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Essa Pharma Inc

(EPIX-NASDAQ)

EPIX: *IND Filing for EPI-7386 in 1Q20…*

Based on our probability adjusted DCF model that takes into account potential future revenues from EPI-7386, EPIX is valued at $9.50/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 (02/18/20)	$5.35
Valuation	**$9.50**

OUTLOOK

On February 13, 2020, Essa Pharma Inc. (EPIX) presented additional preclinical data on the company's lead clinical candidate, EPI-7386, at the 2020 American Society of Clinical Oncology Genitourinary Cancers Symposium. New data presented by the company included the use of EPI-7386 in a patient-derived xenograft model in which it inhibited tumor growth by 58% compared to no tumor growth inhibition shown by enzalutamide. Pharmacokinetic data supports once a day dosing and toxicology studies show that the drug is well tolerated at high doses in tox species. We anticipate the company filing an IND for EPI-7386 in the first quarter of 2020 with a Phase 1 clinical trial initiating shortly thereafter.

SUMMARY DATA

52-Week High	**$6.00**
52-Week Low	**$1.46**
One-Year Return (%)	**47.19**
Beta	**2.01**
Average Daily Volume (sh)	**29,443**
Shares Outstanding (mil)	**21**
Market Capitalization ($mil)	**$111**
Short Interest Ratio (days)	**1**
Institutional Ownership (%)	**59**
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	**-7.0**
P/E using 2021 Estimate	**-7.5**

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)
2019	0 A	0 A	0 A	0 A	0 A
2020	0 A	0 E	0 E	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	-$0.17 E	-$0.17 E	-$0.17 E	-$0.72 E
2021					-$0.55 E
2022					-$0.56 E

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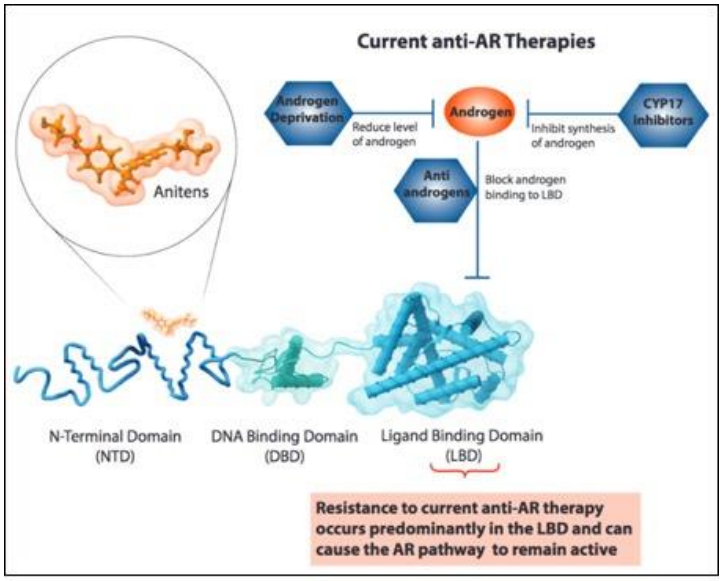
WHAT'S NEW

Business Update

Additional Preclinical Data Presented on EPI-7386

On February 13, 2020, ESSA Pharma Inc. (EPIX) announced additional preclinical data was presented at the 2020 American Society of Clinical Oncology (ASCO) Genitourinary Cancers Symposium (the poster can be found here) for its lead clinical 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 of the N-terminal domain (NTD), which is unique compared to other available anti-androgen therapies that target the ligand binding domain (LBD).

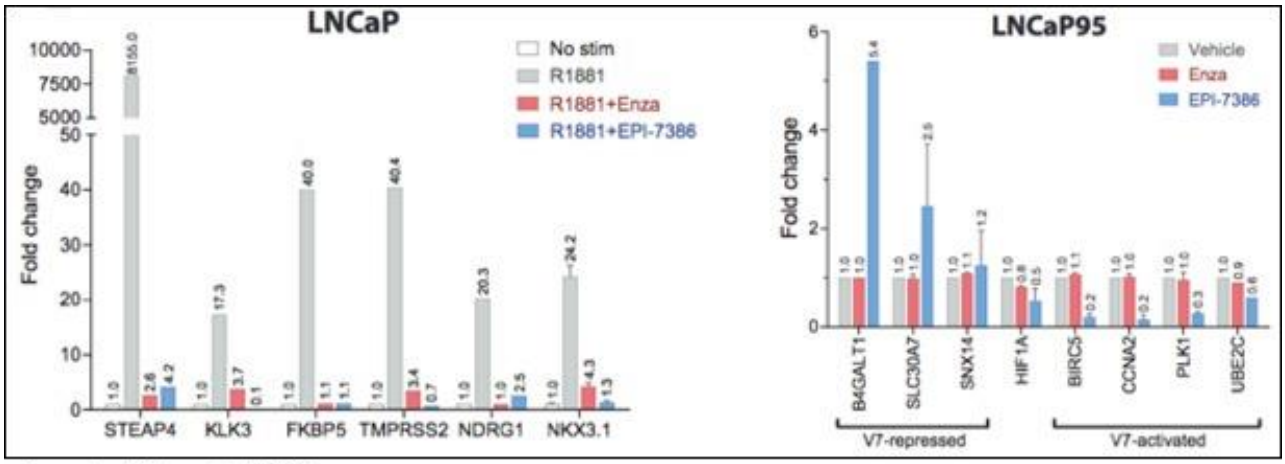
The company previously completed a Phase 1 trial with a first-generation aniten compound, EPI-506, that confirmed the safety and tolerability of this class of compounds. However, due to its short half-life and other negative pharmaceutical properties, the development of EPI-506 was discontinued while research continued on the development of next-generation anitens. This work led to the discovery of EPI-7386, a next-generation aniten that has a number of advantages compared to first-generation anitens. 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: Le Moigne *et al.*, 2020

The data presented at the 2020 ASCO Genitourinary Cancers Symposium built upon results previously presented by the company (see here for a discussion of those results). Additional experiments with EPI-7386 included examining its activity in both full-length AR (AR-FL) and AR-V7 models. AR V7 is a splice variant of AR that lacks the LBD and is correlated with poor survival, progression, and resistance to anti-androgen therapy.

The following figures show gene expression activity for genes controlled by AR-FL (lower left) and AR-V7 (lower right) in LNCaP and LNCaP95 cells, respectively. R1881 (methyltrienolone) is a synthetic androgen and considered the "gold standard" AR agonist, which is shown by the high gene expression levels in LNCaP cells treated with it. The following figure on the left shows that EPI-7386 is just as effective as enzalutamide in knocking down R1881-induced gene expression, thus showing it can inhibit AR activity. In the AR-V7 model, EPI-7386 can prevent AR-V7 from reducing the expression of certain genes (V7-repressed means that those genes are down regulated by AR-V7) and prevents AR-V7 from activating 'V7-activated' genes. This is in contrast to enzalutamide, which does not exhibit activity in the AR-V7 model. These results show that EPI-7386 can inhibit AR activity regardless if it is the fully length protein or an LBD-lacking variant.



Source: Le Moigne *et al.*, 2020

EPI-7386 has been tested in a number of preclinical prostate cancer xenograft models utilizing both AR-dependent and AR-independent tumors. The following table summarizes results from these studies. We believe the most interesting data from the table is in regards to the HID28 model, which utilizes cells derived from a prostate cancer patient and which is castration-resistant. In that model, EPI-7386 exhibited 58% tumor growth inhibition compared to placebo treatment while enzalutamide showed no tumor growth inhibition. This is additional data that differentiates EPI-7385 from enzalutamide and shows how it may be active against tumors in which enzalutamide is no longer effective.

in vivo model	AR status	Male Mice Condition	Compound	Dose (mg/kg)	Formulation	Regimen	TGI (%)	p value
LNCaP	AR FL	Castrated	Enzalutamide	30	Solution	qd24	>100%	p<0.0001
			EPI-7386	60			93%	p<0.0001
VCaP	Amplified AR Some AR-V7	Castrated	Enzalutamide	15	Solution	qd24	66%	p<0.05
			EPI-7386	3			54%	p<0.01
			EPI-7386	10			95%	p<0.0001
			EPI-7386	30			>100%	p<0.0001
LNCaP95	High level AR-V7 Other oncogenic pathways	Castrated	Enzalutamide	15	Solution	qd24	<0%	NS
			EPI-7386	30			54%	p<0.0001
22Rv1	High level AR-V7 Other oncogenic pathways	Castrated	EPI-7386	30	Solution	qd28	48%	p<0.0001
HID28	AR +, PSA + AR-V7 unknown	Castrated	Enzalutamide	15	Solution	qd28	<0%	NS
			EPI-7386	60	Suspension		58%	p<0.05
PC-3	Non functional AR Other oncogenic pathways	Intact	Enzalutamide	15	Solution	qd28	0%	NS
			EPI-7386	30			0%	NS

Statistics: 2-way ANOVA with Dunnett correction for multiple comparisons. NS: Non significant. TGI: Tumor Growth Inhibition

Source: Le Moigne *et al.*, 2020

ESSA Pharma has conducted a number of pharmacokinetic (PK) and toxicity studies in animals as part of the requirements for an IND filing. The following two tables show the results of 14-day dose range finding toxicology studies in rats (lower left) and beagles (lower right). Tolerability of EPI-7386 was shown at AUC ≤ 2,000,000 ng*h/mL.

Male SD rat dose range finding

Day of dosing	Dose Level (mg/kg/day)	C_{max} (ng/mL)	AUC_{0-24h} (ng-h/mL)	Toxicology conclusion
14	81	96,600	1,400,000	Below NOAEL
	162	147,000	2,000,000	NOAEL
	324*	195,000	3,340,000	Not tolerated

NOAEL: No-observed -adverse-event level.
Repeat dose showed an accumulation of 1.3-fold in AUC from day 1 to day 14.
* On day 8, animals dosed with the highest dose of 324 mg/kg/day were sacrificed.

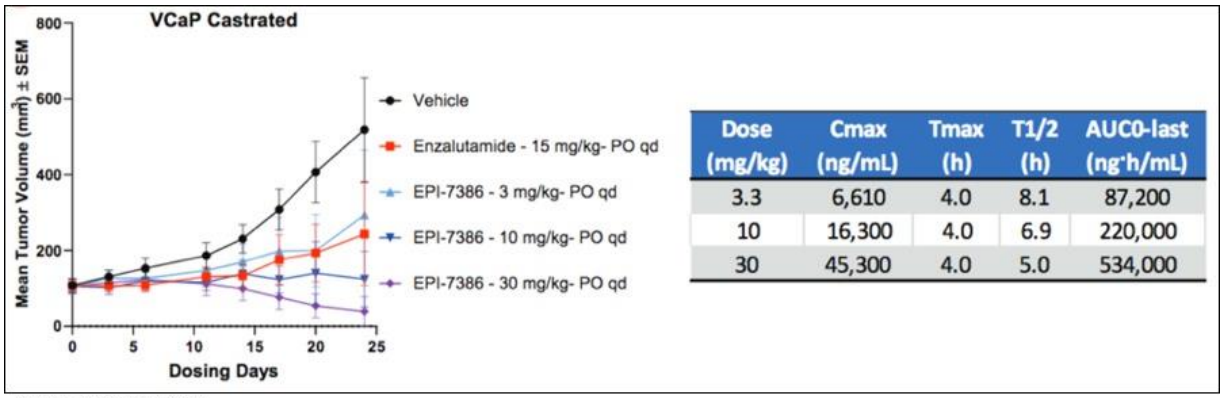
Male Beagle dog dose range finding

Day of dosing	Dose Level (mg/kg/day)	C_{max} (ng/mL)	AUC_{0-24h} (ng-h/mL)	Toxicology conclusion
14	26	27,800	507,000	Below NOAEL**
	64	93,000	1,870,000	NOAEL**
	162*	154,000	3,270,000	Not tolerated**

NOAEL: No-observed -adverse-event level.
Repeat dose showed an accumulation of 2-fold in AUC from day 1 to day 14.
* On day 8, 1 out of 3 dogs was sacrificed due to dose limiting clinical observations.
** Anti-androgen effects observed on target organs.

Source: Le Moigne *et al.*, 2020

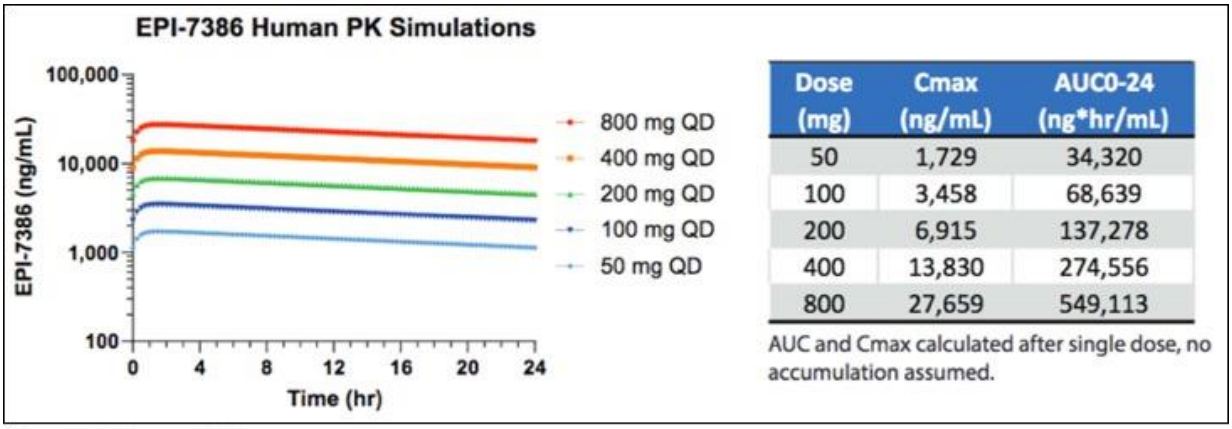
To put that data into perspective, the following table shows PK parameters for EPI-7386 when tested in the VCaP model. At 30 mg/kg, EPI-7386 showed >100% tumor growth inhibition and had an AUC of 534,000 ng*h/mL, which is well below the AUC value of 2,000,000 ng*hr/mL for the NOAEL dosage in rats.



Dose (mg/kg)	Cmax (ng/mL)	Tmax (h)	T1/2 (h)	AUC0-last (ng*h/mL)
3.3	6,610	4.0	8.1	87,200
10	16,300	4.0	6.9	220,000
30	45,300	4.0	5.0	534,000

Source: Le Moigne *et al.*, 2020

Lastly, estimated PK data was determined from *in vitro in vivo* correlation (IVIC). The following figures show estimated PK curves for single doses of EPI-7386 ranging from 50 mg to 800 mg once a day. Estimated PK parameters for those doses show that the expected AUC is well below the AUC of the NOAEL dosage in rats. These PK parameters also support once a day dosing for the upcoming Phase 1 studies. It should be noted that this model is for single dosing and that accumulation could occur with repeat dosing, however since the AUC levels are several fold lower than the NOAEL level we don't believe that toxicity will be an issue even if the modeled data is on the conservative side.



Dose (mg)	Cmax (ng/mL)	AUC0-24 (ng*hr/mL)
50	1,729	34,320
100	3,458	68,639
200	6,915	137,278
400	13,830	274,556
800	27,659	549,113

AUC and Cmax calculated after single dose, no accumulation assumed.

Source: Le Moigne *et al.*, 2020

EPI-7386 IND Filing in 1Q20; Phase 1 Clinical Trial to Start Shortly Thereafter

We anticipate the company filing an IND for EPI-7386 in the first quarter of 2020 and a Phase 1 clinical trial initiating soon thereafter in patients who are resistant to second-generation anti-androgen therapies (e.g., enzalutamide). The trial will include both a dose escalation phase with approximately 28 patients and a dose expansion phase with approximately 10 patients. 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. Given the above PK and toxicity data, we believe the company will be able to initiate with a high dose that may be close to the relevant exposure range and thus could identify the Phase 2 dose relatively quickly.

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 a combination trial with EPI-7386 and a 'lutamide' (enzalutamide, apalutamide, or darolutamide) in mCRPC patients due to the robust preclinical data showing increased activity with combination therapy. We estimate that the company is fully financed to conduct all three trials (the dose escalation trial, the dose expansion trial, and the combination trial).

Financial Update

On February 13, 2020, ESSA Pharma announced financial results for the first quarter of fiscal year 2020 that ended December 31, 2019. The company reported a net loss of $4.6 million, or $0.22 per share, for the first quarter of fiscal year 2020 compared to a net loss of $2.7 million, or $0.43 per share, for the first quarter of fiscal year 2019. R&D expenses for the three months ending Dec. 31, 2019 were $2.6 million compared to $1.3 million for the three months ending Dec. 31, 2018. The increase was related to the costs associated with preparing the IND for EPI-7386. G&A expenses in the first quarter of fiscal year 2020 were $2.1 million compared to $1.2 million in the first quarter of fiscal year 2019. The increase was primarily due to increased share-based compensation expenses.

As of Dec. 31, 2019, ESSA Pharma had approximately $45.9 million of cash and cash equivalents. During the first quarter of fiscal year 2020, the company repaid the remaining balance of its debt facility of approximately $3.6 million and the company no longer has any debt on its balance sheet. We estimate that ESSA Pharma has sufficient capital to fund operations through fiscal year 2022.

As of Dec. 31, 2019, the company had approximately 20.8 million shares outstanding, and when factoring in the 12.2 million reasonably priced warrants and the 5.3 million stock options there is a fully diluted share count of approximately 38.2 million.

Valuation

We value ESSA using a probability adjusted discounted cash flow model that takes into account potential future revenues for EPI-7386. We model for ESSA to partner the asset and to receive a 15% royalty on net sales.

For EPI-7386, we estimate that the company will initiate a Phase 1 trial in 2020, a Phase 3 trial in 2023, and file for approval in 2025. While the opportunity could exist for accelerated approval with exceptional results, we believe our timeframe is a bit more conservative of an estimate. For the initial indication, which is patients with mCRPC who are no longer responding to therapy, we estimate there are approximately 30,000 in the U.S. and 80,000 in the E.U. who would be eligible for treatment based on the number of deaths attributed to prostate cancer each year. While this represents a potential billion dollar opportunity on its own, we believe the much larger opportunity exists in combination therapy with earlier stage patients. We estimate there are approximately 160,000 patients who have either non-metastatic CRPC, metastatic hormone sensitive PC, or ADT-failing metastatic CRPC. When including these patients in our model we believe EPI-7386 could achieve peak sales of $4 billion worldwide. Using a 30% chance of approval along with a 13% discount rate leads to a net present value for EPI-7386 of $316 million. Combining the net present value of EPI-7386 with the company's current estimated cash balance and dividing by an estimated fully diluted share count of 38.2 million leads to a valuation of approximately $9.50 per share.

PROJECTED FINANCIALS

ESSA Pharma Inc.	FY2019 A	Q1FY20 A	Q2FY20 E	Q3FY20 E	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	$2.0	$2.0	$2.0	$8.6	$10.0	$12.0
Financing Costs	$0.6	$0.2	$0.0	$0.0	$0.0	$0.2	$0.0	$0.0
General & Administrative	$5.5	$2.1	$1.4	$1.4	$1.4	$6.3	$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)	($3.4)	($3.4)	($3.4)	($15.1)	($16.0)	($19.0)
Operating Margin	-	-	-	-	-	-	-	-
Non-Operating Expenses (Net)	$2.4	($0.0)	$0.0	$0.0	$0.0	($0.0)	$0.0	$0.0
Pre-Tax Income	($10.4)	($4.9)	($3.4)	($3.4)	($3.4)	($15.2)	($16.0)	($19.0)
Income Taxes	$0.0	($0.3)	$0.0	$0.0	$0.0	($0.2)	$0	$0
Tax Rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*
Net Income	**($10.4)**	**($4.6)**	**($3.4)**	**($3.4)**	**($3.4)**	**($14.9)**	**($16.0)**	**($19.0)**
Net Margin	-	-	-	-	-	-	-	-
Reported EPS	**($1.24)**	**($0.22)**	**($0.16)**	**($0.16)**	**($0.16)**	**($0.72)**	**($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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