Zacks Small-Cap Research

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ESSA Pharma Inc

(EPIX-NASDAQ)

EPIX: Dose Escalation Data for Combination of Masofaniten (EPI-7386) and Enzalutamide Presented at PCF Retreat…

Based on our probability adjusted DCF model that takes into account potential future revenues from EPI-7386 and the ANITAC program, EPIX is valued at $27/share. This model is highly dependent upon continued clinical success of EPI-7386/TPD and will be adjusted accordingly based upon future clinical results.

Current Price (10/30/23)	$4.42
Valuation	**$27.00**

OUTLOOK

On October 26, 2023, ESSA Pharma Inc. (EPIX) announced updated data from the dose escalation portion of the Phase 1/2 clinical trial of masofaniten (EPI-7386) in combination with enzalutamide was presented at the 30th Annual Prostate Cancer Foundation Scientific Retreat. The data show that the combination of masofaniten and enzalutamide is well tolerated and causes deep and sustained decreases in prostate-specific antigen (PSA) in patients with metastatic castration-resistant prostate cancer (mCRPC). Across all dose cohorts, 88% of patients (14/16) achieved PSA50, 81% of patients (13/16) achieved PSA90, and 56% of patients (9/16) achieved PSA <0.2 ng/mL. The company has selected a dose of 600 mg BID for masofaniten and 160 mg daily of enzalutamide (the full dose per label) for the Phase 2 portion of the study, which is currently enrolling.

SUMMARY DATA

52-Week High	**$4.59**
52-Week Low	**$2.35**
One-Year Return (%)	**0.23**
Beta	**2.02**
Average Daily Volume (sh)	**379,547**
Shares Outstanding (mil)	**44**
Market Capitalization ($mil)	**$195**
Short Interest Ratio (days)	**1**
Institutional Ownership (%)	**75**
Insider Ownership (%)	**12**
Annual Cash Dividend	**$0.00**
Dividend Yield (%)	**0.00**
5-Yr. Historical Growth Rates	
Sales (%)	**N/A**
Earnings Per Share (%)	**N/A**
Dividend (%)	**N/A**
P/E using TTM EPS	**N/A**
P/E using 2020 Estimate	**-4.2**
P/E using 2021 Estimate	**-3.3**

Risk Level	**High**
Type of Stock	**Small-Value**
Industry	**Med-Drugs**

ZACKS ESTIMATES

Revenue
(in millions of $)

	Q1 (Dec)	Q2 (Mar)	Q3 (Jun)	Q4 (Sep)	Year (Sep)
2022	0 A	0 A	0 A	0 A	0 A
2023	0 A	0 A	0 A	0 E	0 E
2024					0 E
2025					0 E

Earnings per Share

	Q1 (Dec)	Q2 (Mar)	Q3 (Jun)	Q4 (Sep)	Year (Sep)
2022	-$0.21 A	-$0.25 A	-$0.20 A	-$0.14 A	-$0.80 A
2023	-$0.15 A	-$0.16 A	-$0.17 A	-$0.25 E	-$0.72 E
2024					-$0.98 E
2025					-$1.09 E

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WHAT'S NEW

Business Update

Dose Escalation Data Presented at ESMO 2023

On October 26, 2023, ESSA Pharma Inc. (EPIX) announced that updated data from the dose escalation portion of the Phase 1/2 trial of masofaniten (EPI-7386) and enzalutamide (Enz) was presented at the 30th Annual Prostate Cancer Foundation Scientific Retreat. This is an open-label trial enrolling patients with metastatic castration-resistant prostate cancer (mCRPC) that are currently on androgen deprivation therapy and are naïve to second-generation antiandrogens (1 line of prior chemotherapy in the metastatic hormone sensitive (mHSPC) setting is allowed) (NCT05075577). The primary and secondary endpoints of the Phase 1 portion of the study were to evaluate the safety and pharmacokinetics (PK) of masofaniten and Enz when co-administered in order to establish a recommended Phase 2 combination dose (RP2CD) as well as to evaluate possible drug-drug interactions (DDIs). A copy of the poster can be found here.

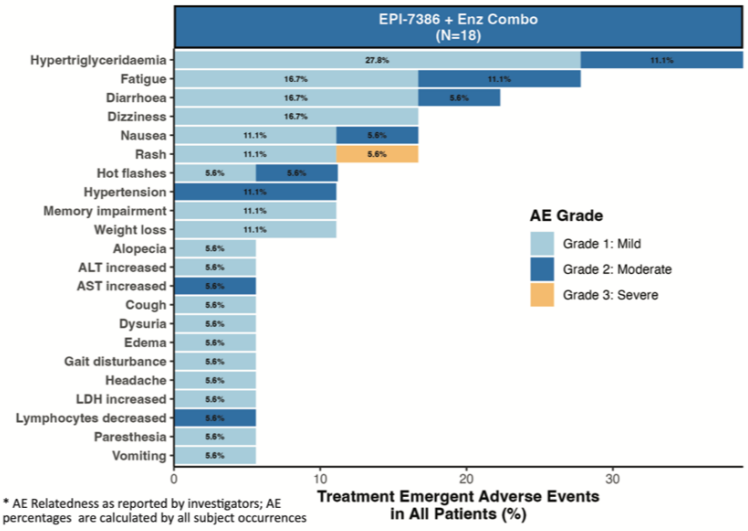
The Phase 1 portion of the study enrolled 18 patients in four dose cohorts, with 16 patients evaluable for efficacy as per protocol. The following table gives an overview of the patients baseline characteristics for each dosing cohort.

Parameter N=18	Cohort 1 Masofaniten 600mg QD + Enz 120mg QD n=3[1]	Cohort 2 Masofaniten 800mg QD + Enz 120mg QD n=4[1]	Cohort 3 Masofaniten 600mg BID + Enz 120mg QD n=4	Cohort 4 Masofaniten 600mg BID + Enz 160mg QD n=7
Median age (range), yrs.	70.0 (68-73)	73.5 (61-86)	72.0 (60-75)	75.0 (65-89)
ECOG performance status, n (%)				
0	0 (0%)	2 (50.0%)	2 (50.0%)	5 (71.4%)
1	3 (100.0%)	2 (50.0%)	2 (50.0%)	2 (28.6%)
Bone Only Disease	1 (33.3%)	4 (100.0%)	3 (75.0%)	1 (14.3%)
Prior Chemotherapy, n (%)	2 (66.6%)	3 (75.0%)	1 (25.0%)	2 (28.6%)
Median Baseline PSA (range), ng/mL	24.9 (2.6-26.4)	2.54 (1.84-1209)	2.13 (1.35- 20.6)[2]	13.5 (1.18-565)[3]

[1]2 of the 3 subjects from the masofaniten 600mg QD cohort dose escalated to the masofaniten 800mg QD cohort after 9 cycles. 2 of the 3 subjects from the masofaniten 800mg QD cohort dose escalated to the masofaniten 600mg BID cohort after 8-10 cycles
[2] Masofaniten 600mg BID + Enza 120mg QD, 1/4 baseline PSA result was obtained with local lab
[3] Masofaniten 600mg BID + Enza 160mg QD , 1/7 baseline PSA result was obtained with local lab

Source: Laccetti *et al.*, 2023

The combination of masofaniten and Enz is safe and well tolerated, with an adverse event profile that is consistent with single-agent Enz. The following table shows that the most frequent adverse events (AEs) were either related to androgen receptor inhibition or gastrointestinal tract irritation and were Grade 1 or 2 in severity. In Cohort 4, there was a report of a Grade 3 rash that was deemed to be possibly related to study drug. It was observed after administration of masofaniten and Enz in combination during the dose-limiting toxicity period. The patient has since discontinued the study due to disease progression. It should be noted that the monotherapy study of masofaniten did not report a similar rash, while Enz's Phase 1 dose escalation study had a rash as a dose limiting toxicity at higher Enz exposures.

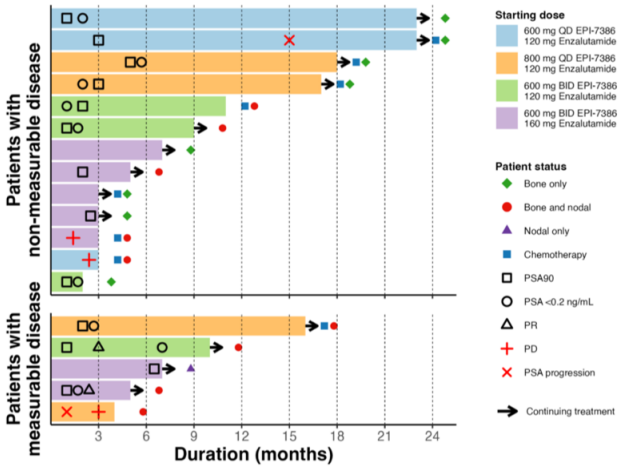


* AE Relatedness as reported by investigators; AE percentages are calculated by all subject occurrences

Source: Laccetti *et al.*, 2023

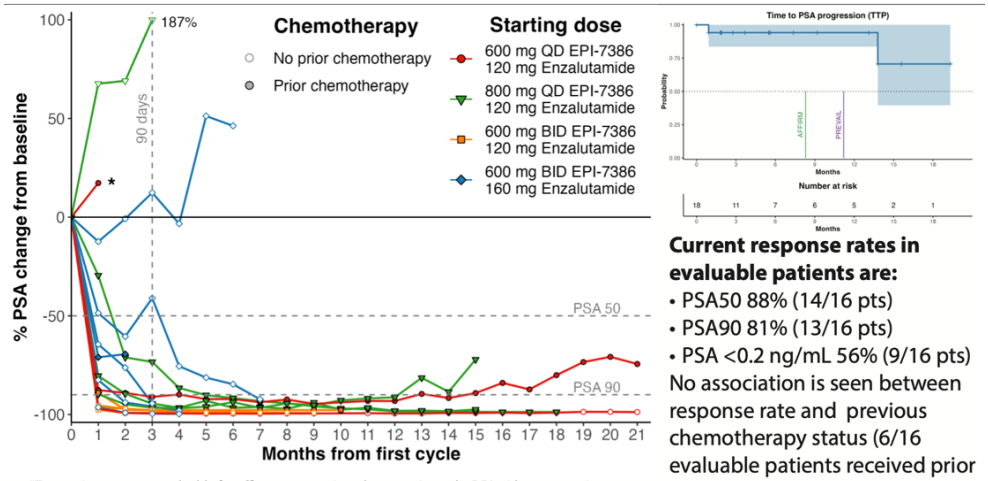
To investigate drug-drug interactions (DDIs), a 7-day run-in period with masofaniten was initiated at the beginning of Cycle 1 for each dose before introducing Enz. Serum levels of masofaniten, Enz, and N-desmethyl Enz were measured. The results show that masofaniten does not affect the metabolism of Enz with similar PK parameters regardless of the dose of masofaniten or Enz. However, Enz does affect the metabolism of masofaniten, resulting in a decrease in PK parameters such as AUC and Cmax. After switching the masofaniten dosing from 600 mg QD to 600 mg BID, the drop in exposure caused by Enz was partially mitigated and masofaniten stayed at clinically relevant levels.

The following chart shows the current patient disposition. Of the 18 patients enrolled in the trial, 13 are still on treatment and five have discontinued (disease progression = 3; brain abscess = 1 (non-related event); non-cancer related death = 1). Of the 18 enrolled patients, 13 have non-measurable disease while five have measurable disease. Of the five with measurable disease, two had a partial response, two had stable disease, and one had progressive disease.



Source: Laccetti *et al.*, 2023

Across all dosing cohorts, patients showed a rapid, deep, and durable decrease in prostate-specific antigen (PSA). The following chart shows the PSA outcomes for all enrolled patients, including for patients from Cohort 4. The current response rates in evaluable patients show that 88% (14/16) have achieved PSA50 (a 50% decrease in PSA levels from baseline), 81% (13/16) have achieved PSA90 (a 90% decrease in PSA levels from baseline), and 56% (9/16) have achieved PSA <0.2 ng/mL. In addition, the graph in the upper right shows the time to PSA progression and how that compares to the Phase 3 PREVAIL trial and the P3 AFFIRM trial, which examined Enz in the pre-chemotherapy and post-chemotherapy setting, respectively.



*Two patients are not evaluable for efficacy: one patient that experienced a DDI with a concomitant drug, and another DLT patient (not plotted past baseline)

Source: Laccetti *et al.*, 2023

While difficult to do cross-trial comparisons, the Phase 3 clinical trials of Enz show what is to be expected when treating patients either pre-chemotherapy (PREVAIL trial; Beer *et al*., 2014) or post-chemotherapy (AFFIRM trial; Scher *et al*., 2012) with single agent Enz. The following table summarizes the data from those trials in regards to PSA response.

	N	PSA50	PSA90	PSA <0.2ng/mL
Enz+Mas	16	88%	81%	56%
PREVAIL	854	78%	47%	11%
AFFIRM	731	54%	25%	ND

Sources: Beer *et al*., 2014; Scher *et al*., 2012; ESSA Pharmaceuticals Inc.; Zacks SCR

PSA response is an important prognosticator, as it was shown to be correlated with a number of positive outcomes from the PREVAIL study (Armstrong *et al*., 2019). This agrees with multiple other studies of hormone-sensitive prostate cancer (HSPC) patients that show greater PSA responses are associated with better long-term prognoses. In addition, PSA response was shown to correlated with five-year survival in the PREVAIL study:

- Armstrong *et al*., 2020: This was a long-term safety and efficacy analysis of the PREVAIL trial that evaluated 5-year survival and its correlation with various pretreatment prognostic factors and post-treatment PSA declines. The results showed that the 5-year survival rate for those with a best overall PSA decline of < 0.2 ng/mL was 71% compared to just 11% for those with no PSA decline or < 30% confirmed decline. Even for those who achieved PSA90, the 5-year survival rate was only 42%. This exemplifies the importance of achieving PSA < 0.2 ng/mL and how that can have a positive impact on long-term survival. Approximately 11% (100/872) of patients treated with Enz in PREVAIL achieved PSA < 0.2 ng/mL.

PSA responses of < 0.2 ng/mL do not appear to be commonly reported in studies of mCRPC patients, however the Phase 3 ACIS study showed that 25% of mCRPC patients treated with apalutamide plus abiraterone acetate and prednisone achieved a PSA level < 0.2 ng/mL at any time during treatment compared to 19% treated with just abiraterone acetate and prednisone (Saad *et al*., 2021).

Conclusion

We're very encouraged by the Phase 1 data presented for masofaniten in combination with enzalutamide, which shows the combination is well tolerated and produces PSA50 and PSA90 rates that compare very favorably to single agent Enz therapy. ESSA is continuing to enroll patients into the Phase 2 trial of masofaniten and Enz, with an expected enrollment of approximately 120 patients and we look forward to updates on the trial in 2024. With no changes to our model, our valuation remains at $27 per share.

PROJECTED FINANCIALS

ESSA Pharma Inc.	FY2022 A	Q1FY23 A	Q2FY23 A	Q3FY23 A	Q4FY23 E	FY2023 E	FY2024 E	FY2025 E
EPI-7386	$0	$0	$0	$0	$0	$0	$0	$0
Total Revenues	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**
Cost of Sales	$0	$0	$0	$0	$0	$0	$0	$0
Research & Development	$24.4	$5.3	$4.5	$6.3	$7.5	$23.6	$30.0	$35.0
Financing Costs	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
General & Administrative	$12.5	$2.5	$3.7	$2.6	$3.3	$12.2	$14.0	$15.0
Other (Income) Expense	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Operating Income	($37.0)	($7.87)	($8.2)	($8.9)	($10.8)	($35.8)	($44.0)	($50.0)
Operating Margin	-	-	-	-	-	-	-	-
Non-Operating Expenses (Net)	$1.8	$1.1	$1.2	$1.6	$0.0	$3.9	$0.0	$0.0
Pre-Tax Income	($35.2)	($6.74)	($7.1)	($7.3)	($10.8)	($31.9)	($44.0)	($50.0)
Income Taxes	($0.1)	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Tax Rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*
Net Income	**($35.1)**	**($6.7)**	**($7.1)**	**($7.3)**	**($10.8)**	**($31.9)**	**($44.0)**	**($50.0)**
Net Margin	-	-	-	-	-	-	-	-
Reported EPS	**($0.80)**	**($0.15)**	**($0.16)**	**($0.17)**	**($0.25)**	**($0.72)**	**($0.98)**	**($1.09)**
YOY Growth	-	-	-	-	-	-	-	-
Basic Shares Outstanding	44.0	44.1	44.1	44.1	44.1	44.1	45.0	46.0

Source: Zacks Investment Research, Inc. *David Bautz, PhD*

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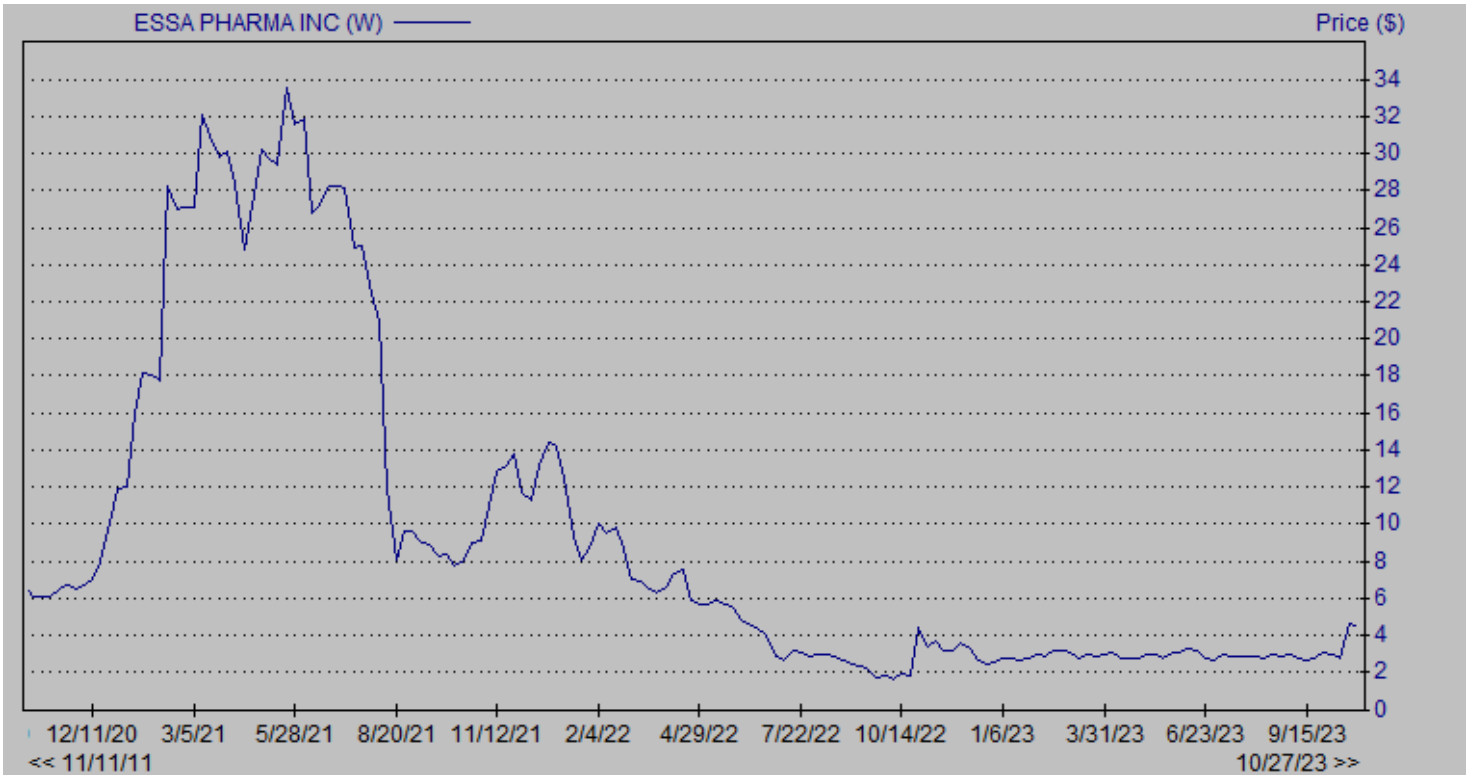
HISTORICAL STOCK PRICE



Source: Zacks SCR

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