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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: $45 Million Financing Includes Investment from Pfizer; Dosing Begins in Phase 1 Trial of EPI-7386…

Based on our probability adjusted DCF model that takes into account potential future revenues from EPI-7386, EPIX is valued at $16.50/share. This model is highly dependent upon continued clinical success of EPI-7386 and will be adjusted accordingly based upon future clinical results.

Current Price (08/12/20)	$6.75
Valuation	**$16.50**

OUTLOOK

On August 6, 2020, ESSA Pharma, Inc. (EPIX) announced financial results for the third quarter of fiscal year 2020 and provided a business update. The company recently completed a public financing of approximately $45 million. A number of new investors participated in the financing, including Pfizer, Inc. (PFE), who now owns 6% of the outstanding shares. During the quarter, ESSA initiated the Phase 1 clinical trial of EPI-7386 in patients with metastatic castration-resistant prostate cancer (mCRPC). The company also presented preclinical data on EPI-7386 at the 2020 AACR Virtual Meeting that included gene expression analysis and the exhibition of full-length androgen receptor (AR) engagement in a cellular thermal shift assay.

SUMMARY DATA

52-Week High	**$6.99**
52-Week Low	**$1.46**
One-Year Return (%)	**306.63**
Beta	**1.76**
Average Daily Volume (sh)	**168,160**
Shares Outstanding (mil)	**21**
Market Capitalization ($mil)	**$141**
Short Interest Ratio (days)	**1**
Institutional Ownership (%)	**68**
Insider Ownership (%)	**N/A**
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	**-5.6**
P/E using 2021 Estimate	**-6.6**

Risk Level	**Below Avg.**
Type of Stock	**Small-Growth**
Industry	**Med-Drugs**

ZACKS ESTIMATES

Revenue
(in millions of $)

	Q1 (Dec)	Q2 (Mar)	Q3 (Jun)	Q4 (Sep)	Year (Sep)
2019	0 A	0 A	0 A	0 A	0 A
2020	0 A	0 A	0 A	0 E	0 E
2021					0 E
2022					0 E

Earnings per Share

	Q1 (Dec)	Q2 (Mar)	Q3 (Jun)	Q4 (Sep)	Year (Sep)
2019	-$0.42 A	-$0.54 A	-$0.52 A	-$0.07 A	-$1.24 A
2020	-$0.22 A	-$0.45 A	-$0.24 A	-$0.16 E	-$1.10 E
2021					-$0.53 E
2022					-$0.54 E

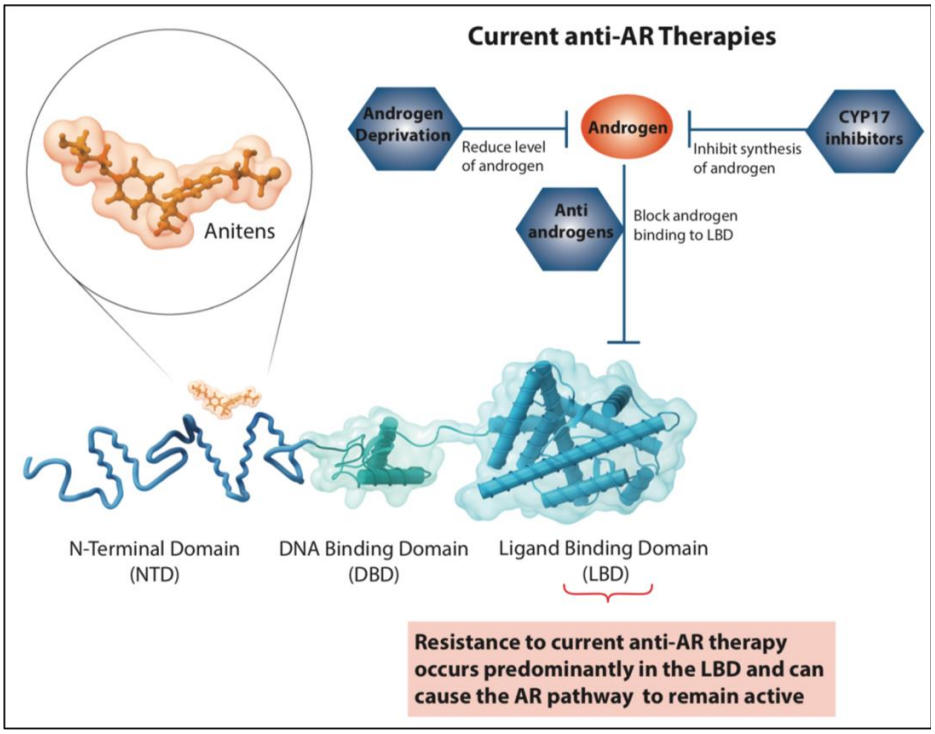
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WHAT'S NEW

Business Update

Additional Preclinical Data Presented at AACR 2020

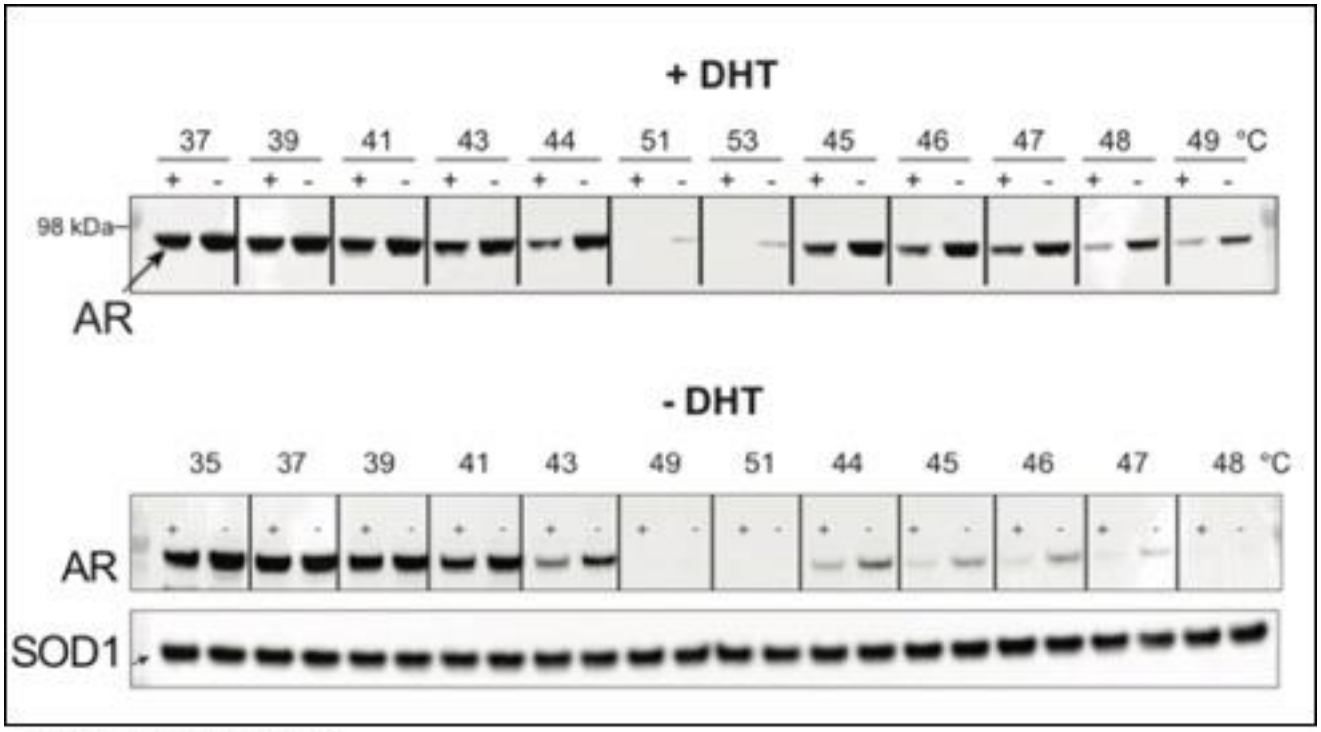
On June 22, 2020, ESSA Pharma Inc. (EPIX) announced new preclinical data was presented at the 2020 American Association for Cancer Research (AACR) Virtual Annual Meeting II (the poster can be accessed here) for its lead clinical development candidate EPI-7386, which is part of a novel class of compounds known as 'anitens' to treat prostate cancer in patients that are progressing on standard of care therapy. Anitens target the androgen receptor (AR), which is the main signaling mechanism driving the growth of prostate tumors, through binding to the N-terminal domain (NTD), which is unique compared to other available anti-androgen therapies that the target the ligand binding domain (LBD). The following graphic shows where anitens bind on the AR compared to currently available anti-AR therapies, which fully differentiates anitens from other prostate cancer therapies that target the AR.



Source: Hong *et al.*, 2020

The data presented at the 2020 AACR Annual Meeting built upon results previously presented by the company (see here for a discussion of the results presented at the 2020 ASCO Genitourinary Cancers Symposium and here for a discussion of the results presented at the 2020 AUA Annual Meeting). Additional data presented on EPI-7386 at AACR included AR target engagement shown in a cellular thermal shift assay and RNAseq analysis showing EPI-7386 inhibits AR transcriptional activity similarly to enzalutamide in cells with full length AR and in a superior fashion to enzalutamide in AR-V7-driven cellular models.

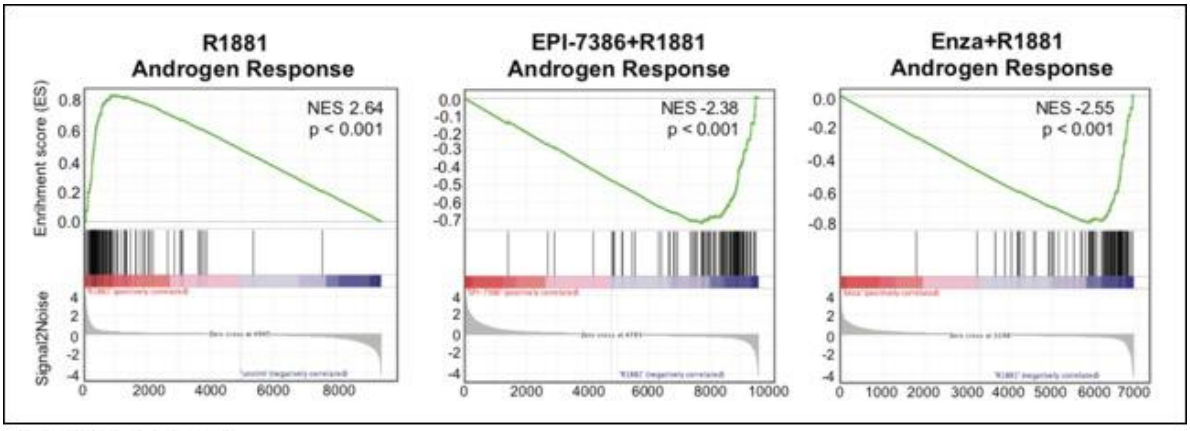
The cellular thermal shift assay (CETSA) is designed to show direct binding of a compound to a target protein through alteration of the protein's melting temperature (Molina *et al.*, 2013). As the temperature is raised, proteins begin to denature and fall out of solution, thus when analyzed by Western blot a decrease in the amount of protein is seen. When a compound directly binds to a protein, its melting profile changes as evidenced by a change in the amount of protein detected by Western blot. This change can either be an increase or decrease, depending on whether the protein increases or decreases the thermal stability of the protein. The following figures show that EPI-7386 decreases the thermal stability of the AR as shown by a decrease in the amount of protein seen by Western blot in the "+" lanes. This effect is seen whether dihydroxytestosterone (DHT) is added or not. This is in contrast to enzalutamide, which only binds to AR in the presence of DHT (Shaw *et al.*, 2018).



Source: Hong *et al.*, 2020

The most important takeaway from that assay is that EPI-7386 binds directly to the AR, thus showing that it is not off-target effects but direct interaction with the AR that is driving the anti-cancer response seen in preclinical models.

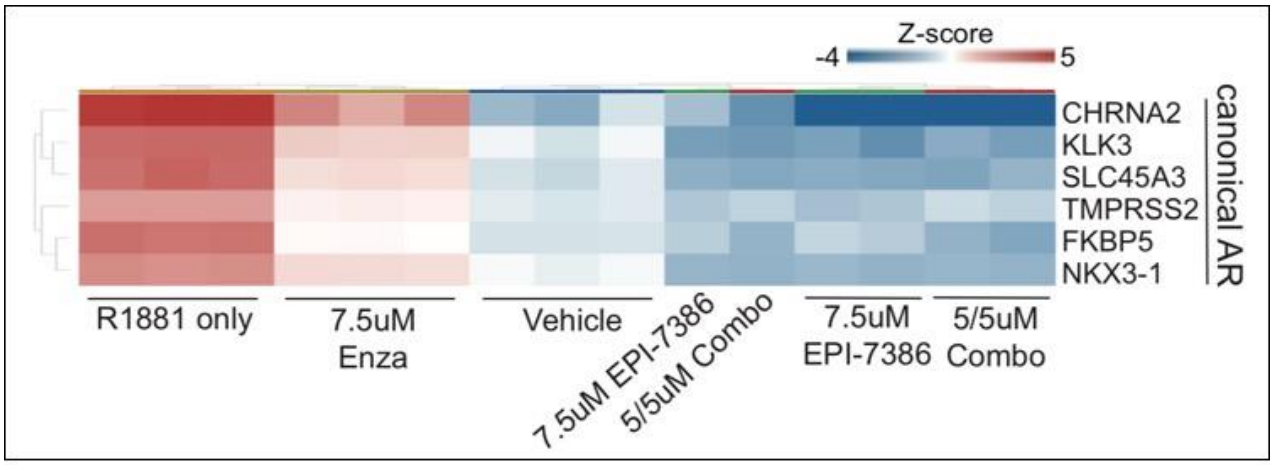
While the company had previously performed transcriptomic analysis on a select set of genes, for this study ESSA performed RNAseq analysis to examine the transcriptome in as much detail as possible. The following figures show the androgen response gene expression signature in the presence of R1881, EPI-7386 + R1881, or enzalutamide + R1881. Both EPI-7386 and enzalutamide alter the androgen response gene expression in a similar fashion.



Source: Hong *et al.*, 2020

In contrast to the similarity in response seen to EPI-7386 and enzalutamide in cells with native AR, in cells with AR-V7-driven growth there is a substantial difference in gene expression in the presence of EPI-7386 and enzalutamide. The following figure shows gene expression for a group of genes regulated by the AR in an AR-V7-driven cell line. Red represents up-regulation with blue representing down-regulation. When examining genes that are regulated by the AR it is clear that their expression in an AR-V7 model are down-regulated more efficiently by EPI-7386 than by enzalutamide. In addition, there is little difference between EPI-7386 monotherapy and combination therapy with enzalutamide, thus confirming that enzalutamide has a limited effect in AR-V7-driven prostate cancer cells. As a reminder, many prostate cancers are initially driven by full-length AR before mutations such as AR-V7 render the disease refractory to treatment with agents like enzalutamide. The fact that EPI-7386

shows an ability to alter gene expression in an AR-V7 driven model means that while combination therapy may make sense in early stage patients, monotherapy with EPI-7386 could be an appropriate approach for late-stage patients with AR mutations.



Source: Hong *et al.*, 2020

In summary, the new data presented by ESSA confirms that EPI-7386 binds directly to the AR, alters androgen response gene expression in a manner similar to enzalutamide, and decreases expression of AR-regulated genes in an AR-V7 model.

Dosing Initiated in Phase 1 Clinical Trial of EPI-7386

On July 15, 2020, ESSA announced that the first patient had been enrolled in the Phase 1 clinical trial of EPI-7386 in patients with metastatic castration-resistant prostate cancer that failed standard of care treatments, including second generation anti-androgens.

We anticipate the trial enrolling approximately 18 patients to evaluate the safety, pharmacokinetics, and maximum-tolerated dose of the compound in multiple-dose escalations. It will encompass a standard 3+3 trial design (three patients enrolled per dose cohort) with an estimated 10 patients being enrolled in the dose expansion cohort. The initial dose will be 200 mg, followed by 400 mg, 600 mg, 800 mg, and 1000 mg.

The primary objective of the dose escalation portion is to establish the safety and efficacy of EPI-7386 with the secondary objective being to determine the maximum tolerated dose and the recommended Phase 2 dose. In the dose expansion portion of the trial, the primary objective will be to further evaluate the safety, tolerability, and preliminary anti-tumor activity of the recommended Phase 2 dose.

The company is also planning to initiate multiple combination trials with EPI-7386 and different anti-androgen therapies (enzalutamide, apalutamide, darolutamide, etc.) in mCRPC patients due to the robust preclinical data showing increased activity with combination therapy. Following the company's recent financing, we estimate that the company is fully financed to conduct all planned trials (the dose escalation trial, the dose expansion trial, and multiple combination trials).

Financial Update

On August 6, 2020, ESSA announced financial results for the third quarter of fiscal year 2020 that ended June 30, 2020. The company reported a net loss of $4.9 million, or $0.24 per share, compared to a net loss of $3.3 million, or $0.52 per share, for the third quarter of fiscal year 2019. R&D expenses for the third quarter of fiscal year 2020 were $2.7 million, compared to $2.0 million for the third quarter of fiscal year 2019. The increase was primarily due to costs related to preparing the IND for EPI-7386, preparatory clinical costs, manufacturing costs, and share-based compensation. G&A expenses for the three months ending June 30, 2020 were $2.2 million, compared to $1.2 million for the three months ending June 30, 2019. The increase was primarily due to non-cash share-based payments.

As of June 30, 2020, ESSA had approximately $36.5 million of cash and cash equivalents. On July 31, 2020, ESSA announced the closing of an underwritten public offering of a total of approximately 8.2 million shares (which included 1.065 million shares granted to the underwriters) at an offering price of $6.00 per share. Total net proceeds

to ESSA were approximately $45.0 million. Pfizer, Inc. (PFE) was a new investor and acquired 1.675 million shares and now own 6% of outstanding shares. Additional institutional investors who acquired shares in this financing include Avidity Partners, CAM Capital, Point72, Ridgeback Capital, Sphera Healthcare, and Vivo Capital.

As of June 30, 2020, ESSA had approximately 20.8 million shares outstanding and following the recent financing we estimate that the company currently has approximately 29.0 million shares and, when factoring in stock options and warrants, a fully diluted share count of approximately 46.4 million.

Valuation

ESSA continues to show very encouraging preclinical data for EPI-7386 and we imagine that a number of Big Pharma companies would be interested in testing currently available anti-androgen therapies in combination studies with EPI-7386. We believe that Pfizer now owning 6% of the outstanding shares of ESSA is indicative of the type of interest that the company will be receiving (and likely already is) from potential collaborators.

We have adjusted our model to account for the company's recent financing and we now utilize a net margin percentage of up to 35% on gross sales instead of a 15% royalty for U.S. sales, as we believe this is closer to how a potential Big Pharma acquirer would value EPI-7386. These changes have led to an increase in our valuation to $16.50, and we eagerly await initial results from the Phase 1 trial, which may be shared at a scientific meeting in the first half of 2021.

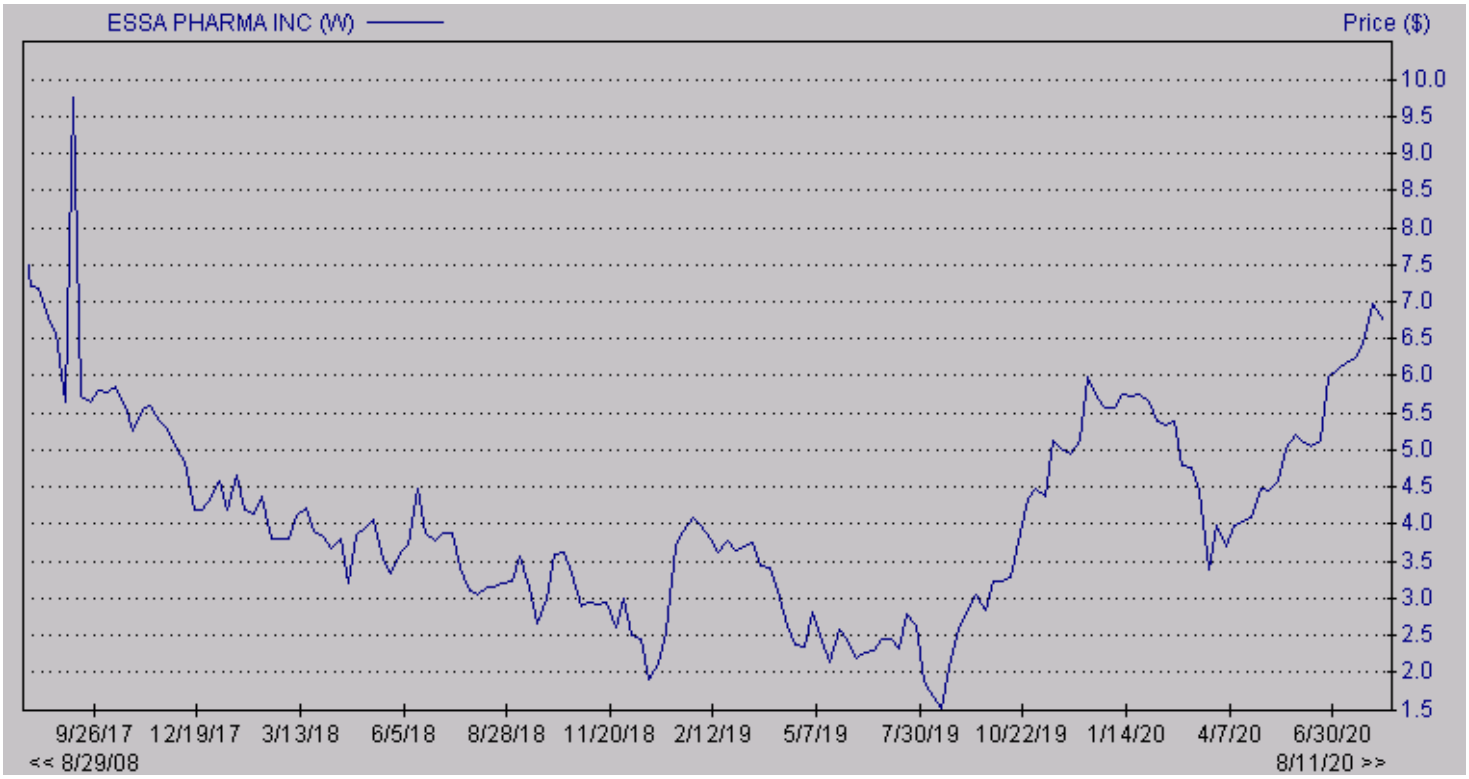
PROJECTED FINANCIALS

ESSA Pharma Inc.	FY2019 A	Q1FY20 A	Q2FY20 A	Q3FY20 A	Q4FY20 E	FY2020 E	FY2021 E	FY2022 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
Product Gross Margin	-	-	-	-	-	-	-	-
Research & Development	$6.7	$2.6	$4.6	$2.7	$2.0	$11.9	$10.0	$12.0
Financing Costs	$0.6	$0.2	$0.1	$0.2	$0.0	$0.5	$0.0	$0.0
General & Administrative	$5.5	$2.1	$4.9	$2.2	$1.4	$10.6	$6.0	$7.0
Other (Income) Expense	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Operating Income	($12.8)	($4.9)	($9.6)	($5.1)	($3.4)	($23.0)	($16.0)	($19.0)
Operating Margin	-	-	-	-	-	-	-	-
Non-Operating Expenses (Net)	$2.4	($0.0)	($0.2)	$0.1	$0.0	($0.1)	$0.0	$0.0
Pre-Tax Income	($10.4)	($4.9)	($9.4)	($4.9)	($3.4)	($23.1)	($16.0)	($19.0)
Income Taxes	$0.0	($0.3)	$0.0	$0.0	$0.0	($0.3)	$0	$0
Tax Rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*
Net Income	**($10.4)**	**($4.6)**	**($9.4)**	**($4.9)**	**($3.4)**	**($22.9)**	**($16.0)**	**($19.0)**
Net Margin	-	-	-	-	-	-	-	-
Reported EPS	**($1.24)**	**($0.22)**	**($0.45)**	**($0.24)**	**($0.16)**	**($1.10)**	**($0.53)**	**($0.54)**
YOY Growth	-	-	-	-	-	-	-	-
Basic Shares Outstanding	8.4	20.8	20.8	20.8	20.8	20.8	30.0	35.0

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

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Source: Zacks SCR

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