October 25, 2019

Zacks Small-Cap Research

Brian Marckx, CFA
bmarckx@zacks.com
Ph (312) 265-9474

Sponsored – Impartial - Comprehensive

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

Aethlon Medical (AEMD-NASDAQ)

FDA IDE Approval of Human Cancer Study is Major Milestone (and clearly underappreciated by the Street)

We are maintaining our sum-of-the-parts valuation methodology in which we place a value of $90M for Hemopurifier in virus, pathogen, bioterror and cancer applications and value ESI at $30M. Sum-of-the-parts values AEMD at approximately $120M or ~$90/share.

Current Price (10/25/19)	$4.34
Valuation	**$90.00**

OUTLOOK

FDA IDE approval of Hemopurifier clinical cancer study is a major milestone as while it had previously been tested in human subjects – with no instances of serious safety concerns – the totality of clinical experience to-date has been modest and in disease areas (hepatitis C virus) that would likely not have nearly the commercial opportunity as would oncological applications. EFS (n= 10 – 12) will combine Hemopurifier with the checkpoint inhibitor Keytruda (Merck), a revolutionary cancer therapy approved in over 22 indications, in patients with unresectable head and neck cancer. More evidence continues to support targeting of exosomes to fight certain solid cancers including recent studies showing removal of cancer-associated exosomes slows cancer growth (even in tumors resistant to checkpoint inhibitors), some solid cancers appear to be resistant to these drugs – suggesting that effective treatment may require the direct targeting of tumor derived exosomes, and that targeting cancer exosomes provides incremental benefit (i.e. suppression of tumor growth) beyond that of the most effective cancer drugs available today. FDA approval of final site documentation is a near-term expectation and, given its small size and single location, we think there may be opportunities for potential value-moving events on a regular basis shortly after the study begins.

SUMMARY DATA

52-Week High	**$26.10**
52-Week Low	**$3.00**
One-Year Return (%)	**-74.43**
Beta	**-0.10**
Average Daily Volume (sh)	**20,314**
Shares Outstanding (mil)	**1**
Market Capitalization ($mil)	**$5**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**15**
Insider Ownership (%)	**7**
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	**N/A**
P/E using 2021 Estimate	**N/A**
Zacks Rank	**N/A**

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

ZACKS ESTIMATES

Revenue
(in '000 of $)

	Q1 (Jun)	Q2 (Sep)	Q3 (Dec)	Q4 (Mar)	Year (Mar)
2018	0.0 A	0.0 A	0.1 A	0.1 A	0.2 A
2019	0.2 A	0.0 A	0.0 A	0.1 A	0.2 A
2020	0.0 A	0.2 E	0.2 E	0.2 E	0.6 E
2021					1.1 E

Earnings per Share

	Q1 (Jun)	Q2 (Sep)	Q3 (Dec)	Q4 (Mar)	Year (Mar)
2018	-$3.14 A	-$2.17 A	-$1.22 A	-$1.20 A	-$6.92 A
2019	-$0.97 A	-$1.17 A	-$1.67 A	-$1.30 A	-$5.12 A
2020	-$1.63 A	-$1.10 E	-$1.03 E	-$0.95 E	-$4.71 E
2021					-$2.96 E

Zacks Projected EPS Growth Rate - Next 5 Years % **N/A**

© Copyright 2019, Zacks Investment Research. All Rights Reserved.

IDE Approved. Hemopurifier U.S. Clinical Cancer Program On-Deck…

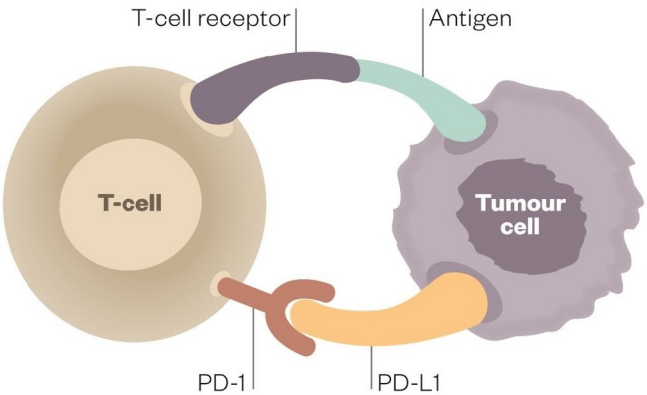
When Aethlon reported fiscal Q1 2020 financial results in August, management noted that they anticipated imminent filing of an Investigational Device Exemption (IDE) seeking approval to initiate U.S.-based clinical studies for their Hemopurifier device in cancer patients. Not only did that filing happen but on October 7th AEMD announced that the IDE was approved by FDA. While initiation of the clinical program is contingent on standard trial-site sign-off, IDE approval means the most significant hurdle is cleared.

The IDE relates to an Early Feasibility Study (EFS) – analogous to a Phase 1 safety-oriented study – using Hemopurifier in conjunction with pembrolizumab in patients with advanced head and neck cancer. Pembrolizumab, marketed by Merck (MRK) as Keytruda, is a next-gen cancer therapy used in immunotherapy against a variety of advanced cancers. A humanized antibody which was initially approved by FDA in 2014, pembrolizumab is one of a new class of drugs known as checkpoint inhibitors which work by manipulating immune system function. In June 2019 FDA approved Keytruda for first-line (i.e. standard of care) treatment of patients with metastatic or unresectable recurrent head and neck squamous cell carcinoma (HNSCC).

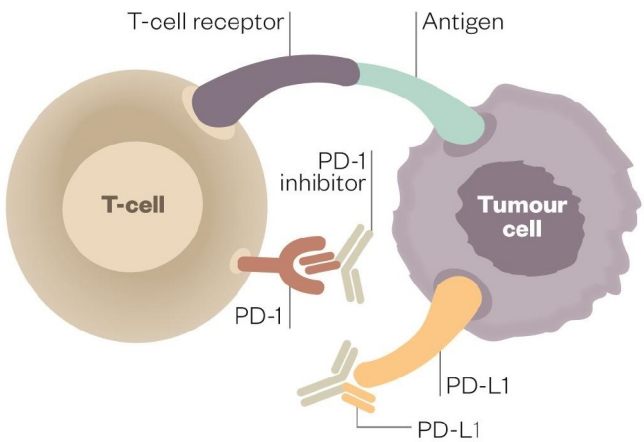
Pembrolizumab targets PD-1 ('programmed cell death protein 1'), a protein found on and responsible for turning on and off T cells' immunity response. When T cells encounter normal healthy cells, PD-1 attaches to PD-L1 ('programmed death-ligand 1'), a protein on the healthy cell which lets the immune cell know not to attack it. PD-L1 is also found on some cancer cells, however, which use it as a defense mechanism by tricking T cells into not destroying it.

In cancers that overexpress PD-L1, pembrolizumab inhibits tumor growth by targeting PD-1. More specifically, pembrolizumab attaches to the PD-1 receptor, thereby blocking PD-L1 (from turning the immune response off) and exposing PD-L1 overexpressed cancer cells to attack by the body's immune system.

Tumor Uses PD-L1 as Defense Mechanism



PD-1 Inhibitor Blocks Tumor's Defense Mechanism



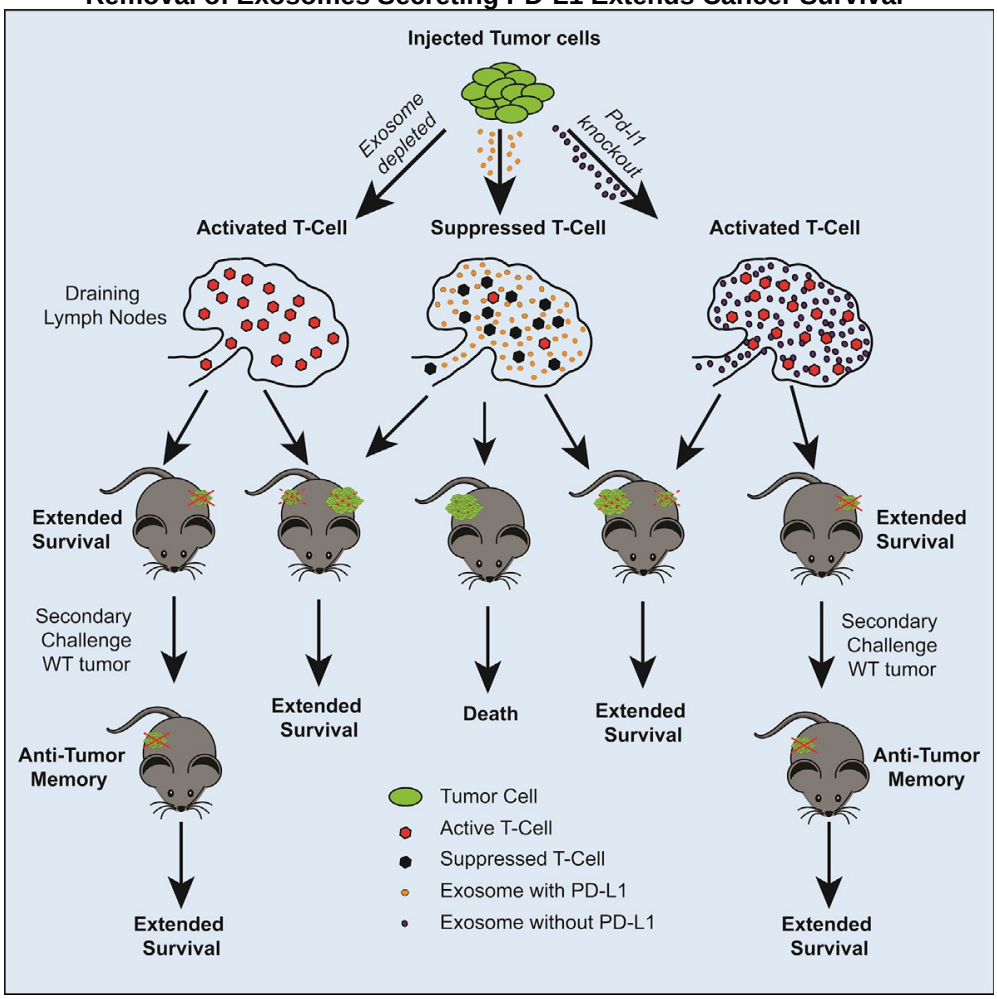
Source: The Pharmaceutical Journal, Nov 2014. Malini Guha

The hypothesis behind combining the inhibition of PD-1 (via pembrolizumab) and physical removal of tumor-derived exosomal PD-L1 (via Hemopurifier) from the body is to evaluate whether it is more effective than PD-1 inhibition alone in fighting these unresectable tumors. As it relates to the latter, more and more evidence continues to support therapeutic targeting of exosomes to fight certain solid cancers.

This includes compelling findings from a study (*Suppression of Exosomal PD-L1 Induces Systemic Anti-tumor Immunity and Memory*, April 2019) published earlier this year in the journal Cell which showed that not only do exosomes play a role in cancer, but also that removal of exosomal PD-L1 inhibits tumor growth (even with tumors resistant to anti-PD-L1 antibodies) and exposure to exosomal PD-L1-deficient tumor cells may result in anti-tumor memory and immunity. Moreover, exosomal PD-L1 of some solid cancers appears to be resistant to anti-PD-L1 therapy – suggesting that effective treatment may require the direct targeting of tumor derived exosomes. Perhaps the most compelling conclusion of the study is the finding that targeting exosomal PD-L1 provides incremental benefit (i.e. suppression of tumor growth) to that of checkpoint inhibitors. AEMD's EFS study, while small and not

necessarily powered for conclusive efficacy, might still provide some insight into the potential utility of Hemopurifier in additive cancer therapy.

Removal of Exosomes Secreting PD-L1 Extends Cancer Survival[1]



Potential Opportunity for Hemopurifier as Keytruda Adjunct…

Even if this EFS study is successful, there is no way for us to know what AEMD's next-steps will be for their cancer program (i.e. a formal U.S. regulatory program using Hemopurifier in combination with pembrolizumab would seem to be the most obvious, although other options could potentially be in play as well). So, while too early to even suggest that there is a reasonable chance that Hemopurifier could one day be used in combination with Keytruda in the treatment of certain cancers, we offer some background on the success of this cancer drug for some context of the significance of this market and the possible opportunity for AEMD.

Keytruda has shown to be a revolutionary drug in the treatment of cancer. Keytruda generated $7.2B in revenue in 2018, is expected to bring in approximately $10B in sales in 2019 and is Merck's most important product. Analysts are predicting that it could reach over $22B in revenue by 2025 and become the best-selling drug of all time. Keytruda has been successfully used to treat 25 different types of cancer, has regulatory approval in more than 22 oncological indications (including non-small cell lung cancer, head and neck cancer, melanoma, cervical cancer and many more) and has been used in over 1,000 clinical trials.[2]

Specific to head and neck cancer (i.e. subject of the EFS study), Keytruda is the only checkpoint inhibitor that has FDA approval as a first-line treatment for this indication (Bristol-Myers' Opdivio is FDA approved for patients that fail chemotherapy), which FDA granted in June of this year. An estimated 65k people in the U.S. are diagnosed each

[1] Poggio et al., *Suppression of Exosomal PD-L1 Induces Systemic Anti-tumor Immunity and Memory* 2019, Cell 177, 414–427
[2] BioSpace, Oct 4, 2019. Alex Keown

year with head and neck cancer. Which, given the approximate $12k per month cost of Keytruda treatment, means this indication alone (and just in the U.S.) represents an estimated annual market of more than $9B.

Early Feasibility Study
The design of the Early Feasibility Study is consistent with the indication granted to Hemopurifier under FDA's Breakthrough Device designation which, as a reminder was awarded in November 2018 and relates to "the treatment of individuals with advanced or metastatic cancer who are either unresponsive to or intolerant of standard of care therapy, and with cancer types in which exosomes have been shown to participate in the development or severity of the disease. Therapy with the Hemopurifier device should be an adjunct to standard of care for cancer."

Per Aethlon's press release earlier this month, this initial human cancer study will enroll between 10 and 12 patients at a single trial site. Like all Phase 1 studies, the primary endpoint will be related to safety. The study will assess efficacy-related performance with secondary endpoints measuring exosome clearance and characterization as well as response and survival rates.

IDE approval is a major milestone in our opinion as while Hemopurifier has previously been tested in human subjects – with no instances of serious safety concerns – the totality of clinical experience to-date has been modest and in disease areas (hepatitis C virus) that would likely not have nearly the commercial opportunity as would oncological applications. To be clear, we are not trivializing the significance of the findings that have come from development to-date of Hemopurifier – including establishment of a safety profile sufficient to clear FDA's relatively stringent benefit-risk assessment and gain IDE approval. And much of that work likely has cross-over applicability to follow-on development in cancer applications – even more encouraging given that we have always believed (since we initiated coverage of AEMD in 2012; *March 13, 2012: Initiating With Neutral Rating*) that any commercial opportunity for Hemopurifier in HCV (AEMD's initial therapeutic target) would be limited and not particularly attractive from a development-spending or investment standpoint.

And while previous clinical testing has shown that Hemopurifier can successfully and safely remove viral toxins from the blood and preclinical testing has demonstrated its ability to remove tumor-derived exosomes, this Early Feasibility Study will be the first real world-type evaluation of whether it may have utility in the treatment of cancer. Unlike HCV, which new drugs have turned into a highly treatable and even curable disease, cancer cures (with some rare exceptions) remain elusive. Treatment of metastatic disease is largely related to one or more of a combination of investigational (drugs, immunotherapy, radiation) therapies and focused on marginal life extension (often with poor quality of life) and palliative care.

As such, cancer not only represents a potentially enormous commercial market but the (unfortunate) terminality and incidence of metastatic disease means that development-related opportunities (potentially including non-dilutive funding, partnerships, clinical trials, regulatory-related resources, etc) are likely much more abundant than what would be the case in most other diseases. In addition, the finality of terminal diseases means that demonstration of 'effectiveness' (as well as 'acceptable safety') may be comparably less onerous than in less serious conditions or those with currently available treatment options. Moreover, as side effects of some cancer drugs can be particularly challenging to manage and cope with, 'effectiveness' might also be defined (for example) as an improvement to quality of life.

These reasons underscore why we view FDA approval of the IDE as such a significant event. If all goes well it will also eventually prove to represent a development and commercial inflection in focus for AEMD. In the meantime, FDA's regulatory framework for clinical evaluation of novel therapeutics should provide ample opportunity over time to help judge the potential utility of the Hemopurifier in the treatment of cancer – and, by extension, regular and multiple opportunities for inflection in the market value of AEMD.

Outlook Valuation
Given the difficulty in designing clinical studies around highly virulent viruses, we think the BDD for cancer could be a game-changer for Aethlon. While cancer is just as impossible to effectively control and treat as are the deadly viruses that would fall under the purview of the initial Breakthrough program, it is obviously relatively widely prevalent and more chronic as compared to infection from highly virulent viruses (which, if exposed, could result in death in relatively short period of time). This makes cancer a much more practical target to build a clinical and regulatory program around. And with Hemopurifier already having shown substantive efficacy in reducing or eliminating circulating tumor derived exosomes from the blood, coupled with existing human safety data, it is possible that a cancer pursuit could be relatively fast-moving.

We think that there is reason to believe that a cancer indication for the Hemopurifier is an eventual realistic outcome. Already-completed clinical studies should provide at least some support for the safety of the device, while preclinical studies support Hemopurifiers' ability to capture exosomes. Moreover, the fact that the BDD indication is for metastasized cancers and for which standard of care has failed (i.e. patients which are essentially out of options), implies a lower safety hurdle. Meanwhile, successful capture of exosomes in preclinical studies in a variety of cancers including breast, ovarian and metastatic melanoma certainly lends credence to the effectiveness of the Hemopurifier in removing exosomes from the circulation of cancer patients. And, finally, receipt and successful competition of grants from the National Cancer Institute related to this topic – that is, removal of exosomes from circulation as a cancer therapy means that this is a pursuit that is not just of interest to Aethlon but to the U.S. government as well. Importantly, in September 2019 AEMD announced that NCI awarded them the Phase 2 (follow-on) grant related to isolation of melanoma exosomes (for diagnostic and treatment monitoring). The grant, which will pay $1.86M over two years, lends further validation to the potential utility of their technology in cancer treatment.

And, encouragingly, there is no shortage of new evidence supporting the role of exosomes in the progression of cancer and, similarly, that removing tumor-derived exosomes from circulation may inhibit tumor growth and/or potentially improve the effectiveness of immunotherapies. As this describes the basis for Aethlon's pursuit of the Hemopurifier in a potential cancer indication, a growing database of evidence can have important consequences including potentially influencing key opinion leaders and regulators alike.

Relative to ESI, in September 2019 AEMD announced a collaboration with Hoag Memorial Hospital Presbyterian (Newport Beach, CA) with a focus on learning more about exosomes in cancer including identifying unique exosome-based biomarkers with the intent of using these in the development of an early-stage cancer liquid biopsy. The idea is to develop a liquid biopsy which will be able to identify individuals at high risk of developing cancers that could benefit from Hemopurifier treatment.

ESI also continues to work on the ongoing CTE study which we continue to expect will provide more definitive information relative TauSome's place in the detection of CTE (as well as potentially its relationship to other diseases such as Alzheimer's) – a goal that has escaped the clinical community so far and one that would be a major breakthrough and likely be instrumental in helping to shape the diagnosis, treatment and monitoring of the disease.

While we view IDE approval of the EFS study as a major milestone (for the reasons listed above) and one that could lead to meaningful inflection in the value of AEMD, we are currently maintaining our (sum-of-the-parts based) valuation. FDA approval of final site documentation is a near-term milestone we will be looking for and, given the its small size and single location, expect there may be opportunities for potential value-moving events on a regular basis shortly after the study begins.

We also note that while it is too early to gauge the potential value of the AEMD / SeaStar collaboration, that significant progress towards a joint product development program (or related synergies with AEMD's current individual pursuits) could offer value-creation and/or value-enhancement opportunity.

So, while our price target remains subject to change, we continue to see fair value of Hemopurifier in virus, pathogen, bioterror and cancer applications at ~$90M and value ESI at $30M. Sum-of-the-parts values AEMD at approximately $120M or ~$90/share. The shares underwent a 1-for-15 reverse split effective Oct 15th and currently trade at $4.34 each, representing total equity value of just $5.9M (with ~1.35M shares currently o/s) – grossly undervaluing the company in our opinion.

PROJECTED INCOME STATMENT

Aethlon Medical, Inc.

	2017 A	2018 A	Q1 A	Q2 A	Q3 A	Q4 A	2019 A	Q1 A	Q2 E	Q3 E	Q4 E	2020 E	2021 E
Revenue	$392.1	$149.6	$149.6	$0.0	$0.0	$80.0	$229.6	$30.0	$188.4	$187.5	$187.5	$593.4	$1,125.0
YOY Growth	*-55.8%*	*3128.2%*	-	-	-	*6.9%*	*53.5%*	*-79.9%*	-	-	*134.4%*	*158.4%*	*89.6%*
Cost of Goods Sold	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Gross Income	$392.1	$149.6	$149.6	$0.0	$0.0	$80.0	$229.6	$30.0	$188.4	$187.5	$187.5	$593.4	$1,125.0
Gross Margin	*100.0%*	-	-	-	-	-	-	-	-	-	-	-	-
SG&A	$5,817.4	$4,402.1	$1,052.1	$1,139.2	$1,720.0	$1,430.7	$5,342.0	$1,347.3	$1,329.0	$1,383.0	$1,448.0	$5,507.3	$5,527.0
% SG&A	*1483.8%*	-	-	-	-	-	-	-	-	-	-	-	-
R&D	$673.0	$578.6	$194.8	$207.8	$243.8	$240.2	$886.6	$248.9	$262.0	$244.0	$278.0	$1,032.9	$1,147.0
% R&D	*171.7%*	-	-	-	-	-	-	-	-	-	-	-	-
Impairment	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0	$0.0
Operating Income	($6,098.4)	($4,831.1)	($1,097.3)	($1,347.0)	($1,963.9)	($1,590.9)	($5,999.1)	($1,566.2)	($1,402.6)	($1,439.5)	($1,538.5)	($5,946.8)	($5,549.0)
Operating Margin	*-1555.4%*	-	-	-	-	-	-	-	-	-	-	-	-
Other Expense, total	$1,208.4	$868.7	$55.1	$55.1	$55.1	$55.2	$220.5	$501.1	$15.2	$0.0	$0.0	$69.3	$0.0
Pre-Tax Income	($7,306.7)	($5,699.8)	($1,152.4)	($1,402.1)	($2,019.0)	($1,646.1)	($6,219.5)	($2,067.3)	($1,417.8)	($1,439.5)	($1,538.5)	($6,016.1)	($5,549.0)
Taxes (benefit)	$0.0	$0.0	$0.0	$0.0	$0.0	$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%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*	*0.0%*
Net Income	($7,276.1)	($5,679.6)	($1,146.2)	($1,393.4)	($2,013.0)	($1,642.1)	($6,194.8)	($2,066.4)	($1,412.1)	($1,433.7)	($1,532.3)	($6,444.7)	($5,526.8)
Net Margin	*-1855.8%*	-	-	-	-	-	-	-	-	-	-	*-1086.1%*	*-491.3%*
EPS	($14.06)	($6.92)	($0.97)	($1.17)	($1.67)	($1.30)	($5.12)	($1.63)	($1.10)	($1.03)	($0.95)	($4.71)	($2.96)
YOY Growth	*42.2%*	*65.1%*	-	-	-	-	-	-	-	-	-	-	-
Diluted Shares O/S	518	821	1,184	1,186	1,203	1,260	1,208	1,270	1,288	1,392	1,605	1,389	1,867

Brian Marckx, CFA

© Copyright 2019, Zacks Investment Research. All Rights Reserved.

HISTORICAL STOCK PRICE



Source: Zacks Investment Research

© Copyright 2019, Zacks Investment Research. All Rights Reserved.

DISCLOSURES

The following disclosures relate to relationships between Zacks Small-Cap Research ("Zacks SCR"), a division of Zacks Investment Research ("ZIR"), and the issuers covered by the Zacks SCR Analysts in the Small-Cap Universe.

ANALYST DISCLOSURES

I, Brian Marckx, CFA, hereby certify that the view expressed in this research report accurately reflect my personal views about the subject securities and issuers. I also certify that no part of my compensation was, is, or will be, directly or indirectly, related to the recommendations or views expressed in this research report. I believe the information used for the creation of this report has been obtained from sources I considered to be reliable, but I can neither guarantee nor represent the completeness or accuracy of the information herewith. Such information and the opinions expressed are subject to change without notice.

INVESTMENT BANKING AND FEES FOR SERVICES

Zacks SCR does not provide investment banking services nor has it received compensation for investment banking services from the issuers of the securities covered in this report or article.
Zacks SCR has received compensation from the issuer directly, from an investment manager, or from an investor relations consulting firm engaged by the issuer for providing non-investment banking services to this issuer and expects to receive additional compensation for such non-investment banking services provided to this issuer. The non-investment banking services provided to the issuer includes the preparation of this report, investor relations services, investment software, financial database analysis, organization of non-deal road shows, and attendance fees for conferences sponsored or co-sponsored by Zacks SCR. The fees for these services vary on a per-client basis and are subject to the number and types of services contracted. Fees typically range between ten thousand and fifty thousand dollars per annum. Details of fees paid by this issuer are available upon request.

POLICY DISCLOSURES

This report provides an objective valuation of the issuer today and expected valuations of the issuer at various future dates based on applying standard investment valuation methodologies to the revenue and EPS forecasts made by the SCR Analyst of the issuer's business.
SCR Analysts are restricted from holding or trading securities in the issuers that they cover. ZIR and Zacks SCR do not make a market in any security followed by SCR nor do they act as dealers in these securities. Each Zacks SCR Analyst has full discretion over the valuation of the issuer included in this report based on his or her own due diligence. SCR Analysts are paid based on the number of companies they cover. SCR Analyst compensation is not, was not, nor will be, directly or indirectly, related to the specific valuations or views expressed in any report or article.

ADDITIONAL INFORMATION

Additional information is available upon request. Zacks SCR reports and articles are based on data obtained from sources that it believes to be reliable, but are not guaranteed to be accurate nor do they purport to be complete. Because of individual financial or investment objectives and/or financial circumstances, this report or article should not be construed as advice designed to meet the particular investment needs of any investor. Investing involves risk. Any opinions expressed by Zacks SCR Analysts are subject to change without notice. Reports or articles or tweets are not to be construed as an offer or solicitation of an offer to buy or sell the securities herein mentioned.