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MediciNova, Inc. (MNOV-NASDAQ)

MNOV: $20M Investment to Fund Multiple Programs…

Based on our probability adjusted DCF model that takes into account potential future revenues from MN-166 in ALS, progressive MS and addiction; MN-001 in NASH and IPF; and the SARS-CoV-2 vaccine, MNOV is valued at $26.50/share. This model is highly dependent upon continued clinical success of the company's assets and will be adjusted accordingly based upon future clinical results.

Current Price (01/25/21)	$5.96
Valuation	**$26.50**

OUTLOOK

MediciNova, Inc. (MNOV) recently entered into a securities purchase agreement whereby the company has agreed to issue $20 million in shares of its common stock to 3D Opportunity Master Fund. The company is planning to use the proceeds primarily for three programs: 1) the initiation of a new clinical trial of MN-166 (ibudilast) for the treatment of glioblastoma, which could be a pivotal trial; 2) to develop an intravenous formulation for MN-166, which would be utilized for treatment of amyotrophic lateral sclerosis (ALS) patients who have difficulty swallowing; and 3) to initiate a Phase 2 clinical trial of MN-166 in nonalcoholic steatohepatitis (NASH). It is encouraging to see a single investor make such a substantial investment in the company.

SUMMARY DATA

52-Week High	**$11.00**
52-Week Low	**$2.90**
One-Year Return (%)	**-6.07**
Beta	**1.40**
Average Daily Volume (sh)	**245,858**
Shares Outstanding (mil)	**45**
Market Capitalization ($mil)	**$268**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**22**
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	**Above Avg.**
Type of Stock	**Small-Blend**
Industry	**Med-Biomed/Gene**

ZACKS ESTIMATES

Revenue
(In millions of $)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
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 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2019	-$0.11 A	-$0.09 A	-$0.05 A	-$0.04 A	-$0.30 A
2020	-$0.06 A	-$0.10 A	-$0.08 A	-$0.09 E	-$0.34 E
2021					-$0.34 E
2022					-$0.35 E

WHAT'S NEW

Business Update

$20 Million Investment to Fund Multiple Pipeline Programs

On January 11, 2021, MediciNova, Inc. (MNOV) announced it entered into a securities purchase agreement in which $20 million worth of shares of its common stock would be sold to 3D Opportunity Master Fund, a fund managed by 3D Investment Partners Pte. Ltd., a value-oriented investment manager based in Singapore. On January 21, 2021, 3D Investment Partners filed a Schedule 13D which disclosed total ownership of 5.502 million shares of MNOV (11.3% of the issued and outstanding shares) which includes 1.846 million shares acquired in open market purchases in addition to the shares from the securities purchase agreement. Under the "Purpose of the Transaction" section of the Schedule 13D, 3D Investment Partners stated that they "believe that the Issuer's common stock is undervalued and is an attractive investment."

The company is planning to use the proceeds from the securities purchase agreement primarily to advance the following three programs:

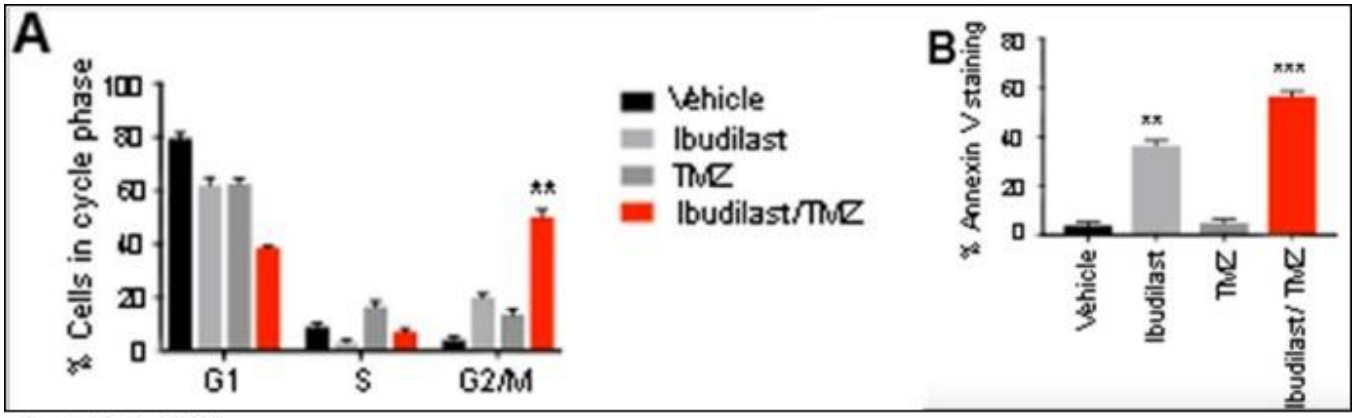
1) The initiation of a second clinical trial of MN-166 (ibudilast) for glioblastoma, which may be a pivotal trial
2) The development of an intravenous formulation of MN-166 to be used in treating amyotrophic lateral sclerosis (ALS) patients that have difficulty swallowing
3) The initiation of a Phase 2 clinical trial of MN-001 (tipelukast) in nonalcoholic steatohepatitis (NASH)

MN-166 for Glioblastoma

MediciNova is currently conducting a Phase 1/2 clinical trial of MN-166 in combination with temozolomide (TMZ) for the treatment of glioblastoma (GBM) that is divided into a dose-escalation phase (Part 1) and a fixed-dose phase (Part 2) (NCT03782415). A total of 15-18 adults are expected to be enrolled in Part 1 where the safety and tolerability of MN-166 given in combination with TMZ will be determined along with the optimal dose to evaluate in Part 2 of the study. Part 2 of the study is expected to enroll approximately 32 subjects and will evaluate the efficacy of MN-166 given in combination with TMZ as measured by six-month progression free survival. Additional outcomes include overall survival and response rate.

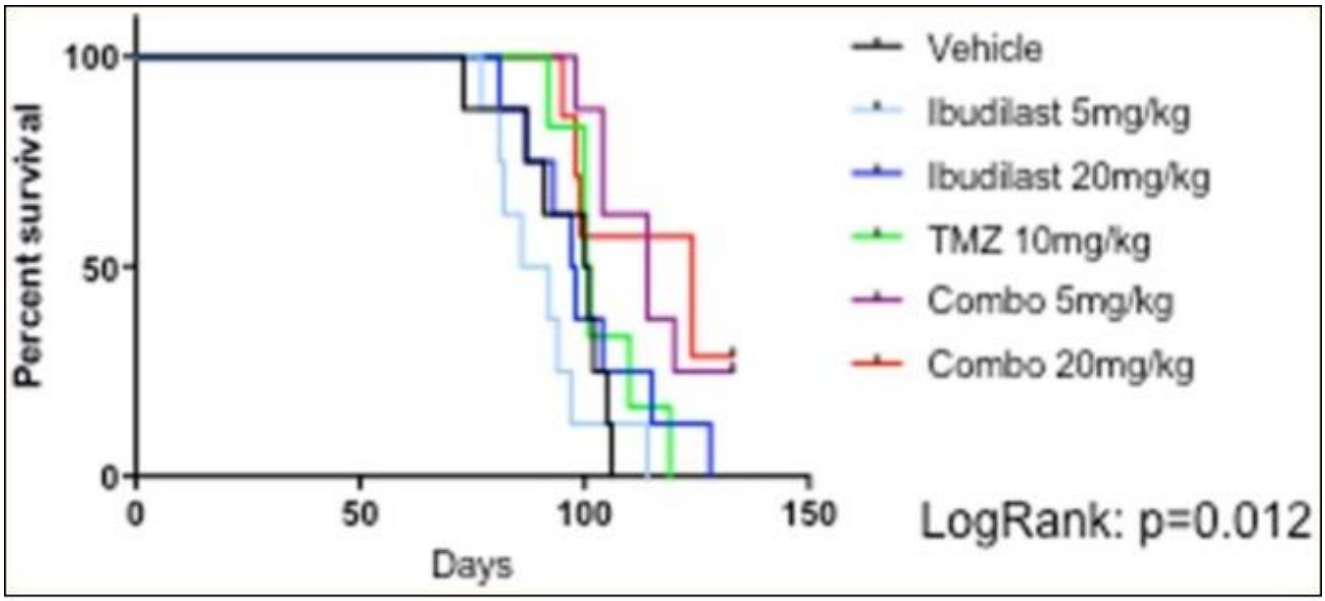
The rationale for testing MN-166 in GBM is based on its activity in preclinical GBM models:

Ha *et al*., 2019: This study identified macrophage inhibitory factor (MIF) as a protein overexpressed in GBM samples from patients with MGMT methylation, which is typically a positive prognostic factor, but who had poor overall survival. MN-166 showed modest anti-proliferative activity as a single agent against patient derived cell lines, however when combined with TMZ significant synergism was observed. The following figure shows a significant effect on cell cycle arrest (lower left) that resulted in an increase in apoptosis, as shown by an increase in Annexin V staining (lower right), in the RN1 unmethylated MGMT cell line.



Source: Ha *et al*., 2020

To examine the effect of MN-166 on survival, RN1 cells were implanted intracranially into immunocompromised Balb/c mice. MN-166 was administered by oral gavage (5 mg/kg or 20 mg/kg) while TMZ was administered by intraperitoneal injection (10 mg/kg). The following graph shows that combination therapy with MN-166 and TMZ resulted in significantly longer survival at both 5 mg/kg MN-166 (*P*=0.005) and 10 mg/kg MN-166 (*P*=0.014).



Source: Ha *et al.*, 2020

Alban *et al*., 2020: Previous research showed that GBM patients had higher levels of myeloid-derived suppressor cells (MDSCs) that were dependent on MIF for survival. This study showed that monocytic MDSCs (M-MDSCs) expressed high levels of the MIF cognate receptor CD74 in the tumor microenvironment. MN-166 is a known inhibitor of the CD74/MIF interaction and it was shown to inhibit the generation of M-MDSCs in an *in vitro* MDSC induction model. Thus far, immune stimulating therapies have been ineffective against GBM, however the researchers posit that combination therapy with an immune stimulating agent and MN-166 could be an effective strategy since MN-166 can decrease the levels of the immune dampening MDSCs.

GBM Background

GBM is the most aggressive of the category of tumors known as gliomas, which all arise from glia cells within the central nervous system. There are four grades of gliomas, with the highest grade, Grade 4 or GBM, being the most aggressive and the most common form in humans. Unfortunately, most patients with GBM don't live much longer than one or two years, and this has not changed appreciably over the years. The reason these tumors are so difficult to treat is multi-dimensional and has to do with the both the genetic make-up of the tumor (most GBM cells have multiple activating mutations and other genetic anomalies) as well as the way the tumors grow (they are highly infiltrative and arise in many different regions of the brain).

Current standard-of-care (SOC) treatment for GBM consists of surgery to resect as much of the tumor as possible followed by radiation and chemotherapy (TMZ) to kill any tumor cells that were not removed through surgery. While some types of solid tumors can be cured surgically, this is very rare in GBM due to the diffuse nature of the tumor.

Gliomas are the most common type of intracranial cancer, accounting for 81% of all malignant brain cancers, and GBM accounts for 45% of all gliomas (Ostrom *et al*., 2014). There are approximately 25,000 people diagnosed with malignant brain cancer each year in the U.S. Since GBM is mostly diagnosed in older individuals (median age = 65 years), the aging demographics of the Western world has resulted in the incidence of GBM increasing from 5.1 per 100,000 in the 1970's to 10.6 per 100,000 in the 1990's (Chakrabarti *et al*., 2005). Those diagnosed with the disease have a very grim prognosis, with the median survival time of untreated patients being only 4.5 months. Current standard of care treatment only provides a 12-14 month median overall survival after diagnosis (Johnson *et al*., 2012).

<u>IV Formulation of MN-166</u>

MediciNova is currently conducting a Phase 2b/3 clinical trial of MN-166 in patients with (ALS). An estimated 230 patients will be randomized 1:1 to receive either 100 mg MN-166 or placebo daily along with a stable dose of riluzole in the double-blind, placebo-controlled trial (NCT04057898). Treatment will last for 12 months followed by a six-month open label extension period. The primary outcome of the trial is the change from baseline in the ALS function rating scale – revised (ALSFRS-R) and survival time.

MediciNova previously announced positive topline results from a Phase 2 study of MN-166 in ALS patients. The Phase 2 trial was a single center, double-blind, placebo-controlled study in which patients were randomized 2:1 to receive riluzole plus MN-166 (60 mg/day) or placebo. The six-month double-blind portion of the trial 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).

Results from the Phase 2 trial showed that MN-166 could be safely administered to ALS patients along with riluzole and there were positive efficacy trends in favor of MN-166 for ALSFRS-R. The trial showed that 29.4% (10/34) of MN-166-treated patients were responders compared to 17.6% (3/17) of placebo-treated patients. A responder was defined as someone who had ≤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. Given the clear dose-dependent response of MN-166 observed in multiple studies, the company believes that the higher dose of 100 mg/day being used in the Phase 2b/3 ALS trial should produce better efficacy data than was observed with the 60 mg/day dose used in the Phase 2 trial.

MN-166 is currently administered to patients in all trials as a pill. However, many ALS patients suffer from difficulty in swallowing or have decreased swallowing ability as the disease progresses. For this reason, MediciNova will be developing an intravenous formulation of MN-166, which would be advantageous for ALS patients, particularly those that have difficulty swallowing.

MN-001 in NASH

MediciNova is planning to evaluate MN-001 (tipelukast) as a potential treatment for NASH in a Phase 2 clinical trial. MN-001 is a novel, orally available small molecule compound that works through several mechanisms to produce anti-fibrotic and anti-inflammatory effects in preclinical models. The compound is a leukotriene (LT) receptor antagonist, a PDE inhibitor (mainly 3 and 4), and it also inhibits 5-lipoxygenase (5-LO). The 5-LO/LT pathway is thought to be a pathogenic factor in fibrosis development (Zeldin *et al*., 2002).

Two separate studies in mouse models of NASH have shown MN-001 to have both anti-NASH and anti-fibrotic activity.

Study #1: MN-001 was administered orally once daily (10, 30, or 100 mg/kg) for three weeks in the STAM™ (NASH-HCC) mouse model of NASH. The model is created by a combination of chemical and dietary interventions in a standard laboratory mouse strain through the use of a single dose of streptozotocin shortly after birth and a continuous high-fat diet.

Treatment with MN-001 resulted in a dose-dependent reduction in liver fibrosis as demonstrated by a reduction in liver hydroxyproline content (P<0.01). In addition, there was a significant improvement (P<0.01) in the NAFLD activity score (NAS), which is a summation of the separate scores for steatosis (0–3), hepatocellular ballooning (0–2) and lobular inflammation (0–3). Concurrently, MN-001 was shown to significantly down-regulate (P<0.01) the expression of MCP-1, CCR2, collagen type-1, and TIMP-1; all of which are genes associated with the formation of fibrosis.

Study #2: In a second study, the same STAM™ (NASH-HCC) mouse model of NASH was utilized, however the mice were at a more advanced stage of NASH. MN-001 was administered orally once daily (10, 30, or 100 mg/kg) beginning at eight weeks of age for four weeks.

Once again, treatment with MN-001 resulted in a statistically significant decrease in NAS score (P<0.001), owing mostly to a decrease in hepatocyte ballooning score and lobular inflammation score. Fibrosis area was also significantly reduced in the MN-001 treated group (P<0.01). MN-001 was once again shown to decrease expression levels of the previously tested genes along with LOXL2, a gene shown to be upregulated in fibrotic livers (Barry-

Hamilton *et al*., 2010). Importantly, treatment with MN-001 had no effect on body weight or general condition of the mice compared to placebo.

In addition to the aforementioned preclinical studies in NASH, MediciNova previously announced positive results from a Phase 2 clinical trial of MN-001 in patients with NASH and NAFLD with hypertriglyceridemia. A total of 15 patients completed eight weeks of treatment with MN-001 (four weeks at 250 mg/day and four weeks at 500 mg/day), and MN-001 reduced serum triglyceride levels in 14/15 subjects. The average pre-treatment serum triglyceride level was 328.6 mg/dL, which was reduced to an average 192.9 mg/dL following eight weeks of treatment (-41.3%, *P*=0.02). The company also analyzed the data excluding an outlier subject that had an extremely high serum triglyceride level of 1288 mg/dL prior to treatment that was reduced to 300 mg/dL after treatment. That analysis showed 13/14 subjects with a reduction in serum triglycerides, from an average 260.1 mg/dL prior to treatment to an average 185.2 mg/dL following treatment (-28.8%, *P*=0.00006). Importantly, there were no clinically significant safety or tolerability issues during the study.

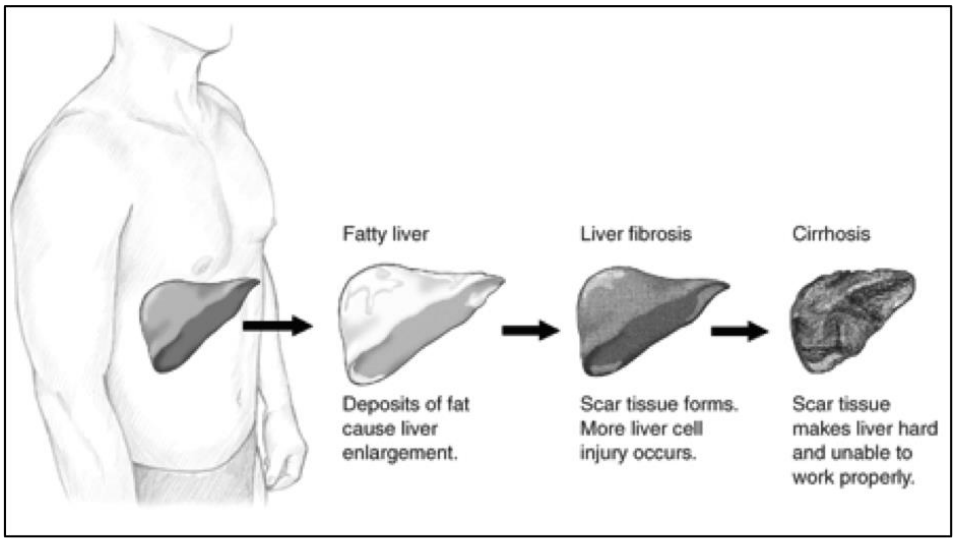
Background on NASH

NASH is inflammation and damage in the liver brought on by a buildup of fat. The disease is an often “silent” liver disease as most people with NASH feel well and are not aware that they have a liver problem. Nevertheless, NASH can be severe and can lead to cirrhosis, in which the liver is permanently damaged and scarred and no longer works properly.

NASH is the most severe form of nonalcoholic fatty liver disease (NAFLD), a type of fatty liver where there is deposition of fat (steatosis) in the liver brought on by something other than alcohol consumption and is often due to obesity. Approximately 30 to 40 percent of individuals in the U.S. have fat in their liver but no indication of inflammation, while NASH affects 3 to 12 percent of people in the U.S (NIDDK).

Both NASH and NAFLD are becoming more common, possibly because of the greater number of Americans with obesity. In the past 10 years, the rate of obesity has doubled in adults and tripled in children. Obesity also contributes to diabetes and high blood cholesterol, which can further complicate the health of someone with NASH.

People with NASH usually have few or no symptoms. Patients generally feel well in the early stages and only begin to have symptoms — such as fatigue, weight loss, and weakness — once the disease is more advanced or cirrhosis develops. The progression of NASH can take years or even decades, can stop on its own and even get better without therapy, or it can slowly worsen and cause fibrosis, or scarring, of the liver. As fibrosis worsens, cirrhosis develops; the liver becomes seriously scarred, hardened, and unable to function normally. Not every person with NASH develops cirrhosis, but once serious scarring or cirrhosis is present there are few treatments that can halt the progression. Liver transplantation is the only treatment for advanced cirrhosis with liver failure, and transplantation is increasingly performed in people with NASH. NASH ranks as one of the major causes of cirrhosis in America, behind hepatitis C and alcoholic liver disease.



Source: NIDDK

Elevated liver enzymes, such as alanine aminotransferase (ALT) or aspartate aminotransferase (AST), are the first sign that a person may have NASH. If further evaluation shows no apparent reason for liver disease (such as medications, viral hepatitis, or excessive use of alcohol) and x-rays or imaging studies of the liver show fat, NASH is suspected. The only means of proving a diagnosis of NASH and separating it from simple fatty liver is a liver biopsy. NASH is diagnosed when examination of liver tissue shows fat along with inflammation and damage to liver cells. If the tissue shows fat without inflammation and damage, simple fatty liver or NAFLD is diagnosed. An important piece of information learned from the biopsy is whether scar tissue has developed in the liver. Currently, no blood tests or scans can reliably provide this information.

While NASH has become more common since it was first diagnosed over 30 years ago (Ludwig *et al*., 1980), its exact cause is still uncertain. Since it is associated with fat accumulation in the liver, it is not surprising that many patients with NASH have elevated blood cholesterol and triglycerides. However, some patients with NASH are not overweight, do not have diabetes, and have normal blood cholesterol and triglyceride levels. Thus, while they are contributory factors, NASH is not simply a consequence of obesity or elevated blood lipid levels.

Conclusion

The $20 million investment from 3D Opportunity Master Fund is a positive development for MediciNova and will allow the company to advance multiple programs in its pipeline. We believe that fund likely became interested in MediciNova due to the low valuation currently assigned to the company along with the multiple large market opportunities being pursued, which include not only the aforementioned programs but also progressive multiple sclerosis (MS), chemotherapy induced peripheral neuropathy (CIPN), substance dependence, degenerative cervical myelopathy (DCM), idiopathic pulmonary fibrosis (IPF), and a COVID-19 vaccine and treatment. We look forward to updates on these programs as the year advances and with no changes to our model the valuation remains at $26.50.

PROJECTED FINANCIALS

MediciNova Inc.
Income Statement

MediciNova, Inc.	2019 A	Q1 A	Q2 A	Q3 A	Q4 E	2020 E	2021 E	2022 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	$6.079	$1.251	$2.199	$2.238	$1.800	$7.488	$9.000	$10.000
General & Administrative	$7.952	$1.674	$2.311	$1.492	$2.400	$7.877	$8.500	$9.000
Other Expenses	$0	$0	$0	$0	$0	$0	$0	$0
Operating Income	($14.0)	($2.9)	($4.5)	($3.7)	($4.2)	($15.4)	($17.5)	($19.0)
Operating Margin	-	-	-	-	-	-	-	-
Non-Operating Expenses (Net)	$1.1	$0.2	$0.1	$0.0	$0.1	$0.4	$0.4	$0.4
Pre-Tax Income	($12.9)	($2.7)	($4.5)	($3.7)	($4.1)	($15.0)	($17.1)	($18.6)
Income Taxes Paid	($0)	$0	$0	$0	($0)	$0	$0	$0
Tax Rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*
Net Income	**($12.9)**	**($2.7)**	**($4.5)**	**($3.7)**	**($4.1)**	**($15.0)**	**($17.1)**	**($18.6)**
Net Margin	-	-	-	-	-	-	-	-
Reported EPS	**($0.30)**	**($0.06)**	**($0.10)**	**($0.08)**	**($0.09)**	**($0.34)**	**($0.34)**	**($0.35)**
YOY Growth	-	-	-	-	-	-	-	-
Basic Shares Outstanding	43.159	43.949	44.092	44.644	44.800	44.371	50.000	53.000

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

HISTORICAL STOCK PRICE

Source: Zacks Small Cap Research

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