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David Bautz, PhD
312-265-9471
dbautz@zacks.com

scr.zacks.com
10 S. Riverside Plaza, Chicago, IL 60606

ESSA Pharma Inc

(EPIX-NASDAQ)

EPIX: Updated Data for Phase 1 Trial of Masofaniten Shows 63% of Patients Achieved PSA <0.2 ng/mL…

Based on our probability adjusted DCF model that takes into account potential future revenues from masofaniten and the ANITAC program, EPIX is valued at $29/share. This model is highly dependent upon continued clinical success of masofaniten/TPD and will be adjusted accordingly based upon future clinical results.

Current Price (01/26/24)	$6.80
Valuation	**$29.00**

OUTLOOK

On January 25, 2023, ESSA Pharma Inc. (EPIX) announced the presentation of updated dose escalation data from the Phase 1/2 clinical trial of masofaniten (formerly EPI-7386) in combination with enzalutamide at the 2024 ASCO Genitourinary Cancers Symposium. The data includes 18 patients across four cohorts. The combination of masofaniten and enzalutamide continues to be well tolerated through 25 cycles of dosing in some patients. In patients evaluable for efficacy (n=16), 88% (14/16) achieved PSA50, 81% (13/16) achieved PSA90, 69% (11/16) achieved PSA90 in less than 90 days, and 63% (10/16) achieved PSA < 0.2 ng/mL. In addition, although the data are still maturing, the current median time to PSA progression is 16.6 months, which compares very well with data from the Phase 3 AFFIRM and PREVAIL studies of enzalutamide monotherapy.

SUMMARY DATA

52-Week High	**$9.94**
52-Week Low	**$2.60**
One-Year Return (%)	**153.73**
Beta	**1.90**
Average Daily Volume (sh)	**146,363**
Shares Outstanding (mil)	**44**
Market Capitalization ($mil)	**$300**
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 2024 Estimate	**-8.1**
P/E using 2025 Estimate	**-6.1**

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

ZACKS ESTIMATES

Revenue
(in millions of $)

	Q1 (Dec)	Q2 (Mar)	Q3 (Jun)	Q4 (Sep)	Year (Sep)
2023	0 A	0 A	0 A	0 A	0 A
2024	0 E	0 E	0 E	0 E	0 E
2025					0 E
2026					0 E

Earnings per Share

	Q1 (Dec)	Q2 (Mar)	Q3 (Jun)	Q4 (Sep)	Year (Sep)
2023	-$0.15 A	-$0.16 A	-$0.17 A	-$0.12 A	-$0.60 A
2024	-$0.15 E	-$0.15 E	-$0.15 E	-$0.16 E	-$0.61 E
2025					-$0.61 E
2026					-$0.67 E

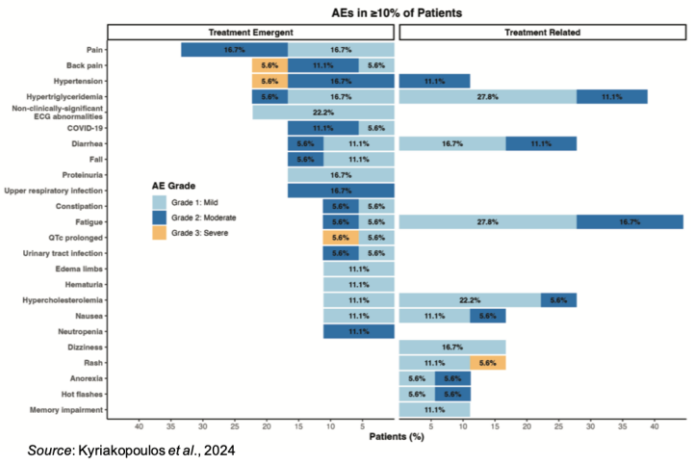
WHAT'S NEW

Business Update

Updated Phase1/2 Data for Masofaniten Presented at ASCO Genitourinary Cancers Symposium

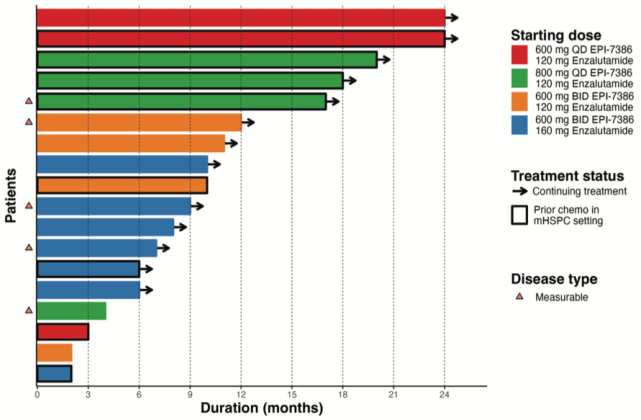
On January 25, 2024, ESSA Pharma, Inc. (EPIX) announced that updated Phase 1/2 clinical trial data for masofaniten (formerly EPI-7386) in combination with enzalutamide (Enz) was presented at the 2024 ASCO Genitourinary Cancers Symposium. A copy of the poster presentation can be found here.

The Phase 1/2 trial is enrolling patients with metastatic castration-resistant prostate cancer (mCRPC) who are naïve to second-generation antiandrogens. The Phase 1 portion of the study enrolled 18 patients in four dose cohorts, with 16 patients evaluable for efficacy as per protocol. 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 adverse events (AEs) occurring in ≥10% of patients, with most 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 probably 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. Lastly, there were no serious adverse events (SAEs) observed.



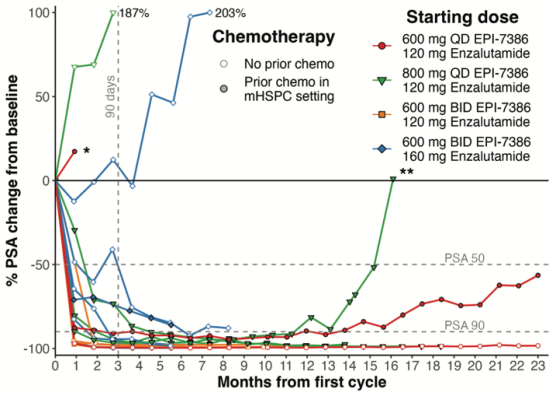
Source: Kyriakopoulos *et al.*, 2024

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.

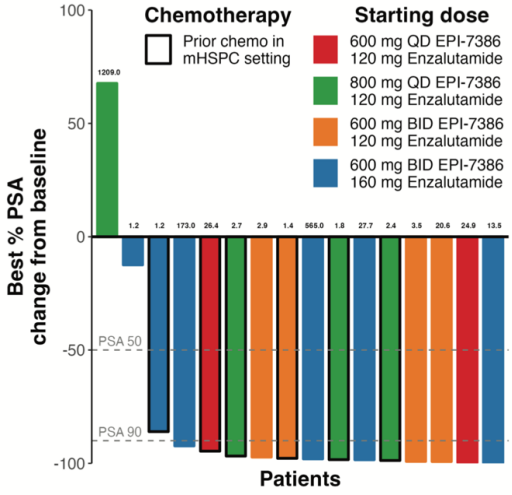


Source: Kyriakopoulos *et al.*, 2024

Across all dosing cohorts, patients showed a rapid, deep, and durable decrease in prostate-specific antigen (PSA). The following chart on the left shows the PSA outcomes for all enrolled patients. 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), 69% (11/16) achieved PSA90 within 90 days, and 63% (10/16) have achieved PSA <0.2 ng/mL. The graph on the right shows the best % PSA change from baseline for each patient.



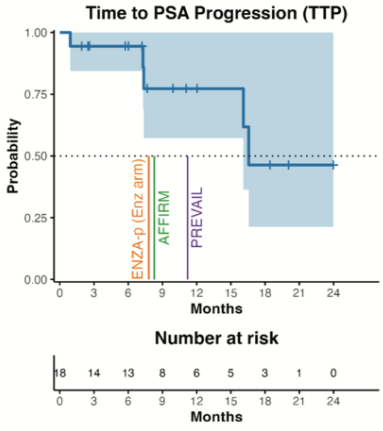
*Two patients are not evaluable for efficacy: one patient that experienced a DDI with a concomitant drug, and another DLT patient (not plotted past baseline).
**Unconfirmed PSA progression.
Source: Kyriakopoulos *et al.*, 2024



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 on the left summarizes the data from those trials (along with the ENZA-p Phase 2 trial of ^{177}Lu-PSMA-617 in combination with enzalutamide) in regards to PSA response. The figure on the right shows the current time to PSA progression (16.6 months), which while immature compares quite favorably to data from both the AFFIRM (8.3 months) and PREVAIL (11.2 months) trials.

Drug	Masofaniten + Enz	Lu-PSAM-617 + Enz		Enz		Enz	
Study	EPI-7386-CS-010 Phase 1	ENZA-p[1] Phase 2		AFFIRM[2] Phase 3		PREVAIL[3] Phase 3	
Cohort	Phase 1 pooled	Lu+Enz	Enz	Enz	Placebo	Enz	Placebo
n	18	83	79	800	399	872	845
PSA baseline (ng/mL)	3.2	39	33	107.7	128.3	54	44
Prior Chemo	44%	53%	56%	100%	100%	0%	0%
Prior abiraterone	0%	14%	11%	0%	0%	0%	0%
PSA-PFS (months)	16.6 (immature)	13	7.8	8.3	3	11.2	2.8
PSA90	81%	78%	37%	25%	1%	47%	1%
PSA90 (90 days)	69%	N/A	N/A	13%	N/A	37%	N/A
PSA50	88%	93%	68%	54%	2%	78%	3%
PSA<0.2 ng/mL	63%	N/A	N/A	3%	N/A	11%	N/A
≥Gr3 AE	6%	10%	4%	45%	53%	43%	37%

[1]ESMO 2023 presentation; [2]Scher et al, 2012; Armstrong et al, 2017; [3]Beer et al, 2014
Source: Kyriakopoulos *et al.*, 2024



The median PSA baseline for this study was 3.2 ng/mL, which on the surface may look like it is quite different from the other studies listed in the table above. However, this value is for all 18 patients, including the two that were not evaluable for efficacy. For the patients just listed in the waterfall plot above, the median PSA at baseline was 8.5 ng/mL. In addition, if you exclude the post-chemo patients (who had a median PSA at baseline of 2.1 ng/mL), the median PSA at baseline for the pre-chemo patients was 22.8 ng/mL, which is not far from the 33 ng/mL reported in the ENZA-p study. Lastly, the 22.8 ng/mL baseline PSA for pre-chemo patients is also in line with the ACIS study of apalutamide and abiraterone acetate in chemotherapy naïve patients with mCRPC (Saad *et al.*, 2021). Thus, we believe the cross-trial comparisons are appropriate to help put the results seen thus far with masofaniten in context with other therapies in similar patient populations.

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

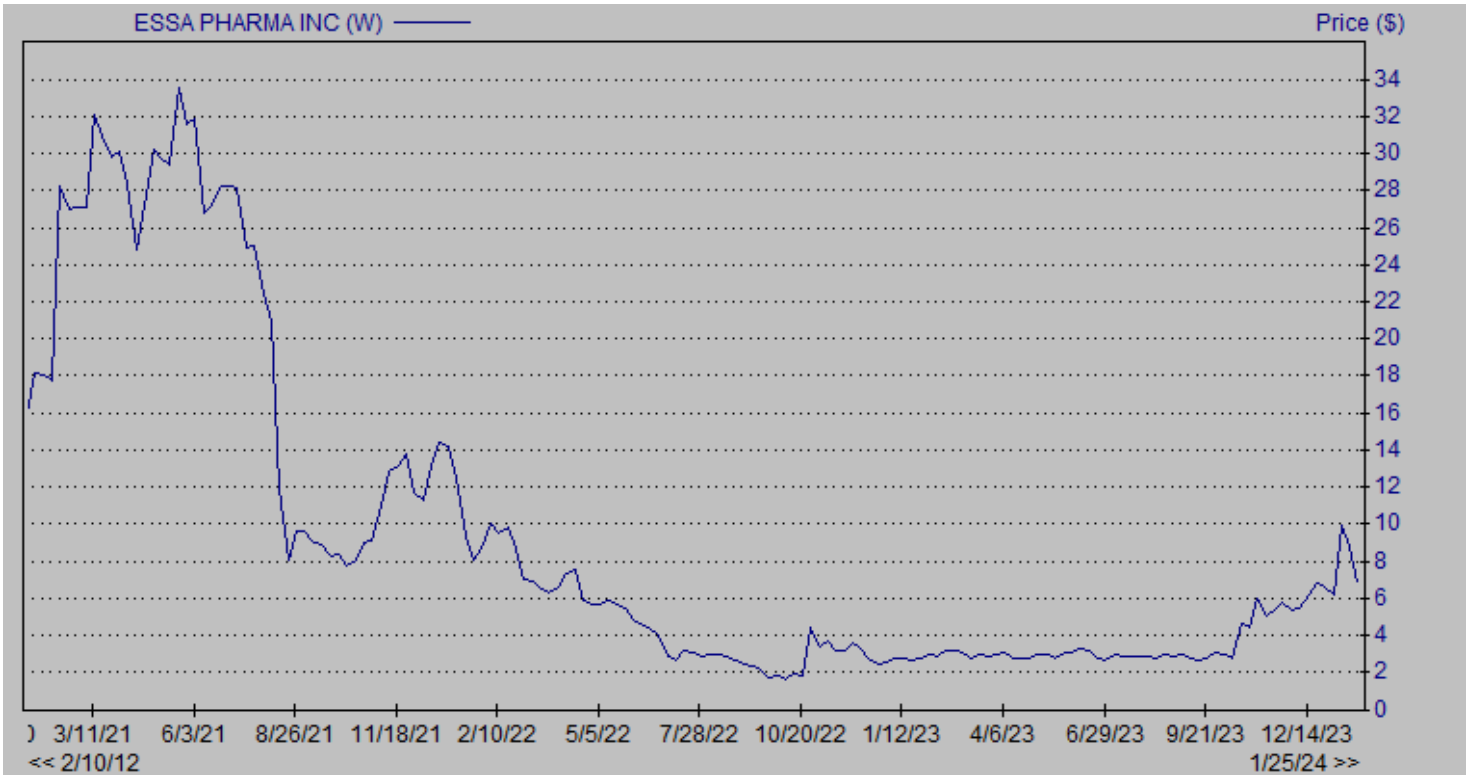
The data from the ongoing Phase 1/2 clinical trial of masofaniten and Enz continues to be very encouraging, as the combination therapy is well tolerated and results in deep and durable decreases in PSA. The company is continuing to enroll patients in the dose expansion portion of the Phase 2 trial of masofaniten and Enz and we anticipate initial data from the study being reported later in 2024. With no changes to our model our valuation remains at $29 per share.

PROJECTED FINANCIALS

ESSA Pharma Inc.	FY2023 A	Q1FY24 E	Q2FY24 E	Q3FY24 E	Q4FY24 E	FY2024 E	FY2025 E	FY2026 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	$21.3	$5.3	$5.4	$5.5	$5.6	$21.8	$23.0	$25.0
Financing Costs	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
General & Administrative	$10.8	$2.6	$2.7	$2.7	$2.9	$10.9	$11.0	$12.0
Other (Income) Expense	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Operating Income	($32.1)	($7.95)	($8.1)	($8.2)	($8.5)	($32.8)	($34.0)	($37.0)
Operating Margin	-	-	-	-	-	-	-	-
Non-Operating Expenses (Net)	$5.6	$1.5	$1.5	$1.5	$1.5	$6.0	$6.0	$6.0
Pre-Tax Income	($26.6)	($6.45)	($6.6)	($6.7)	($7.0)	($26.8)	($28.0)	($31.0)
Income Taxes	$0.0	$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	**($26.6)**	**($6.4)**	**($6.6)**	**($6.7)**	**($7.0)**	**($26.8)**	**($28.0)**	**($31.0)**
Net Margin	-	-	-	-	-	-	-	-
Reported EPS	**($0.60)**	**($0.15)**	**($0.15)**	**($0.15)**	**($0.16)**	**($0.61)**	**($0.61)**	**($0.67)**
YOY Growth	-	-	-	-	-	-	-	-
Basic Shares Outstanding	44.1	44.1	44.1	44.1	44.1	44.1	46.0	46.0

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

HISTORICAL STOCK PRICE



Source: Zacks SCR

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