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ESSA Pharma Inc

(EPIX-NASDAQ)

EPIX: Updated Masofaniten plus Enzalutamide Dose Escalation Data to be Presented at ESMO 2024…

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 (08/08/24)	$4.55
Valuation	**$29.00**

OUTLOOK

On August 5, 2024, ESSA Pharma Inc. (EPIX) announced financial results for the third quarter of fiscal year 2024 that ended June 30, 2024 and provided a business update. ESSA is currently studying its lead compound, masofaniten (EPI-7386), in two clinical trials: EPI-7386-CS-001 and EPI-7386-CS-010. Full results from the monotherapy arm of the -001 trial will be presented at a scientific conference in the second half of 2024 while enrollment continues in the two combination arms. Preliminary results from the dose equilibrium portion of the -010 study were presented in January 2024 at ASCO-GU and we anticipate updated data being reported at the ESMO 2024 congress in September 2024. Lastly, the Phase 2 portion of the -010 study evaluating EPI-7386 in combination with enzalutamide versus enzalutamide monotherapy is expected to complete enrollment in 1Q25 with preliminary results to be reported in mid-2025.

SUMMARY DATA

52-Week High	**$10.65**
52-Week Low	**$2.65**
One-Year Return (%)	**63.08**
Beta	**1.82**
Average Daily Volume (sh)	**32,891**
Shares Outstanding (mil)	**44**
Market Capitalization ($mil)	**$202**
Short Interest Ratio (days)	**1**
Institutional Ownership (%)	**75**
Insider Ownership (%)	**15**
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	**-6.4**
P/E using 2025 Estimate	**-4.9**

Risk Level	**Above Avg.**
Type of Stock	**Small-Value**
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 A	0 A	0 A	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	-$0.14 A	-$0.20 A	-$0.16 A	-$0.16 E	-$0.66 E
2025					-$0.62 E
2026					-$0.67 E

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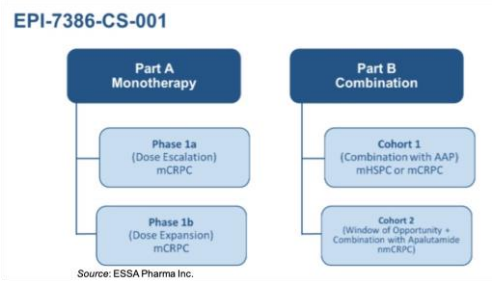
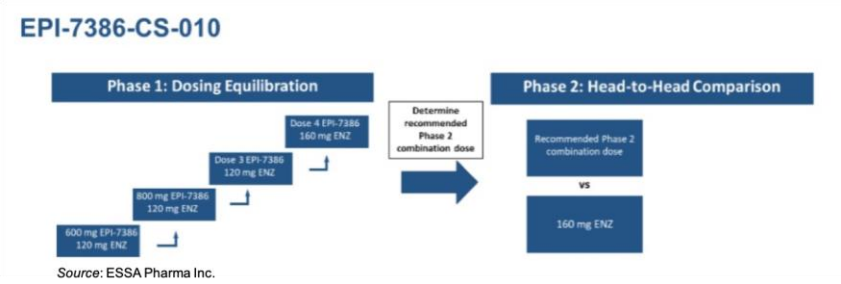
WHAT'S NEW

Business Update

ESSA Pharma Inc. (EPIX) is developing masofaniten (EPI-7386), its next-generation aniten molecule that is designed to target the N-terminal domain (NTD) of the androgen receptor (AR) as a treatment for prostate cancer. Masofaniten is currently being evaluated in two clinical trials: EPI-7386-CS-001 and EPI-7386-CS-010.





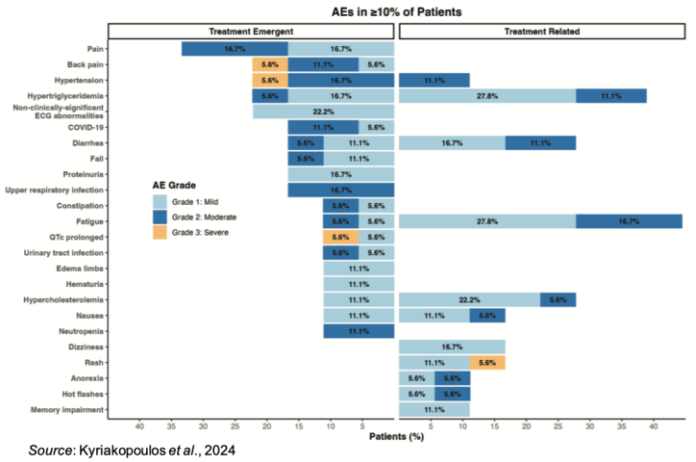
EPI-7386-CS-001 has a monotherapy and combination arm in patients with metastatic castration resistant prostate cancer (mCRPC). The company completed the Phase 1a dose escalation portion of the monotherapy arm in which 600 mg QD and 600 mg BID were the two doses selected to advance into the dose expansion portion of the trial. For the dose expansion portion of the study, the 600 mg BID cohort of 12 patients has been fully enrolled and the 600 mg QD cohort of patients has completed enrollment. Trial EPI-7386-CS-001 also has a combination component: Cohort 1 is evaluating masofaniten with abiraterone acetate/prednisone in patients with metastatic hormone sensitive prostate cancer (mHSPC) or mCRPC; Cohort 2 is evaluating masofaniten 600 mg BID for a limited window of time (up to 12 weeks before patients start standard of care) in non-metastatic CRPC (nmCRPC) patients. Following the 12-week dosage of masofaniten, the company will evaluate masofaniten in combination with apalutamide. Full results from the monotherapy portion of the study are expected to be presented at a scientific conference in the second half of 2024.

EPI-7386-CS-010 is a combination trial of masofaniten and enzalutamide (Enz). The company has completed the dose escalation portion of the trial (see below for results presented at ASCO GU in January 2024) and the recommended Phase 2 combination doses are masofaniten 600 mg BID and Enz 160 mg. The Phase 2 trial is currently enrolling and we anticipate enrollment completing in the first quarter of 2025 and initial data in mid-2025. Updated results from the dose escalation portion of the trial are expected to be reported at the European Society for Medical Oncology (ESMO) 2024 congress in September 2024.

Phase 1/2 Data for Masofaniten Plus Enzalutamide Presented at ASCO Genitourinary Cancers Symposium

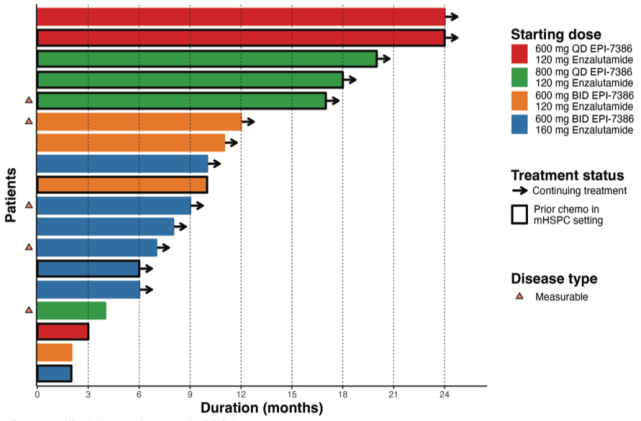
In January 2024, ESSA announced that updated Phase 1/2 clinical trial data for masofaniten (formerly EPI-7386) in combination with Enz was presented at the 2024 ASCO Genitourinary Cancers Symposium. A copy of the poster presentation can be found here.

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.



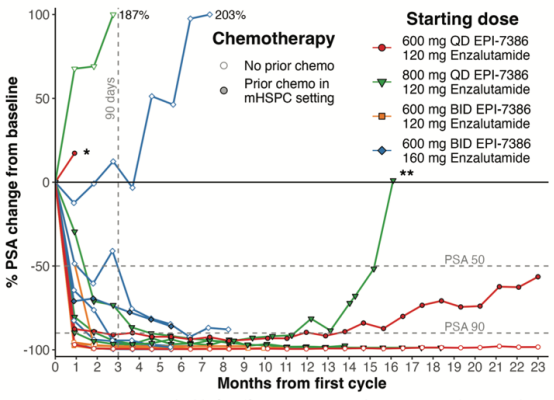
Source: Kyriakopoulos *et al.*, 2024

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.



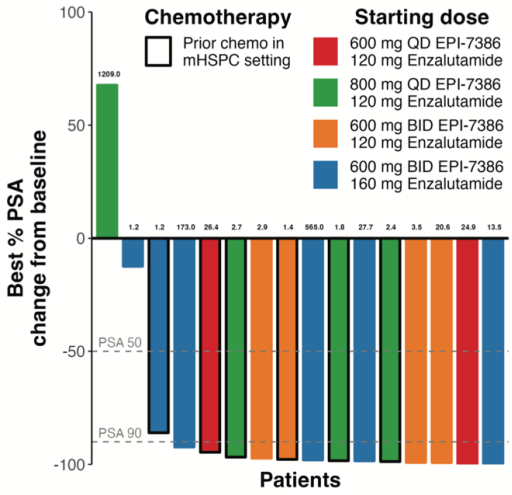
Source: Kyriakopoulos *et al.*, 2024

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.

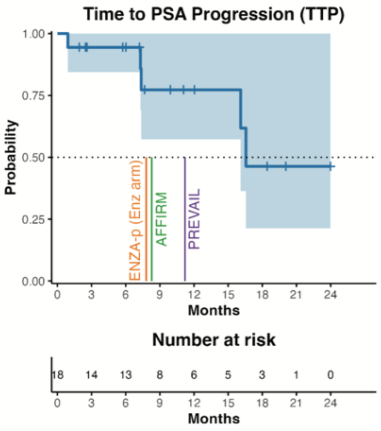
Source: Kyriakopoulos *et al.*, 2024



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 be 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).

Financial Update

On August 5, 2024, ESSA announced financial results for the third quarter of fiscal year 2024 that ended June 30, 2024. For the third quarter of fiscal year 2024, the company reported a net loss of $7.2 million, or $0.16 per share, compared to a net loss of $7.3 million, or $0.17 per share, for the third quarter of fiscal year 2023. R&D expenses for the third quarter of fiscal year 2024 were $5.5 million compared to $6.3 million for the third quarter of fiscal year 2023. The decrease was primarily due to reductions in preclinical work to focus on ongoing clinical trials. G&A expenses for the third quarter of fiscal year 2024 were $3.2 million compared to $2.6 million for the third quarter of

fiscal year 2023, which included $1.7 million in share-based payments in the third quarter of fiscal year 2024 compared to $0.6 million for the third quarter of fiscal year 2023. The net decrease (net of share-based payments) was primarily due to the timing of corporate projects and lower insurance premiums.

As of June 30, 2024, ESSA had approximately $130.7 million in cash, cash equivalents, and short-term investments. We estimate the company has sufficient capital to fund operations beyond 2025. As of August 5, 2024, the company had approximately 44.4 million shares outstanding and, when factoring in stock options and warrants, a fully diluted share count of approximately 56.6 million.

Conclusion

We look forward to updated data from the Phase 1 dose escalation study of masofaniten and enzalutamide at the ESMO 2024 congress in September 2024 and initial data from the Phase 2 dose expansion portion of the trial in mid-2025. In addition, we anticipate the full data set from the Phase 1a monotherapy study to be presented at a scientific conference in the second half of 2024. As we await the updated data presentations our valuation remains at $29.

PROJECTED FINANCIALS

ESSA Pharma Inc.	FY2023 A	Q1FY24 A	Q2FY24 A	Q3FY24 A	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	$5.4	$6.2	$5.5	$5.6	$22.6	$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	$2.2	$4.3	$3.2	$2.9	$12.6	$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)	($7.59)	($10.5)	($8.6)	($8.5)	($35.2)	($34.0)	($37.0)
Operating Margin	-	-	-	-	-	-	-	-
Non-Operating Expenses (Net)	$5.6	$1.7	$1.5	$1.4	$1.5	$6.1	$6.0	$6.0
Pre-Tax Income	($26.6)	($5.9)	($9.0)	($7.2)	($7.0)	($29.2)	($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)	($5.9)	($9.0)	($7.2)	($7.0)	($29.2)	($28.0)	($31.0)
Net Margin	-	-	-	-	-	-	-	-
Reported EPS	($0.60)	($0.14)	($0.20)	($0.16)	($0.16)	($0.66)	($0.62)	($0.67)
YOY Growth	-	-	-	-	-	-	-	-
Basic Shares Outstanding	44.1	44.1	44.2	44.4	44.5	44.3	45.0	46.0

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

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