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Edesa Biotech, Inc. (EDSA-NASDAQ)

EDSA: First Patient Enrolled in COVID-19 Trial…

Based on our probability adjusted DCF model that takes into account potential future revenues of EB01 and EB02, EDSA is valued at $15.00/share. This model is highly dependent upon continued clinical success of the company's pipeline and will be adjusted accordingly based on future clinical results.

Current Price (12/10/20)	$4.31
Valuation	**$15.00**

OUTLOOK

On December 7, 2020, Edesa Biotech, Inc. (EDSA) announced financial results for fiscal year 2020 that ended September 30, 2020. The company recently initiated a Phase 2/3 clinical trial of EB05 as a potential treatment for hospitalized COVID-19 patients. The trial is scheduled to take place at up to 40 clinical sites in the U.S. and Canada and is expected to enroll approximately 316 patients. We look forward to updates from the company regarding patient recruitment over the next few months. The ongoing coronavirus pandemic has created a challenging environment for getting patients enrolled into the Phase 2b clinical trial of EB01 in patients with chronic allergic dermatitis, however Edesa took actions to facilitate enrollment into the study and recently reported that 50% of the patients planned for the first cohort have been enrolled.

SUMMARY DATA

52-Week High	**$9.45**
52-Week Low	**$1.64**
One-Year Return (%)	**-3.58**
Beta	**0.65**
Average Daily Volume (sh)	**84,012**
Shares Outstanding (mil)	**11**
Market Capitalization ($mil)	**$45**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**1**
Insider Ownership (%)	**61**
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 2019 Estimate	**-3.5**
P/E using 2020 Estimate	**-2.7**

Risk Level	**Above Avg.**
Type of Stock	**Small-Growth**
Industry	**Med-Biomed/Gene**

ZACKS ESTIMATES

Revenue
(in millions of $)

	Q1 (Dec)	Q2 (Mar)	Q3 (Jun)	Q4 (Sep)	Year (Sep)
2020	0.1 A	0.1 A	0.1 A	0.1 A	0.4 A
2021	0.1 E	0.1 E	0.1 E	0.1 E	0.4 E
2022					0.4 E
2023					0.4 E

Earnings per Share

	Q1 (Dec)	Q2 (Mar)	Q3 (Jun)	Q4 (Sep)	Year (Sep)
2020	-$0.15 A	-$0.17 A	-$0.19 A	-$0.22 A	-$0.74 A
2021	-$0.16 E	-$0.17 E	-$0.19 E	-$0.19 E	-$0.71 E
2022					-$0.61 E
2023					-$0.65 E

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WHAT'S NEW

Business Update

First Patient Enrolled in COVID-19 Trial of EB05

On November 30, 2020, Edesa Biotech, Inc. (EDSA) announced that the first patient was enrolled in a Phase 2/3 clinical trial of EB05 in hospitalized COVID-19 patients. This is a randomized, multicenter, double blind, placebo-controlled trial that is expected to enroll approximately 316 patients across 40 hospitals (NCT04401475). It will evaluate the safety and efficacy of EB05 in adult hospitalized patients with moderate to severe COVID-19 that could eventually progress to acute lung injury (ALI) and acute respiratory distress syndrome (ARDS), both of which are life threatening and require intensive medical care. Patients will receive a single dose of either EB05 (15 mg/kg) + standard of care (SOC) or SOC only. If the results look promising the protocol allows for continuation of enrollment as a pivotal Phase 3 trial.

Background on TLR4 and ARDS

EB05 is a monoclonal antibody that targets toll-like receptor 4 (TLR4). Toll-like receptors (TLRs) belong to the pattern recognition receptor family of proteins and are an important part of the innate immune system. They are responsible for detecting invading pathogens and initiating an immediate immune response. TLR4 recognizes a number of different pathogens, including bacterial lipopolysaccharide (LPS) (Miller *et al*., 2005), mannuronic acid polymers from Gram-negative bacteria (Flo *et al*., 2002), and viral components (Haynes *et al*., 2001). Its activation leads to production of pro-inflammatory cytokines and chemokines (Janssens *et al*., 2003).

In addition to being involved in the innate immune response to pathogens, TLRs are known to be involved in exaggerated immune responses, with TLR4 shown to induce inflammatory responses that can lead to ALI (Jiang *et al*., 2005). Additional examples for TLR4's role in ALI and ARDS include:

- Imai *et al*., 2008: This study looked at the role of TLR4 in ALI. Mice deficient in TLR4 (*Tlr4*$^{-/-}$) were resistant to acid-induced ALI and while H5N1 influenza rapidly induced ALI in wild-type mice, TLR4 deficient mice were resistant to H5N1-induced ALI, suggesting a causative role for TLR4 in ALI.

- Shirey *et al*., 2016: This research group had previously reported that *Tlr4*$^{-/-}$ mice are resistant to influenza-induced lethality and a novel small molecule TLR4 inhibitor (eritoran) reduced influenza-induced lethality. In this study, an anti-TLR4 antibody protected mice from lethal influenza infection.

- Perrin-Cocon *et al*., 2017: A novel small molecule TLR4 antagonist (FP7) was tested in an *in vivo* mouse model of influenza. FP7 blocked TLR4 stimulation and protected mice from influenza-induced lethality and reduced inflammatory cytokine expression and ALI.

- Zhou *et al*., 2018: An anti-TLR4 monoclonal antibody was studied in a rat model of ARDS. The rats treated with the anti-TLR4 antibody showed lower respiratory frequency, lung permeability, lung edema, inflammatory infiltration, and tumor necrosis factor (TNF)-α and interleukin (IL)-1β expression levels in lungs along with lower TLR4, TLR9, MyD88, and nuclear factor (NF)-κB expression in macrophages.

- Domitrovic 2018: TLR4 monoclonal antibodies were evaluated both *in vitro* and in a rat model of ARDS. Stimulating macrophages with TNF-α along with anti-TLR4 antibody eliminated the upregulation and secretion of cytokines. Pre-treating rats with anti-TLR4 antibody prior to ventilation decreased lung injury, inflammatory infiltration, lung edema, and TLR4, TLR9, MyD88, and NF-κB expression.

- Zhang *et al*., 2019: This study examined the role of TLR4 and NF-κB in ALI and found inhibition of the TLR4/NF-κB signaling pathway decreased oxidative stress and improved ALI.

A number of studies have been published this year showing how TLR4 signaling is involved in COVID-19, including data showing that the level of TLR4 ligands (specifically calprotectin) can differentiate patients with severe COVID-19 compared to mild cases. Calprotectin, otherwise known as S100A8/A9, is a TLR4 ligand that promotes NF-κB activation (Riva *et al*., 2012) and the secretion of multiple inflammatory proteins such as IL-6 (Wang *et al*., 2018). Taken together, these studies provide the rationale for testing TLR4 signaling inhibition as a treatment for COVID-19.

- Silvin *et al*., 2020: This study examined peripheral blood cells in patients suffering from COVID-19 and included 27 with mild disease, 16 with moderate disease, and 43 with severe disease. The results showed that high levels of calprotectin correlated with severe COVID-19. The authors propose that calprotectin may trigger the cytokine release syndrome seen in severe COVID-19.

- Shi *et al*., 2020: This retrospective study examined the level of calprotectin in 172 COVID-19 patients and showed that all of the patients had elevated levels of calprotectin compared to healthy controls. In addition, when examined on day 1 or 2 of hospitalization (n=94 patients), calprotectin levels were significantly higher in patients who would go on to require mechanical ventilation (n=32) compared to those who were not intubated (P<0.0001).

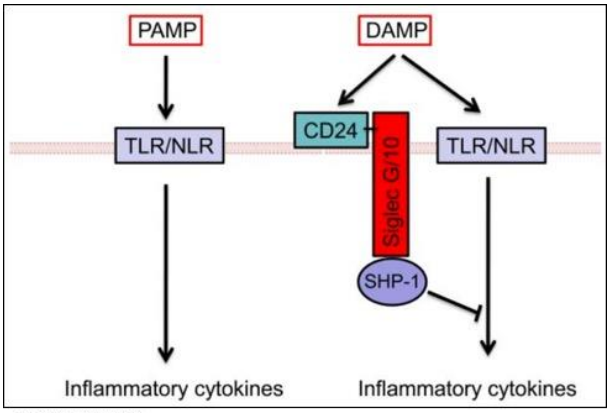
- Chen *et al*., 2020: This was a prospective study of 121 COVID-19 patients with 40 in the ICU and 81 in general wards at enrollment. Results showed that higher calprotectin resulted in significantly worse overall survival (P<0.0001). In addition, the level of calprotectin correlated with a range of inflammatory cytokines and chemokines, with three myeloid chemokines (IL-8, MCP-3, MCP-1) being the most significantly correlated and representing a distinct cytokine storm signature in COVID-19 patients.

Acquisition of OncoImmune Shows Potential for COVID-19 Therapeutics

In November 2020, Merck (MRK) announced the acquisition of OncoImmune, a privately held, clinical stage biopharmaceutical company for $425 million in cash along with the potential for OncoImmune shareholders to receive sales-based and milestone-based payments.

OncoImmune recently announced positive results from a Phase 3 study of CD24Fc for the treatment of patients with severe and critical COVID-19 (NCT04317040). This was a randomized, double blind, placebo controlled trial in which hospitalized COVID-19 patients who required oxygen support (including supplemental oxygen, high flow oxygen, and non-invasive ventilation) were assigned to receive either standard of care (SOC) plus a single dose of CD24Fc (SACCOVID™) or SOC plus placebo. The trial had planned to enroll 270 patients, however the trial was stopped after an interim efficacy analysis was performed when 146 patients had achieved clinical recovery from COVID-19, which occurred after enrollment of 203 patients. Patients who received CD24Fc had a 60% better chance of clinical recovery than those on placebo (P=0.005) and the risk of death from respiratory failure was reduced by more than 50%.

CD24Fc is a fusion protein consisting of CD24 and an immunoglobulin Fc domain. CD24 is a small glycosylated protein that was originally discovered by its ability to provide costimulatory signals to T cells (Liu *et al*., 1992). It binds to Siglec-10 and acts as an innate immune checkpoint against danger-associated molecular patterns (DAMPs), which are intracellular proteins that are released during cellular injury, through their binding to either CD24 or TLR (Kono *et al*., 2008). The innate immune system is also activated by pathogen-associated molecular patterns (PAMPs), which are mostly recognized by TLRs. The following figure shows how CD24 (and TLRs) sit at the apex of the inflammatory signaling pathway that is initiated by PAMPs and DAMPs (Liu *et al*., 2009).

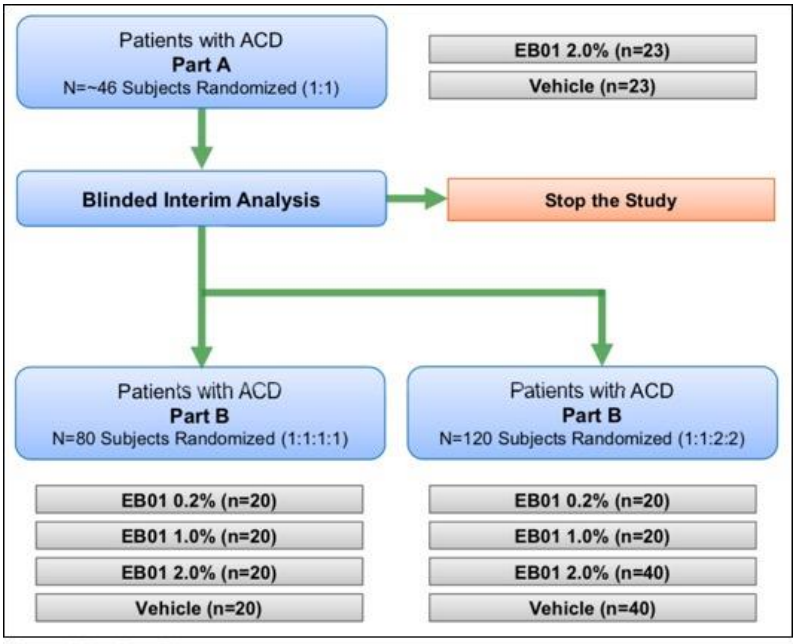


Source: Liu *et al.*, 2009

While simplified, the figure above shows that binding of TLR by their ligands (PAMPs or DAMPs) initiates an inflammatory cytokine signaling pathway and that CD24 binding of DAMPs works to inhibit the DAMP-induced signal. In COVID-19, the death of pneumocytes, and consequently the release of DAMPs, is a prominent feature and can ultimately lead to the development of ARDS. It is thought that CD24Fc both binds to DAMPs to prevent their interaction with TLRs as well as binding to Siglec-10 to inhibit inflammatory signaling through the DAMP/TRL pathway. Just like CD24Fc, EB05 is designed to inhibit the interaction of DAMPs with TLR so that the inflammatory signaling cascade is not initiated. Since CD24Fc appears to have a positive effect on COVID-19 pathogenicity (based on the results released by OncoImmune), it stands to reason that a similar intervention in the TLR pathway could also lead to positive results in COVID-19 patients.

Update on Phase 2b Trial of EB01

Edesa is currently conducting a Phase 2b clinical trial of EB01 2.0% cream in patients with (allergic contact dermatitis (ACD). The randomized, double blind, placebo controlled, sample size adaptive design trial is expected to enroll approximately 46 patients in Part A randomized 1:1 between EB01 and placebo for 28 days of treatment. Following the enrollment of the first cohort, a blinded interim analysis will be conducted that can have the following outcomes: 1) stop the study for futility; 2) continue to the dose ranging portion of the trial with 80 additional subjects; or 3) continue to the dose ranging portion of the trial with 120 additional subjects. The primary endpoint of the trial will measure the mean percent change from baseline in CDSI at Day 29, with secondary endpoints examining symptom reduction, dose-response relationships, and safety. An outline of the trial is shown below.



Source: Edesa Biotech, Inc.

In April 2020, the company filed a protocol amendment with the FDA for the ongoing Phase 2b trial. The amendment was filed such that changes to the study protocol could be made to mitigate the impact of the ongoing coronavirus pandemic. Included in the amendment were allowances for a reduction in the number of in-person office visits, remote telehealth appointments, and other procedural updates to simplify enrollment and patient care. In November 2020, the company announced that the trial has now enrolled >50% of the planned first cohort.

Financial Update

On December 7, 2020, Edesa announced financial results for the fiscal year 2020 that ended September 30, 2020. The comparable period is the nine months ending September 30, 2019 as the company changed its fiscal year to end in September following the reverse merger. The company reported revenues of $0.33 million, which was derived from the sale of product inventory obtained in the reverse merger in June 2019, compared to sales of $0.41 million for the nine-months ending September 30, 2019. We anticipate product sales to continue to decline as a result of the discontinuation of legacy operations. The cost of sales and services was $0.02 million for fiscal year 2020, due to the sales of product inventory obtained in the reverse merger acquisition. R&D expenses in fiscal year 2020 were $3.3 million, compared to $1.1 million for the nine months ending September 30, 2019. The increase was primarily due to increased expenses associated with the clinical trials of EB01 and EB05. G&A expenses totaled $3.4 million for fiscal year 2020 compared to $2.1 million for the nine months ending September 30, 2019. The increase was primarily due to increased salary and personnel expenses.

As of September 30, 2020, Edesa had approximately $7.2 million in cash and cash equivalents. Subsequent to the end of the fiscal year, Edesa raised approximately $2.0 million from the exercise of warrants and issuance shares under the at-the-market (ATM) program. We estimate that the company has sufficient capital to fund operations through the end of 2021. As of December 2, 2020, Edesa had approximately 10.5 million shares outstanding and when factoring in the Series A-1 convertible preferred, stock options, and warrants a fully diluted share count of approximately 13.5 million.

Conclusion

We are glad that the Phase 2/3 clinical trial of EB05 for the treatment of moderate to severe COVID-19 patients is underway and we look forward to updates from the company regarding the pace of enrollment. COVID-19 cases continue to increase in the U.S., and even with successful vaccines there will continue to be a need for effective therapeutics. The acquisition of OncoImmune shows what an effective COVID-19 therapy, particularly for patients with serious to severe disease, could be worth. Based on the positive results from OncoImmune and the similarities between the CD24 and TLR signaling pathways, we have increased our probability of success for EB05 in treating COVID-19 to 40%. This has increased our valuation to $15.00.

PROJECTED FINANCIALS

Edesa Biotech, Inc.	FY2020 A	Q1FY21 E	Q2FY21 E	Q3FY21 E	Q4FY21 E	FY2021 E	FY2022 E	FY2023 E
EB01	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
EB02	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Other Income	$0.3	$0.1	$0.1	$0.1	$0.1	$0.4	$0.4	$0.4
Total Revenues	**$0.3**	**$0.1**	**$0.1**	**$0.1**	**$0.1**	**$0.4**	**$0.4**	**$0.4**
Cost of Sales	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Product Gross Margin	-	-	-	-	-	-	-	-
Research & Development	$3.3	$1.0	$1.0	$1.1	$1.1	$4.2	$5.0	$6.0
General & Administrative	$3.4	$0.8	$0.9	$1.0	$1.1	$3.8	$4.0	$4.2
Other (Income) Expense	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Operating Income	($6.4)	($1.7)	($1.8)	($2.0)	($2.1)	($7.6)	($8.6)	($9.8)
Operating Margin	-	-	-	-	-	-	-	-
Non-Operating Expenses (Net)	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Pre-Tax Income	($6.4)	($1.7)	($1.8)	($2.0)	($2.1)	($7.6)	($8.6)	($9.8)
Income Taxes	$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	**($6.4)**	**($1.7)**	**($1.8)**	**($2.0)**	**($2.1)**	**($7.6)**	**($8.6)**	**($9.8)**
Net Margin	-	-	-	-	-	-	-	-
Reported EPS	**($0.74)**	**($0.16)**	**($0.17)**	**($0.19)**	**($0.19)**	**($0.71)**	**($0.61)**	**($0.65)**
YOY Growth	-	-	-	-	-	-	-	-
Basic Shares Outstanding	8.6	10.5	10.7	10.8	11.0	10.8	14.0	15.0

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

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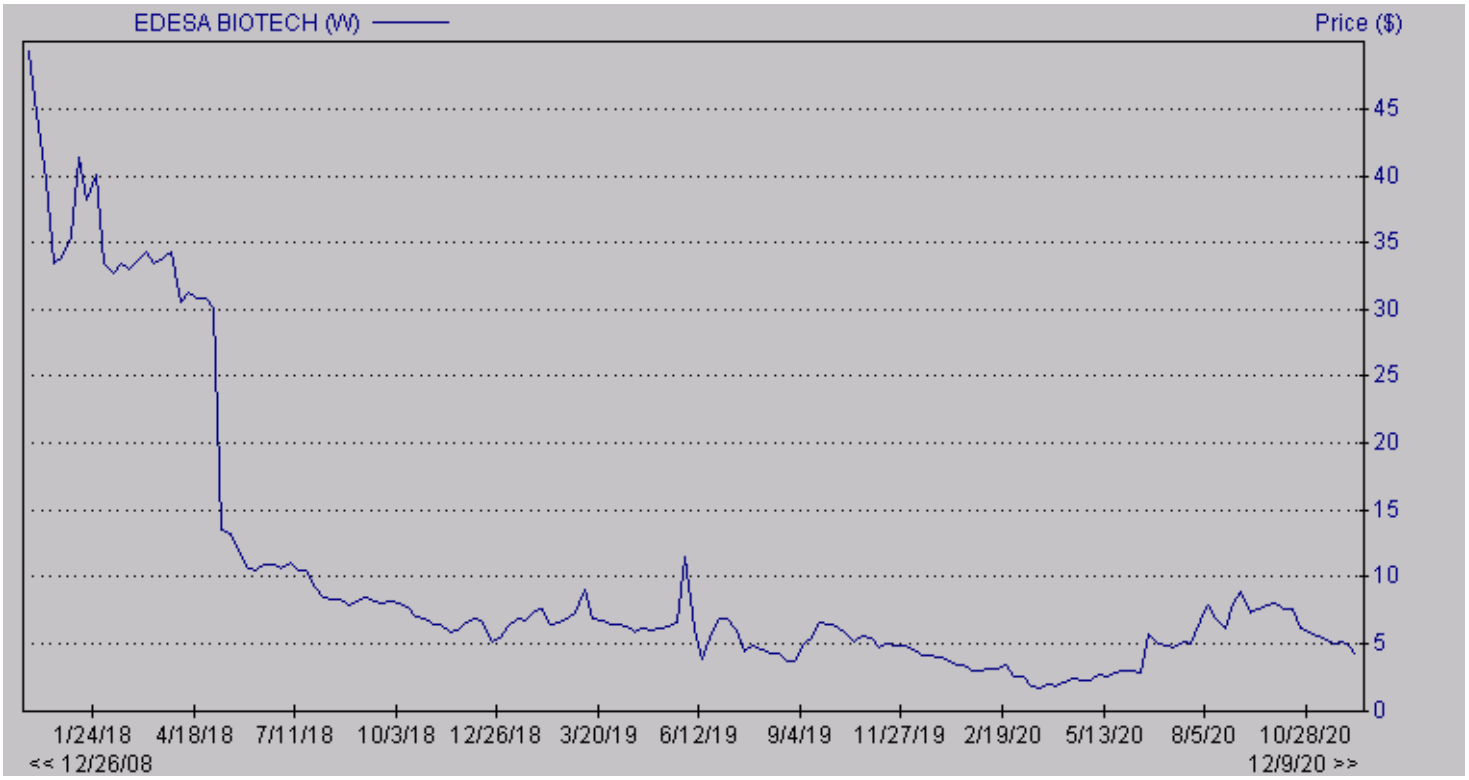
HISTORICAL STOCK PRICE



Source: Zacks Small Cap Research

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