UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
PURSUANT TO SECTION 13 OR 15(d)
OF THE SECURITIES EXCHANGE ACT OF 1934

Date of Report (Date of earliest event reported): January 5, 2023

eFFECTOR Therapeutics, Inc.
(Exact name of registrant as specified in its charter)

Delaware	**001-39866**	**85-3306396**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(I.R.S. Employer Identification No.)**

142 North Cedros Avenue, Suite B **Solana Beach, California** **(Address of principal executive offices)**	**92075** **(Zip Code)**

(858) 925-8215
(Registrant's telephone number, including area code)

(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common stock, $0.0001 par value per share	EFTR	Nasdaq Capital Market
Warrants to purchase common stock	EFTRW	Nasdaq Capital Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (Sec.230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (Sec.240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

On January 5, 2023, eFFECTOR Therapeutics, Inc. (the "Company") hosted a conference call with accompanying slides to discuss updates to the Company's clinical program and other matters. A copy of the slide presentation is filed as Exhibit 99.1 hereto and incorporated herein by reference.

The information in Item 7.01 of this Current Report on Form 8-K, including the slides incorporated herein by reference, is being furnished and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, and it shall not be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or under the Exchange Act, whether made before or after the date hereof, except as expressly set forth by specific reference in such filing to this Item 7.01 of this Current Report on Form 8-K.

Item 8.01 Other Events.

On January 5, 2023, the Company provided an update of its ongoing clinical development programs with both zotatifin, in Phase 2 expansion cohorts for the treatment of ER+ breast cancer ("ER+ BC") and KRAS non-small cell lung cancer ("KRAS NSCLC") as well as Phase 1 development for SARS-CoV-2 ("COVID-19"), and tomivosertib, in Phase 2 development for treatment of non-small cell lung cancer ("NSCLC") in combination with pembrolizumab, an established anti-immune checkpoint inhibitor used to treat various types of cancer. The below data update for the zotatifin Phase 2 program is as of a data cutoff date of December 15, 2022.

In the ECBF+A cohort (n=7) receiving zotatifin, fulvestrant and abemaciclib, two patients experienced confirmed partial responses ("PRs"), and a third patient had stable disease continuing beyond 24 weeks, for an objective response rate ("ORR") of 29% (2/7) and a clinical benefit rate ("CBR") of 43% (3/7). Zotatifin was generally safe and well-tolerated in this triplet combination. ORR and CBR data for the remaining 11 patients is anticipated to be available in the first half of 2023.

In addition, in the ECBF cohort (n=18) receiving zotatifin and fulvestrant, one patient experienced a confirmed PR continuing beyond Week 52 and one patient had stable disease continuing beyond 24 weeks. Zotatifin was generally safe and well-tolerated in this doublet combination. Dose-dependent target engagement was observed by two independent methods, without obvious signs of target saturation. Therefore, the Company has resumed dose escalation with topline data anticipated in the second half of 2023.

The Company is deferring initiation of the Cyclin D1 amplification cohort in ER+ BC and pausing enrollment in the KRAS G12C lung cancer cohort until completion of dose escalation.

The Company has also completed enrollment in the third and final cohort in its Phase 1b study with zotatifin in COVID-19, and anticipates providing topline data from this trial in the first half of 2023.

With respect to the tomivosertib program, the Company has experienced enrollment challenges across both cohorts resulting from staffing issues across clinical sites and competition from other trials. The Company is focusing its efforts on completing enrollment in the front-line PD-L1 $\geq$50% cohort and now anticipates topline data from this cohort in the second half of 2023. The Company is discontinuing further enrollment of the PD-L1 $\geq$1% maintenance cohort.

Based on its updated development plans, the Company believes its existing cash resources will be sufficient to fund operations into the first quarter of 2024.

Cautionary Note Regarding Forward-Looking Statements

The Company cautions you that statements contained in this report regarding matters that are not historical facts are forward-looking statements. The forward-looking statements are based on our current beliefs and expectations and include, but are not limited to: the future clinical development of our product candidates, including expectations on enrollment and the timing of reporting data from ongoing clinical trials; the planned expanded

development of zotatifin and the timing thereof; the potential therapeutic benefits of our product candidates; the potential market opportunity for our product candidates; and our expected cash runway and the sufficiency of our capital resources to allow clinical trial data readouts and the expansion of our clinical development programs. Actual results may differ from those set forth in this report due to the risks and uncertainties inherent in our business, including, without limitation: 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; additional disruptions to our operations from the COVID-19 pandemic, including clinical trial and manufacturing delays; 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; we may use our capital resources sooner than expected and they may be insufficient to allow clinical trial readouts; regulatory developments in the United States and foreign countries; 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; any future impacts to our business resulting from the conflict between Russia and Ukraine and other risks described in our prior filings with the Securities and Exchange Commission. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof, and we undertake no obligation to update such statements to reflect events that occur or circumstances that exist after the date hereof. 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.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Slide Presentation
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

eFFECTOR Therapeutics, Inc.

Date: January 5, 2023

By: /s/ Michael Byrnes
Name: Michael Byrnes
Title: Chief Financial Officer

Exhibit 99.1

Zotatifin Clinical Data and Corporate Update

January 5, 2023

eFFECTOR

Disclaimer

FORWARD-LOOKING STATEMENTS

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 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; additional disruptions to our operations from the COVID-19 pandemic, including clinical trial and manufacturing delays; 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; we may use our capital resources sooner than expected and they may be insufficient to allow clinical trial readouts; regulatory developments in the United States and foreign countries; 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; any future impacts to our business resulting from the conflict between Russia and Ukraine 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.

CLINICAL INVESTIGATION/FDA

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.

TRADEMARKS

This presentation contains trademarks, service marks, and trade names of the Company and other companies, which are the property of their respective owners.

Zotatifin Clinical Data and Corporate Update

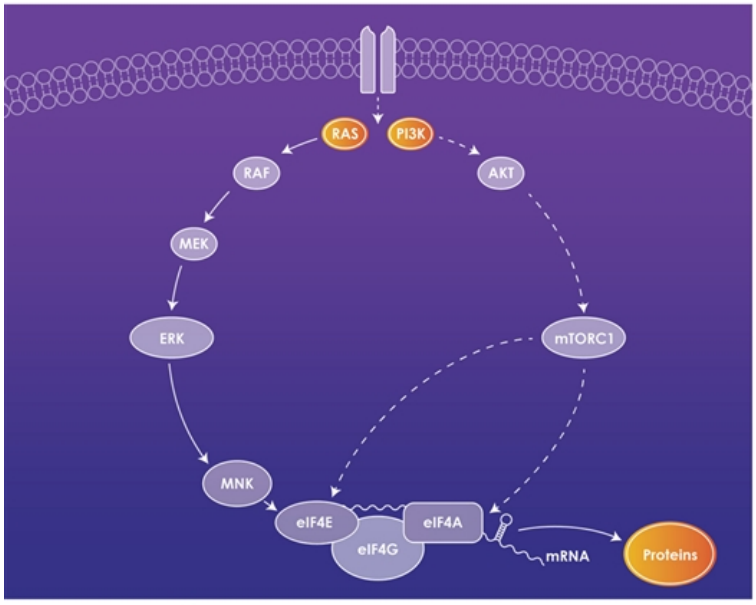
Participants

- Steve Worland, Ph.D., President & CEO
- Doug Warner, M.D., Chief Medical Officer
- Mike Byrnes, Chief Financial Officer

Agenda

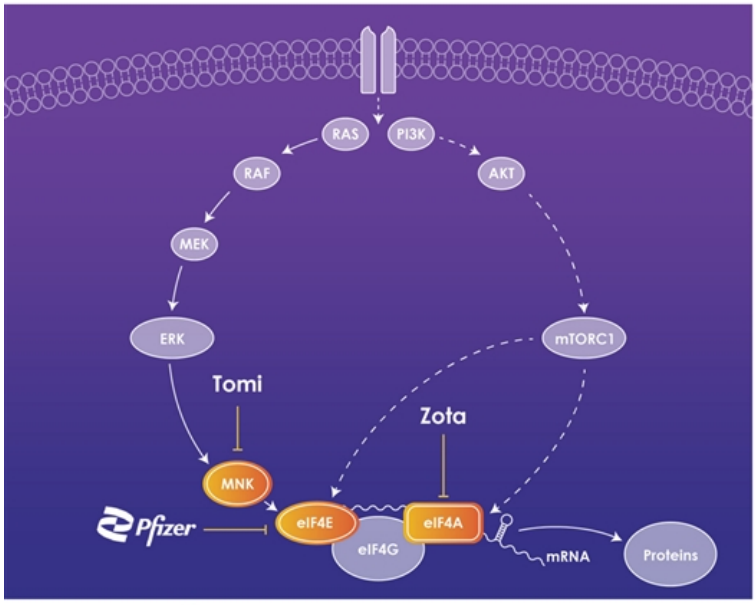
- Introductory Remarks
- Zotatifin Oncology Update
- Zotatifin COVID Update
- Tomivosertib Update
- Business Update and Closing Remarks
- Q&A

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

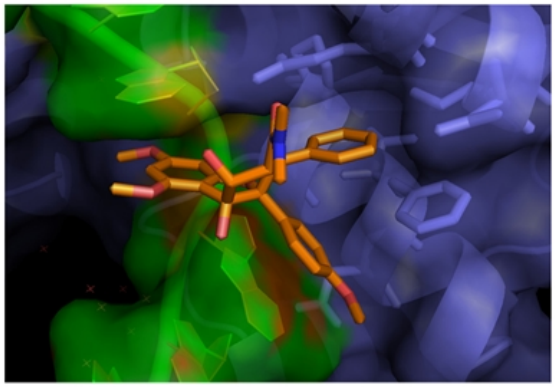
Selective Translation Regulator Inhibitor (STRI) Platform: Controlling the Outputs of Tumor-driving Pathways



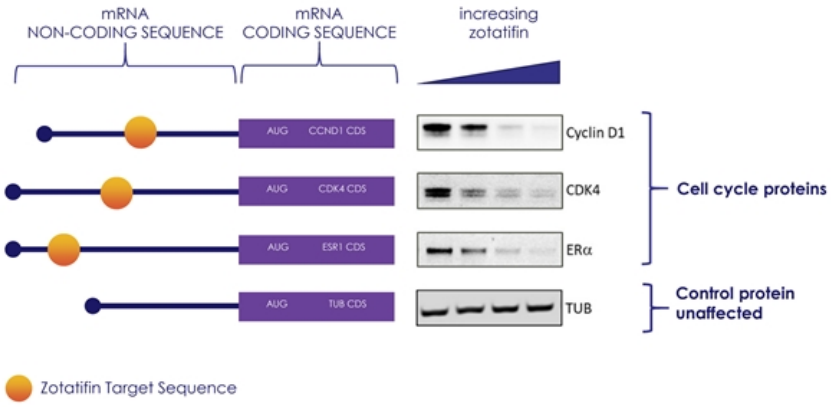
- Focused on three targets that drive translation:
  - **MNK:** kinase phosphorylates RNA-binding proteins
  - **eIF4A:** helicase unwinds RNA secondary structures
  - **eIF4E:** binds 5'-cap of mRNA
- Each target controls production of a distinct set of proteins
  - STRI platform enabled identification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

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]



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

Zotatifin Phase 1/2 Dose Escalation and Expansion Trial

Part 1 Dose Escalation

- Open label 3+3 design in mixed population
- Weekly dosing transitioned to two weeks on/one week off
- **Primary Objectives** include
  - Safety, tolerability, MTD and RP2D
- **Secondary Objectives** include
  - Preliminary anti-tumor activity

Part 2 Expansion Cohorts

- Simon 2-stage design (Stage 1, N=7; Stage 2, N=11)
- Dose of 0.07 mg/kg given on Day 1 and 8 of 21-day cycle
- **Primary Objectives** include
  - Preliminary anti-tumor activity as monotherapy and in combination
  - MTD or RP2D of zotatifin as combination therapy
- **Secondary Objectives** include
  - Safety of zotatifin as monotherapy and as combination therapy
  - Progression free survival (PFS)

Expansion Cohorts in ER+ BC Combined with fulvestrant +/- abemaciclib

ECBF ER+ BC zotatifin + fulvestrant	Post-endocrine and CDK4/6 therapy No limit to prior lines
ECBF + A ER+/HER2- zotatifin + fulvestrant + abemaciclib	Post-endocrine therapy No limit to prior lines

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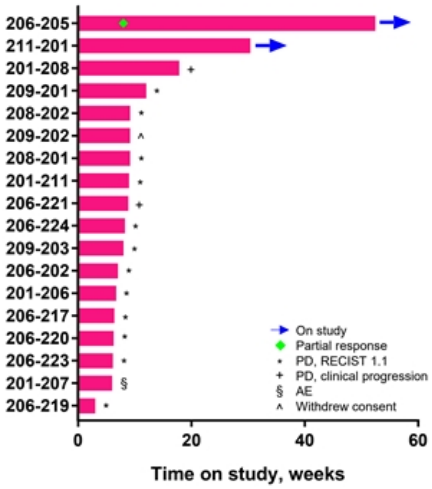
ECBF Cohort
Zotatifin plus Fulvestrant



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

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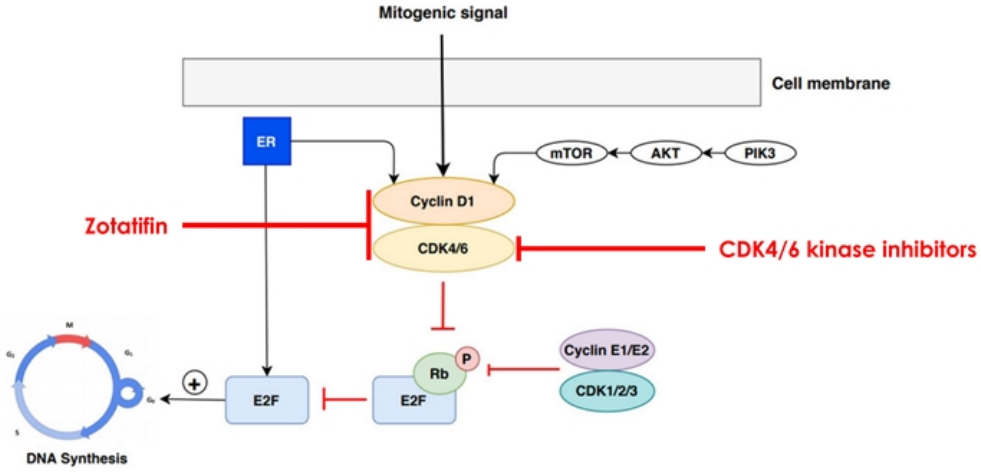
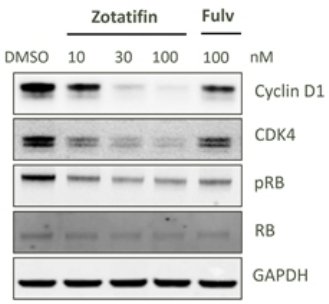
Preliminary results from ongoing trial prior to database lock
Data cutoff December 15, 2022

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

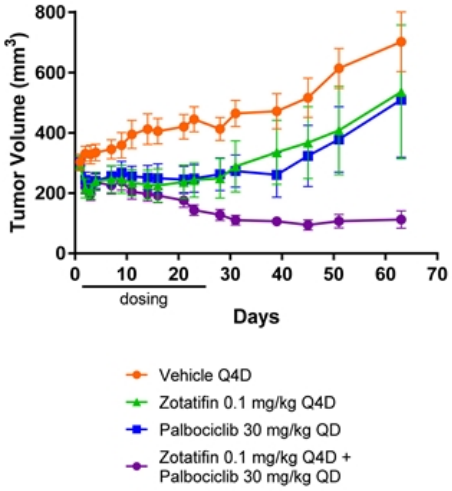


Zotatifin Downregulated Cyclin D1 and CDK4/6 *in vitro*
Combination of Zotatifin with Palbociclib Was Highly Active *in vivo*

Zotatifin Blocked Production of Key Cell Cycle Targets in Cells

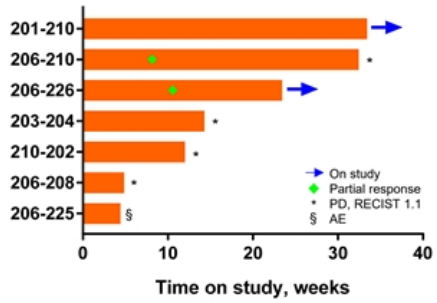


Zotatifin Was Active in Preclinical Models of ER+ BC and Showed Combination Benefit with Palbociclib



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
- 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

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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.

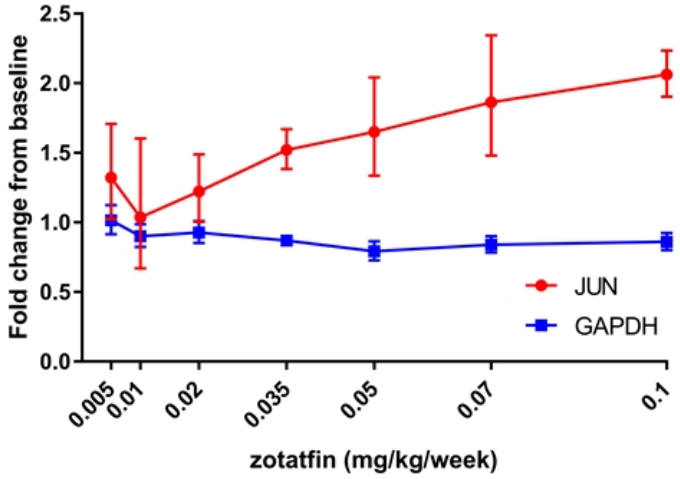
ECBF+A Cohort (Zotatifin plus Fulvestrant and Abemaciclib) Summary of Treatment-Emergent Adverse Events, cont'd

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 Stabilization of Zotatifin-Sensitive RNA in Whole Blood

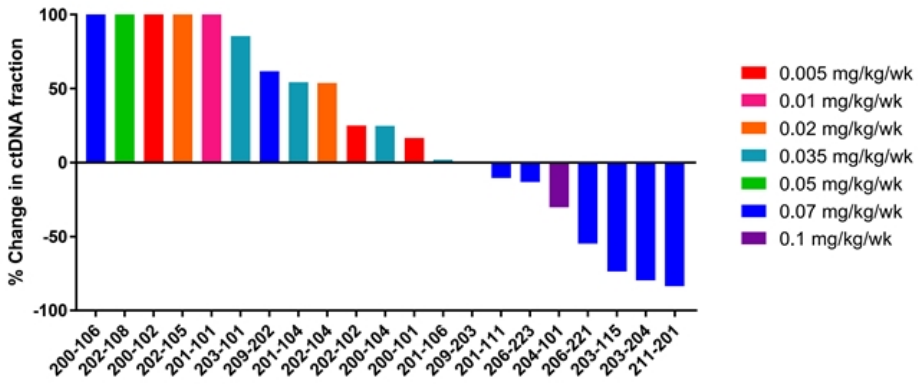
Formation of ternary complex between zotatifin, eIF4A and RNA resulted in selective, dose-dependent stabilization of JUN RNA relative to housekeeping gene GAPDH



RNA levels in whole blood, assayed by Nanostring ® methodology, are plotted as geometric mean of fold-induction 4 and 8 hrs after zotatifin administration
Preliminary results with a 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



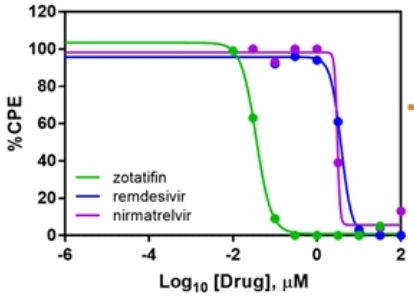
Fraction of ctDNA relative to total DNA was measured at baseline and after treatment with zotatifin. % change in ctDNA fraction after treatment relative to baseline is plotted. Preliminary results with a data cutoff of December 15, 2022

Good Safety Results with Zotatifin To Date Motivate Additional Dose Escalation

- Resumed dose escalation at 0.1 mg/kg dosed every other week (Q2W)
  - Preclinical *in vivo* data showed full retention of anti-tumor activity with extended-interval dosing
- Also plan to resume testing weekly (QW) dosing, starting at 0.07 mg/kg
  - Testing weekly dosing in case relationships between pharmacokinetics, pharmacodynamics and activity are different between human disease and mouse models
- Expect data from both dosing regimens 2H 2023

Zotatifin Well Positioned as Host-Directed Therapeutic for COVID-19 and Beyond

Zotatifin observed to be more potent *in vitro* than remdesivir and nirmatrelvir*



Phase 1b Double-Blind Trial Ongoing

- N=36, non hospitalized patients with mild to moderate COVID-19 severity
- Sequential cohort dosing:
  - 0.01 mg/kg
  - .02 mg/kg
  - .035 mg/kg

Future Development

- Continued widespread COVID-19 cases and potential for future zoonotic transmissions suggests pressing need for continued development of novel anti-coronavirus therapeutics

- Zotatifin inhibits eIF4A, preventing production of the viral proteins needed for SARS-CoV-2 replication
- Sub-cutaneous formulation with single injection aligns with Test to Treat initiative
- COVID-19 program funded by $5M cooperative agreement with DARPA and UCSF
- **Enrollment in all three cohorts now completed**

Topline safety and antiviral data expected in 1H 2023

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*tested head-to-head in same assay against Omicron BA.2 strain of SARS-CoV-2

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

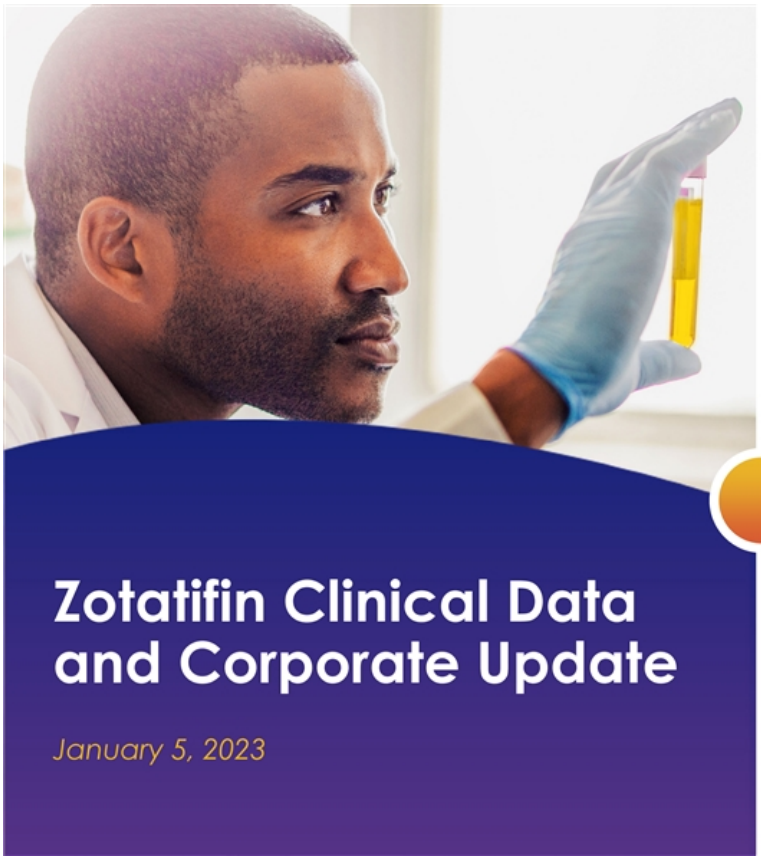
- **Topline data readout anticipated 2H 2023**

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 P1b dose escalation cohorts		●	
	Initiate potentially registrational P2b study			●
Zotatifin COVID-19	Top line data from Phase 1b study	●		

eFFECTOR

Q&A



Zotatifin Clinical Data and Corporate Update

January 5, 2023

eFFECTOR