Zacks Small-Cap Research
*Sponsored – Impartial - Comprehensive*

July 18, 2019
David Bautz, PhD
312-265-9471
dbautz@zacks.com

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

# MediciNova, Inc. (MNOV-NASDAQ)

## *MNOV: Readying for Phase 3 Trial in Multiple Sclerosis…*

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 $22/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 (07/18/19) | $9.67 |
| **Valuation** | **$22.00** |

## OUTLOOK

MediciNova, Inc. (MNOV) recently received feedback from the U.S. FDA regarding the planned Phase 3 clinical trial for MN-166 (ibudilast) in progressive multiple sclerosis (MS). The company is planning to conduct a single Phase 3 trial in patients with secondary progressive MS (SPMS) without relapses. The primary endpoint will be the time to 3-month confirmed disability progression, as measured by the Expanded Disability Status Scale (EDSS), which is the same primary endpoint that was used by other drugs recently approved for progressive MS. The MS market is currently valued at $23 billion (the vast majority of which is for drugs approved for only relapsing remitting MS [RRMS]). With >50% of RRMS patients converting to SPMS, and 80% of SPMS patients not experiencing relapses, SPMS without relapses represents an enormous potential opportunity.

## SUMMARY DATA

| | |
|---|---|
| **52-Week High** | **$13.22** |
| **52-Week Low** | **$6.82** |
| **One-Year Return (%)** | **14.40** |
| **Beta** | **1.20** |
| **Average Daily Volume (sh)** | **115,635** |
| **Shares Outstanding (mil)** | **43** |
| **Market Capitalization ($mil)** | **$441** |
| **Short Interest Ratio (days)** | **N/A** |
| **Institutional Ownership (%)** | **21** |
| **Insider Ownership (%)** | **15** |
| **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-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 |

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

## WHAT'S NEW

**Business Update**

*Planning for a Phase 3 Trial in Progressive Multiple Sclerosis*

On July 11, 2019, MediciNova, Inc. (MNOV) announced plans for a Phase 3 clinical trial for MN-166 (ibudilast) in progressive multiple sclerosis (MS) following feedback received from the U.S. Food and Drug Administration (FDA). The company is planning to conduct a single Phase 3 trial in patients with secondary progressive MS (SPMS) without relapses with the primary endpoint being the time to 3-month confirmed disability progression as measured by Expanded Disability Status Scale (EDSS). The EDSS is the 'gold standard' for assessing disability progression in patients with MS (Kurtzke, 1983). The EDSS consists of 19 disease steps on a scale between 0 and 10 and measures impairment or activity limitation in eight functional systems along with ambulation. The most commonly used method for determining disability progression is through repeat measurements of EDSS.

We believe there is ample justification for the company's decisions for each of the three main points of the trial:

1) **A single Phase 3 trial to support a regulatory filing for MN-166 in SPMS**. The FDA has recently approved two new therapies for the treatment of relapsing forms of MS (including RRMS and relapsing SPMS) and SPMS with relapses. Mayzent® (siponimod) was approved for SPMS with relapses based on the results of the EXPAND Phase 3 clinical trial (Kappos *et al*., 2018). Mavenclad® (cladribine) was approved for relapsing forms of MS based on the results of a 2010 Phase 3 clinical trial (Giovannoni *et al*., 2010). Thus, we believe that positive results from a single Phase 3 trial will suffice to support an NDA for MN-166 in SPMS patients without relapses.

2) **Focusing on SPMS patients without relapse**. In April 2019, MediciNova announced the results of a subgroup analysis of the Phase 2b SPRINT-MS trial of MN-166 in patients with progressive MS. The subgroup analysis performed was done to better understand which type of progressive MS responds best to treatment with MN-166 in regards to confirmed disability progression as measured by EDSS. The following table shows that the greatest treatment effect for MN-166 occurred in patients with SPMS without relapse, as demonstrated by a 46% risk reduction and a hazard ratio of 0.538.

| Subgroup | # subjects | | Hazard Ratio | Risk Reduction |
|---|---|---|---|---|
| | MN-166 | Placebo | | |
| PPMS | 68 | 66 | 0.707 | 29% |
| SPMS with relapse | 9 | 6 | 1.153 | -15% |
| SPMS without relapse | 52 | 54 | 0.538 | 46% |

*Source* : MediciNova, Zacks SCR

There are only three drugs currently approved for the treatment of progressive MS. Ocrevus® is only approved for PPMS while Mayzent® and Mavenclad® are approved for both RRMS and SPMS with relapse, while no medications are currently approved for the treatment of SPMS without relapses.

3) **Primary endpoint will be the time to 3-month confirmed disability progression as measured by EDSS**. The primary endpoints in the Phase 3 clinical trials for Mayzent® and Ocrevus® was the time to 3-month confirmed disability progression as measured by EDSS. The Phase 3 trial for Mavenclad® used that endpoint as a secondary outcome. Based upon this, the FDA agreed that it was an acceptable primary endpoint for a Phase 3 trial of MN-166 in SPMS patients without relapse.

Full details of the Phase 3 clinical trial protocol of MN-166 in SPMS patients without relapse will be finalized soon as the company prepares for an 'end-of-Phase 2' meeting with FDA later this year. We anticipate learning additional details about the trial following that meeting and for the trial to initiate in early 2020.

*How MN-166 Compares to Other Progressive MS Treatments*

We believe that the data presented thus far for MN-166 from the Phase 2b clinical trial compare quite favorably to the data presented for both ocrelizumab and siponimod, potentially making MN-166 a best in disease treatment for patients with both primary and secondary MS, as shown in the following table. Treatment with MN-166 results in a

46% reduction in disability progression in SPMS patients without relapse, compared to siponimod's study which showed only a 13% reduction in disability progression in SPMS patients without relapse (and a 21% reduction for all SPMS subjects) in those treated with siponimod (Mayzent® prescribing information). The weak trend shown by siponimod in SPMS patients without relapse is the reason the FDA limited its approved indication to relapsing SPMS.

| Drug | Type of Progressive MS | Route of Administration | Phase / Study Size | Reduction in Brain Atrophy after 2 Years | Reduction in Disability Progression |
|---|---|---|---|---|---|
| ocrelizumab | PPMS | intravenous infusion | Phase 3 n=732 | 17.5% | 24% |
| siponimod | SPMS | oral | Phase 3 n=1651 | 15% | 21% |
| **MN-166** | **PPMS and SPMS** | **oral** | **Phase 2b n=255** | **48%** | **PPMS: 29% SPMS without Relapse: 46%** |

*Source:* MediciNova, Inc.

In addition to exhibiting better efficacy than already approved products, MN-166 had a very favorable safety and tolerability profile as shown by no increases in serious adverse events and no safety signals. In contrast to the excellent safety profile for MN-166, treatment with ocrelizumab resulted in an increase in malignancies, serious infusion reactions, and infections, while treatment with siponimod increased infections, bradyarrhythmias, macular edema, respiratory effects, liver injury, increased blood pressure, and fetal risk. We don't believe that Mavenclad® will ever command more than 1-2% of the total market for SPMS with relapses due to a black box warning about an increased risk of malignancies.

| Drug | Safety Issues | Most Common Adverse Reactions |
|---|---|---|
| ocrelizumab (OCREVUS) | • malignancies including breast cancer<br>• serious infusion reactions<br>• Infections | • upper respiratory tract infections<br>• infusion reactions<br>• skin infections<br>• lower respiratory tract infections |
| siponimod (MAYZENT)* | • infections<br>• macular edema<br>• bradyarrhythmia<br>• respiratory effects<br>• liver injury<br>• increased blood pressure<br>• fetal risk | • headache<br>• hypertension<br>• transaminase increased<br>• falls<br>• edema peripheral |
| **MN-166** | • **None** | • **gastrointestinal side effects** |

*Source:* MediciNova, Inc.

*How Large is the SPMS Without Relapse Market?*

Three recent papers in the journal Neurology attempted to accurately estimate the prevalence of MS in the U.S. (Nelson *et al*., 2019; Culpepper *et al*., 2019; Wallin *et al*., 2019). The methodology described in those papers resulted in an estimate of approximately 700,000 individuals in the U.S. with MS. Up until then, most estimates of the number of individuals in the U.S. with MS suggested there were approximately 300,000 to 400,000 (Dilokthornsakul *et al*., 2016). While the new, larger estimate is certainly interesting, we will continue to use what we view as a more conservative estimate of 400,000 MS patients in the U.S., which we believe is supported by total sales of MS drugs (discussed below).

Of the patients diagnosed with MS, approximately 85% will be initially diagnosed with RRMS while approximately 15% will be diagnosed with primary progressive MS (PPMS). Of those diagnosed with RRMS, we estimate that at least 50% of them will go on to develop SPMS, although over a longer period of time (20+ years) that number may

be much higher. Of those with SPMS, we estimate that approximately 20% will have relapses (based on a 19% rate of relapse in placebo patients in the Mayzent® Phase 3 clinical trial). Based on a total of 400,000 MS patients in the US, this represents a potential market of >130,000 patients with SPMS without relapse.

According to EvaluatePharma, the MS market was approximately $23 billion in 2018. The following table shows the leading MS drugs according to 2018 worldwide sales. Tecfidera® was the highest-grossing MS drug in 2018 with approximately $4.3 billion in sales out of a total of 18 drugs available to treat those with RRMS. While there are a large number of drugs available for patients with RRMS, as previously mentioned there are only three drugs currently approved for treating progressive MS: Ocrevus® (only approved for PPMS), Mayzent® (approved for RRMS and SPMS with relapse), and Mavenclad® (approved for RRMS and SPMS with relapse), and none that are approved for treating SPMS without relapses.

| Company | Product | Indication | WW 2018 Sales (Millions) |
|---|---|---|---|
| Biogen | Tecfidera | RRMS | $4,274 |
| Novartis | Gilenya | RRMS | $3,341 |
| Roche | Ocrevus | RRMS/PPMS | $2,406 |
| Teva | Copaxone | RRMS | $2,366 |
| Sanofi | Aubagio | RRMS | $1,945 |
| Biogen | Avonex | RRMS | $1,915 |
| Biogen | Tysabri | RRMS | $1,864 |
| Merck KGaA | Rebif | RRMS | $1,699 |
| Bayer | Betaseron | RRMS | $643 |
| OTHER | | | $2,616 |
| | | **TOTAL** | $23,069 |

*Source*: EvaluatePharma

**Valuation and Conclusion**

Based upon an analysis of the MS market, we have adjusted our valuation for MediciNova. We continue to use an estimate for a total number of MS patients in the US of 400,000 based upon total sales of MS drugs in the U.S. Based on $23 billion in sales in 2018 and 300,000 MS patients being treated, that works out to approximately $76,667 per patient per year, which is fairly close to estimated yearly costs for MS drugs (Hartung *et al*., 2015; Managed Care).

If MN-166 is approved for the treatment of SPMS without relapse, it will be the only drug available for that condition. Tecfidera®, with sales of $4.3 billion in 2018, is a good example of the type of revenues that a safe and successful MS drug can generate (and that is in a very crowded market with 18 approved drugs), thus we now estimate $5 billion in peak worldwide sales is achievable for MN-166 for SPMS without relapse.

We believe MediciNova is ready to move ahead with the Phase 3 trial on its own, however partnering discussions are likely going on in the background. Partnering for a Phase 3 trial is certainly not a requirement for a smaller biotech company, for example both TG Therapeutics (TGTX) and Atara Biotherapeutics (ATRA) are conducting Phase 3 trials in MS without a larger biopharma partner. In addition, Receptos, Inc. was conducting two Phase 3 clinical trials in RRMS on its own when it was acquired by Celgene in 2015 for $7.4 billion. We believe the data compiled for MN-166 fully supports the initiation of a Phase 3 program and that even if no partnership is established prior to initiation of the Phase 3 trial that does not preclude one occurring during the trial or after the trial's conclusion.

We estimate the Phase 3 clinical trial for MN-166 in MS will begin in 2020 and approval will be in 2024, with peak sales of $5 billion approximately seven years after launch. Based on a 65% probability of approval and using a 15% discount rate, MN-166 in SPMS has a net present value of approximately $600 million. Based on this we are increasing our valuation for MediciNova from $19 to $22.

## 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*

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

## HISTORICAL STOCK PRICE




© 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, David Bautz, PhD, 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 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.