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MediciNova, Inc. (MNOV-NASDAQ)

MNOV: Plans in Place for Phase 3 Trial in ALS…

Based on our probability adjusted DCF model that takes into account potential future revenues from MN-166 in ALS, progressive MS and addiction and MN-001 in NASH and IPF, MNOV is valued at $19/share. This model is highly dependent upon continued clinical success of both MN-166 and MN-001 and will be adjusted accordingly based upon future clinical results.

Current Price (05/09/19)	$12.47
Valuation	**$19.00**

OUTLOOK

MediciNova, Inc. (MNOV) recently completed a subgroup analysis of the SPRINT-MS Phase 2b trial of MN-166 (ibudilast) in progressive multiple sclerosis (MS). Results showed that treatment with MN-166 resulted in a 46% risk reduction in confirmed disability progression compared to placebo (hazard ratio=0.538) in secondary progressive MS (SPMS) patients without relapse, while in SPMS patients with relapse there was no treatment effect. The FDA recently approved two new therapies for patients with SPMS with relapse, and there are currently no approved long-term therapies for SPMS without relapse, thus representing a large market opportunity. The company is planning a meeting with the FDA to discuss plans for the Phase 3 trial in progressive MS.

SUMMARY DATA

52-Week High	**$12.83**
52-Week Low	**$6.82**
One-Year Return (%)	**18.76**
Beta	**1.25**
Average Daily Volume (sh)	**134,274**
Shares Outstanding (mil)	**43**
Market Capitalization ($mil)	**$537**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**21**
Insider Ownership (%)	**16**
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 2018 Estimate	**N/A**
P/E using 2019 Estimate	**N/A**

Risk Level	**High**
Type of Stock	**Small-Growth**
Industry	**Med-Biomed/Gene**

ZACKS ESTIMATES

Revenue
(In millions of $)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2018	0 A	0 A	0 A	0 A	0 A
2019	0 A	0 E	0 E	0 E	0 E
2020					0 E
2021					0 E

Earnings per Share

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2018	-$0.12 A	-$0.08 A	-$0.16 A	-$0.00 A	-$0.36 A
2019	-$0.11 A	-$0.14 E	-$0.15 E	-$0.15 E	-$0.55 E
2020					-$0.56 E
2021					-$0.56 E

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WHAT'S NEW

Business Update

Ready to Move MN-166 into Phase 3 Trial in ALS

On April 15, 2019, MediciNova, Inc. (MNOV) announced that following review of the protocol the U.S. Food and Drug Administration (FDA) has determined that the company may proceed with the Phase 2b/3 clinical trial of MN-166 (ibudilast) in amyotrophic lateral sclerosis (ALS). If successful, results from this trial are expected to support a New Drug Application (NDA) for MN-166 in ALS.

The Phase 2b/3 clinical trial will be a multi-center, two-arm, randomized, double blind, placebo controlled trial that will compare MN-166 to placebo in 150 patients with ALS. Participants in the trial will be randomized 1:1 between placebo and 100 mg/day of MN-166 for nine months of treatment. The primary endpoint of the trial is the mean change in ALS functional rating scale-revised (ALSFRS-R) (Cedarbaum *et al*., 1999). The ALSFRS-R consists of a series of 12 questions on basic tasks (speech, salivation, swallowing, handwriting, cutting food, dressing and hygiene, turning in bed, walking, climbing stairs, dyspnea, orthopnea, and respiratory insufficiency) that are rated on a five-point scale where 0 = can't do and 4 = normal ability. The individual items are summed to produce a score of between 0 = death and 48 = best. The ALSFRS-R score is utilized to keep track of the health of all ALS patients, and is a common outcome measure in ALS clinical trials as well as an established FDA-approvable endpoint. Secondary endpoints in the trial include the mean change from baseline in muscle strength and quality of life, the utilization of and time to clinically indicated prescription for non-invasive ventilation, and safety and tolerability.

Important inclusion criteria include onset of ALS no more than 18 months prior to screening, at least one documented ALSFRS-R score between three and six months before screening, the use of riluzole for at least 30 days prior to initiation of the study drug, and an ALSFRS-R score of at least 35 at screening. Patients currently taking Radicava® (edaravone) or Nuedexta® (dextromethorphan/quinidine) may be eligible as long as they cease taking those treatments three months prior to entering the trial.

Radicava® Most Recently Approved ALS Treatment

Radicava (edaravone) was approved for the treatment of ALS by the FDA in May 2017. Edaravone is a potent scavenger of oxygen radicals. While the underlying mechanisms responsible for causing ALS are unknown, it is believed that oxidative stress plays some role in the development of the disease. This is supported by the fact that mutations in superoxide dismutase 1 (SOD1) cause familial ALS. SOD1 is responsible for converting superoxide radicals to oxygen and hydrogen peroxide.

In an ALS mouse model that involves a mutation in SOD1, administration of edaravone resulted in reduced motor decline and preserved motor neurons in the spinal cord (Ito *et al*., 2008). Similar results were seen in a rat model of ALS (Aoki *et al*., 2011). Based on these results, edaravone was tested in ALS patients in three different clinical trials.

Edaravone Clinical Trials

Edaravone was originally tested in a Phase 2 clinical trial involving 20 ALS patients (Yoshino *et al*., 2006). The study was an open-label comparison study that evaluated patients before and after treatment with edaravone. Results showed a statistically significant difference in the change in ALSFRS-R before treatment (4.7 points) compared to during the treatment period (2.3 points; P=0.036).

The first Phase 3 clinical trial of edaravone was conducted in 205 patients randomized to receive edaravone (n=101) or placebo (n=104) (Abe *et al*., 2014). Treatment consisted of intravenous infusions given over 60 min for the first 14 days of cycle 1 (followed by 14 days off drug), and then 10 of the first 14 days during cycles two through six, with 14 days off drug following treatment in each cycle. The primary endpoint was the change in ALSFRS-R during the 24-week treatment period. Results showed that the change in ALSFRS-R scores were -5.70 and -6.35 in the edaravone and placebo groups, respectively, which did not represent a statistically significant difference (P=0.411). No serious adverse events were reported and the level and frequency of adverse events were similar between the two treatment groups. A post-hoc analysis suggested that edaravone could be efficacious in a restricted subgroup that includes recently diagnosed patients with milder disease symptoms.

Based on the post-hoc analysis, a second Phase 3 clinical trial was conducted that was restricted to patients with a disease duration of <2 years and independent activity of daily living (Tanaka *et al*., 2015). A total of 134 patients were randomized to receive edaravone (n=68) or placebo (n=66) for six months, with treatment given the same as in the first Phase 3 clinical trial. The change in ALSFRS-R score from baseline at six months was -5.01 in the edaravone group and -7.50 in the placebo group (*P*=0.001). Once again, adverse events were similar between the edaravone and the placebo groups.

Positive Results from Phase 2 Trial of MN-166 in ALS

MediciNova previously studied MN-166 in a Phase 2 trial in ALS. This was a single center, double blind, placebo controlled six-month study with patients randomized 2:1 to receive riluzole (100 mg/day) plus either MN-166 (60 mg/day) or placebo. The six-month double blind portion was followed by a six-month open label extension phase during which all patients received MN-166. The intent-to-treat (ITT) population consisted of 51 patients who were randomized to placebo (n=17) or MN-166 (n=34) for the double-blind portion of the study. The per protocol (PP) population consisted of 44 patients that completed the double-blind portion of the study (n=15 for placebo; n=29 for MN-166) and 35 patients that completed the open label extension (n=12 for placebo; n= 23 for MN-166).

Since this was the first time MN-166 was tested in ALS patients the primary outcome of the study was safety and tolerability of the drug when administered along with riluzole (100 mg/day), the standard of care for ALS patients. The study achieved the primary outcome with no serious or life-threatening treatment-related adverse events (TRAEs). There were six subjects that had a total of seven serious adverse events (five for MN-166 group and one for placebo group), however none of them were related to treatment.

	# of Subjects or # of Events	
	Placebo N=17	Ibudilast N=34
# of Subject with at Least one TRAEs	n= 3	n= 4
Total events # of TRAEs	5	8
Severe or Life-threatening TRAEs	0	0
Serious TRAEs	0	0
	# of Subjects	
	Placebo N = 17	Ibudilast N = 34
At Least one TEAEs	n = 17	n = 34
Severe or Life threatening TEAEs	n = 2	n = 4
Serious Adverse Events	n = 1	n = 5
Treatment Related Adverse Events	n = 10	n = 13

Source: Brooks *et al*., 2017

In addition to the primary endpoint of safety and tolerability, the study also evaluated secondary efficacy endpoints. These secondary endpoints, which included an analysis of ALSFRS-R, were not powered for statistical significance but were evaluated to look for positive trends that could help guide the design of future clinical trials. For this study, a responder was defined as someone who had a ≤1 point decline in the ALSFRS-R during the six-month double blind period while a non-responder was defined as someone who had >1 point decline in ASLFRS-R. For the ITT population, the following table shows that 29.4% (10/34) of MN-166-treated patients were responders, compared to 17.6% (3/17) of placebo-treated patients. The third and fourth columns in the table show the percentage of patients who were responders in the open-label six-month extension phase during which all patients received MN-166. In the open-label extension, 35.3% (6/17) of the patients who had received placebo during the double blind portion of the study were responders when taking MN-166. This compares quite favorably with the 29.4% of patients who were responders with MN-166 during the double blind portion of the study.

Double-Blind Phase		Open Label Phase		Overall
Placebo (N = 17)	Ibudilast (N = 34)	Ibudilast 0-6 mon treatment (N = 17)	Ibudilast 6-12 mon treatment (N = 34)	Ibudilast 0-12 mon treatment combined (N = 51)
3 / 17 (17.6 %)	10 / 34 (29.4 %)	6 / 17 (35.3 %)	3 * / 34 (8.8 %)	19 * / 51 (37.3 %)

Source: Brooks *et al*., 2017

For the PP population, the following table shows that 34.5% (10/29) of MN-166-treated patients were responders, compared to 20.0% (3/15) of placebo-treated patients. Again, the open-label extension results showing 50.0% (6/12) of patients who had received placebo during the double blind portion of the study were responders when taking MN-166 compared well with the 34.5% of patients that were responders when taking MN-166 in the double blind portion of the study.

Double-Blind Phase		Open Label Phase		Overall
Placebo (N = 15)	Ibudilast (N = 29)	Ibudilast 0-6 mon treatment (N = 12)	Ibudilast 6-12 mon treatment (N = 23)	Ibudilast 0-12 mon treatment combined (N = 35)
3 / 15 (20.0 %)	10 / 29 (34.5 %)	6 / 12 (50.0 %)	3 * / 23 (13.0 %)	19 * / 35 (54.3 %)

Source: Brooks *et al*., 2017

We believe these results show that MN-166 was having a positive effect on ALSFRS-R and that this effect is likely to increase in the Phase 3 trial, as the company will be testing a 100 mg/day dose, compared to the 60 mg/day dose that was utilized in the Phase 2 trial.

Similarities Between Edaravone Phase 3 Trial and Proposed Phase 3 Trial for MN-166

MediciNova has designed the Phase 3 clinical trial of MN-166 in a similar manner as the successful edaravone Phase 3 trial, as shown in the following table.

Comparison Between Edaravone Phase 3 Trial and Planned MN-166 Phase 3 Trial		
	Edaravone	MN-166
# Patients	134	150
Randomization	1:1	1:1
Time since diagnosis	< 2 years	< 1.5 years
Treatment duration	24 weeks	36 weeks
Primary Outcome	Δ ALSFRS-R	Δ ALSFRS-R

Sources: Tanaka *et al*., 2015, MediciNova, Zacks SCR

While the mechanisms of action for edaravone and MN-166 are not the same, we believe that designing a similar clinical trial to the successful edaravone Phase 3 trial is a smart move, as the placebo group response is likely to be the same as was seen in the edaravone trial. Success for MN-166 would be a significant event for the company as any successful ALS treatment could become a blockbuster.

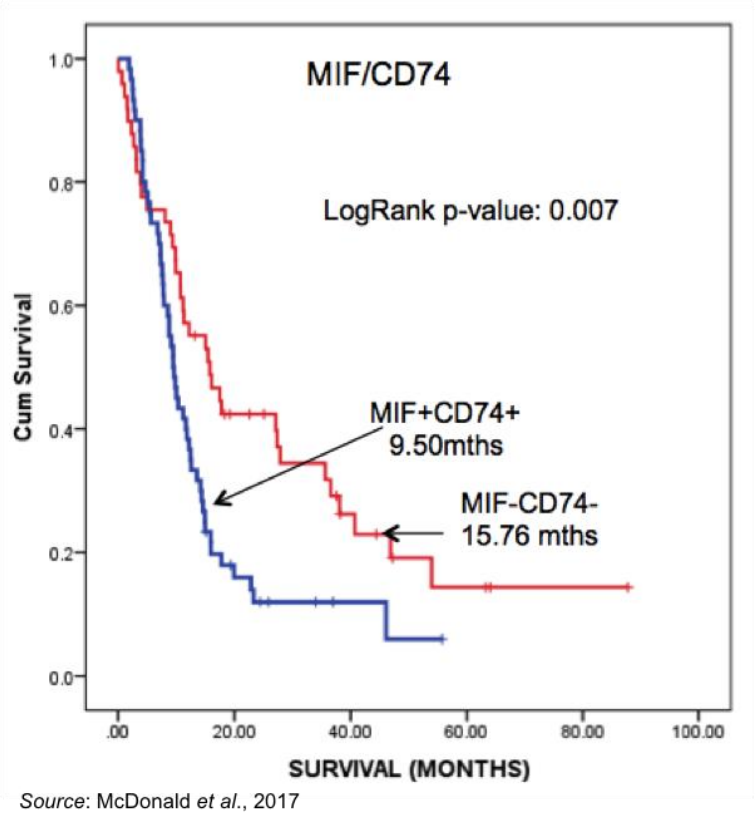
New Patent for MN-166 in Treatment of Glioblastoma

On April 23, 2019, MediciNova announced that the U.S. Patent and Trademark Office has issued a Notice of Allowance for a patent covering the use of MN-166 in the treatment of glioblastoma (GBM). The patent claims cover a method for treating glioblastoma or recurrent glioblastoma with MN-166 as part of a combination therapy, including laquinimod in addition to radiation therapy, electric field therapy, and various other therapies including the standard of care chemotherapeutic agent temozolomide. The patent is expected to expire no earlier than December 2037.

On January 8, 2019, MediciNova announced that the first patient has been enrolled in the clinical trial of MN-166 in combination with temozolomide for the treatment of recurrent glioblastoma. The principal investigators for the study are Dr. Patrick Y. Wen, Professor of Neurology, Harvard Medical School and Director, Neuro-Oncology Division at the Dana-Farber Cancer Institute in Boston, and Dr. Kerrie McDonald, Associate Professor and Head of Biomarkers and Translational Research at the Lowy Cancer Research Centre, University of New South Wales, Australia.

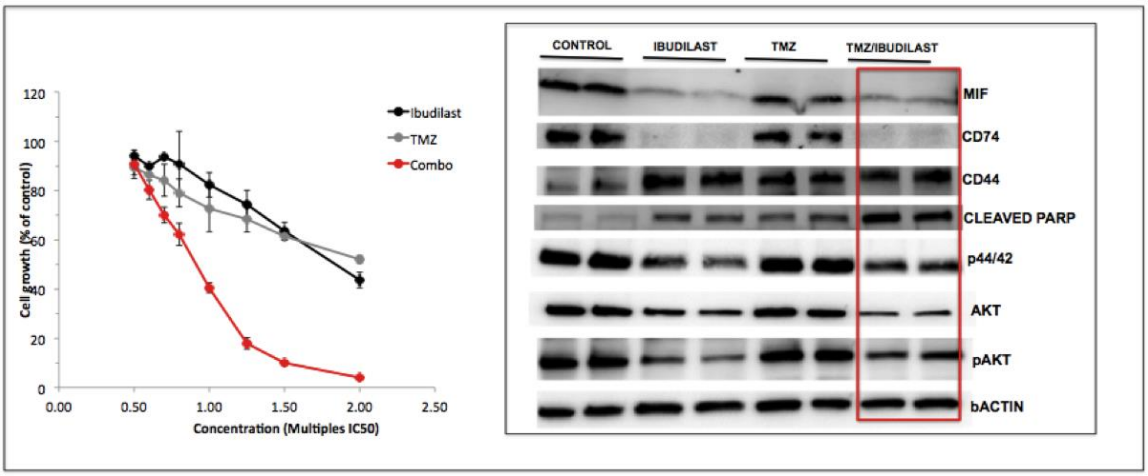
Dr. McDonald presented results from a preclinical study of MN-166 in the treatment of GBM at the 2017 American Society of Clinical Oncology (ASCO) Annual Meeting. The aims of the study were to compare proteomic profiles of tumors from two groups of patients with GBM (grouped according to survival, ± 1 year) such that novel biomarkers could be identified and explored as potential therapeutic targets.

Proteomic profiling of samples from 30 GBM patients revealed macrophage migration inhibitory factor (MIF) as a protein that was expressed in “poor responders” (e.g., those that lived < 1 year). MIF is an inflammatory-related cytokine that is secreted by cancer stem cells. The researchers then examined an additional 168 GBM samples and found co-expression of MIF and its receptor CD74 in 57% of the samples. In addition, co-expression of MIF and CD74 was significantly associated with poor survival, as shown in the following graph. These results point to MIF being a suitable target for GBM treatment.



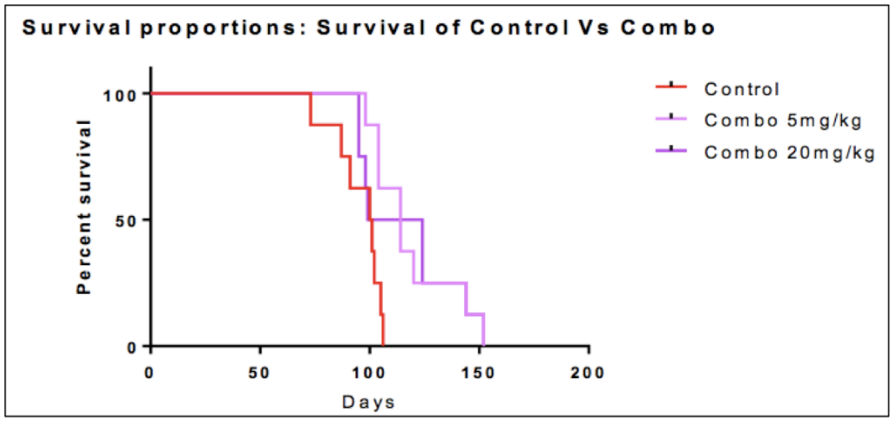
Source: McDonald *et al*., 2017

MN-166 is an inhibitor of MIF (Cho *et al*., 2010). To determine if MN-166 could show an effect in GBM, the researchers first treated patient derived GBM cell lines with MN-166, temozolomide (TMZ, the standard of care chemotherapeutic for GBM) or a combination of the two and evaluated the effect on cell growth and protein expression. Results showed that in all cell lines tested, the combination of MN-166 and TMZ resulted in significant synergy in inhibiting cell growth, as well as decreases in MIF, CD74, and AKT expression.



Source: McDonald *et al*., 2017

An *in vivo* study was performed using RN1 GBM cells, which were intracranially injected into the brains of mice followed by no treatment or a combination of TMZ and MN-166 at two different concentrations. Results showed that mice treated with the combination of TMZ and MN-166 had significantly enhanced survival (median overall survival 114 days vs. 100.5 days, *P*=0.005) with suppression of MIF and CD74 expression also noted.



Source: McDonald *et al*., 2017

The company had previously announced that the FDA granted MN-166 orphan drug designation (ODD) to MN-166 as adjunctive therapy to TMZ for the treatment of GBM. ODD carries a number of incentives for the company, including seven years of market exclusivity following approval for the treatment of GBM, tax credits, and a waiver of PDUFA fees.

Financial Update

On April 25, 2019, MediciNova filed form 10-Q with financial results for the first quarter of 2019. As expected, the company did not report any revenues for the first quarter of 2019. Net loss for the first quarter of 2019 was $4.7 million, or $0.11 per share, compared to a net loss of $4.5 million, or $0.12 per share, in the first quarter of 2018. R&D expenses for the first quarter of 2019 were $1.6 million compared to $1.7 million in the first quarter of 2018. The decrease was due to the completion of the MN-001 clinical trial in NASH/NAFLD in 2018. G&A expenses were $3.3 million for the first quarter of 2019 compared to $3.0 million for the first quarter of 2018. The increase was primarily due to higher stock-based compensation expenses.

Total operating burn for the first quarter of 2019 was $3.0 million and the company exited the first quarter of 2019 with approximately $63.2 million in cash and cash equivalents. As of Apr. 24, 2019, MediciNova had approximately 43.1 million common shares outstanding and when factoring in the approximately 6.8 million stock options a fully diluted share count of 49.9 million.

Conclusion

We look forward to the initiation of the Phase 2b/3 clinical trial of MN-166 in ALS, as we believe the Phase 2 study provided ample justification for moving MN-166 into a pivotal study: 1) it showed that MN-166 can be safely administered to ALS patients who are also taking riluzole, and 2) there were positive efficacy trends in favor of MN-166 for ALSFRS-R, which is an approvable endpoint. Based on the clear dose-dependent response observed in an earlier study in relapsing multiple sclerosis (MS), we believe the higher dose of 100 mg/day will demonstrate better efficacy than the 60 mg/day dose that was used in the Phase 2 trial. In addition, we believe moving to 100 mg/day will be safe and well tolerated based on the fact that the company demonstrated the safety of 100 mg/day in the progressive MS Phase 2b study.

The treatment of ALS is a potential blockbuster opportunity. With only two drugs approved to treat the disease there is a huge unmet medical need for better treatment options. Given the limited therapeutic options and high costs associated with patient care, if shown to be safer or more effective than the existing drugs, we believe MN-166 would command a premium price, which is supported by the yearly list price of $145,000 for Radicava®. We estimate this could lead to worldwide sales of approximately $2 billion annually for MN-166.

We anticipate additional updates from the company this year regarding plans for a Phase 3 trial in progressive multiple sclerosis (MS) and the initiation of enrollment in a trial in degenerative cervical myelopathy (DCM). With multiple clinical programs advancing and two potential blockbuster indications in progressive MS and ALS, we remain positive on MediciNova and our current valuation remains at $19 per share.

PROJECTED FINANCIALS

MediciNova Inc.
Income Statement

MediciNova, Inc.	2018 A	Q1 A	Q2 E	Q3 E	Q4 E	2019 E	2020 E	2021 E
MN-166 (Multiple Sclerosis)	$0	$0	$0	$0	$0	$0	$0	$0
MN-166 (ALS)	$0	$0	$0	$0	$0	$0	$0	$0
MN-166 (Addiction)	$0	$0	$0	$0	$0	$0	$0	$0
MN-001 (NASH)	$0	$0	$0	$0	$0	$0	$0	$0
MN-001 (IPF)	$0	$0	$0	$0	$0	$0	$0	$0
Grants & Collaborative Revenue	$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	$5.626	$1.634	$2.500	$3.000	$3.500	$10.634	$15.500	$17.000
General & Administrative	$9.961	$3.345	$3.500	$3.500	$3.600	$13.945	$11.000	$11.500
Other Expenses	$0	$0	$0	$0	$0	$0	$0	$0
Operating Income	($15.6)	($5.0)	($6.0)	($6.5)	($7.1)	($24.6)	($26.5)	($28.5)
Operating Margin	-	-	-	-	-	-	-	-
Non-Operating Expenses (Net)	$0.9	$0.3	$0.1	$0.1	$0.1	$0.6	$0.4	$0.4
Pre-Tax Income	($14.7)	($4.7)	($5.9)	($6.4)	($7.0)	($24.0)	($26.1)	($28.1)
Income Taxes Paid	($0)	$0	$0	$0	($0)	$0	$0	$0
Tax Rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*
Net Income	**($14.7)**	**($4.7)**	**($5.9)**	**($6.4)**	**($7.0)**	**($24.0)**	**($26.1)**	**($28.1)**
Net Margin	-	-	-	-	-	-	-	-
Reported EPS	**($0.36)**	**($0.11)**	**($0.14)**	**($0.15)**	**($0.15)**	**($0.55)**	**($0.56)**	**($0.56)**
YOY Growth	-	-	-	-	-	-	-	-
Basic Shares Outstanding	41.125	42.468	43.000	44.000	46.000	43.867	47.000	50.000

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

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