

- 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
  - Showed encouraging activity in multiple tumor types*
- Clinical benefit was most prominent in NSCLC patients (N=17)
  - Increasing metastatic disease on anti-PD-(L)1 therapy prior to adding tomivosertib
    - 16 patients had RECIST-defined progressive disease, 17th patient had 13% increase in SLD score
  - 2 confirmed partial responses (PR), including one which went on to confirmed CR on extension
    - 12% ORR compares favorably to 3% for vibostolimab+pembrolizumab in PD-(L)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.*

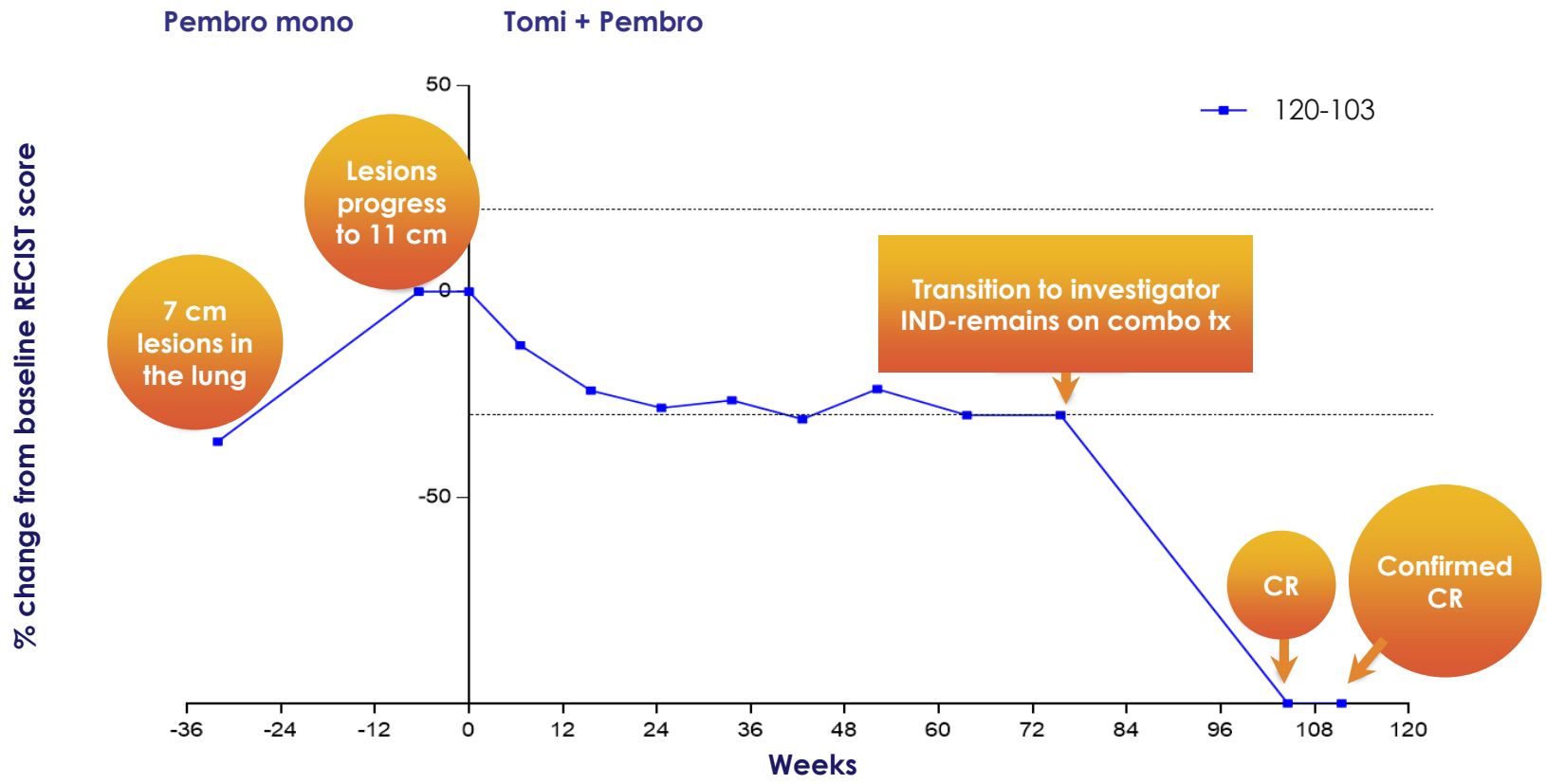
*FOR ILLUSTRATIVE PURPOSES ONLY: **Data for vibostolimab+pembrolizumab from trial NCT02964013. Differences exist between trial designs and subject characteristics, and caution should be exercised when comparing data across trials.*

Tomivosertib Was Generally Well-Tolerated In Combination with Checkpoint Inhibitors in Phase 2a Trial

Tomivosertib 200 mg BID In Combination with Anti-PD-(L)1 Inhibitors		
	Drug-related TEAEs	
MedDRA term	All Grades N(%)	Grade 3 or higher N(%)
Nausea	16 (41.0)	0 (0.0)
Tremor	15 (38.5)	0 (0.0)
Fatigue	11 (28.2)	0 (0.0)
Vomiting	9 (23.1)	0 (0.0)
Alanine aminotransferase increased	7 (17.9)	2 (5.1)
Aspartate aminotransferase increased	7 (17.9)	0 (0.0)
Diarrhea	7 (17.9)	0 (0.0)
Gamma-glutamyltransferase increased	7 (17.9)	1 (2.6)
Rash	5 (12.8)	0 (0.0)
Blood alkaline phosphatase increased	4 (10.3)	0 (0.0)
Decreased appetite	4 (10.3)	0 (0.0)
Dyspepsia	4 (10.3)	0 (0.0)
Headache	4 (10.3)	0 (0.0)
Insomnia	4 (10.3)	0 (0.0)

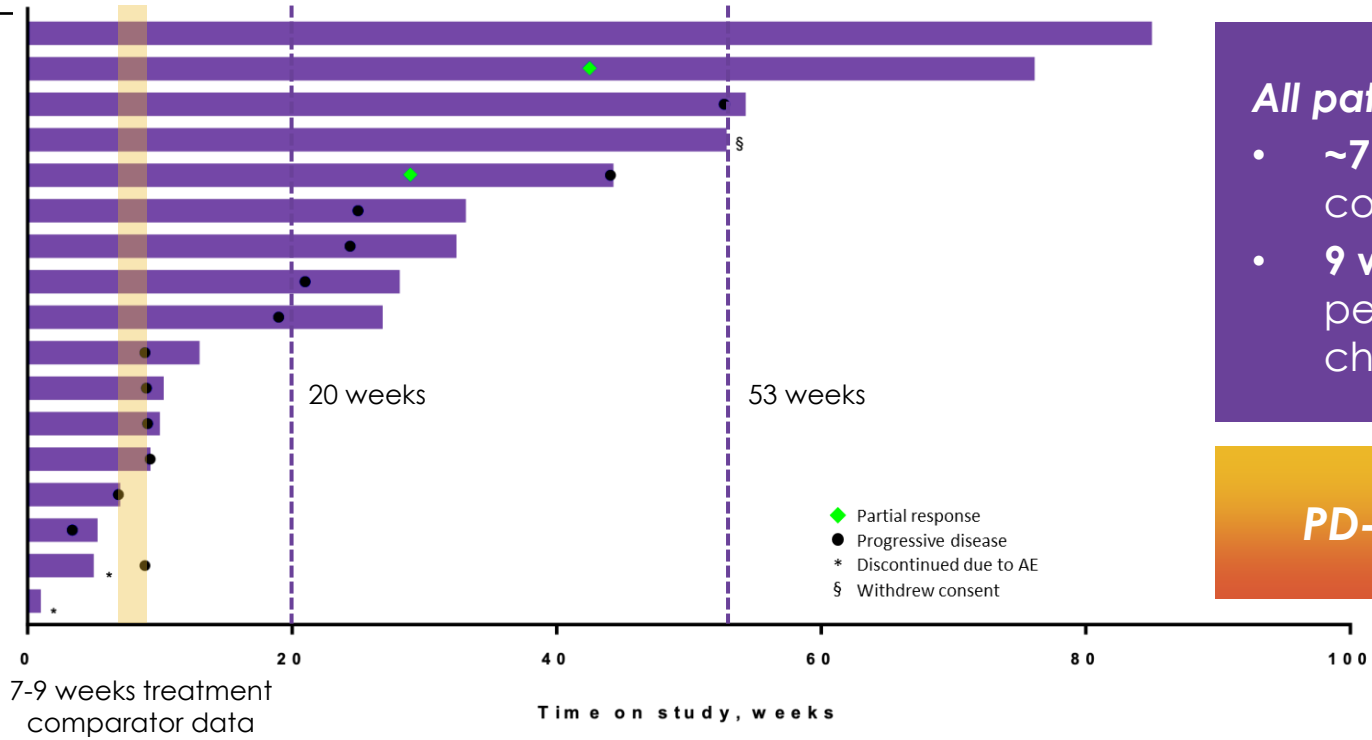
Drug-related Treatment-Emergent Adverse Events >10% Incidence from interim data at study conclusion.
Tomivosertib was dosed 200 mg BID in fasted state in combination with pembrolizumab, nivolumab, durvalumab or atezolizumab at approved dose of each anti-PD-(L)1 inhibitor.

Example: Patient on Tomi/Pembro Combo With Confirmed Complete Response after ~2 Years



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*

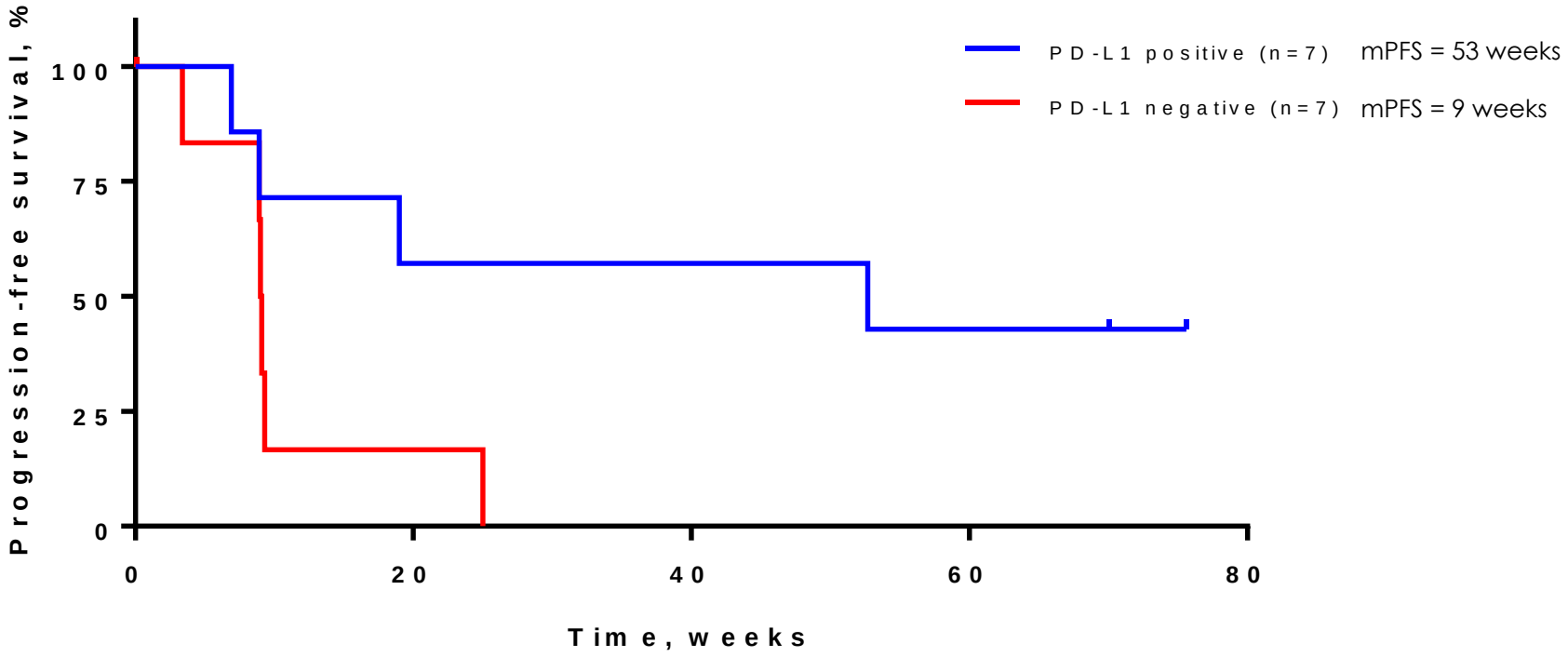
PD-L1+ patients: mPFS of 53 weeks

**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.

PD-L1 Positive Patients Showed Longer PFS

A post-hoc analysis of data from the Phase 2a trial showed that the median PFS in PD-L1 positive patients was 53 weeks vs 9 weeks in PD-L1 negative patients



**data as of study completion September 2020. PD-L1 status available from site communications or central testing for 14 of 17 patients. Analysis of median PFS between PD-L1 positive and negative patients is from Kaplan Meier analysis of PFS curves.*

PFS and OS for Tomi Added After PD in Phase 2a Trial Exceed PFS and OS in OAK Trial Treatment Beyond Progression Cohort

Criteria	EFTR Phase 2a Trial NSCLC subset	OAK Trial Treatment Beyond Progression Cohort[1]	OAK Trial Full Atezo Cohort[2]
ORR	11.8%	7.1%	13.6%
PFS	20.0 weeks	~6.5 weeks[3]	12.1 weeks
OS	19.0 months	12.7 months	13.8 months
PD-L1+ subset of pts[4] ORR PFS OS	 14.3% 53 weeks >20 months (not reached)	 7.5% not reported but not enriched in waterfall plot not reported	 18% 12.1 weeks 15.7 months

[1]Rittmeyer et al., Lancet 2017
[2]Gandara et al., J. Thoracic Oncology 2018
[3]reported as time to discontinue therapy
[4]PD-L1 detected on tumor cells or immune cells (TC or IC) in OAK trial, TC only in eFFECTOR trial

Differences exist between trial designs and subject characteristics, and caution should be exercised when comparing data across trials.

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

- Tomi dosed 100 mg BID with food
- Progression Free Survival (PFS) is primary endpoint
- Trial design enriched for PD-L1+ patients who received the most benefit in the P2a trial

- **Topline data readout anticipated 2H 2023**

How We Define Success in KICKSTART

Clinically meaningful results:

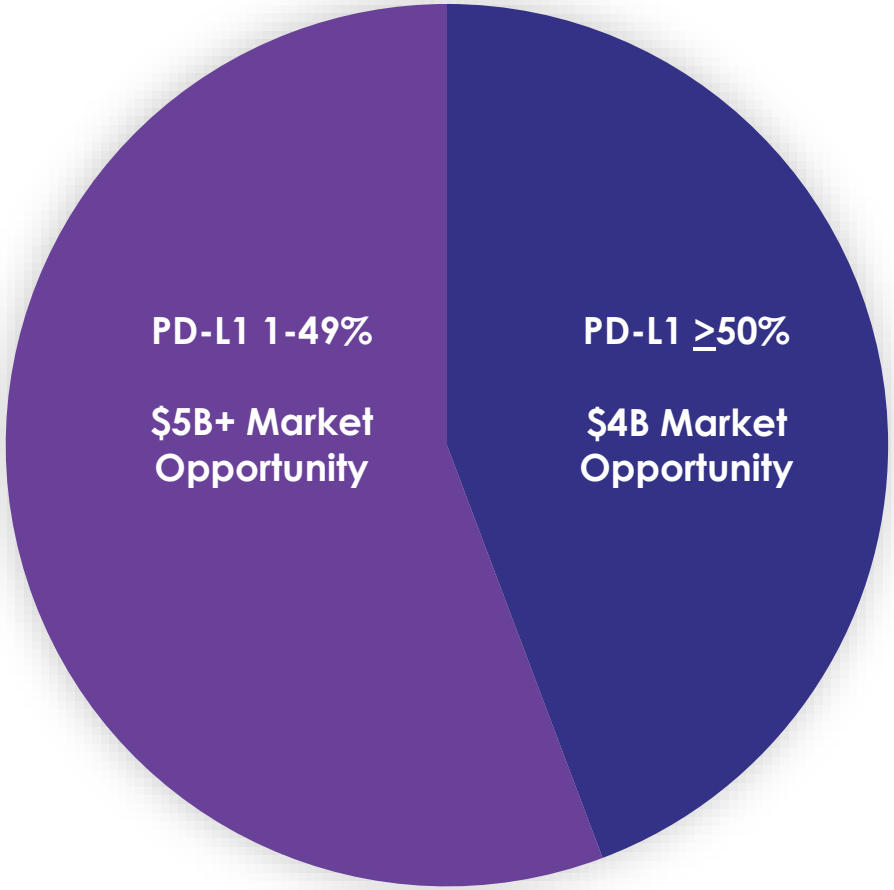
- PFS Hazard Ratio (HR) of 0.65 (p ≤0.2)
  - HR of 0.65 corresponds to 50% improvement in PFS
- Illustrative example
  - mPFS in control arm is expected to be ~7 months*
  - 50% improvement corresponds to mPFS of ~11 months

We believe HR of 0.65 or better is achievable in KICKSTART:

- In Phase 2a trial PFS benefit after progression was ~200% greater than comparator data from OAK trial
- KICKSTART is enrolling patients before progression
- KICKSTART is being enriched for PD-(L)1+ patients who demonstrated best results in Phase 2a (mPFS = 53 weeks)

* derived from KEYNOTE 042

$4 Billion U.S. Market Opportunity for Tomivosertib Represented by Patients with PD-L1≥50%

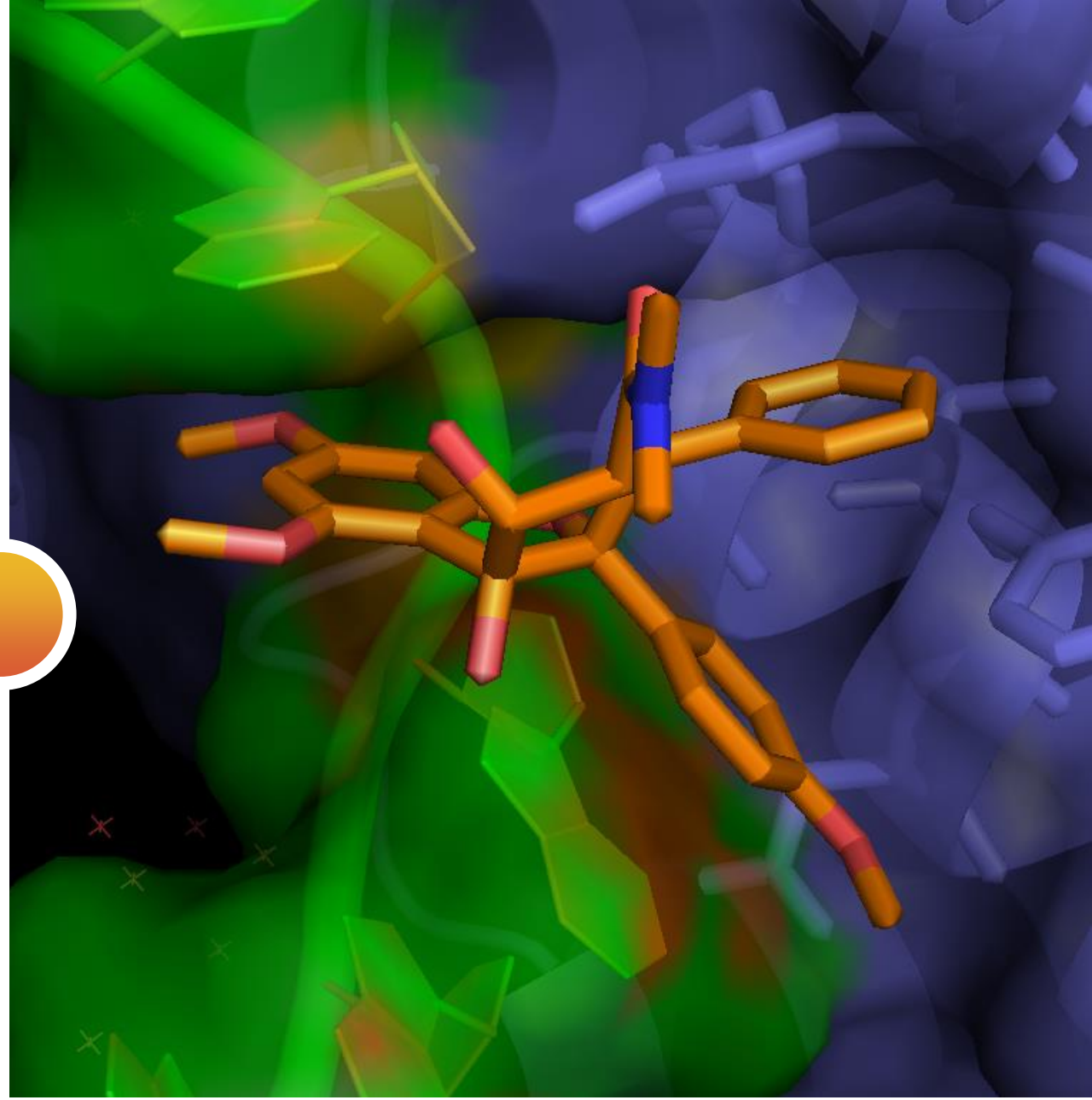


- KICKSTART trial focused on NSCLC patients with PD-L1 ≥ 50%
  - 27,000 patients annually in US
- Tomivosertib's mechanism also has potential to enhance response in patients with PD-L1 1-49%
  - Additional 43,000 patients annually in US

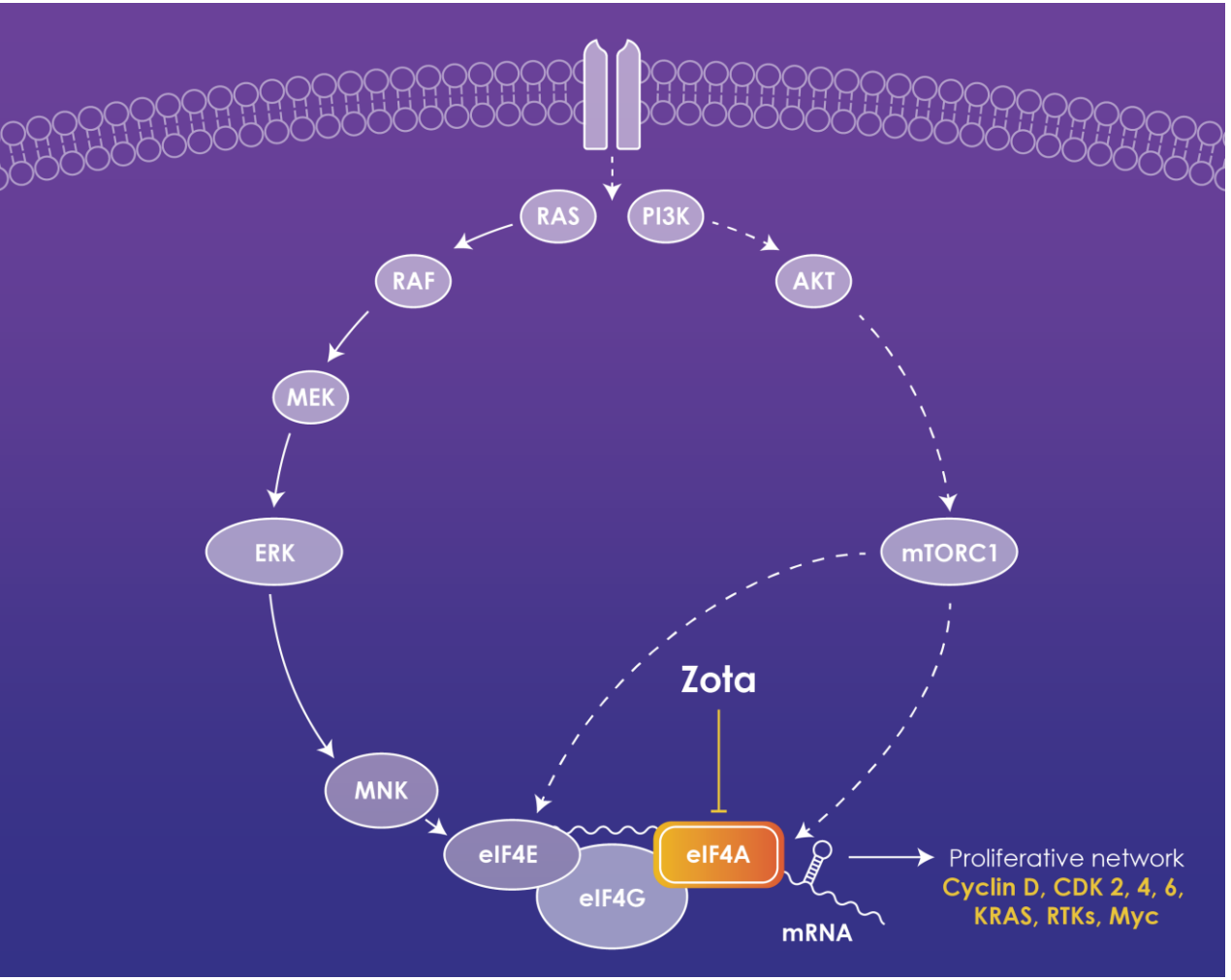
Zotatifin

eIF4A Helicase Inhibitor

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



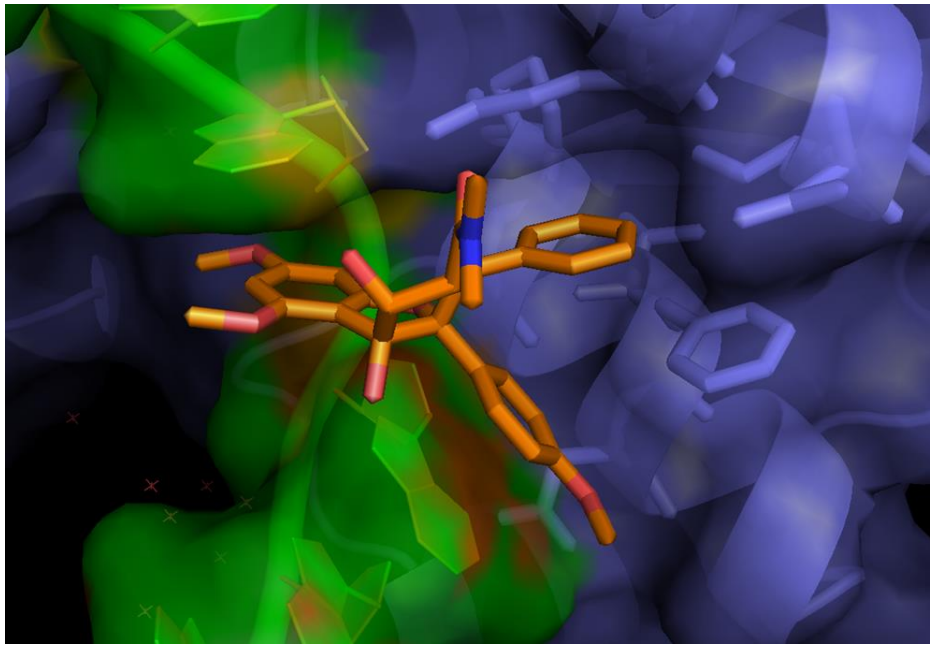
Zotatifin Designed to Suppress a Network of Important Tumor-Driving Proteins by Inhibiting eIF4A



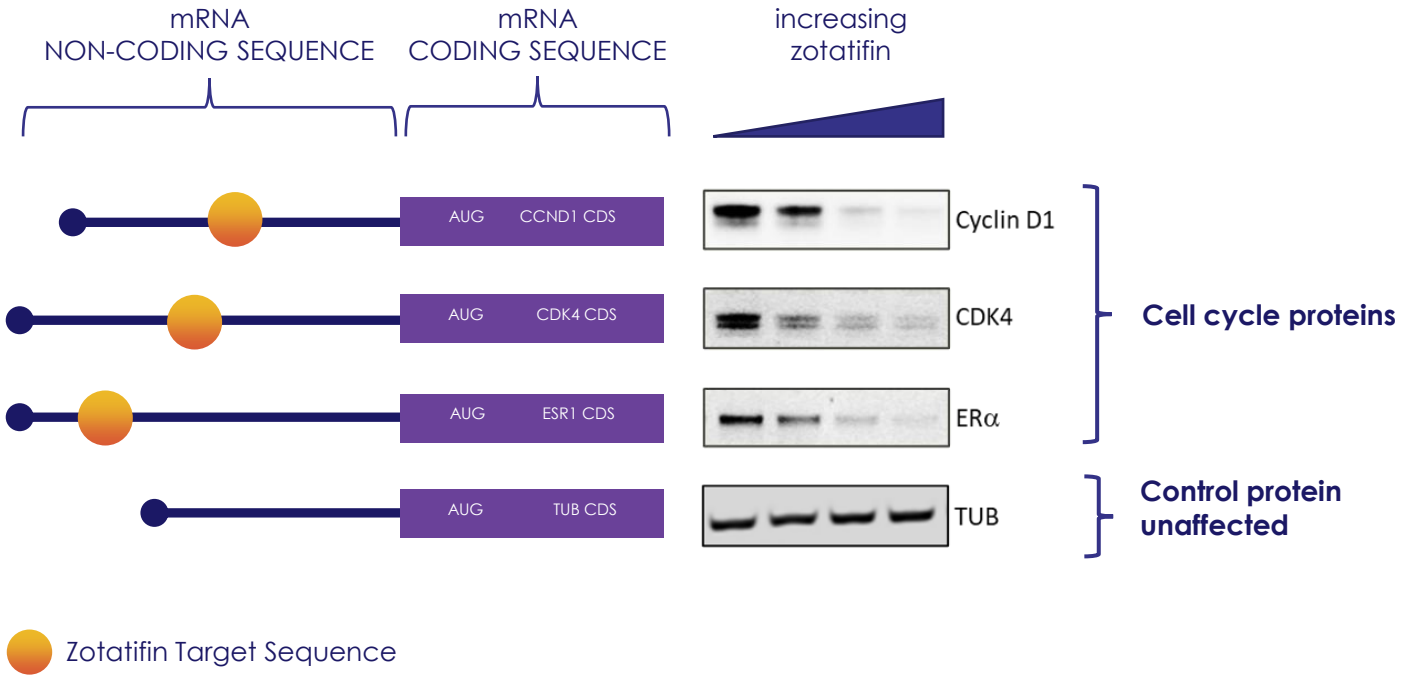
- Cancer signaling **activates eIF4A** to upregulate a network of tumor promoting proteins
- Zotatifin designed to **suppress the network** in a single product
- In preclinical studies, zotatifin downregulated a network of cell-cycle proteins and oncoproteins including:
  - **Cyclin D1** and **CDKs 2, 4, 6**
  - Estrogen receptor (**ERα**)
  - **RTKs** and **KRAS**

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



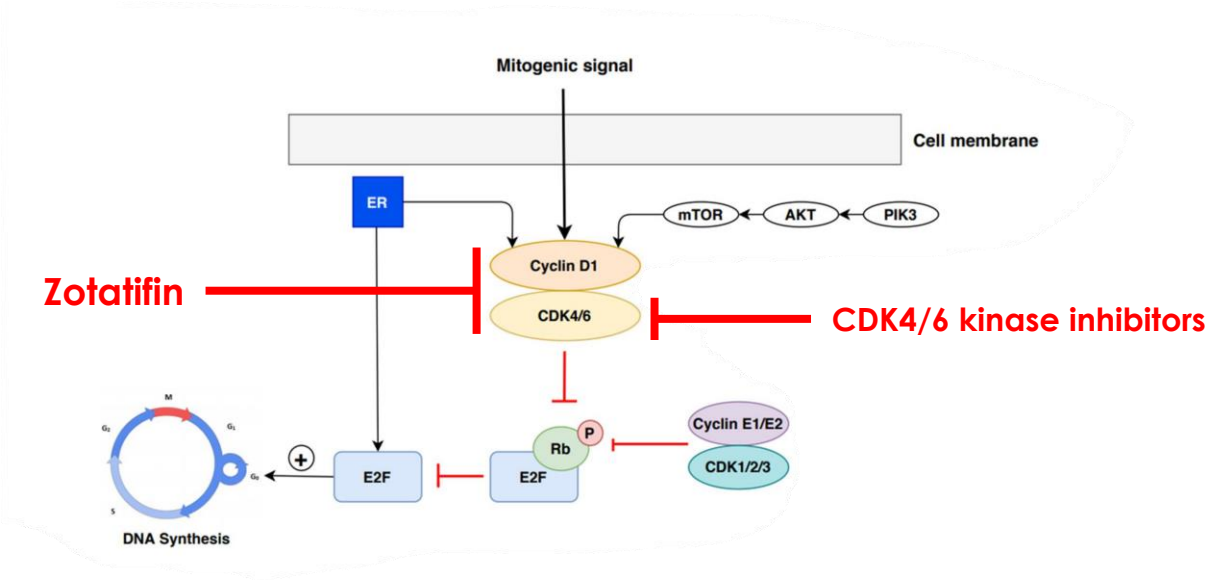
Experimental structure of natural product RocA bound to eIF4A and zotatifin RNA target sequence[1]



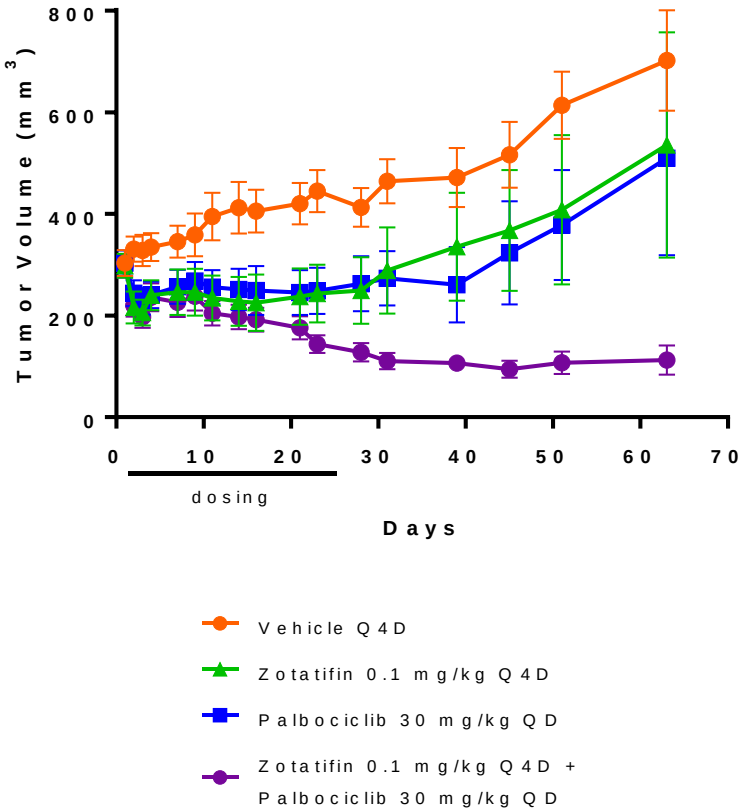
[1]Iwaski et al. 2019 Mol Cell (73) 738-748

Zotatifin Downregulation of Cyclin D1 and CDK4/6 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 Phase 1/2 Dose Escalation and Expansion Trial

COMPLETED

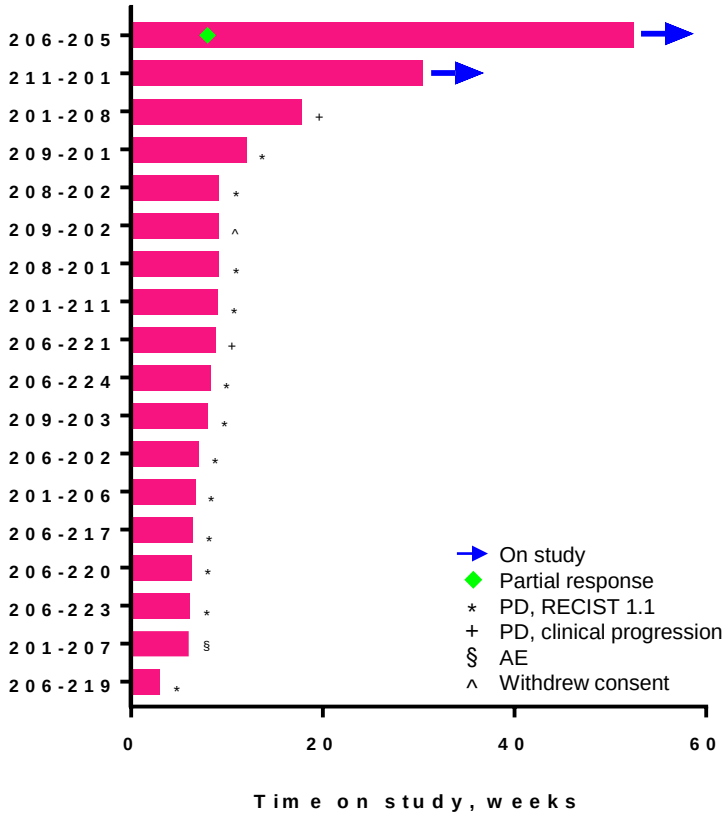
- Phase 1 dose escalation (3+3)
  - Identified 0.07 mg/kg on Days 1 and 8 of 21-day cycle as initial RP2D
- Confirmed PRs observed in early expansion cohorts in ER+ breast cancer
- Generally well tolerated as monotherapy and combined with fulvestrant
  - Low incidence of G3 AEs (each <10%)
  - Most common G 1/2 AEs were GI symptoms and anemia

ONGOING

- Expansion of triplet Z/F/A from 7 to 18 patients
  - Saw ORR of 29% and CBR of 43% in first 7 patients
  - **Data anticipated H1 2023**
- Based on good tolerability to date, resumed dose escalation as doublet with fulvestrant using every other week or weekly dosing
  - **Data anticipated H2 2023**

Z/F/A: zotatifin combined with fulvestrant and abemaciclib

ECBF Cohort
Zotatifin plus Fulvestrant



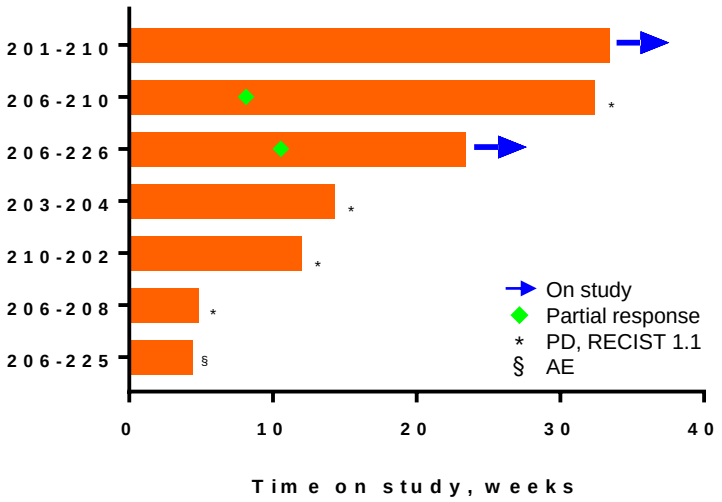
Genetics and Prior Treatments

- 206-205
  - Confirmed PR continuing at Week 52
  - Cyclin D1^{amp}, ESR1^{mut}
  - 7 lines of prior treatment including fulvestrant, palbociclib and ribociclib
- 211-201
  - Stable Disease ongoing at Week 30
  - PIK3CA^{mut}
  - 3 lines of prior treatment including fulvestrant and abemaciclib

Preliminary results from ongoing trial prior to database lock
Data cutoff December 15, 2022

ECBF+A Cohort
Zotatifin plus Fulvestrant and Abemaciclib

ORR 29% (2/7)
CBR 43% (3/7)



Clinical Benefit Rate (CBR) defined as proportion of patients with Confirmed Responses or Stable Disease lasting ≥ 24 weeks

Genetics and Prior Treatments

- 201-210
  - Stable Disease continuing at Week 33
  - Cyclin D1^{amp}, FGFR1^{amp}
  - 7 lines of prior treatment including palbociclib and letrozole
- 206-210
  - Confirmed PR, PFS of 28 Weeks
  - PIK3CA^{mut}
  - 3 lines of prior treatment including palbociclib, fulvestrant and alpelisib
- 206-226
  - Confirmed PR ongoing at Week 23
  - FGFR1^{amp}, NSD3^{amp}
  - 3 lines of prior treatment including palbociclib and fulvestrant

Preliminary results from ongoing trial prior to database lock
Data cutoff December 15, 2022

ECBF Cohort (Zotatifin plus Fulvestrant) Summary of Treatment-Emergent Adverse Events

TEAE Listing for ECBF	TEAEs (All Grades) N (%)	Grade 3 or Higher N (%)
	n=18	n=18
Nausea	7 (39%)	0 (%)
Constipation	5 (27%)	0 (%)
Abdominal pain	4 (22%)	0 (%)
Anemia	4 (22%)	1 (6%)
Diarrhea	4 (22%)	1 (6%)
Vomiting	4 (22%)	0 (%)
Dizziness	3 (17%)	0 (%)
Dry eye	3 (17%)	0 (%)
Dry mouth	3 (17%)	0 (%)
Fatigue	3 (17%)	0 (%)
Headache	3 (17%)	0 (%)
Alopecia	2 (11%)	0 (%)
Aspartate aminotransferase increased	2 (11%)	0 (%)
Contusion	2 (11%)	0 (%)
Cough	2 (11%)	0 (%)
Dyspnea	2 (11%)	1 (6%)
Hypotension	2 (11%)	1 (6%)
Non-cardiac chest pain	2 (11%)	0 (%)
Edema peripheral	2 (11%)	0 (%)
Sinus tachycardia	2 (11%)	0 (%)
Urinary tract infection	2 (11%)	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 and Maximum Reported CTCAE Grade for Subjects. Percentage is calculated using the number of treated subjects as the denominator. Preliminary results with data cutoff of December 15, 2022.

ECBF+A Cohort (Zotatifin plus Fulvestrant and Abemaciclib) Summary of Treatment-Emergent Adverse Events

TEAE Listing for ECBF+A	TEAEs (All Grades) N (%)	Grade 3 or Higher N (%)
	n=7	n=7
Diarrhea	5 (71%)	0 (%)
Nausea	4 (57%)	0 (%)
Dry mouth	3 (43%)	0 (%)
Fatigue	3 (43%)	0 (%)
Vomiting	3 (43%)	0 (%)
Constipation	2 (29%)	0 (%)
Dysgeusia	2 (29%)	0 (%)
Dyspnea	2 (29%)	0 (%)
Epistaxis	2 (29%)	0 (%)
Muscle spasms	2 (29%)	0 (%)
Myalgia	2 (29%)	0 (%)
Atrial fibrillation	1 (14%)	1 (14%)
Blood creatine phosphokinase increased	1 (14%)	1 (14%)
Corona virus infection	1 (14%)	0 (%)
Ear congestion	1 (14%)	0 (%)
Gastroesophageal reflux disease	1 (14%)	0 (%)
Hypomagnesaemia	1 (14%)	0 (%)
Limb discomfort	1 (14%)	0 (%)
Muscular weakness	1 (14%)	0 (%)
Non-cardiac chest pain	1 (14%)	0 (%)
Esophagitis	1 (14%)	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 and Maximum Reported CTCAE Grade for Subjects. Percentage is calculated using the number of treated subjects as the denominator. Preliminary results with data cutoff of December 15, 2022.

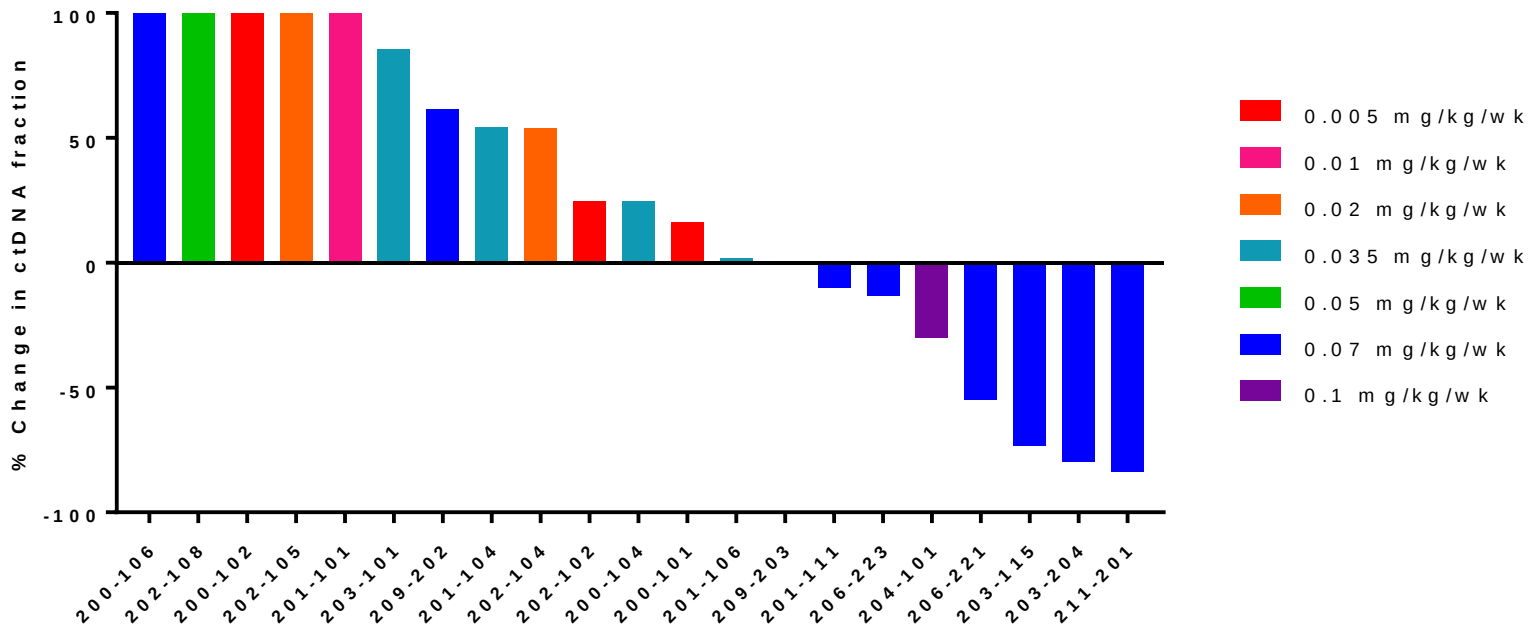
ECBF+A Cohort (Zotatifin plus Fulvestrant and Abemaciclib) Summary of Treatment-Emergent Adverse Events, cont'd

TEAE Listing for ECBF+A	All TEAEs (All Grades) (N %)	Grade 3 or Higher N(%)
	n=7	n=7
Pain in extremity	1 (14%)	0 (%)
Palpitations	1 (14%)	0 (%)
Pleural effusion	1 (14%)	0 (%)
Presyncope	1 (14%)	0 (%)
Proteinuria	1 (14%)	1 (14%)
Pruritus	1 (14%)	0 (%)
Rash maculo-papular	1 (14%)	0 (%)
Rhabdomyolysis	1 (14%)	1 (14%)
Sinus tachycardia	1 (14%)	0 (%)
Stomatitis	1 (14%)	0 (%)
Thrombocytopenia	1 (14%)	0 (%)
Vertigo	1 (14%)	0 (%)
Vision blurred	1 (14%)	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 and Maximum Reported CTCAE Grade for Subjects. Percentage is calculated using the number of treated subjects as the denominator. Preliminary results with data cutoff of December 15, 2022.

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

Fraction of ctDNA decreased at higher doses of zotatifin



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. Preliminary results with a data cutoff of December 15, 2022

Zotatifin Clinical Summary and Next Steps

- Clinical activity observed in ER+ breast cancer
- Multiple demonstrations of pharmacodynamic effects
  - Highly selective down-regulation of specific proteins with <1% deviation in overall protein levels
  - Target engagement demonstrated by selective stabilization of zotatifin-sensitive RNA
  - Decrease in fraction of ctDNA observed at 0.07 and 0.1 mg/kg
- Zotatifin has been generally well tolerated to date as monotherapy and in doublet or triplet combinations
- ECBA+A cohort has been expanded from 7 to 18 patients
- Given safety results to date, have resumed dose escalation in combination with fulvestrant
- Steady flow of data anticipated in 2023
  - Topline data for full 18 patients in ECBF+A in H1 2023
  - Topline data from dose escalation expected in H2 2023

Additional Program Opportunities

Tomivosertib

- Expand to additional segments of NSCLC based on PD-L1 status
- Expansion into other immuno-responsive tumors (renal, bladder, MSI-H)

Zotatifin – Oncology

- Expansion into additional biomarker-specific cohorts

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

- Cash, cash equivalents and short-term investments as of December 31, 2022 = **$26.3M**
  - Cash used in operating activities for FY22 = $25.9M

- Current cash expected to fund operations into Q1-24 and allow for readout of:
  - Topline data from P2b KICKSTART trial evaluating tomivosertib in combination with pembrolizumab in patients with NSCLC
  - Initial ORR data from additional 11 patients added to ECBF+A P2a expansion cohort of zotatifin (n=18 total)
  - Data from P1b dose escalation cohorts with zotatifin

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 remaining 11 patients in ECBF+A P2a (n=18) expansion cohort	●		
	Data from dose escalation cohorts		●	
	Initiate potentially registrational P2b study			●

Next Generation Targeted Therapy for Cancer

Corporate Presentation | April 2023

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