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David Bautz, PhD
312-265-9471
dbautz@zacks.com

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

MediciNova, Inc. (MNOV-NASDAQ)

MNOV: Ibudilast Identified as Promising Development Candidate in Alcohol Use Disorder and Degenerative Cervical Myelopathy…

Based on our probability adjusted DCF model that takes into account potential future revenues from MN-166 in ALS, progressive MS, addiction, and as an MCM; and MN-001 in NASH, MNOV is valued at $27.00/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 (03/01/22)	$2.39
Valuation	**$27.00**

OUTLOOK

MediciNova, Inc. (MNOV) is developing MN-166 (ibudilast) as a treatment for alcohol use disorder (AUD) and degenerative cervical myelopathy (DCM). Recently, two publications have identified MN-166 as a promising development candidate for each of those diseases. The compound is currently being evaluated in a Phase 2 clinical trial for the treatment of AUD and a Phase 3 clinical trial for the treatment of DCM. In addition, trials for MN-166 continue in amyotrophic lateral sclerosis (ALS), acute respiratory distress syndrome (ARDS) caused by COVID-19, chemotherapy-induced peripheral neuropathy (CIPN), glioblastoma (GBM), methamphetamine dependence, and it is Phase 3 ready for progressive multiple sclerosis (MS).

SUMMARY DATA

52-Week High	**$8.74**
52-Week Low	**$2.21**
One-Year Return (%)	**-57.92**
Beta	**1.24**
Average Daily Volume (sh)	**172,938**
Shares Outstanding (mil)	**49**
Market Capitalization ($mil)	**$117**
Short Interest Ratio (days)	**N/A**
Institutional Ownership (%)	**16**
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-Value**
Industry	**Med-Biomed/Gene**

ZACKS ESTIMATES

Revenue
(In millions of $)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2021	4 A	0 A	0 A	0 A	0 A
2022	0 E	0 E	0 E	0 E	0 E
2023					0 E
2024					0 E

Earnings per Share

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2021	-$0.00 A	-$0.09 A	-$0.07 A	-$0.04 A	-$0.21 A
2022	-$0.08 E	-$0.08 E	-$0.09 E	-$0.09 E	-$0.34 E
2023					-$0.36 E
2024					-$0.40 E

WHAT'S NEW

Business Update

MN-166 Identified as Promising Development Candidate for Alcohol Use Disorder

On February 22, 2022, MediciNova, Inc. (MNOV) announced that a recent publication identified MN-166 (ibudilast) as a promising pharmacological agent for the treatment of alcohol use disorder (AUD) (Burnette *et al*., 2022). In the U.S., approximately 44.6 million adults per year suffer from AUD and approximately 93.4 million (~1/3rd) adults will meet or have met AUD criteria during their lifetime (Grant *et al*., 2015). Surprisingly, less than 10% of adults in the U.S. with AUD are treated for the condition with either pharmacotherapies and/or psychotherapy treatment (Hasin *et al*., 2007). There are a number of reasons why there is such limited use of pharmacotherapies for AUD patients, including a lack of addiction treatment training for physicians, reluctance to prescribe, the perceived lack of efficacy of AUD therapies, undesirable side effects, and the negative stigma associated with being treated for AUD.

Currently, there are three FDA approved therapies for the treatment of AUD: disulfiram (Antabuse), acamprosate, and naltrexone (oral or extended-release injection). In Europe, the EMA has approved those three therapies along with nalmefene.

Disulfiram – This drug was approved by the FDA for the treatment of AUD in 1951. It is an aldehyde dehydrogenase inhibitor that blocks the metabolism of alcohol and increases the concentration of acetaldehyde. This results in nausea, vomiting, sweating, flushing, and heart palpitations upon alcohol consumption. A review of 22 randomized controlled trials (RCTs) showed that disulfiram was better than placebo at treating AUD in open-label studies, however blinded trials showed no statistical significance between disulfiram and placebo (Skinner *et al*., 2014). When disulfiram is used under supervision (in order to increase adherence), its success rate is better compared to non-supervised treatment. However, since adherence is such an issue and given that the side effects of disulfiram treatment following alcohol consumption can be potentially serious, the drug is typically only used for the maintenance of alcohol abstinence and not as a medication to reduce drinking.

Acamprosate – This is thought to be an N-methyl-D-aspartic acid (NMDA) receptor partial co-agonist. While this may lead to a reduction in neuronal hyperexcitability, the exact mechanism by which the drug works to treat AUD is currently unknown. A review of 27 RCTs showed that acamprosate reduced the risk of abstinent drinkers beginning to drink again, however it did not reduce the risk of binge drinking (Jonas *et al*., 2014). A Cochrane meta-analysis of 24 RCTs showed that acamprosate significantly reduced the risk of any drinking and increased cumulative duration of abstinence (Rösner *et al*., 2010). It is generally well tolerated and is FDA approved for abstinence maintenance in AUD patients who are abstinent when beginning treatment.

Naltrexone – This is a mu opioid receptor antagonist that was originally developed as a treatment for opioid use disorder. It was approved for AUD in 1994 following two 12-week trials that showed naltrexone significantly reduced drinking days and relapse rates (O'Malley *et al*., 1992; Volpicelli *et al*., 1992). It is available both orally and as an extended-release injectable that is administered once monthly (Vivitrol). Alkermes reported $311 million in revenues for Vivitrol in 2020, with $84 million of that for AUD (EvaluatePharma). Both oral and injectable forms of naltrexone are generally well tolerated and can significantly reduce both the risk of return to any drinking and return to binge drinking, however both of these associations were modest in magnitude (Mark *et al*., 2009).

A recent study showed that only 1.6% of adults in the US with AUD received an approved pharmacotherapy (Han *et al*., 2021), and based on the fact that the three approved products have limited efficacy and some can have severe side effects, it is clear that additional treatment options are warranted. A therapy with greater efficacy and tolerability will likely have a positive impact on patient and prescriber acceptance and should increase the percentage of patients that receive pharmacotherapy.

Ibudilast for the Treatment of AUD

Ibudilast (MN-166) is a macrophage migration inhibitory factor (MIF) and phosphodiesterase (PDE)-3, 4, -10, and 11 inhibitor. It leads to a decrease in pro-inflammatory cytokines, and since AUD can cause increases in inflammation (Mayfield *et al*., 2017), ibudilast is thought to treat AUD through its anti-inflammatory and pro-neurotrophic mechanisms. Preclinical results showed that ibudilast decreased drinking in alcohol-dependent mice

(Bell *et al*., 2015), which agrees with multiple other preclinical studies showing PDE inhibition decreases alcohol intake (Wen *et al*., 2012; Blednov *et al*., 2014).

Two previous clinical trials showed that ibudilast was well tolerated and showed positive effects against alcohol consumption. The first trial was a 7-day crossover study in which 24 non-treatment seeking individuals with mild-to-severe AUD were administered 50 mg ibudilast twice daily and then subjected to a stress-exposure session, an alcohol cue-exposure session, and an intravenous alcohol administration session (Ray *et al*., 2017). Ibudilast improved mood during exposure to alcohol and stress cues and attenuated the stimulant and mood-altering effects of alcohol in depressed patients. The second trial involved 52 non-treatment seeking individuals with AUD who were randomized to receive ibudilat (n=24) or placebo (n=28) for two weeks, during which time they filled out daily reports on their drinking, mood, and craving (Grodin *et al*., 2021). Results showed that ibudilast reduced the odds of heavy drinking by 45% (OR=0.55; 95%CI: 0.30, 0.98) compared to placebo, reduced alcohol craving on non-drinking days (*P*=0.02), and attenuated alcohol cue-related activation in the ventral striatum (reward response) compared to placebo (*P*=0.01).

Ibudilast is currently being evaluated in a double blind, placebo controlled trial in which approximately 132 treatment-seeking individuals with AUD will be randomized to receive ibudilast (50 mg) or placebo twice a day (NCT03594435). In-person follow-up visits will occur at Weeks 4, 8, and 12 and telephone assessments will occur at Weeks 2, 6, and 10. The primary outcome is the percent heavy drinking days with secondary outcomes including drinks per day, percent days abstinent, and percent subjects with no heavy drinking days.

MN-166 Identified as Promising Development Candidate for Degenerative Cervical Myelopathy

On February 28, 2022, MediciNova announced that a recent publication identified ibudilast as a promising candidate for the treatment of degenerative cervical myelopathy (DCM) (Gharooni *et al*., 2022). DCM is the leading cause of spinal cord dysfunction (Fehlings *et al*., 2013). It is typically caused by degeneration of the vertebral column, which can include changes to the vertebrae or the ligamentum flavum and/or posterior longitudinal ligament. These changes result in compression of the spinal cord (primary injury) as well as multiple secondary injuries including loss of neurons, dymyelination, and axonal degeneration. Even with surgical decompression, less than 5% of patients will make a full recovery (Fehlings *et al*., 2015).

Ibudilast was identified as a promising pharmacological agent for DCM based on its anti-inflammatory, neuroprotective, and neuroregenerative properties through its inhibition of macrophage migration inhibitory factor (MIF) and phosphodiesterase (PDE)-3, 4, -10, and 11. An increase in activated microglia and macrophages are observed where chronic spinal cord compression is occurring, and this results in an increase in pro-inflammatory cytokines that leads to cell death by necrosis and apoptosis. A compound such as ibudilast that can alleviate this pro-inflammatory state and potentially regrow lost nerve tissue could be beneficial to patients by preventing excessive cell death following decompression surgery and accelerating recovery.

Ibudilast is currently being evaluated in the Phase 3 randomized, double blind, placebo controlled RECEDE (Regeneration in Cervical Degenerative Myelopathy) clinical trial (NCT04631471). This is a two-part trial; the plan is to enroll 25-80 subjects in part 1 with a targeted enrollment of 362 subjects enrolled in the study. Patients will be administered MN-166 (up to 100 mg/day) for two to three months prior to decompression surgery and then MN-166 treatment will continue for six months following surgery. The primary endpoints assess changes in pain and function 6 months after surgery using the visual analog scale (VAS) for monitoring neck pain and the modified Japanese Orthopaedic Association (mJOA) Score, which assesses neurological function through evaluating motor function in upper and lower extremities, sensation, and bladder sphincter dysfunction.

Financial Results

On February 16, 2022, MediciNova filed Form 10-K with financial results for the full year 2021. The company reported $4.0 million of revenue for the year ending December 31, 2021, compared to no revenue for the year ending December 31, 2020. The revenue was related to the achievement of milestones from an assignment agreement with Genzyme related to gene therapy. Net loss for 2021 was $10.1 million, or $0.21 per share, compared to a net loss of $13.9 million, or $0.31 per share, for 2020. R&D expenses in 2021 were $8.5 million compared to $7.5 million in 2020. The increase was primarily due to higher clinical trial expenses from the ongoing clinical trial of MN-166 in ALS. G&A expenses in 2021 were $5.7 million compared to $6.7 million in 2020. The decrease was primarily due to decreased non-cash stock-based compensation and lower legal expenses.

MediciNova exited 2021 with approximately $71.4 million in cash and cash equivalents. We estimate the company has sufficient capital to fund operations at least through the end of 2023, and it's likely it can finance operations for

years beyond then as the company has a successful track record of managing expenses efficiently and raising capital when needed. As of February 14, 2022, the company had approximately 49.0 million shares outstanding and when factoring in stock options a fully diluted share count of approximately 57.0 million.

Conclusion

It's encouraging to see ibudilast identified by outside research groups as a promising candidate for both AUD and DCM, two indications for which the drug is currently being evaluated in clinical trials. In addition to those two indications, the compound is also currently being studied in a Phase 3 trial in amyotrophic lateral sclerosis (ALS), a Phase 2 trial for acute respiratory distress syndrome (ARDS) caused by COVID-19, a Phase 2 trial for chemotherapy-induced peripheral neuropathy (CIPN), a Phase 2 trial for glioblastoma (GBM), a Phase 2 trial for methamphetamine dependence, and is Phase 3 ready for progressive multiple sclerosis (MS). We look forward to updates from those trials throughout 2022. With no changes to our model our valuation remains at $27.

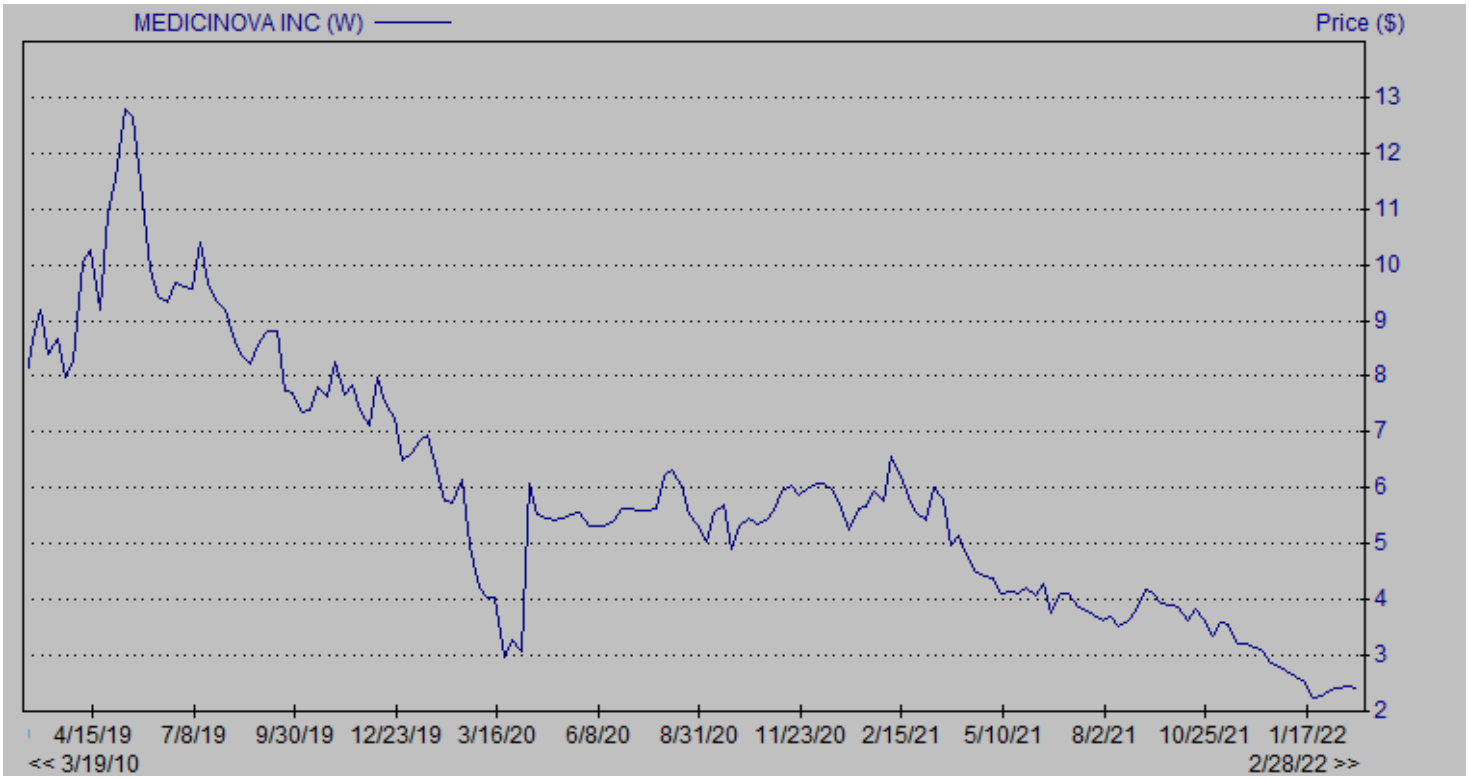
PROJECTED FINANCIALS

MediciNova Inc.
Income Statement

MediciNova, Inc.	2021 A	Q1 E	Q2 E	Q3 E	Q4 E	2022 E	2023 E	2024 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-166 (DCM)	$0	$0	$0	$0	$0	$0	$0	$0
MN-001 (NASH)	$0	$0	$0	$0	$0	$0	$0	$0
Grants & Collaborative Revenue	$4.0	$0	$0	$0	$0	$0	$0	$0
Total Revenues	**$4**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**
Cost of Sales	$0	$0	$0	$0	$0	$0	$0	$0
Product Gross Margin	-	-	-	-	-	-	-	-
Research & Development	$8.5	$2.2	$2.3	$2.3	$2.4	$9.2	$10.0	$12.0
General & Administrative	$5.7	$1.8	$1.8	$1.9	$2.0	$7.5	$8.0	$9.0
Other Expenses	$0	$0	$0	$0	$0	$0	$0	$0
Operating Income	($10.2)	($4.0)	($4.1)	($4.2)	($4.4)	($16.7)	($18.0)	($21.0)
Operating Margin	-	-	-	-	-	-	-	-
Non-Operating Expenses (Net)	$0.1	$0.0	$0.0	$0.0	$0.0	$0.1	$0.1	$0.1
Pre-Tax Income	($10.1)	($4.0)	($4.1)	($4.2)	($4.4)	($16.6)	($17.9)	($20.9)
Income Taxes Paid	$0	$0	$0	$0	$0	$0	$0	$0
Tax Rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*
Net Income	**($10.1)**	**($4.0)**	**($4.1)**	**($4.2)**	**($4.4)**	**($16.6)**	**($17.9)**	**($20.9)**
Net Margin	-	-	-	-	-	-	-	-
Reported EPS	**($0.21)**	**($0.08)**	**($0.08)**	**($0.09)**	**($0.09)**	**($0.34)**	**($0.36)**	**($0.40)**
YOY Growth	-	-	-	-	-	-	-	-
Basic Shares Outstanding	48.596	48.600	48.800	49.000	49.200	48.900	50.000	52.000

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

HISTORICAL STOCK PRICE



Source: Zacks Small Cap Research

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