Zacks Small-Cap Research

December 16, 2015
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MediciNova, Inc. (MNOV - Nasdaq)

MNOV: Positive Interim Safety and Clinical Data Presented at 26th International Symposium on ALS/MND…

Current Recommendation	**Buy**
Prior Recommendation	N/A
Date of Last Change	05/12/2015
Current Price (12/16/15)	$3.53
Target Price	**$8.00**

UPDATE

On December 14, 2015, MediciNova announced the presentation of positive interim safety and clinical data from the company's ongoing Phase 2 clinical trial of MN-166 in patients with amyotrophic lateral sclerosis (ALS). The blinded data was presented at the 26th International Symposium on ALS/MND and included a total of 36 subjects, 33 of which had completed six months of treatment on study drug (MN-166 or placebo in a 2:1 ratio).

The data showed MN-166 to be safe and well-tolerated with no cluster of adverse events. In addition, the rate of decline in accepted measures of ALS patient health were below that historically seen in other ALS studies.

SUMMARY DATA

52-Week High	**$4.96**
52-Week Low	**$2.79**
One-Year Return (%)	**5.06**
Beta	**0.87**
Average Daily Volume (sh)	**31,955**
Shares Outstanding (mil)	**26**
Market Capitalization ($mil)	**$92**
Short Interest Ratio (days)	**9.29**
Institutional Ownership (%)	**23**
Insider Ownership (%)	**27**
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 2015 Estimate	**N/A**
P/E using 2016 Estimate	**N/A**

Risk Level	**Above Average**
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)
2014	0 A	0 A	0 A	0 A	0 A
2015	0 A	0 A	0 A	0 E	0 E
2016					0 E
2017					0 E

Earnings per Share

(EPS is operating earnings before non-recurring items)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2014	-$0.10 A	-$0.09 A	-$0.10 A	-$0.09 A	-$0.38 A
2015	-$0.09 A	-$0.09 A	-$0.06 A	-$0.08 E	-$0.32 E
2016					-$0.39 E
2017					-$0.44 E

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WHAT'S NEW

Interim Data From Phase 2 Study of MN-166 in ALS

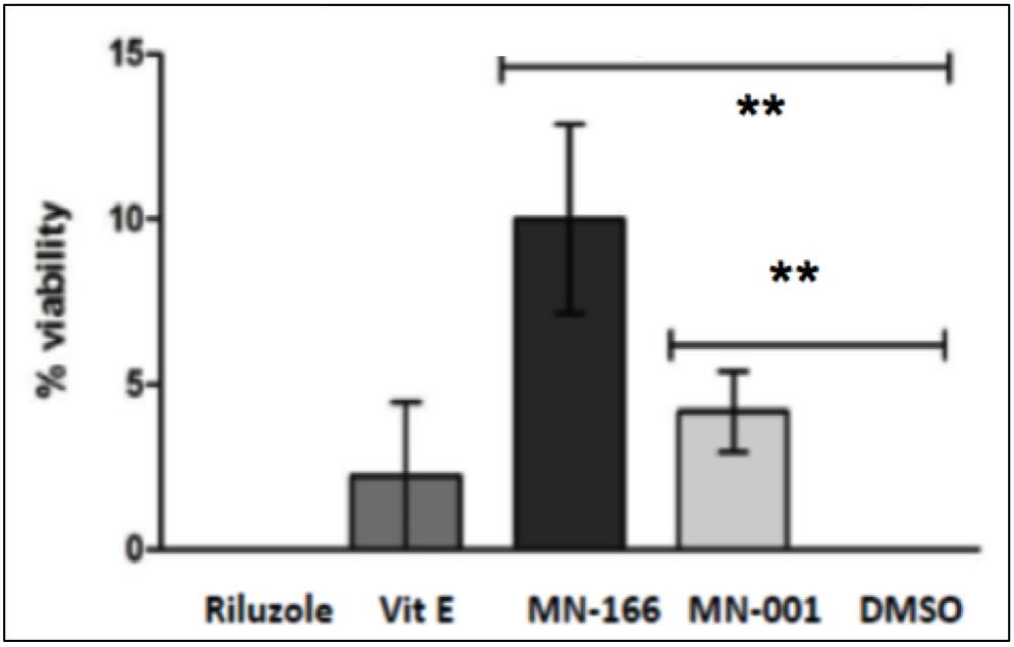
On December 14, 2015, MediciNova, Inc. (MNOV) announced the presentation of positive interim safety and clinical data from the company's ongoing Phase 2 clinical trial of MN-166 in patients with amyotrophic lateral sclerosis (ALS). The blinded data was presented at the 26th International Symposium on ALS/MND and included a total of 36 subjects, 33 of which had completed six months of treatment on study drug (MN-166 or placebo in a 2:1 ratio).

Background on MN-166

MN-166 is an anti-inflammatory drug that has been utilized for over 20 years in Japan to treat asthma (Rolan *et al*., 2009). It acts as a phophodiesterase (PDE) inhibitor (Suzumura *et al*., 1999) and preferentially inhibits PDE-4 (Huang *et al*., 2006). The drug has shown anti-inflammatory activity in both the peripheral immune system and in the CNS via attenuation of glial cells, which play a role in certain neurological conditions. In addition, delivery of a PDE-4 inhibitor was shown to lead to enhanced differentiation of oligodendrocyte progenitor cells within areas of demyelination and a consequent acceleration of remyelination (Syed *et al*., 2013).

Preclinical work performed with MN-166 showed that the compound can suppress neuronal cell death induced by activated microglia (Mizuno *et al*., 2004). MN-166 was shown to suppress the production of TNF-α and IL-6 by microglia as well as enhance the production of the anti-inflammatory cytokine IL-10 and neurotrophic factors such as NGF, GDNF, and NT-4. These data are in agreement with an earlier study of MN-166 in a chronic cerebral hypoperfusion model that showed it could inhibit the activation of microglia cells and prevent the formation of white matter lesions (Wakita *et al*., 2003). This inhibitory effect was shown to be dose dependent and involve the suppression of TNF-α production.

MN-166 has previously been studied in preclinical models of ALS with the use of the fruit fly (*Drosophila melanogaster*). One such model uses the transgenic overexpression of a mutated VAMP-associated protein (VAP P58S) that results in reduced viability of fly larvae. Mutations of VAP in humans are known to cause a number of motor neuron diseases, including ALS8, which is an inherited form of ALS. The addition of MN-166, and to a lesser extent MN-001 and Vitamin E, resulted in an increase in fly viability in the VAP P58S model, while dimethylsulfoxide (DMSO) and Riluzole® (the only drug to ever be approved for the treatment of ALS), had no effect on viability, thus supporting the study of MN-166 in ALS patients.



Source: Brooks *et al*., 2015

Phase 2 Clinical Trial of MN-166 in ALS

In September 2014, MediciNova initiated a Phase 2 study of MN-166 in patients with ALS (NCT02238626). This is a single center, randomized, double blind, placebo controlled six-month study to evaluate the safety, tolerability, and clinical responsiveness of MN-166 (60 mg/day) when administered as an adjunct to riluzole (100 mg/day) in 60 subjects with ALS. Patients in the study will be randomized 2:1 to receive either MN-166 or placebo. The study will consist of a three month screening phase, a six-month double blind treatment phase, and an open label six-month phase and is taking place at the Carolinas Healthcare System in Charlotte, NC. The primary endpoint of the study is the safety and tolerability of MN-166 when administered with riluzole in ALS patients. A number of secondary endpoints are being evaluated including change in ALSFRS-R, respiratory function, muscle strength, and non-invasive ventilation.

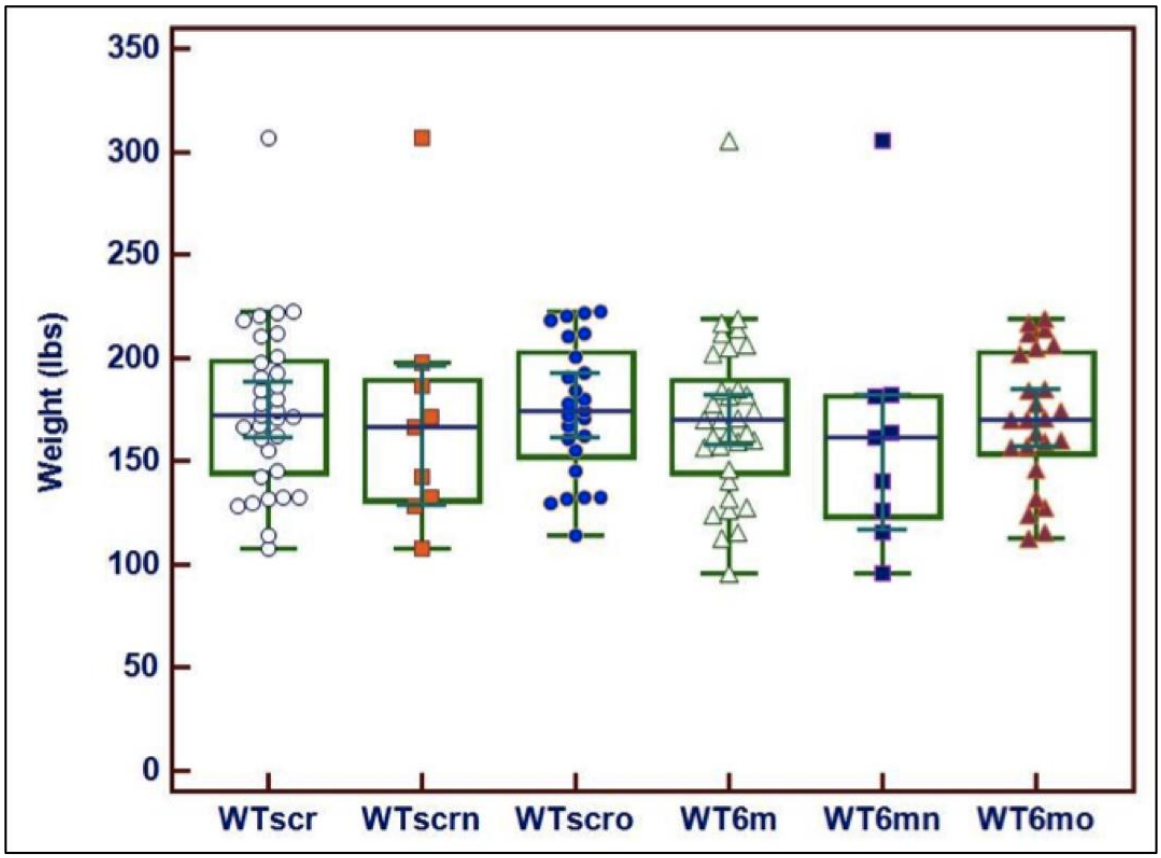
On April 21, 2015, MediciNova announced positive interim safety data from the study that showed no difference in safety or tolerability between MN-166 and placebo in the first 21 subjects enrolled in the study following three months of treatment. Importantly, the independent safety medical monitor recommended that the study continue as planned. In February 2015 the company announced the enrollment of 30 of the 60 patients for the trial.

On September 2, 2015, MediciNova announced that the first ALS patient using non-invasive ventilation (NIV) was enrolled in the ongoing Phase 2 clinical trial. As ALS progresses, the muscles that control breathing become weaker, which leads to impairment of breathing function and an increased susceptibility for lung infections. In addition, patients may experience shortness of breath, fatigue, sleep apnea, and weakened cough. NIV is administered through a removable face mask that is placed around the nose and mouth and is utilized by ALS patients that can still breathe on their own but are beginning to experience the aforementioned effects of decreased breathing capabilities. The use of NIV typically signifies that a patient is more advanced in the course of the disease than a patient not using NIV.

MediciNova amended the clinical protocol to allow for the recruitment of 60 patients with advanced ALS using NIV in addition to the already planned recruitment of 60 patients with ALS that are not using NIV. Since the trial is now enrolling both NIV and non-NIV patients, we are unsure of when enrollment will be completed. We do anticipate that the two sets of patients (non-NIV and NIV) will be evaluated separately, thus depending upon the rate of enrollment, we are hopeful that the data for the non-NIV patients will be available in 2016, with the data for the NIV patients most likely not available until 2017.

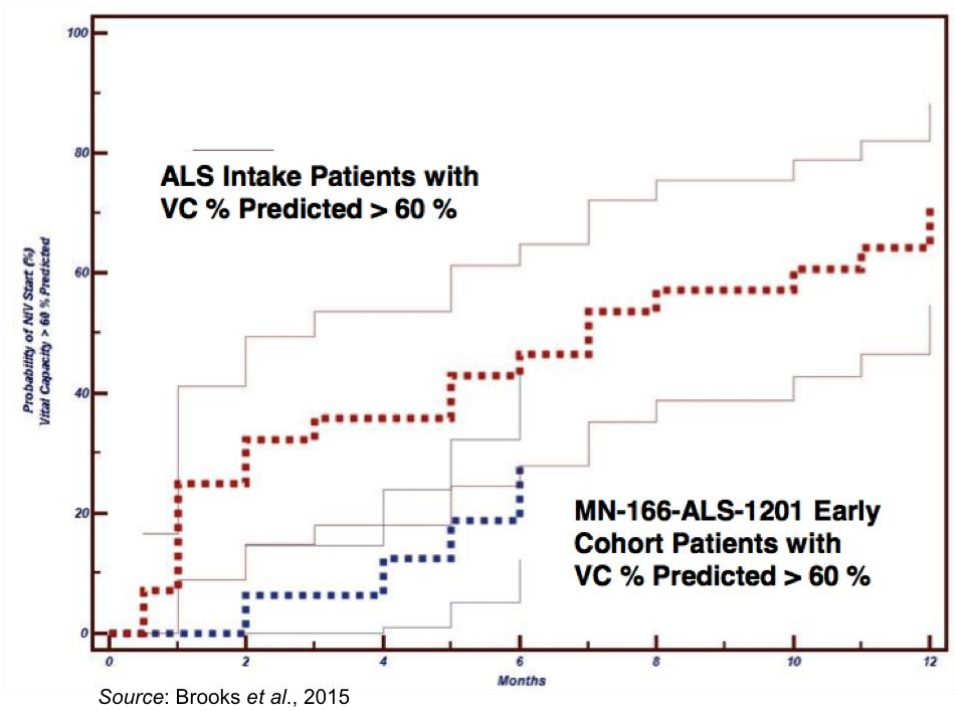
Interim Analysis of Safety and Clinical Data

Below, we present findings from the interim analyses that were recently presented by Dr. Benjamin Brooks at the 26th International Symposium on ALS/MND. It is important to keep in mind that the interim analysis is reporting data that is still blinded, thus there is no way at this point to compare MN-166 and placebo treated patients; they are only looked at as a group. For the interim analysis, a total of 36 patients were included with 33 of them having been on study drug for at least six months. Thus far MN-166 has been safe and well-tolerated as there have been no differential cluster of adverse events in placebo and active treatment subjects. As the following graph shows, there has been virtually no overall weight change following six months in the study (WT = weight; scr = at screening; 6m = after 6 months on study medication; n = those requiring NIV; o = no NIV required).



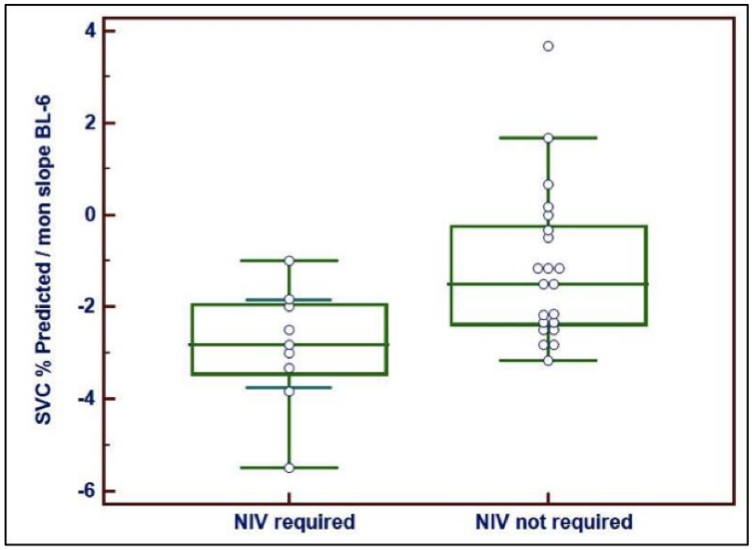
Source: Brooks *et al.*, 2015

Perhaps the most interesting bit of safety data to emerge from this trial involves the need for NIV due to progression of respiratory failure. Thus far, nine of 32 patients required NIV, and as the following graph shows, NIV utilization is lower in patients from the ongoing clinical trial when compared with the deployment of NIV in a sample of patients referred to the ALS Multidisciplinary Clinic with vital capacity greater than 60% predicted. The difference was close to being statistically significant (*P*=0.071). Whether this effect is due to treatment with MN-166 is unknown at this time.



Source: Brooks *et al.*, 2015

Even though the data is still blinded, there are still a couple of other data points that are intriguing given their difference from historical controls. The first has to do with the decline in percentage predicted slow vital capacity (SVC). SVC is a test of lung function that measures how much air the patient can slowly exhale after inhaling as deep a breath as possible. It is typically reported as a percentage of a predicted value based on a patient's age, gender, height, and weight. Values close to 100% are the most normal, with anything above 80% often considered normal. The following chart shows that for patients who did not require NIV, the average % predicted SVC declined at a much lower rate (1.5% per month) than for those patients requiring NIV. In addition, the decline in % predicted SVC for those patients not requiring NIV was lower than what has been seen in previous clinical studies.

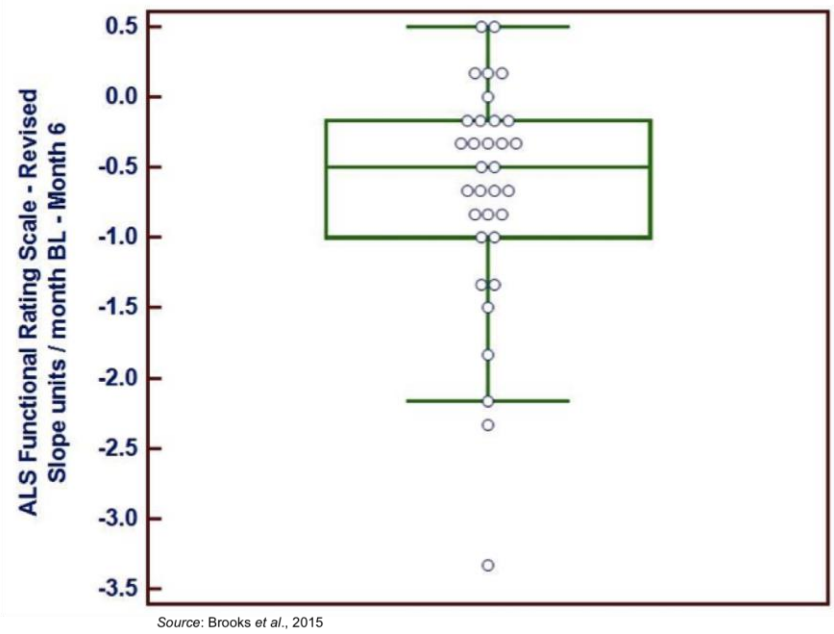


Source: Brooks *et al.*, 2015

Treatment	N	VC % Predicted ± SD	VC % Predicted / month ± SD
Philadelphia Cohort Before NIV	122	85 ± 20	- 4.6 ± 2.9
Philadelphia Cohort On NIV > 4 hr / d Group 1	38	83 ± 18	- 3.5 ± 5.3
Philadelphia Cohort On NIV < 4 hr / d Group 2	32	87 ± 24	- 5.9 ± 4.8
Philadelphia Cohort NIV not used Group 3	52	85 ± 13	- 8.3 ± 5.0
Pro-Act Cohort Before NIV	8404	86 ± 24	- 2.2 ± 6.9
Brisbane Cohort Before NIV	34	95 ± 19	- 3.1 ± 3.7
Penn State Cohort Before NIV	139	93 ± 16	- 2.4 ± 4.1
BCAA Cohort Before NIV	85	75 ± 21	- 3.1 ± 18.3
Memantine Cohort Before NIV	63	93 ± 16	- 2.6 ± 21.4
Charlotte Cohort Before Trilogy NIV	31	89 ± 22	- 2.8 ± 13.2
Charlotte CHS Cohort On Trilogy NIV > 4 hr / d	55	77 ± 18	- 1.2 ± 20.5
Charlotte CHS Ibudilast Safety Cohort Before Trilogy NIV	33	88 ± 15	- 1.3 ± 7.7

Source: Brooks *et al.*, 2015

The last data point examined for the interim analysis was the rate in decline of the "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 score it utilized to keep track of the health of all ALS patients, and is a common outcome measure in ALS clinical trials. The following figure shows that the overall rate of decline for patients in the Phase 2 study (both on MN-166 and placebo) was approximately -0.5 points/month, which is lower than has been observed in previous clinical trials (-1.2 points/month when looking at the totality of data from the Pro-Act Database).



Source: Brooks *et al*., 2015

Conclusion

The interim data presented on the Phase 2 clinical trial of MN-166 in ALS patients is quite encouraging, both because of the promising safety data and the lower rates of decline for both % predicted SVC and ALSFRS-R score compared to historical controls. The fact that the need for NIV is lower in this cohort of patients compared to historical controls is also encouraging, as most ALS patients die from respiratory failure, thus the ability to delay this result could be quite clinically beneficial. However, it must be reiterated that these are blinded data, thus it is impossible to know at this point how patients from each treatment cohort are faring, which we will not know until the data is unblinded. We are hopeful to see the unblinded data from the placebo controlled portion of the study before the end of 2016.

The treatment of ALS is a potential blockbuster opportunity. There has only ever been one drug approved for treating ALS, thus there is a huge unmet medical need for better treatment options for these patients. Given the limited treatment options and high costs associated with patient care, we believe an effective ALS treatment would command a premium price, possibly as high as $100,000 per patient per year. We estimate that a successful ALS treatment could bring in peak revenues of greater than $2 billion. The FDA just recently granted MN-166 Fast Track designation for the treatment of ALS, which includes a number of incentives for the company including increased interactions with the FDA to discuss the drug's development plan and the chance for priority review and accelerated approval.

In addition to targeting ALS, MN-166 is also being tested as a treatment for multiple sclerosis (MS) and various addiction disorders. The company's Phase 2b clinical trial of MN-166 in patients with progressive MS is now fully enrolled, and we anticipate an interim analysis will take place in the second half of 2016, with final results available in 2017. The company also recently announced positive results from a clinical study of MN-166 in alcohol use disorder that showed an ability for the drug to reduce alcohol craving. Clinical trials of the company's other lead compound, MN-001, in both idiopathic pulmonary fibrosis (IPF) and nonalcoholic steatohepatitis (NASH) will soon be underway. With multiple clinical studies both underway and set to be initiated in large target markets, we believe the stock is currently undervalued. Our probability adjusted discounted cash flow model gives a target price of $8 per share, and we continue to maintain a 'Buy' rating.

PROJECTED FINANCIALS

MediciNova Inc.
Income Statement

MediciNova, Inc.	2014 A	Q1 A	Q2 A	Q3 A	Q4 E	2015 E	2016 E	2017 E
MN-166 (Multiple Sclerosis)	$0	$0	$0	$0	$0	$0	$0	$0
YOY Growth	-	-	-	-	-	-	-	-
MN-166 (ALS)	$0	$0	$0	$0	$0	$0	$0	$0
YOY Growth	-	-	-	-	-	-	-	-
MN-166 (Addiction)	$0	$0	$0	$0	$0	$0	$0	$0
YOY Growth	-	-	-	-	-	-	-	-
MN-001 (NASH)	$0	$0	$0	$0	$0	$0	$0	$0
YOY Growth	-	-	-	-	-	-	-	-
MN-001 (IPF)	$0	$0	$0	$0	$0	$0	$0	$0
YOY Growth	-	-	-	-	-	-	-	-
Grants & Collaborative Revenue	$0	$0	$0	$0	$0	$0	$0	$0
YOY Growth	-	-	-	-	-	-	-	-
Total Revenues	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**
YOY Growth	-	-	-	-	-	-	-	-
Cost of Sales	$0	$0	$0	$0	$0	$0	$0	$0
Product Gross Margin	-	-	-	-	-	-	-	-
Research & Development	$3.260	$0.720	$0.797	$0.587	$0.900	$3.003	$5.000	$7.000
General & Administrative	$5.963	$1.495	$1.480	$1.007	$1.600	$5.583	$8.000	$10.000
Other Expenses	$0	$0	$0	$0	$0	$0	$0	$0
Operating Income	($9.223)	($2.215)	($2.277)	($1.594)	($2.500)	($8.586)	($13.0)	($17.0)
Operating Margin	-	-	-	-	-	-	-	-
Non-Operating Expenses (Net)	$0.028	$0.00	($0.01)	($0.01)	($0.01)	($0.03)	($0.5)	($0.5)
Pre-Tax Income	($9.195)	($2.212)	($2.285)	($1.607)	($2.510)	($8.614)	($13.5)	($17.5)
Income Taxes Paid	$0	$0	$0	$0	$0	$0	$0	$0
Tax Rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*
Net Income	**($9.195)**	**($2.215)**	**($2.287)**	**($1.608)**	**($2.510)**	**($8.614)**	**($13.5)**	**($17.5)**
Net Margin	-	-	-	-	-	-	-	-
Reported EPS	**($0.38)**	**($0.09)**	**($0.09)**	**($0.06)**	**($0.08)**	**($0.32)**	**($0.39)**	**($0.44)**
YOY Growth	-	-	-	-	-	-	-	-
Basic Shares Outstanding	24.068	24.539	24.828	26.932	30.000	26.574	35.000	40.000

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

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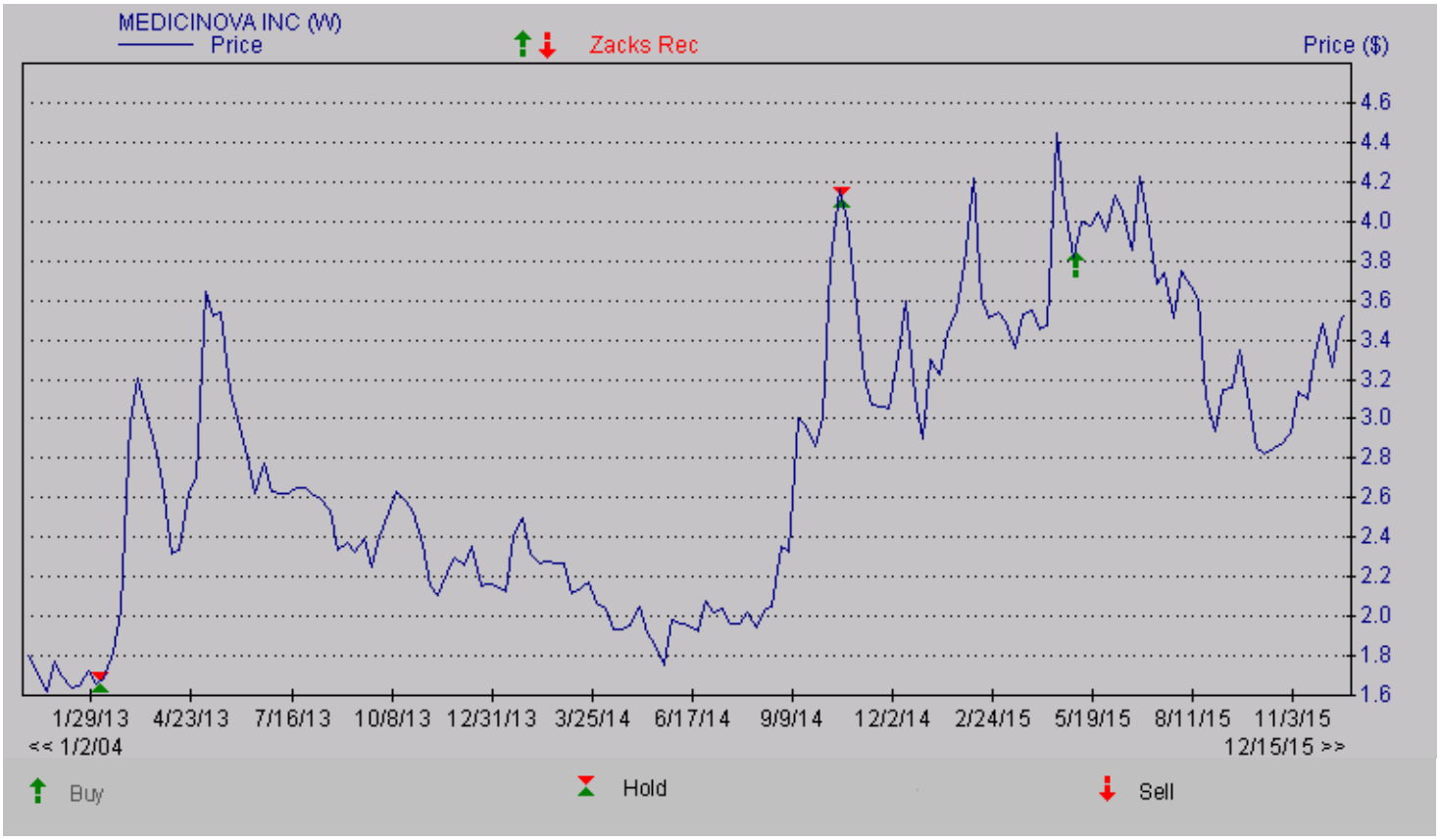

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Sell/Underperform: The analyst expects the company will underperform the broader U.S. Equity market over the next one to two quarters.

The current distribution is as follows: Buy/Outperform- 25.4%, Hold/Neutral- 56.4%, Sell/Underperform – 14.1%. Data is as of midnight on the business day immediately prior to this publication.