### D. Boral Capital による当社レポートの発表に関するお知らせ

現地時間の12月2日、米国ニューヨークに本拠を置く投資銀行D. Boral Capitalのアナリストである Jason Kolbert 氏による、当社レポートが発表されましたので、参考情報としてお知らせいたします。

なお、当該レポートは、恐れ入りますが、権利の都合上、英文のままでのご案内となります ので、ご了承ください。

【D. Boral Capital 公式 web サイト】

https://dboralcapital.com/

※当該レポートは、本書の下部にございますので、スクロールしてご確認ください。

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Health Care: Biotechnology

# MediciNova, Inc. (MNOV)

**INITIATING COVERAGE** 

December 2, 2024

# Lou Gehrig Would be Proud—ReTasking Ibudilast; Initiate Buy and \$9 PT

MediciNova is retasking an old drug (Ibudilast - originally used in Japan for asthma) to battle ALS. MediciNova has explored multiple CNS and inflammatory-related conditions for Ibudilast, also known as MN-166. The data in ALS shows a significant efficacy signal. The drug is known to be very safe. This combination suggests it may find broad use in ALS and, ultimately, some of the other target indications, such as Multiple Sclerosis (MS). Despite the significant market potential MediciNova's valuation is distressed. The company and its founder, Dr. Iwaki MD PhD, an accomplished transplant surgeon, has funded the drug's clinical with non-dilutive capital such as NIH grants. We are initiating coverage with a Buy rating and \$9.00 price target.

How does Ibudilast's work? The drug's mechanism of action in ALS is through its ability to inhibits phosphodiesterases (PDE-4 and PDE-10), increasing cyclic AMP levels, which helps suppress neuroinflammation. It also reduces activation of microglia and astrocytes, the CNS's immune cells, thereby lowering the production of proinflammatory cytokines like TNF- $\alpha$  and mitigating neurotoxicity. Additionally, Ibudilast promotes neurotrophic factors, supporting neuronal survival and reducing oxidative stress, which collectively contribute to its potential to slow ALS progression.

**Ibudilast (MN-166)** is currently being evaluated in the **COMBAT-ALS** Phase 2b/3 clinical trial, which assesses its efficacy, safety, and tolerability in ALS patients. The trial builds on promising Phase 1 and 2 data and plans to enroll 230 participants across 30 sites in the U.S., Canada, and Europe. It includes a 12-month treatment period with a placebocontrolled design, followed by an open-label extension phase. The primary endpoint is the change in ALSFRS-R scores, with secondary endpoints focusing on muscle strength, quality of life, and survival time.

**History:** Ibudilast was initially developed by **Kyorin** (4569-JP; not rated) in Japan in the 1980s and was approved for treating **asthma** and **cerebrovascular disorders**. Over time, its neuroprotective effects drew attention, leading to its exploration in **neurodegenerative diseases** like **multiple sclerosis** (**MS**) and **amyotrophic lateral sclerosis** (**ALS**). In 2008, **MediciNova** acquired the rights to Ibudilast for development in the U.S. and Europe. However, in 2013, Otsuka regained the rights to Ibudilast in a move to prioritize its own internal programs. Following this, in 2015, MediciNova reacquired global rights to the drug, including in Japan, after Otsuka decided to return the rights to MediciNova. In July 2022 Otsuka's involvement with MN-166 ended.

**Valuation:** For the purpose of our model we value MN-166 in ALS. We apply a probability of success factor of 30% based on the fact that its in pivotal trial. In addition, we have selected a 30% discount rate (r) for our forecasting models. We assume additional capital will be raised in our final share count. We then apply these projections to our Free Cash Flow to the firm, or FCFF discounted EPS or dEPS, and sum-of-the-parts or SOP models, which are equal-weighted, averaged, and rounded to the nearest whole number to derive our 12-month price target of \$9.00.

**Risk Factors:** These include Clinical/Regulatory Risk, Partnership and Financial Risk, Commercial Risk, Legal and Intellectual Property Risk, and Market Share Risk.

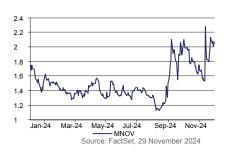
#### Jason Kolbert

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MARKET DATA	
Rating	Buy
Price Target	\$9.00
Price	\$2.07
Average Daily Volume (000)	50
52-Week Range (\$)	\$1.12-\$2.55
Market Cap (M)	\$102
Enterprise Value (M)	\$60
Book Value	\$1.27
Dividend Yield	0.0%
Cash (M)	\$42
Qrtly Burn Rate (M)	\$(3)

ESTIMATES			
	2023A	2024E	2025E
Revenue (M)	\$1.0	\$0.0	\$0.0
Total Expenses (M)	\$11	\$13	\$30
GAAP EPS	\$(0.17)	\$(0.21)	\$(0.50)

#### **One Year Performance Chart**



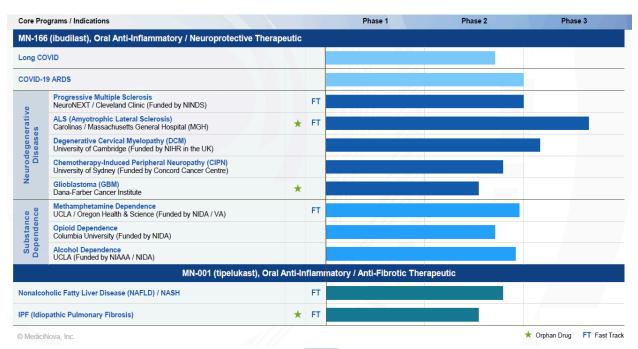
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Please see analyst certification and important disclosures on page 30 of this report.



Company Overview. MediciNova, Inc. is a biopharmaceutical company dedicated to developing innovative therapies targeting serious diseases with unmet medical needs, primarily for the U.S. market. Its lead candidate, MN-166 (ibudilast), is under development for a wide range of neurological and other conditions, including progressive multiple sclerosis (MS), amyotrophic lateral sclerosis (ALS), glioblastoma, and substance dependence. Notable achievements include positive results from Phase 2b trials in progressive MS and ALS, with both programs granted Fast Track and Orphan Drug designations by the FDA. Another pipeline asset, MN-001 (tipelukast), is being investigated for fibrotic diseases such as idiopathic pulmonary fibrosis (IPF) and nonalcoholic fatty liver disease (NAFLD). The company also has additional candidates addressing acute asthma, cancer, and other conditions. Leveraging partnerships with leading academic and clinical institutions, MediciNova aims to address critical gaps in treatment while pursuing regulatory pathways for expedited development and approval.

**Exhibit 1. Pipeline and Milestones.** MediciNova's pipeline showcases a robust portfolio of innovative therapies targeting significant unmet needs across neurological, respiratory, and fibrotic diseases. The lead candidate, MN-166, is advancing in late-stage trials for progressive multiple sclerosis (MS) and amyotrophic lateral sclerosis (ALS), with additional potential in substance use disorders. Complementing this is MN-001 (tipelukast), a first-in-class compound targeting fibrotic diseases such as nonalcoholic steatohepatitis (NASH) and idiopathic pulmonary fibrosis. With multiple programs benefiting from regulatory designations like orphan drug and fast-track status, the pipeline reflects MediciNova's strategic focus on high-impact areas and its commitment to developing transformative therapies.



# MN-166 (ibudilast)

- Phase 3 updates for ALS and DCM
- Update on ARDS program
- Update on Long COVID trial
- Update on other programs

Source: MediciNova, Inc

# MN-001 (tipelukast)

 Phase 2 update in NAFLD, Type 2 diabetes and hypertriglyceridemia



Exhibit 2. Mechanism of Action: MN-166 is a multi-functional therapeutic agent with several mechanisms of action aimed at addressing neuroinflammatory and neurodegenerative conditions. Its first key mechanism involves macrophage migration inhibitory factor (MIF) inhibition, which has been linked to reduced disease progression in animal models of multiple sclerosis (MS), highlighting its potential in modulating immune response in the central nervous system. Secondly, phosphodiesterase-4 (PDE4) inhibition leads to an increase in cyclic adenosine monophosphate (cAMP), a signaling molecule that dampens pro-inflammatory cytokines such as IL-1, TNF- $\alpha$ , and IL-6, resulting in both anti-inflammatory and neuroprotective effects. Lastly, MN-166 attenuates the activity of glial cells, which are a type of macrophage activated during brain damage. Persistent activation of glial cells can drive neurodegeneration; by mitigating their activation, MN-166 offers a protective effect against further neurological damage. Together, these mechanisms underscore its potential in treating conditions characterized by inflammation and neurodegeneration.

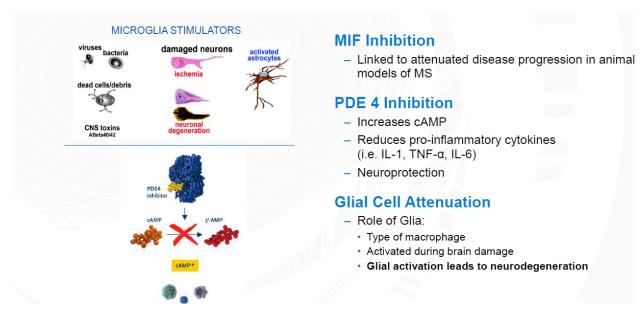


Exhibit 3. A Phase 2 clinical trial evaluating MN-166 in amyotrophic lateral sclerosis (ALS) demonstrated positive results, meeting its primary endpoint of safety and tolerability. The study enrolled 51 ALS patients who were not using non-invasive ventilation. MN-166 showed a favorable safety profile, with no severe or life-threatening treatment-related adverse events (TRAEs). Among seven serious adverse events (SAEs) reported, none were related to the study drug. Mild to moderate TRAEs were the most common, including nausea, anorexia, and loss of appetite—side effects consistent with both riluzole and MN-166. In terms of efficacy, the trial showed encouraging trends. During the 6-month double-blind period, 29.4% of patients receiving MN-166 were ALSFRS-R responders (defined as those whose total scores improved, remained unchanged, or declined by only 1 point), compared to 17.6% in the placebo group. Further support for efficacy came from the 6-month open-label extension (OLE), where 35.3% of placebo-treated patients became responders when switched to MN-166. These findings suggest MN-166 may offer both a safe and potentially effective treatment option for ALS.

Achieved Primary Endpoint Safety And Tolerability	<ul> <li>N=51 ALS subjects not using non-invasive ventilation</li> <li>MN-166 (ibudilast) demonstrated a favorable safety and tolerability profile</li> <li>7 serious adverse events (SAEs) but none were related to the study drug</li> <li>All treatment-related adverse events (TRAEs) were mild to moderate</li> <li>No severe or life-threatening TRAEs</li> <li>Most frequently reported TRAEs: nausea, anorexia, and loss of appetite were expected and are common side effects of both riluzole and MN-166 (ibudilast)</li> </ul>
	<ul> <li>Responder was defined as a subject who improved on the ALSFRS-R total score*, had no change on the score, or the score declined by 1 point</li> </ul>
Efficacy Trends ALSFRS-R Responders	• 6-month, Double-Blind Period: 29.4% of subjects in the MN-166 (ibudilast) group were responders compared to 17.6% of subjects in the placebo group
	<ul> <li>6-month, Open-Label Extension (OLE): 35.3% of subjects on placebo in the double-blind period were responders when taking MN-166 (ibudilast) in OLE</li> </ul>

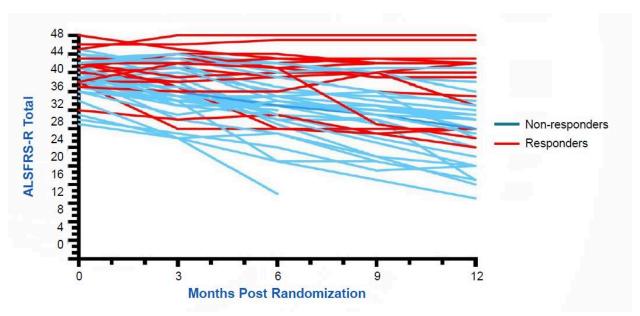
Source: MediciNova, Inc

**Financials:** MediciNova's Q3-2024 financial results: Research and development (R&D) expenses for the quarter were approximately \$1.96M, marking a slight decrease compared to \$2.03M in Q2 2024. Similarly, selling, general, and administrative (SG&A) expenses were \$1.64M, slightly up from \$1.58M in the prior quarter. As of the quarter's end, MediciNova reported \$41.3M in cash and cash equivalents, a decline from \$44.6M in Q2 2024, underscoring a careful cash burn strategy amidst ongoing operational activities.

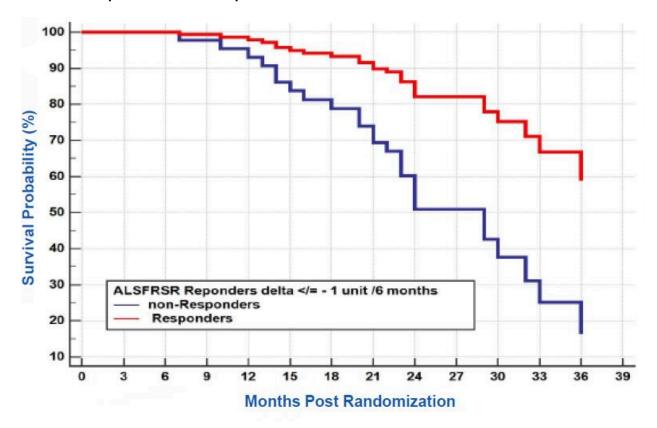
MediciNova has utilized various grants and non-dilutive funding sources to advance its clinical programs while conserving capital. A notable example is the NIH-funded ALS trial, which supports a Phase 2-3 Expanded Access study of MN-166 with no direct financial burden on the company. Additionally, MediciNova is participating in a Health Canada-funded clinical trial evaluating MN-166 for Long COVID, with most costs covered by the Canadian Institutes of Health Research. The company has also benefited from investigator-sponsored trials funded by U.S. government agencies like BARDA and international institutions. These strategic collaborations enable MediciNova to expand its pipeline and conduct critical research while minimizing expenses.

**Exhibit 4. Responders Showed Less Functional Decline.** The chart demonstrates the efficacy of MN-166 in slowing the progression of ALS as measured by changes in ALS Functional Rating Scale-Revised (ALSFRS-R) scores. The analysis defines responders as individuals who experienced improvements, no change, or only a minimal decline (1 point) in their ALSFRS-R scores during the study period. Results from the 6-month double-blind period show that 29.4% of patients treated with MN-166 met this definition, compared to only 17.6% of those receiving a placebo. Furthermore, during the open-label extension phase, where placebo patients were transitioned to MN-166, 35.3% of this group achieved responder status, indicating potential treatment benefits even after a delayed start.

The data emphasizes that responders maintained greater functional stability, suggesting MN-166 may help preserve motor and respiratory function for longer, potentially improving quality of life. This benefit, coupled with the drug's safety profile—characterized by mild to moderate treatment-related adverse events such as nausea and appetite changes—supports the potential of MN-166 to address an urgent unmet need in ALS treatment. By decelerating functional decline, MN-166 may delay critical milestones of disease progression, such as loss of ambulation or reliance on ventilation, offering hope for improved patient outcomes.



Source: MediciNova, Inc Responder was defined as a subject who improved on the ALSFRS-R total score, had no change on the score, or the score declined by 1 point. Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised (ALSFRS-R) total score measures the functional activity of an ALS subject.



**Exhibit 5. Responders Showed Improved Survival** 

Source: MediciNova, Inc.

MediciNova is conducting two clinical trials for ALS (Amyotrophic Lateral Sclerosis) focused on evaluating its lead asset, MN-166, an oral small molecule with anti-inflammatory properties.

- 1. **COMBAT-ALS Trial**: This is MediciNova's company-sponsored Phase 2/3 clinical trial, designed as a 12-month study to assess the efficacy and safety of MN-166 in ALS patients. The goal is to evaluate the drug's impact on disease progression in a controlled, comprehensive setting.
- 2. NIH-Funded Expanded Access Program (EAP): This is a six-month trial funded by the National Institutes of Health (NIH) under the ACT for ALS law. It focuses on providing MN-166 to ALS patients who are ineligible for the COMBAT-ALS trial, particularly those in advanced stages of the disease. Conducted across 17 institutions, the trial leverages NIH support to minimize MediciNova's financial burden while generating additional clinical insights.

MediciNova is advancing its ALS program with an ongoing Phase 3 clinical trial evaluating MN-166. This trial is a multi-center, two-arm, randomized, double-blind, placebo-controlled study involving approximately n=230 ALS patients. Participants are randomized 1:1 to receive either a placebo or MN-166 at 100 mg/day for 12 months. The primary endpoint focuses on the change in ALS Functional Rating Scale-Revised (ALSFRS-R) scores and survival time over the treatment period. ALSFRS-R is a widely used measure in ALS studies, assessing patient capabilities across 12 functional tasks, with scores ranging from 0 (worst) to 48 (best). Secondary endpoints include changes in muscle strength and quality of life, the proportion of responders, time to survival, and safety/tolerability. Key inclusion criteria require patients to have an ALS onset within 18 months of screening, be on riluzole for at least 30 days before the trial, and have specific respiratory and ALSFRS-R benchmarks.

Building on insights from its Phase 2 trial, MediciNova has optimized its Phase 3 design by increasing the MN-166 dose to 100 mg/day, lengthening the treatment duration to 12 months, targeting patients in the early stages of the disease, and excluding slow progressors to enhance the chances of detecting a treatment effect. Notably, Phase 2 data suggested that MN-166 responders, defined as those with stable or slightly improved ALSFRS-R scores, experienced slower functional decline and longer survival times, emphasizing the potential of MN-166 to alter ALS progression meaningfully.

**Exhibit 6. Phase 3 ALS Trial Ongoing: MN-166 is being supported under an NIH-sponsored Expanded Access Protocol (EAP).** Announced this past September 30, 2024, this trial aims to evaluate the drug's impact on neurofilament light chain (NfL), a biomarker for neuron damage associated with ALS progression. This initiative, supported by a \$22 million NIH grant, aligns with the Accelerating Access to Critical Therapies for ALS Act, enabling broader access to investigational treatments for patients who may not qualify for conventional clinical trials. MediciNova is also advancing MN-166 in its Phase 2b/3 COMBAT-ALS trial.

	N=230 subjects
Titl Buston	Phase 3 multicenter, randomized, double-blind trial
Trial Design	Duration: 12 months of double-blind treatment + open label extension (6 months)
	Dosing: 100 mg/day of MN-166 (ibudilast) or placebo (1:1 randomization)
Objections	Primary Endpoint: Change from baseline in ALSFRS-R score at Month 12 and survival time (global rank test)
Objectives	Other Endpoints: Muscle strength (HHD), quality of life (ALSAQ-5), responder analysis (ALSFRS-R), survival time, safety and tolerability

## **Higher Dose**

- Phase 3 is using a higher dose of 100 mg/day of MN-166 (ibudilast) vs. 60 mg/day used in Phase 2
- Safety of 100 mg/day has been established in other clinical trials including progressive MS
- Dose-dependent response of MN-166 (ibudilast) expected to result in better efficacy at the higher dose

#### **Longer Treatment Period**

- Phase 3 has a 12-month double-blind treatment period vs. a 6-month treatment period in Phase 2
- Longer treatment period should make it easier to achieve statistical significance on the primary endpoint as the disease progresses over time

#### Early Stage of Disease

- Early-stage patients showed a better response to MN-166 (ibudilast) than late-stage patients in Phase 2
- Phase 3 is enrolling only early-stage ALS patients (ALS onset of ≤18 months)

#### **No Slow Progressors**

- Including slow progressors makes it more difficult to demonstrate a treatment effect
- Phase 3 excludes ALS patients with a slow rate of progression

(0)



**Exhibit 7. Overview of Completed Phase 2b Progressive MS Trial** 

Trial Design	<ul> <li>N=255 subjects with Primary or Secondary Progressive MS (PPMS or SPMS)</li> <li>Interferon-beta or glatiramer acetate allowed as concomitant medication</li> </ul>
	Phase 2b randomized, double-blind trial; 96-weeks; 28 centers in the U.S. (NeuroNEXT sites)
	Dosing: Up to 100 mg/day (50 mg BID) of MN-166 (ibudilast) or placebo (1:1 randomization)
Objectives	<ul> <li>Primary Endpoint #1: Whole brain atrophy using brain parenchymal fraction (BPF)</li> <li>Primary Endpoint #2: Safety and tolerability</li> </ul>
	<ul> <li>Secondary Endpoint: Disability, imaging analyses of brain and retinal tissue integrity, cortical atrophy, cognitive impairment, quality-of-life, and neuropathic pain</li> </ul>

Source: MediciNova, Inc

**Exhibit 8. MN-166 Achieved Both Primary Endpoints in Phase 2b MS Study.** The Phase 2b trial of MN-166 in progressive multiple sclerosis demonstrated promising results in slowing disease progression. The study involved a two-year evaluation of patients receiving ibudilast in either 30 mg or 60 mg daily doses compared to a placebo. The findings highlighted a significant reduction in sustained disability progression by approximately 50% for patients treated with ibudilast for the full 24 months. Additionally, patients on the higher 60 mg dose experienced a notable reduction in brain volume loss, as measured by MRI, and showed decreased conversion of new inflammatory lesions to persistent black holes—indicators of chronic damage in multiple sclerosis.

These results underscore ibudilast's potential as a disease-modifying treatment for progressive forms of multiple sclerosis, addressing an area of significant unmet need where therapeutic options are limited. The drug was well-tolerated throughout the study duration, supporting its continued clinical development.

Primary Endpoint #1: Brain Atrophy	<ul> <li>MN-166 (ibudilast) demonstrated a statistically significant 48% reduction in the rate of progression of whole brain atrophy vs. placebo (p=0.04) as measured by MRI analysis using brain parenchymal fraction (BPF)</li> </ul>
Primary Endpoint #2:	MN-166 (ibudilast) demonstrated a favorable safety and tolerability profile     No increased rate of serious adverse events in the MN-166 (ibudilast) group compared to the placebo group     No opportunistic infections, no cancers, no cardiovascular events (no heart attacks or strokes), and no deaths related to MN-166 (ibudilast) treatment
Safety And Tolerability	<ul> <li>No statistically significant difference in tolerability between the MN-166 (ibudilast) group and the placebo group</li> <li>The most common treatment-emergent adverse events during the study were gastrointestinal adverse events, which occurred with a higher frequency in the MN-166 (ibudilast) group, and upper respiratory tract infections, which occurred with a higher frequency in the placebo group</li> </ul>
Disability Progression	MN-166 (ibudilast) demonstrated a 26% reduction in the risk of confirmed disability progression vs. placebo (hazard ratio=0.74), measured by EDSS

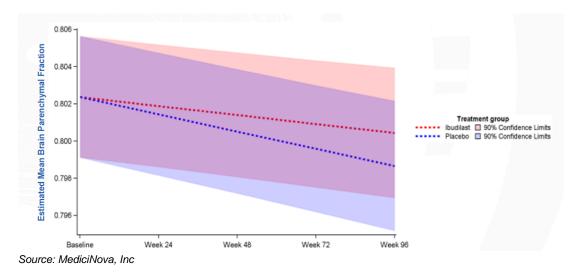
What is Brain Atrophy in MS Patients? Brain atrophy in multiple sclerosis (MS) refers to the gradual loss of brain tissue, including neurons and supporting structures. This neurodegeneration is a hallmark of progressive MS and is associated with the irreversible decline in cognitive and motor function. As MS progresses, particularly in its secondary progressive (SPMS) and primary progressive (PPMS) forms, brain atrophy accelerates, contributing to worsening disability. Unlike the more acute, relapse-driven inflammation seen in relapsing-remitting MS (RRMS), progressive MS involves ongoing neurodegeneration, where the loss of brain volume is considered a key indicator of disease progression.

Brain atrophy in MS patients results from a combination of factors, including inflammation, axonal loss, and demyelination. Demyelination—the breakdown of the protective myelin sheath around nerves—is a key feature of MS. Over time, if the repair mechanisms in the brain are insufficient, this leads to permanent damage and shrinking of the brain tissue. MRI scans can quantify this atrophy by measuring the reduction in brain volume, often referred to as "brain shrinkage." Brain atrophy is closely correlated with clinical symptoms, such as motor impairment, cognitive dysfunction, and overall disability.

In clinical trials, reducing brain atrophy progression is considered an important outcome because it reflects a slowing of the underlying disease process. Treatments that can delay or reduce brain atrophy are highly sought after, especially for progressive MS forms, where few effective therapies currently exist.

**Exhibit 9. MN-166 Reduced Brain Atrophy Progression by 48% (p=0.04).** Reducing brain atrophy progression by 48%, as shown in the chart below is of significant value because brain atrophy is a hallmark of neurodegeneration in multiple sclerosis and strongly correlates with long-term disability. Brain volume loss reflects irreversible damage to neural tissues, leading to impairments in motor function, cognition, and overall quality of life. Slowing this process is a critical goal in treating progressive MS, as it indicates potential preservation of brain function and delaying the progression of disability.

Furthermore, therapies that effectively reduce brain atrophy are rare in progressive MS, where current treatments largely focus on managing relapses rather than halting underlying disease progression. By targeting and slowing atrophy, ibudilast may offer a novel mechanism of action that addresses both inflammation and neurodegeneration, setting it apart from existing therapies. This could improve outcomes for patients, especially in secondary and primary progressive MS, where treatment options remain limited, and prognosis is poor.

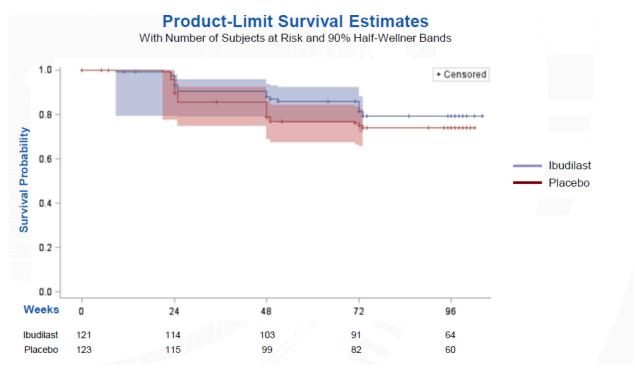




The finding that MN-166 reduced the risk of confirmed disability progression by 26% is highly meaningful for treating progressive multiple sclerosis. Disability progression in MS is often measured by a sustained worsening of symptoms, typically quantified using scales like the Expanded Disability Status Scale (EDSS). A 26% reduction means that ibudilast significantly slowed the worsening of disability compared to placebo, offering patients a better chance of maintaining their mobility, independence, and quality of life for longer periods.

This outcome is particularly noteworthy because confirmed disability progression is an FDA-approvable endpoint for therapies targeting progressive MS. Achieving this endpoint demonstrates that a drug not only manages symptoms but also impacts the underlying disease process in a meaningful way, making it a candidate for regulatory approval. Given that treatment options for progressive MS are extremely limited, a therapy like ibudilast, which addresses both inflammation and neurodegeneration and has shown efficacy in reducing disability progression and brain atrophy, could fill a significant unmet medical need.

Exhibit 10. MN-166 Reduced the Risk of Confirmed, Disability Progression by 26%. Approvable Endpoint for Progressive MS.



Source: MediciNova, Inc.

The 90% Half-Wellner Bands refer to a statistical concept used in survival analysis, specifically in the context of product-limit survival estimates (also known as Kaplan-Meier estimates). These estimates are commonly used in clinical trials to measure the time until an event of interest occurs (such as progression-free survival or overall survival). The Half-Wellner Bands are a type of confidence interval used to express uncertainty around the Kaplan-Meier survival curve. They provide a range of values within which the true survival curve is likely to fall, offering a way to assess the reliability of the survival estimate. Specifically, the 90% Half-Wellner Bands denote the range within which we expect the true survival function to lie, with a 90% level of confidence. These bands are named after the statistical method attributed to Wellner for constructing confidence intervals around the Kaplan-Meier curve. Unlike traditional confidence intervals, which typically use standard deviations or standard errors, the Half-Wellner Bands adjust for the unique properties of survival data, which often includes censoring (where subjects drop out or are lost to follow-up before experiencing the event). The number of subjects at risk is displayed alongside the survival curve and bands, which represents the number of individuals who are still being observed at each time point in the study. This helps contextualize the survival estimates, particularly when the number of subjects at risk decreases over time.



The observation that MN-166 shows the greatest efficacy in secondary progressive multiple sclerosis (SPMS) without relapse, reducing the risk of confirmed disability progression in this subgroup, is a significant finding for several reasons:

- Addressing a Critical Unmet Need: SPMS without relapse represents one of the most challenging forms of MS to treat. Unlike relapsing-remitting MS, where relapses are more predictable and inflammatory, SPMS without relapse involves ongoing neurodegeneration with minimal inflammatory activity. This means that most currently approved MS therapies, which primarily target inflammation, have limited effectiveness in this population.
- 2. Targeting Neurodegeneration: The efficacy of ibudilast in this subgroup suggests that the drug may be addressing mechanisms beyond inflammation, such as neuroprotection and the preservation of neural tissue. This aligns with the reduction in brain atrophy and supports ibudilast's unique mechanism of action, which appears to be more relevant for progressive forms of MS.
- 3. **Potential for Regulatory and Clinical Differentiation:** Demonstrating efficacy in SPMS without relapse positions ibudilast as a novel therapeutic option distinct from existing treatments. This subgroup represents a significant portion of the progressive MS population, and targeting this area could make ibudilast stand out in terms of clinical value and regulatory approval.
- 4. **Enhanced Patient Outcomes:** For patients in this subgroup, slowing disability progression means a longer period of independence and reduced burden on caregivers. This has profound implications for quality of life in a population with few effective treatment options.

These results underscore ibudilast's potential as a first-in-class treatment for progressive MS, particularly in patients without active relapses, addressing a pressing unmet need in neurology.

**Exhibit 11. MN-166 Shows Greatest Efficacy in SPMS Without Relapse.** Risk of Confirmed Disability Progression by Subgroup.

Subgroup	Number of Subjects MN-166	Number of Subjects Placebo	Hazard Ratio*	Risk Reduction
Primary Progressive MS	68	66	0.707	29%
Secondary Progressive MS with Relapse	9	6	1.153	-15%
Secondary Progressive MS without Relapse	52	54	0.538	46%



The exhibit below highlights the unique and differentiated potential of MN-166 in addressing both primary progressive multiple sclerosis (PPMS) and secondary progressive multiple sclerosis (SPMS), particularly the largest and most underserved subgroup of SPMS patients without relapses.

- High Unmet Medical Need in SPMS Without Relapses: This subgroup represents the most significant treatment gap in progressive MS. Unlike relapsing-remitting MS or SPMS with relapses, which are partially addressed by immunomodulatory therapies, SPMS without relapses primarily involves neurodegeneration. Most existing MS drugs target inflammation and offer little to no benefit for these patients.
- 2. **No Approved Long-Term Treatments**: To date, there are no FDA-approved therapies specifically indicated for long-term treatment of SPMS without relapses. This underscores the substantial unmet medical need, as patients in this group experience a steady worsening of disability without acute flare-ups that could be targeted by standard anti-inflammatory therapies.
- 3. Largest Subgroup of Progressive MS Patients: SPMS without relapses accounts for more than 80% of all SPMS cases. This makes it not only a critical clinical population but also a significant market opportunity for ibudilast, which has shown efficacy in reducing brain atrophy and disability progression—key measures of disease impact in this group.

By focusing on this population, ibudilast has the potential to fill a critical gap in the treatment landscape, offering hope to the largest and most underserved segment of progressive MS patients.

#### Exhibit 12. Phase 2b Results Demonstrated Differentiated Potential in Both PPMS and SPMS.

- The unmet medical need is highest in subjects with SPMS without relapses
- No drugs approved for long-term treatment of SPMS without relapses
- It is the largest subgroup of progressive MS patients (>80% of SPMS patients)

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 (ibudilast)	PPMS and SPMS	Oral	Phase 2b n=255	48%	PPMS: 29% SPMS without Relapse: 46%



MN-166 has a unique and differentiated potential of MN-166 in addressing both primary progressive multiple sclerosis (PPMS) and secondary progressive multiple sclerosis (SPMS), particularly the largest and most underserved subgroup of SPMS patients without relapses.

- High Unmet Medical Need in SPMS Without Relapses: This subgroup represents the most significant treatment gap in progressive MS. Unlike relapsing-remitting MS or SPMS with relapses, which are partially addressed by immunomodulatory therapies, SPMS without relapses primarily involves neurodegeneration. Most existing MS drugs target inflammation and offer little to no benefit for these patients.
- 2. No Approved Long-Term Treatments: To date, there are no FDA-approved therapies specifically indicated for long-term treatment of SPMS without relapses. This underscores the substantial unmet medical need, as patients in this group experience a steady worsening of disability without acute flare-ups that could be targeted by standard anti-inflammatory therapies.
- 3. Largest Subgroup of Progressive MS Patients: SPMS without relapses accounts for more than 80% of all SPMS cases. This makes it not only a critical clinical population but also a significant market opportunity for ibudilast, which has shown efficacy in reducing brain atrophy and disability progression—key measures of disease impact in this group.

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#### Exhibit 13. Phase 2b Results Demonstrated Differentiated Potential in Both PPMS and SPMS.

- The unmet medical need is highest in subjects with SPMS without relapses
- No drugs approved for long-term treatment of SPMS without relapses
- It is the largest subgroup of progressive MS patients (>80% of SPMS patients)

Drug	Safety Issues	Most Common Adverse Reactions
ocrelizumab (OCREVUS)	Malignancies Including Breast Cancer     Serious Infusion Reactions     Infections	Upper Respiratory Tract Infections     Infusion Reactions     Skin Infections     Lower Respiratory Tract Infections
siponimod (MAYZENT)*	Infections  Macular Edema  Bradyarrhythmia  Respiratory Effects  Liver Injury  Increased Blood Pressure  Fetal Risk	Headache Hypertension Transaminase Increased Falls Edema Peripheral
MN-166 (ibudilast)	· None	Gastrointestinal Side Effects



ibudilast (MN-166) is a Phase 3 ready asset, with discussions currently underway with potential partners.

- 1. Phase 3 Readiness: The designation of ibudilast as "Phase 3 ready" means that the drug has successfully navigated earlier clinical phases, including Phase 2, and demonstrated sufficient efficacy and safety in treating progressive MS. The Phase 2b results, which showed positive outcomes in reducing disability progression and brain atrophy, have likely provided the necessary data to move forward into a larger, pivotal Phase 3 trial. This step is critical for obtaining regulatory approval and advancing ibudilast to the broader patient population.
- 2. Discussions with Potential Partners: MediciNova is actively seeking collaborations with pharmaceutical companies, possibly for co-development or commercialization. Partnerships are often crucial for securing the necessary resources and expertise to conduct Phase 3 trials and, if successful, to bring the drug to market. A partnership could also help MediciNova expand its reach and increase the chances of success in a competitive and complex therapeutic area like progressive MS.
- 3. **Strategic Positioning for Market Success**: Moving toward Phase 3 trials and engaging with potential partners also positions ibudilast as a potentially valuable asset in the treatment landscape for progressive MS. Given the large unmet need in progressive MS—especially in patients without relapses—ibudilast could represent a key advancement in treating a population with few therapeutic options.

This progress reflects both the clinical promise of ibudilast and its potential to fill a critical gap in the treatment of progressive MS. The combination of positive Phase 2 results and strategic partnership discussions underscores its potential to advance into later-stage development and possibly revolutionize treatment options for MS patients.

Exhibit 14. MN-166: Phase 3 Ready in Progressive MS. Discussions Ongoing with Potential Partners.

Trial Design	<ul> <li>Randomized, double-blind Phase 3 trial</li> <li>Dosing: 100mg/day of MN-166 (ibudilast) or placebo</li> <li>Based on subgroup analyses from Phase 2 trials and discussion with FDA, Phase 3 trial will enroll subjects with SPMS without relapse</li> </ul>
Objectives	Primary endpoint: 3-month confirmed disability progression, as measured by EDSS, as confirmed with FDA
Marketing Potential	<ul> <li>Single Phase 3 trial as the basis for marketing approval</li> <li>FDA approved both MAYZENT and MAVENCLAD for relapsing SPMS in March 2019 after a single Phase 3 trial for each drug</li> </ul>



Degenerative Cervical Myelopathy (DCM), also known as cervical spondylotic myelopathy, is a condition in which the spinal cord is compressed due to degenerative changes in the cervical spine (neck). This compression leads to dysfunction in the spinal cord, resulting in a range of neurological symptoms. DCM is the most common cause of spinal cord impairment in adults, causing significant disability and a reduced quality of life. Patients typically experience symptoms such as pain, numbness, and weakness in the limbs, poor coordination, difficulty with balance, and bladder problems. These symptoms can worsen over time, leading to increased disability if left untreated.

Despite its prevalence, DCM remains largely untreated by pharmaceuticals, as there are currently no approved drugs for its management. Treatment typically involves surgical intervention to relieve compression on the spinal cord or nerve roots. According to the American Association of Neurological Surgeons, more than 200,000 cervical spine surgeries are performed annually in the U.S. to address spinal cord compression, highlighting the substantial burden of this condition on both patients and healthcare systems. The absence of pharmacological treatments for DCM emphasizes the need for further research and development in this area to improve outcomes for patients suffering from this debilitating condition.

Exhibit 15. Phase 3 Trial in DCM Ongoing.

Trial Design	N=362 subjects with degenerative cervical myelopathy (DCM) who are scheduled for first surgical decompression (including enrollment of 25-80 in the pilot stage)
	<ul> <li>Phase 3 randomized, double-blind, multicenter trial</li> <li>Principal Investigator: Dr. Mark Kotter, University of Cambridge</li> </ul>
	Duration: 8 months of double-blind treatment + follow up (6 months)
	Dosing: Up to 100 mg/day of MN-166 (ibudilast) or placebo (1:1 randomization)
Objective	<ul> <li>Primary Endpoint #1: Modified Japanese Orthopaedic Association (mJOA) Score (evaluates motor dysfunction in upper and lower extremities, loss of sensation, and bladder sphincter dysfunction) at 6 months after surgery</li> </ul>
	Primary Endpoint #2: Visual Analogue Scale (VAS) neck pain at 6 months after surgery



Acute Respiratory Distress Syndrome (ARDS) is a severe, life-threatening condition characterized by widespread inflammation in the lungs, leading to fluid accumulation in the air sacs (alveoli). This impairs oxygen exchange and can cause rapid respiratory failure. ARDS typically results from various causes, such as pneumonia, trauma, sepsis, or as a complication of viral infections like COVID-19. Symptoms of ARDS include severe shortness of breath, low blood oxygen levels, and rapid breathing, which require urgent medical intervention, often including mechanical ventilation.

The potential application of **MN-166** in ARDS lies in its known anti-inflammatory and neuroprotective effects. Ibudilast is a phosphodiesterase 4 (PDE4) inhibitor, which has shown promise in modulating the immune response and reducing inflammation. In the context of ARDS, this could be beneficial because inflammation in the lungs plays a critical role in the progression of the disease, leading to further damage to lung tissue and worsening respiratory function. By reducing this inflammation, MN-166 could potentially help mitigate the severity of ARDS, reduce fluid accumulation, and improve oxygen exchange, which is essential for patient recovery.

Ibudilast has been studied in other conditions involving neuroinflammation, such as multiple sclerosis, but its broader anti-inflammatory properties suggest it could be effective in treating conditions like ARDS, where excessive inflammation contributes to tissue damage and dysfunction. Though the drug has not yet been proven in ARDS clinical trials, its mechanism of action suggests it could play a role in controlling the inflammatory response, potentially improving outcomes in patients with ARDS.

#### Exhibit 16. Potential for MN-166 in Acute Respiratory Distress Syndrome

# Anti-inflammatory properties of MN-166 (ibudilast) may be effective in reducing cytokine storm, a key element of COVID-19 induced ARDS

- Cytokine storm is hyperactive immune response characterized by the release of high levels of inflammatory cytokines that cause injury to cells
- Resulting damage causes fluid to leak from the smallest blood vessels, reducing the amount of oxygen that reaches the bloodstream and results in ARDS

# MN-166 (ibudilast) reduces inflammatory cytokines through MIF and PDE4 inhibition

- MN-166 (ibudilast) may prevent or reduce hyperinflammation and cytokine storm, thereby preventing death or enabling a faster recovery.
  - Current rate of death in the hospital is approximately 40% for ARDS patients.

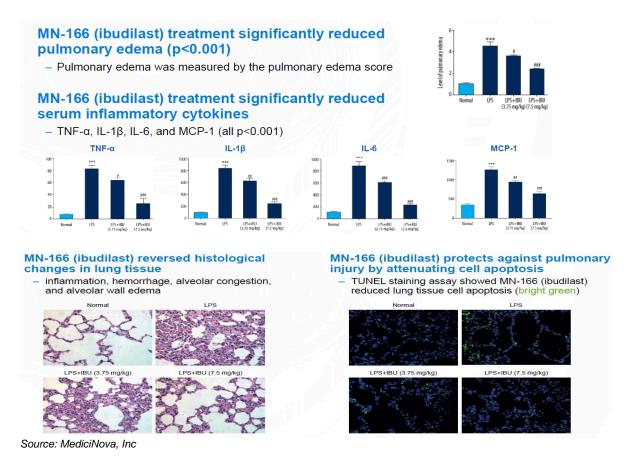


The data showing that MN-166 reduces key inflammatory cytokines in a preclinical model of Acute Respiratory Distress Syndrome provides a promising indication of how the drug could potentially benefit patients suffering from this severe condition. ARDS is driven by an intense inflammatory response, which leads to the release of various pro-inflammatory cytokines—such as TNF- $\alpha$ , IL-6, and IL-1 $\beta$ —that play a critical role in the development and worsening of the syndrome. These cytokines contribute to the injury of lung tissue, disruption of the blood-gas barrier, and impaired oxygenation.

Ibudilast, as a **phosphodiesterase 4 (PDE4) inhibitor**, has been shown to modulate immune responses by reducing the production of these pro-inflammatory cytokines. In preclinical models, ibudilast's ability to lower levels of key cytokines suggests that it could help reduce the overall inflammatory burden in the lungs of ARDS patients, which could prevent further tissue damage, reduce the severity of the condition, and possibly improve outcomes such as respiratory function and recovery times.

In ARDS, controlling inflammation is a key therapeutic target, and this preclinical evidence supports the idea that ibudilast might play a role in modifying the inflammatory process and improving pulmonary function. However, translating these findings from animal models to human patients would require rigorous clinical trials to confirm the efficacy and safety of the treatment in the context of ARDS. The reduction in cytokines observed in these preclinical studies suggests that MN-166 could potentially be developed as a therapeutic for inflammatory lung diseases like ARDS, where few pharmacological treatments currently exist.

**Exhibit 17.** Preclinical Model of ARDS Shows Reduction in Key Inflammatory Cytokines, in the graphs below. In the slides below MN-166 demonstrates Improvements in ARDS animal models.





The positive Phase 2 results in COVID-19-related Acute Respiratory Distress Syndrome reported by the company highlight the potential of MN-166 as a therapeutic option for managing the severe inflammatory response associated with COVID-19. ARDS is a common and serious complication in COVID-19 patients, characterized by severe lung inflammation, fluid buildup in the alveoli, and impaired oxygenation, often leading to respiratory failure and requiring mechanical ventilation.

In the context of COVID-19 ARDS, the Phase 2 trial results demonstrated that MN-166, a **PDE4 inhibitor**, was effective in reducing key inflammatory markers and improving lung function. As a PDE4 inhibitor, ibudilast works by modulating the immune system to decrease the production of pro-inflammatory cytokines, which are central to the inflammatory response seen in ARDS. The positive results from this trial suggest that MN-166 may help reduce the severity of inflammation in the lungs, improve oxygenation, and potentially reduce the need for mechanical ventilation in COVID-19 patients with ARDS.

The data from the trial provide preliminary evidence that ibudilast may offer a new therapeutic strategy for COVID-19-related ARDS, where currently available treatments are limited. This includes the potential to address the underlying inflammation rather than just the symptoms of respiratory failure, a critical component in managing ARDS. However, further clinical trials will be required to confirm these findings and establish the full safety and efficacy profile of MN-166 in this setting.

This positive Phase 2 outcome is particularly relevant in the ongoing search for effective treatments for COVID-19 and its complications, especially in the face of the pandemic's evolving nature. The company's successful results may pave the way for further exploration of ibudilast as a treatment for other inflammatory lung diseases as well.

#### Exhibit 18.Positive Phase 2 Results in COVID-19 ARDS

Trial Basina	N=34 hospitalized COVID-19 patients at risk for developing ARDS and receiving standard of care
	Phase 2 multi-center, randomized, double-blind, placebo-controlled trial
Trial Design	Duration: 7 days of double-blind treatment
	Dosing: 100 mg/day of MN-166 (ibudilast) or placebo (1:1 randomization)
	• Co-primary endpoint: 71% of subjects in the MN-166 (ibudilast) group and 35% of subjects in the placebo group were free of respiratory failure at Day 7 (p=0.02)
	<ul> <li>Co-primary endpoint: 71% of subjects in the MN-166 (ibudilast) group and 47% of subjects in the placebo group had <u>improved clinical status</u> on the NIAID scale at Day 7 (p=0.08)</li> </ul>
Results	<ul> <li>Hospital discharges: 65% of subjects in the MN-166 (ibudilast) group and 29% of subjects in the placebo group were discharged from the hospital at Day 7 (p=0.02)</li> </ul>
	<ul> <li>Worsening of clinical status: 0% of subjects in the MN-166 (ibudilast) group and 24% of subjects in the placebo group had worsened clinical status at Day 7 (p=0.05)</li> </ul>
	Deaths: two deaths in the placebo group and no deaths in the MN-166 (ibudilast) group
	No serious adverse events related to MN-166 (ibudilast)



The company's **BARDA** (Biomedical Advanced Research and Development Authority) partnership is a strategic collaboration focused on the development of **MN-166** for the treatment of **COVID-19-related ARDS** and potentially other inflammatory lung diseases. BARDA, a U.S. government agency under the Department of Health and Human Services (HHS), supports the development of medical countermeasures to respond to public health emergencies, such as pandemics, biological threats, and emerging diseases.

Through this partnership, the company receives funding and resources from BARDA to accelerate the clinical development of MN-166 for ARDS, particularly in the context of COVID-19. The funding supports **preclinical and clinical trials**, as well as regulatory activities, helping the company bring MN-166 to market more quickly. The partnership is particularly important in ensuring that treatments for COVID-19 complications, such as ARDS, are available in a timely manner. In addition to COVID-19, the collaboration may extend to other conditions with similar inflammatory pathways, such as ARDS resulting from influenza or other viral infections.

This partnership highlights the increasing focus on developing anti-inflammatory therapies that can target the root causes of diseases like ARDS, rather than just addressing symptoms. The support from BARDA is critical in mitigating risks associated with developing novel treatments, such as conducting large-scale clinical trials and obtaining regulatory approvals. By working with BARDA, the company is positioning MN-166 as a potential therapeutic for both COVID-19-related complications and other inflammatory conditions, offering new hope for patients with limited treatment options.

The partnership is a reflection of BARDA's ongoing efforts to address the challenges posed by emerging infectious diseases and public health threats, positioning it as a key player in the development of next-generation therapies.

#### Exhibit 19. BARDA Partnership.

Partnership with Biomedical Advanced Research and Development Authority (BARDA) to develop MN-166 (ibudilast) in chlorine gas-induced lung damage such as ARDS and acute lung injury (ALI)

- BARDA provided funding for proof-of-concept studies under Contract No. 75A50121C00022
- First nonclinical efficacy study: Treatment with MN-166 (ibudilast) high dose resulted in greater improvement (p=0.0001) in mean PaO2/FiO2 ratio, a pulmonary function measure and the primary endpoint, than MN-166 (ibudilast) low dose, rolipram, and the negative control in the multi-dose study
  - The mean PaO2/FiO2 ratio decreased (worsened) by 57% from baseline (the end of the chlorine gas exposure) to hour 48 in the negative control group vs. a decrease (worsening) of 36% in the MN-166 (ibudilast) high dose group
  - At hour 48, the last time point measured in the study, the mean PaO2/FiO2 ratio was 46% higher (better) in the MN-166 (ibudilast) high dose group than in the negative control group (327.8 vs. 224.8 mmHg), indicating that the negative control group had mild ARDS but the MN-166 (ibudilast) high dose group no longer had ARDS
- Second nonclinical efficacy study: no evaluable efficacy results as the model was not feasible

#### FDA approval does not require human clinical studies for this indication

- FDA animal rule: development of medical countermeasures (MCMs) does not require human clinical trials to establish efficacy when these trials would not be ethical or feasible
- FDA can grant approval of a drug for a MCM indication based on well-controlled animal studies, when the
  results of these studies establish that the drug is reasonably likely to produce clinical benefit in humans



MN-001 (tipelukast), developed by MediciNova, is an investigational oral therapy with a unique multitarget mechanism of action aimed at addressing inflammation and fibrosis. The drug functions as a leukotriene receptor antagonist, reducing inflammatory and allergic responses, while also inhibiting phosphodiesterase (PDE) activity to enhance anti-inflammatory cyclic AMP signaling. Additionally, MN-001 inhibits 5-lipoxygenase (5-LO), a key enzyme in the production of pro-inflammatory leukotrienes, and demonstrates anti-fibrotic properties by suppressing fibrosis-related gene expression and extracellular matrix deposition. These attributes position MN-001 as a potential treatment for a range of conditions characterized by inflammation and fibrosis, including idiopathic pulmonary fibrosis (IPF), nonalcoholic steatohepatitis (NASH), interstitial lung disease (ILD), and severe asthma. Its differentiated mechanism supports its potential to address unmet needs in these challenging indications.

#### Exhibit 20. MN-001 Overview

### Oral, anti-inflammatory and anti-fibrotic candidate

- Reduced triglycerides in clinical trials
- Anti-fibrotic activity established in preclinical models

# Strong safety profile, with >600 human subjects exposed

Prior asthma studies established safety and tolerability

#### Positive Phase 2 data in NASH / NAFLD

### **Completed Phase 2 trial in IPF**

# Ongoing Phase 2 trial in patients with NAFLD, Type 2 Diabetes and Hypertriglyceridemia

Source: MediciNova, Inc

#### Exhibit 21.MN-001(tipelukast): Differentiated through Multiple Mechanisms of Action

#### **Anti-Fibrotic Activity**

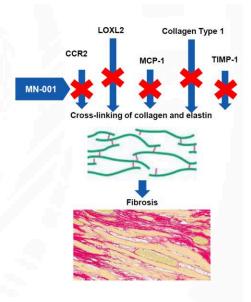
- MN-001 (tipelukast) reduces mRNA expression of genes that are known to promote fibrosis (e.g. LOXL2, Collagen Type 1, TIMP-1)
- MN-001 (tipelukast) inhibits 5-lipoxygenase (5-LO)

# **Anti-Inflammatory Activity**

- MN-001 (tipelukast) inhibits leukotriene (LT) and phosphodiesterases (PDE)
- MN-001 (tipelukast) reduces inflammatory gene expression (e.g. CCR2, MCP-1)

# **Reduces Triglycerides**

- MN-001 (tipelukast) reduced triglycerides in every clinical trial completed (asthma, interstitial cystitis, NASH)
- MN-001 (tipelukast) suppresses CD36 expression and inhibits the uptake of arachidonic acid into hepatocytes





MediciNova conducted a Phase II clinical trial to evaluate MN-001 in patients with idiopathic pulmonary fibrosis (IPF). The study was an open-label, single-arm design aimed at assessing the safety, tolerability, and preliminary efficacy of the drug over a treatment period of 26 weeks. Participants received MN-001 at a dose of 750 mg daily, divided into three doses of 250 mg, with the primary endpoint focused on changes in forced vital capacity (FVC), a key measure of lung function in IPF.

The results demonstrated promising trends in efficacy, with a substantial proportion of patients showing stabilization or improvement in FVC compared to the typical decline observed in untreated IPF patients. Notably, MN-001 appeared to mitigate disease progression, with some patients experiencing an increase in FVC. The safety profile was favorable, with no serious adverse events attributed to the drug, supporting its potential as a well-tolerated treatment option. These findings suggest MN-001 could provide meaningful clinical benefits in IPF, particularly by slowing or halting the decline in lung function, which warrants further investigation in larger, controlled studies.

Exhibit 22. IPF Phase 2 Trial Completed

	N=15 subjects with moderate to severe IPF
Trial Design	<ul> <li>Phase 2 randomized, placebo-controlled, double-blind trial at Penn State Milton S. Hershey Medical Center</li> <li>Principal Investigator: Dr. Rebecca Bascom</li> </ul>
	Duration: 26 weeks of double-blind treatment + open label extension (26 weeks)
	Dosing: 1500 mg/day of MN-001 (tipelukast) or placebo (2:1 randomization)
	<ul> <li>No clinically meaningful trends in favor of MN-001 (tipelukast) for the majority of the clinical outcome measures</li> </ul>
Results	<ul> <li>No worsening IPF events (acute IPF exacerbation or hospitalization due to respiratory symptoms) in the MN-001 (tipelukast) group compared to one worsening IPF event in the placebo group</li> </ul>
	<ul> <li>MN-001 (tipelukast) demonstrated a substantial reduction in LOXL2, a biomarker for IPF, whereas LOXL2 increased in the placebo group</li> </ul>
	MN-001 (tipelukast) was safe and well tolerated

Source: MediciNova, Inc

MediciNova conducted a Phase II clinical trial to evaluate MN-001 in patients with nonalcoholic steatohepatitis (NASH) or nonalcoholic fatty liver disease (NAFLD). This open-label study aimed to assess the safety, tolerability, and efficacy of MN-001 in improving key biomarkers associated with liver disease progression. Patients received MN-001 at a daily dose of 750 mg, administered in three divided doses, over a 12-week treatment period.

The trial focused on changes in liver fat content, as measured by imaging techniques such as MRI-PDFF (proton density fat fraction), along with improvements in liver enzymes, including alanine aminotransferase (ALT) and aspartate aminotransferase (AST). Secondary endpoints included biomarkers of fibrosis, lipid metabolism, and systemic inflammation.

Results from the trial were encouraging, with MN-001 demonstrating a significant reduction in liver fat content and notable improvements in ALT and AST levels, indicative of reduced liver inflammation. Additionally, some patients showed reductions in fibrosis markers, suggesting the drug's potential to slow or reverse liver damage. MN-001 was well-tolerated, with no treatment-related serious adverse events reported. These outcomes highlight the potential of MN-001 as a novel therapeutic option for NASH and NAFLD, conditions for which effective treatments remain a significant unmet medical need.



Exhibit 23. Phase 2 NASH / NAFLD Trial. MN-001 (tipelukast) reduced serum triglycerides (primary endpoint)

	Subjects with NASH or NAFLD with hypertriglyceridemia
Trial Design	Phase 2 multicenter, proof-of-principle, open-label study
	Dosing: MN-001 (tipelukast) 250 mg once daily for 4 weeks, then twice daily for 8 weeks
	MN-001 reduced mean serum triglycerides, reduced mean serum total cholesterol, and reduced mean serum LDL
Results	MN-001 increased mean serum HDL
	No clinically significant safety or tolerability issues
Dest Hea	Compared to subjects without Type 2 diabetes mellitus (T2DM), the T2DM group showed a greater reduction in serum triglyceride levels at Week 8 (50.8% reduction for with T2DM versus 17.8% reduction for without T2DM, p=0.098)
Post-Hoc Subgroup Analysis	<ul> <li>Mean HDL increase was significantly greater in subjects with T2DM than subjects without T2DM at Week 8 (15.8% versus 1.0%, p&lt;0.0002)</li> </ul>
	<ul> <li>In comparison to subjects without T2DM, the T2DM group showed a greater reduction in serum LDL levels at Week 8 (15.4% versus 6.7%)</li> </ul>

Source: MediciNova, Inc.

MediciNova is currently conducting a Phase II clinical trial to evaluate MN-001 in patients with nonalcoholic fatty liver disease (NAFLD), type 2 diabetes, and hypertriglyceridemia. The trial is designed as an open-label, multi-center study aiming to assess the drug's safety, tolerability, and impact on key metabolic and hepatic parameters in this high-risk patient population. The study targets the interplay between metabolic dysfunction and liver disease, a critical area of unmet need in clinical care.

Patients enrolled in the trial receive MN-001 at a daily dose of 750 mg, administered in three divided doses, over a 12-week treatment period. The primary endpoints focus on changes in triglyceride levels and liver fat content, measured through imaging techniques such as MRI-PDFF. Secondary endpoints include improvements in glycemic control, as reflected by HbA1c levels, and reductions in liver enzymes such as ALT and AST. Additional exploratory analyses evaluate changes in biomarkers of fibrosis, systemic inflammation, and lipid metabolism.

This trial builds on the drug's multi-modal mechanism of action, targeting inflammation, lipid dysregulation, and fibrotic pathways, which are central to the pathophysiology of NAFLD and its complications. If successful, the results could position MN-001 as a potential therapeutic option for patients with overlapping metabolic and hepatic disorders, addressing a critical gap in treatment.

Exhibit 24. Phase 2 Trial in NAFLD, Type 2 Diabetes and Hypertriglyceridemia Ongoing.

	N=40 subjects with NAFLD, Type 2 diabetes and hypertriglyceridemia
Trial Design	Multi-center, randomized, double-blind, placebo-controlled Phase 2 trial
	Duration: 24 weeks of double-blind treatment
	• Dosing: 500 mg/day of MN-001 (tipelukast) or placebo (1:1 randomization)
Objectives	<ul> <li>Co-Primary Endpoints:         <ul> <li>(1) change from baseline in liver fat content measured by FibroScan CAP score at Week 24, and</li> <li>(2) change from baseline in fasting serum triglycerides at Week 24</li> </ul> </li> </ul>
	Secondary Endpoints: changes in lipid profile (HDL-C, LDL-C, total cholesterol); safety and tolerability



The incidence and prevalence of Amyotrophic Lateral Sclerosis (ALS) vary geographically, reflecting differences in population demographics and diagnostic practices. Here's a breakdown based on the most recent data:

#### **United States**

- **Prevalence**: 4–6 per 100,000 people.
- **Population estimate**: With a U.S. population of approximately 330 million, this equates to **13,200–19,800 individuals** living with ALS.
- **Source**: The ALS Association confirms the U.S. prevalence of ALS at approximately 16,000 individuals living with the condition at any given time. *Source: The ALS Association.*

#### **Europe**

- **Prevalence**: 5–7 per 100,000 people.
- **Population estimate**: Europe has a population of about 450 million, resulting in **22,500–31,500** individuals living with ALS.
- **Source**: Data aligns with epidemiological studies of ALS prevalence in Europe, which report similar prevalence rates. *Source: The ALS Association.*

#### Japan

- **Prevalence**: 6–8 per 100,000 people.
- Population estimate: Japan's population of 125 million suggests 7,500–10,000 individuals living with ALS.
- **Source**: ALS prevalence studies specific to Japan indicate a higher prevalence compared to Western countries, potentially due to genetic and environmental factors. *Source: The ALS Association.*

#### Rest of the World (ROW)

- 1. **Prevalence**: Estimated at 1.5–3 per 100,000 people, with significant underreporting in some areas.
- 2. **Population estimate**: For a global population of ~8 billion (minus regions above), this suggests ~120,000–240,000 individuals outside the U.S., Europe, and Japan.
- 3. **Source**: These figures reflect lower diagnosis rates in developing countries where healthcare access and reporting systems are limited.



#### **Model Assumptions:**

- 1. We assume MN-166 requires two pivotal trials completed for approval in ALS, as such we model commercialization in the U.S. by 2029, with Europe and Japan staggered a year later.
- 2. We assume a price of \$75,000, which is a moderate estimate and may be impacted by multiple factors, from the Cost of Goods to efficacy.
- 3. We apply a 30% probability of success as MN-166 is a Phase III compound. Investors should recognize that our POS factor is independent of our discount rate (r), which is also at 30%.
- 4. We assume a pretty rapid market share climb as MN-166 safety profile is excellent and any patient with ALS who can benefit is likely to be put on drug. Our exception to this is Rest-of-World where lack of insurance and care become factors for therapeutics use.
- 5. We do not include other indications for MN-166 such as Multiple Sclerosis or Degenerative Cervical Myelopathy (DCM) nor do we include MN-001 (tipelukast) as we believe in the near term ALS is the sole performance driver for the company. Success in ALS, generates resources, sets the stage for these and other indications outlined in this report.

**Exhibit 25. Therapeutic Models** 

US ALS		2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E	2034E
	Prevalance	16,000	16,320	16,646	16,979	17,319	17,665	18,019	18,379	18,747	19,121	19,504	19,894
	Growth Rate	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%	2%
	Market Share	0%	0%	0%	0%	0%	0%	10%	20%	40%	60%	65%	65%
	Treated Patients	-		-	-	-	-	1,802	3,676	7,499	11,473	12,678	12,931
	cost of therapy	75,000	75,000	75,000	75,000	75,000	75,000	75,000	75,750	76,508	77,273	78,045	78,826
	change in cost of therapy	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	1.0%	1.0%	1.0%	1.0%	1.0%
	Probability of Success	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%
Total Revenues (M)	\$	- \$	- \$	- \$	- \$	- \$	- \$	41 \$	84 \$	172 \$	266 \$	297 \$	306
Source: DBoralCapital Estimates													
EU ALS		2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E	2034E
	Prevalance	26,000	26,260	26,523	26,788	27,056	27,326	27,600	27,876	28,154	28,436	28,720	29,007
	Growth Rate of incidence	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%
	Market Share	0%	0%	0%	0%	0%	0%	0%	5%	25%	40%	50%	55%
	Treated Patients	0	0	0	0	0	0	0	1,394	7,039	11,374	14,360	15,954
	Unit Cost of Therapy \$	75,000 \$	75,750 \$	76,508 \$	77,273 \$	78,045 \$	78,826 \$	79,614 \$	80,410 \$	81,214 \$	82,026 \$	82,847 \$	82,847
	Change in Cost of Therapy	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%
	Probability of Success	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%	30%
Total Revenues (M)	\$	- \$	- \$	- \$	- \$	- \$	- \$	- \$	34 \$	171 \$	280 \$	357 \$	397
Source: DBoralCapital Estimates													
Japan ALS		2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E	2034E
	Prevalance	8,000	8,240	8,487									
					8,742	9,004	9,274	9,552	9,839	10,134	10,438	10,751	11,074
	Growth Rate of incidence	3%	3%	3%	3%	3%	3%	3%	3%	3%	3%	3%	3%
	Market Share	0%	3% 0%					3% 0%	3% 10%	3% 35%	3% 65%	3% 70%	3% 70%
	Market Share Total Patients for therapy	0%	0%	3% 0%	3% 0%	3% 0%	3% 0%	3% 0%	3% 10% 984	3% 35% 3,547	3% 65% 6,785	3% 70% 7,526	3% 70% 7,752
	Market Share Total Patients for therapy cost of therapy	0% - 75,000	0% - 75,000	3% 0% - 75,000	3% 0% - 75,000	3% 0% - 75,000	3% 0% - 75,000	3% 0% - 75,000	3% 10% 984 75,000	3% 35% 3,547 75,000	3% 65% 6,785 75,000	3% 70% 7,526 75,000	3% 70% 7,752 75,750
	Market Share Total Patients for therapy cost of therapy change in cost of therapy	0% - 75,000 0.0%	0% - 75,000 0.0%	3% 0% 75,000 0.0%	3% 0% - 75,000 0.0%	3% 0% - 75,000 0.0%	3% 0% - 75,000 0.0%	3% 0% - 75,000 0.0%	3% 10% 984 75,000 0.0%	3% 35% 3,547 75,000 0.0%	3% 65% 6,785 75,000 0.0%	3% 70% 7,526 75,000 0.0%	3% 70% 7,752 75,750 1.0%
	Market Share Total Patients for therapy cost of therapy change in cost of therapy Probability of Success	0% - 75,000 0.0% 30%	0% - 75,000 0.0% 30%	3% 0% - 75,000 0.0% 30%	3% 0% - 75,000 0.0% 30%	3% 0% - 75,000 0.0% 30%	3% 0% - 75,000 0.0% 30%	3% 0% - 75,000 0.0% 30%	3% 10% 984 75,000 0.0% 30%	3% 35% 3,547 75,000 0.0% 30%	3% 65% 6,785 75,000 0.0% 30%	3% 70% 7,526 75,000 0.0% 30%	3% 70% 7,752 75,750 1.0% 30%
	Market Share Total Patients for therapy cost of therapy change in cost of therapy	0% - 75,000 0.0%	0% - 75,000 0.0%	3% 0% 75,000 0.0%	3% 0% - 75,000 0.0%	3% 0% - 75,000 0.0%	3% 0% - 75,000 0.0%	3% 0% - 75,000 0.0%	3% 10% 984 75,000 0.0%	3% 35% 3,547 75,000 0.0%	3% 65% 6,785 75,000 0.0%	3% 70% 7,526 75,000 0.0%	3% 70% 7,752 75,750 1.0% 30%
	Market Share Total Patients for therapy cost of therapy change in cost of therapy Probability of Success	0% - 75,000 0.0% 30%	0% - 75,000 0.0% 30%	3% 0% - 75,000 0.0% 30%	3% 0% - 75,000 0.0% 30%	3% 0% - 75,000 0.0% 30%	3% 0% - 75,000 0.0% 30%	3% 0% - 75,000 0.0% 30%	3% 10% 984 75,000 0.0% 30%	3% 35% 3,547 75,000 0.0% 30%	3% 65% 6,785 75,000 0.0% 30%	3% 70% 7,526 75,000 0.0% 30%	3% 70% 7,752 75,750 1.0%
Source: DBoralCapital Estimates	Market Share Total Patients for therapy cost of therapy change in cost of therapy Probability of Success	75,000 0.0% 30% - \$	0% - 75,000 0.0% 30% - \$	3% 0% - 75,000 0.0% 30% - \$	3% 0% - 75,000 0.0% 30% - \$	3% 0% - 75,000 0.0% 30% - \$	3% 0% - 75,000 0.0% 30% - \$	3% 0% - 75,000 0.0% 30% - \$	3% 10% 984 75,000 0.0% 30% 44 \$	3% 35% 3,547 75,000 0.0% 30% 160 \$	3% 65% 6,785 75,000 0.0% 30% 305 \$	3% 70% 7,526 75,000 0.0% 30% 339 \$	3% 70% 7,752 75,750 1.0% 30% 352
Source: DBoralCapital Estimates	Market Share Total Patients for therapy cost of therapy change in cost of therapy Probability of Success  Prevalance	75,000 0.0% 30% - \$	0% - 75,000 0.0% 30% - \$	3% 0% - 75,000 0.0% 30% - \$	3% 0% - 75,000 0.0% 30% - \$	3% 0% - 75,000 0.0% 30% - \$	3% 0% - 75,000 0.0% 30% - \$	3% 0% - 75,000 0.0% 30% - \$	3% 10% 984 75,000 0.0% 30% 44 \$	3% 35% 3,547 75,000 0.0% 30% 160 \$	3% 65% 6,785 75,000 0.0% 30% 305 \$	3% 70% 7,526 75,000 0.0% 30% 339 \$	3% 70% 7,752 75,750 1.0% 30% 352
Source: DBoralCapital Estimates	Market Share Total Patients for therapy cost of therapy change in cost of therapy Probability of Success  Prevalance Growth Rate of incidence	0% - 75,000 0.0% 30% - \$ 2023E 120,000 1%	0% - 75,000 0.0% 30% - \$ 2024E 121,200 1%	3% 0% - 75,000 0.0% 30% - \$ 2025E 122,412 1%	3% 0% - 75,000 0.0% 30% - \$ 2026E 123,636 1%	3% 0% - 75,000 0.0% 30% - \$ 2027E 124,872 1%	3% 0% - 75,000 0.0% 30% - \$ 2028E 126,121 1%	3% 0% - 75,000 0.0% 30% - \$ 127,382 1%	3% 10% 984 75,000 0.0% 30% 44 \$	3% 35% 3,547 75,000 0.0% 30% 160 \$	3% 65% 6,785 75,000 0.0% 30% 305 \$	3% 70% 7,526 75,000 0.0% 30% 339 \$	3% 70% 7,752 75,750 1.0% 30% 352 0 133,880
Source: DBoralCapital Estimates	Market Share Total Patients for therapy cost of therapy change in cost of therapy Probability of Success  Prevalance Growth Rate of incidence Target Patient Population	0% - 75,000	0% -75,000 0.0% 30% - \$ - 2024E 121,200 1% 121,200	3% 0% - 75,000 0.0% 30% - \$ 2025E 122,412 1% 122,412	3% 0% - 75,000 0.0% 30% - \$ 2026E 123,636 1% 123,636	3% 0% - 75,000 0.0% 30% - \$ 2027E 124,872 1% 124,872	3% 0% - 75,000 0.0% 30% - \$ 2028E 126,121 1% 126,121	3% 0% - 75,000 0.0% 30% - \$ 127,382 196 127,382	3% 10% 984 75,000 0.0% 30% 44 \$ 128,656 1% 128,656	3% 35% 3,547 75,000 0.0% 30% 160 \$	3% 65% 6,785 75,000 0.0% 30% 305 \$ 131,242 1% 131,242	3% 70% 7,526 75,000 0.0% 30% 339 0 132,555 1% 132,555	3% 70% 7,752 75,750 1.0% 30% 352 0 133,880 1% 133,880
Source: DBoralCapital Estimates	Market Share Total Patients for therapy cost of therapy change in cost of therapy Probability of Success  Prevalance Growth Rate of incidence Target Patient Population o have access, insurance-75%	0% -75,000 0.0% 30% - \$ 2023E 120,000 1% 120,000 90,000	0% - 75,000 0.0% 30% - \$ 2024E 121,200 1% 121,200 90,900	3% 0% - 75,000 0.0% 30% - \$ 2025E 122,412 1% 122,412 91,809	3% 0% -75,000 0.0% 30% -\$ 2026E 123,636 1% 123,636 92,727	3% 0% -75,000 0.0% 30% - \$ - 124,872 1% 124,872 93,654	3% 0% - 75,000 0.0% 30% - \$ 2028E 126,121 1% 126,121 94,591	3% 0% 0% 75,000 0.0% 30% - \$ 127,382 1% 127,382 95,537	3% 10% 984 75,000 0.0% 30% 44 \$ 0 128,656 1% 128,656 96,492	3% 35% 3,547 75,000 0.0% 30% 160 \$	3% 65% 6,785 75,000 0.0% 30% 305 \$ 0 131,242 1% 131,242 98,432	3% 70% 7,526 75,000 0.0% 30% 339 \$ 132,555 1% 132,555 99,416	3% 70% 7,752 75,750 1.0% 30% 352 0 133,880 13,880 100,410
Source: DBoralCapital Estimates	Market Share Total Patients for therapy cost of therapy change in cost of therapy change in cost of therapy Probability of Success  Prevalance Growth Rate of incidence Target Patient Population o have access, insurance- 75% Market Share	0%	0% - 75,000 0.0% 30% - \$ 2024E 121,200 1% 121,200 90,900 0%	3% 0% - 75,000 0.0% 30% - \$ 2025E 122,412 1% 122,412 91,809 0%	3% 0% - 75,000 0.0% 30% - \$ 2026E 123,636 1% 123,636 92,727 0%	3% 0% -75,000 0.0% 30% -\$ -\$ -2027E 124,872 1% 124,872 93,654 0%	3% 0% - 75,000 0.0% 30% - \$ 2028E 126,121 1% 126,121 94,591 0%	3% 0% 0% - 75,000 0.0% 30% - \$ 127,382 1% 127,382 95,537 0%	3% 10% 984 75,000 0.0% 30% 44 \$ 0 128,656 1% 128,656 96,492 0%	3% 35% 3,547 75,000 0.0% 30% 160 \$ 0 129,943 1% 129,943 97,457 2%	3% 65% 6,785 75,000 0.0% 30% 305 \$ 0 131,242 1% 131,242 98,432 4%	3% 70% 7,526 75,000 0.0% 30% 339 \$ 132,555 1% 122,555 99,416 5%	3% 70% 7,752 75,750 1.0% 352 133,886 1% 133,880 100,410
Source: DBoralCapital Estimates	Market Share Total Patients for therapy cost of therapy change in cost of therapy Probability of Success  Prevalance Growth Rate of incidence Target Patient Population o have access, insurance-75% Market Share cost of therapy \$	0% - 75,000 0.0% 30% - \$  2023E 120,000 1% 120,000 90,000 9% 75,000 \$	0% - 75,000 0.0% 30% - \$  2024E 121,200 90,900 90,900 90% 75,750 \$	3% 0% - 75,000 0.0% 30% - \$ 2025E 122,412 91,809 0% 76,508 \$	3% 0% - 75,000 0.0% 30% - \$ 2026E 123,636 12,3636 92,727 0% 77,273 \$	3% 0%  75,000 0.0% 30%  \$ 2027E 124,872 124,872 93,654 0% 78,045 \$	3% 0% 0% 1. 75,000 0.0% 30% - \$ 2028E 126,121 126,121 94,591 0% 78,826 \$	3% 0% 0% - 75,000 0.0% 30% - \$ 127,382 127,382 95,537 0% 79,614 \$	3% 10% 984 75,000 0.0% 30% 44 \$ 128,656 96,492 0% 80,410 \$	3% 35% 3.547 75,000 0.0% 30% 160 \$ 129,943 17,457 2% 81,214 \$	3% 65% 6,785 75,000 0.0% 30% 305 \$	3% 70% 7,526 75,000 0.0% 30% 339 \$ 132,555 99,416 132,555 99,416 82,847 \$	3% 70% 7,752 75,750 1.0% 30% 352 (133,886 1% 133,886 100,410 6% 82,847
Source: DBoralCapital Estimates	Market Share Total Patients for therapy cost of therapy change in cost of therapy change in cost of therapy Probability of Success  Prevalance Growth Rate of incidence Target Patient Population o have access, insurance- 75% Market Share cost of therapy S Change in Cost of Therapy	0% - 75,000 0.0% 30% - \$ 2023E 120,000 1% 120,000 90,000 0% 75,000 \$ 1%	0% - 75,000 0.0% 30% - \$ 2024E 121,200 1% 121,200 90,900 0%	3% 0% - 75,000 0.0% 30% - \$ 2025E 122,412 1% 122,412 91,809 0%	3% 0% - 75,000 0.0% 30% - \$ 2026E 123,636 1% 123,636 92,727 0%	3% 0% -75,000 0.0% 30% -\$ -\$ -2027E 124,872 1% 124,872 93,654 0%	3% 0% - 75,000 0.0% 30% - \$ 2028E 126,121 1% 126,121 94,591 0%	3% 0% 0% - 75,000 0.0% 30% - \$ 127,382 1% 127,382 95,537 0%	3% 10% 984 75,000 0.0% 30% 44 \$ 0 128,656 1% 128,656 96,492 0%	3% 35% 3,547 75,000 0.0% 30% 160 \$ 0 129,943 1% 129,943 97,457 2% 81,214 1%	3% 65% 6,785 75,000 0.0% 30% 305 \$	3% 70% 7,526 75,000 0.0% 30% 339 \$  132,555 1% 132,555 194,116 5% 82,847 1%	3% 70% 7,752 75,750 1.0% 30% 352 133,880 100,410 6% 82,847
Source: DBoralCapital Estimates	Market Share Total Patients for therapy cost of therapy cost of therapy change in cost of therapy Probability of Success  Prevalance Growth Rate of incidence Target Patient Population o have access, insurance- 75% Market Share cost of therapy Change in Cost of Therapy Treated Patients	75,000 0.0% 30% - \$ 2023E 120,000 19% 75,000 1%	0% -75,000 0.0% 30% -\$ -\$ -2024E 121,200 1% 121,200 90,900 0% 75,750 \$ 1%	3% 0% - 75,000 0.0% 30% - \$ - \$ - 2025E 122,412 1% 122,412 91,809 0% 76,508 \$ 1%	3% 0% - 75,000 0.0% 30% - \$ 2026E 123,636 123,636 92,727 0% 77,273 \$ 1%	3% 0% - 75,000 0.0% 30% - \$ 2027E 124,872 124,872 93,654 0% 78,045 1%	3% 0% 0%  75,000 0.0% 30%  \$ 2028E 126,121 1% 126,121 94,591 0% 78,826 \$1%	3% 0% 0% 0.00 0.00% 30% - \$ 127,382 1% 127,382 95,537 0% 79,614 1%	3% 10% 984 75,000 0.0% 30% 44 \$ 128,656 1% 128,656 96,492 0% 80,410 \$ 1%	3% 35% 3,547 75,000 0.0% 30% 160 \$ 0 129,943 1% 129,943 97,457 2% 81,214 \$ 1% 1,949	3% 65% 6,785 75,000 0.0% 30% 305 \$	3% 70% 7,526 75,000 0.0% 30% 339 \$ 0 132,555 1% 132,555 99,416 5% 82,847 1,971	3% 70% 7,752 75,750 1.0% 30% 352 0 133,880 1% 133,880 100,410 6% 82,847 1,6,025
Total Revenues (M) Source: DBore/Capital Estimates ROW ALS Patients who	Market Share Total Patients for therapy cost of therapy change in cost of therapy change in cost of therapy Probability of Success  Prevalance Growth Rate of incidence Target Patient Population o have access, insurance- 75% Market Share cost of therapy S Change in Cost of Therapy	0% - 75,000 0.0% 30% - \$ 2023E 120,000 1% 120,000 90,000 0% 75,000 \$ 1%	0% - 75,000 0.0% 30% - \$  2024E 121,200 90,900 90,900 90% 75,750 \$	3% 0% - 75,000 0.0% 30% - \$ 2025E 122,412 91,809 0% 76,508 \$	3% 0% - 75,000 0.0% 30% - \$ 2026E 123,636 12,3636 92,727 0% 77,273 \$	3% 0%  75,000 0.0% 30%  \$ 2027E 124,872 124,872 93,654 0% 78,045 \$	3% 0% 0% 1. 75,000 0.0% 30% - \$ 2028E 126,121 126,121 94,591 0% 78,826 \$	3% 0% 0% - 75,000 0.0% 30% - \$ 127,382 127,382 95,537 0% 79,614 \$	3% 10% 984 75,000 0.0% 30% 44 \$ 128,656 96,492 0% 80,410 \$	3% 35% 3,547 75,000 0.0% 30% 160 \$ 0 129,943 1% 129,943 97,457 2% 81,214 1%	3% 65% 6,785 75,000 0.0% 30% 305 \$	3% 70% 7,526 75,000 0.0% 30% 339 \$  132,555 1% 132,555 194,116 5% 82,847 1%	3% 70% 7,752 75,750 1.0% 30% 352 0 133,880 100,410 6% 82,847 1%

Source: D.Boral Capital Estimates



**Valuation:** Our valuation is based on our models and the assumptions for our projected revenues to 2034. Our models apply a 30% probability of success (POS) factor based on the fact that MN-166 (ibudilast) is a Phase III drug. Our model assumes the company will raise additional capital. Our share count is based on a fully diluted 2034 estimate. In addition to the POS factor, we use a 30% risk rate in our free cash flow to the firm (FCFF), discounted EPS (dEPS), and sum-of-the-parts (SOP) models. We equal weight, average these metrics, and then round to the nearest whole number to derive our price target.

#### **Exhibit 26. Free Cash Flow Model**

	Average \$	9											
	Price Target \$ Year	11 2024											
DCF Valuation Using FCF (mln):													
units ('000)			2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E	2034E
EBIT			(14,935)	(29,673)	(30,140)	(34,040)	(38,010)	(5,947)	98,452	456,277	813,302	963,593	1,042,356
Tax Rate			0%	0%	0%	0%	0%	10%	10%	20%	30%	35%	35%
EBIT(1-t)			(14,935)	(29,673)	(30,140)	(34,040)	(38,010)	(5,352)	88,607	365,021	569,311	626,335	677,531
CapEx													
Depreciation Change in NWC (excash)			\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0	\$0
FCF			(14,935)	(29,673)	(30,140)	(34,040)	(38,010)	(5,352)	88,607	365,021	569,311	626,335	677,531
ror			(14,935)	(29,073)	(30,140)	(34,040)	(36,010)	(5,352)	00,007	365,021	309,311	626,333	677,531
PV of FCF			(14,935)	(22,825)	(17,834)	(15,494)	(13,308)	(1,441)	18,357	58,172	69,792	59,063	49,147
Discount Rate			30%										
Long Term Growth Rate			1%										
Long Term Grown Rate			176										
Terminal Cash Flow			2,359,679										
Terminal Value YE2034			826,189										
NPV			994,881										
NPV-Debt			-										
Projected Shares out (thousands)			87,804	2034E									
NPV Per Share		\$	11										

#### D.Boral Capital Estimates

#### **Exhibit 27. Discounted EPS Model**

	· · · · · · · · · · · · · · · · ·	
Current Year		2024
Year of EPS		2034
Earnings Multiple		15
Discount Factor		30%
Selected Year EPS		7.72
NPV	\$	8.40
Source: DBoralCapital & Company reports		

			Discount Rate and	f Earnings Multi 2034		is Constant	
	8.40	5%	10%	15%	20%	25%	30%
Earnings							
Multiple	1	\$4.74	\$2.97	\$1.91	\$1.25	\$0.83	\$0.56
	5	\$23.68	\$14.87	\$9.54	\$6.23	\$4.14	\$2.80
	10	\$47.37	\$29.75	\$19.07	\$12.46	\$8.28	\$5.60
	15	\$71.05	\$44.62	\$28.61	\$18.69	\$12.43	\$8.40
	20	\$94.73	\$59.49	\$38.14	\$24.92	\$16.57	\$11.19
	25	\$118.42	\$74.37	\$47.68	\$31.15	\$20.71	\$13.99
	30	\$142.10	\$89.24	\$57.21	\$37.38	\$24.85	\$16.79
	35	\$165.78	\$104.11	\$66.75	\$43.61	\$29.00	\$19.59

#### Exhibit 28. Sum-of-the-Parts Model

MedicNova, Inc.	LT Gr	Discount Rate	Yrs. to Peak	% Success	Peak Sales MM's	Term Val
US ALS	1%	30%	5	30%	\$1,019	\$3,515
NPV						\$2.43
EU ALS	1%	30%	6	30%	\$1,322	\$4,558
NPV						\$2.42
Japan ALS	1%	30%	7	30%	\$1,174	\$4,050
NPV					<b>*</b>	\$1.65
ROW ALS	1%	30%	5	30%	\$499	\$1,721
NPV						\$1.19
Net Margin						75%
MM Shrs OS (2034E)	•	•	•	•		88
Total						\$7.7

D.Boral Capital Estimates



#### **Intellectual Property**

**MediciNova's intellectual property is centered on its two** lead compounds, MN-166 (ibudilast) and MN-001 (tipelukast), both of which have broad therapeutic applications and are protected by a robust portfolio of patents.

#### 1. MN-166 (Ibudilast):

- Patents cover multiple methods of administration, including oral, intravenous, subcutaneous, intramuscular, and inhalation routes. They also span a wide range of doses, dosing frequencies, and treatment durations. The exclusivity for these claims extends to at least 2042 in some territories.
- MN-166 is a small molecule inhibitor targeting phosphodiesterase-4 (PDE4), macrophage migration inhibitory factor (MIF), and pro-inflammatory cytokines. It is in clinical trials for neurodegenerative diseases such as ALS, multiple sclerosis, and degenerative cervical myelopathy, and is also being explored for conditions like glioblastoma, Long COVID, and substance use disorders

#### 2. MN-001 (Tipelukast):

- Patents protect its use for treating advanced nonalcoholic steatohepatitis (NASH) and idiopathic pulmonary fibrosis (IPF). This includes reducing hepatic fibrosis and scarring, with claims covering both MN-001 and its major metabolite MN-002. Patent protection extends until at least 2035 in key markets, including the U.S., Europe, Japan, Korea, and Canada
- MN-001 has multiple mechanisms of action, such as leukotriene receptor antagonism, inhibition of phosphodiesterases (PDE3 and PDE4), and 5-lipoxygenase inhibition. These actions reduce inflammation and fibrosis. It is also being investigated for hypertriglyceridemia and other chronic inflammatory and fibrotic conditions

MediciNova's intellectual property strategy ensures long-term exclusivity for its compounds across various diseases, enhancing the value of its late-stage pipeline. This positions the company to maximize opportunities through partnerships or independent development.

**The risks to our thesis include** 1. Clinical/Regulatory Risk, 2. partnership and Financial Risk, 3. Commercial Risk, 4. legal and Intellectual Property Risk, and 5. Market Share Risk.

**Clinical / Regulatory Risk**. MediciNova depends on the outcome of regulatory approvals. Regulatory risk often goes beyond the data and trials and includes the elements associated with the approval process, such as properly submitting the required forms and data.

**Partnership Risk**. MediciNova is a small company that may pursue a partnership deal for U.S. and Rest of the World marketing. It cannot be assured that it will find an appropriate partner and realize attractive partnership terms.

**Financial Risk.** MediciNova is a small capital company that can translate into high volatility and risk for investors. The company has no revenues as such, dependent on the clinical progress of its therapeutics. MediciNova will likely require additional capital raises before it can be self-sustaining, and there is no guarantee that it will raise the needed capital.

**Commercial Risk.** MediciNova hopes to introduce a new treatment paradigm in the CNS-Inflammation, Oncology spaces. However, the company cannot be assured that it can effectively market its products.

**Legal and Intellectual Property**. MediciNova may face multiple legal challenges, specifically IP challenges, which could force the company to defend its patents or claim it infringes on others.



MedicNova, Inc.																
Product Revenues	2023A	1Q24A	2Q24A	3Q24A	4Q24E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E	2034E
US ALS									-	-	40,542	83,532	172,110	265,962	296,827	305,791
EU ALS									-	-	-	33,622	171,490	279,899	356,906	396,522
Japan ALS									-	-	-	44,275	159,613	305,317	338,667	352,315
ROW ALS									-	-	-	-	47,489	96,888	123,544	149,736
Total Product Revenues								-			40,542	161,430	550,702	948,065	1,115,944	1,204,364
Grant Revenue						-										
Milestone and Royalty Revenue																
Total Revenues (\$000)	1,000										40,542	161,430	550,702	948,065	1,115,944	1,204,364
Expenses																
COGS						-	-	-	-	-	8,108	24,215	55,070	94,807	111,594	120,436
% COGS											20%	15%	10%	10%	10%	10%
Research and Development	5,658	1,782	1,646	1,859	1,800	7,087	24,000	20,000	20,000	20,000	20,200	20,402	20,810	21,226	21,651	22,084
Selling, General and Administrative	5,242	1,354	1,400	1,450	1,500	5,704	10,000	10,100	14,000	18,000	18,180	18,362	18,545	18,731	19,105	19,488
Operating expenses	10,900	3,136	3,046	3,309	3,300	12,792	29,638	30,100	34,000	38,000	46,488	62,978	94,426	134,764	152,351	162,008
Oper. Inc. (Loss)	9,900	(3,136)	(3,046)	(3,309)	(3,300)	(12,792)	(29,638)	(30,100)	(34,000)	(38,000)	(5,947)	98,452	456,277	813,302	963,593	1,042,356
Other Income (net)	1,835	398	435	448	500	1,781	500	(40)	(40)	(10)						
Interest Income	(503)	(16)	(17)	9		(24)	-	(/	()	(14)						
Interest Expense	(,	o o	(0)			(0)	-									
Financial Expenses, Net	1,332	382	418	457	500	1,757	(35)	(40)	(40)	(10)	-	-	-	-	-	-
Pretax Income	(8,568)	(2,754)	(2,628)	(2,852)	(2,800)	(11,035)	(29,673)	(30,140)	(34,040)	(38,010)	(5,947)	98,452	456,277	813,302	963,593	1,042,356
Pretax Margin																
Income Tax Benefit (Provision)	(3)						1		·	·	(595)	14,768	91,255	243,990	337,258	364,825
Tax Rate	45.550	0%	0%	0%	0%	0%	0%	0%	0%	0%	10%	15%	20%	30%	35%	35%
GAAP Net Income (loss) Net Margin	(8,571) NM	(2,754) NM	(2,628)	(2,852)	(2,800)	(11,035)	(29,673)	(30,140) NM	(34,040) NM	(38,010) NM	(5,352) NM	83,684 0.52	365,021 0.66	569,311 0.60	626,335 0.56	677,531 0.56
Net loss attributable to non controlling interests	NM	NM				_		NM	NM	NM	NM	0.52	0.66	0.60	0.56	0.56
GAAP-EPS	(0.17)	(0.06)	(0.05)	(0.06)	(0.05)	(0.22)	(0.50)	(0.38)	(0.40)	(0.44)	(0.06)	0.97	4.21	6.54	7.16	7.72
Non GAAP EPS (dil)	(0.17)	(0.06)	(0.05)	(0.06)	(0.05)	(0.21)	(0.50)	(0.38)	(0.40)	(0.44)	(0.06)	0.97	4.21	6.54	7.16	7.72
Wgtd Avg Shrs (Bas)	49.046	49.046	49.046	49,046	59,095	51.559	59,243	71.987	84.806	85,146	85.487	85.830	86,174	86,519	86.865	87,213
Wgtd Avg Shrs (Dil)	49.046	49.046	49.046	49.046	59.537	51,669	59,644	85.008	85.381	85.723	86.066	86,411	86.757	87.105	87.454	87,804

Source: DBoralCapital & Company reports



MedicNova, Inc.																
Assets	2023A	1Q24A	2Q24A	3Q24A	4Q24E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E	2034E
Cash and Cash Equivilents	\$50,999	\$47,139	\$44,338	\$42,281	\$55,380	\$55,380	\$25,707	(\$4,433)	(\$38,473)	(\$76,483)	(\$81,835)	\$1,849	\$366,870	\$936,181	\$1,562,517	\$2,240,048
PrePaid Expenses	\$175	\$725	\$1,168	\$985	\$985	\$985	\$985	\$985	\$985	\$985	\$985	\$985	\$985	\$985	\$985	\$985
Total Current Assets	\$51,174	\$47,864	\$45,506	\$43,265	\$56,365	\$56,365	\$26,692	(\$3,448)	(\$37,488)	(\$75,498)	(\$80,850)	\$2,834	\$367,855	\$937,166	\$1,563,502	\$2,241,033
Goodwill	\$9,600	\$9,600	\$9,600	\$9,600	\$9,600	\$9,600	\$9,600	\$9,600	\$9,600	\$9,600	\$9,600	\$9,600	\$9,600	\$9,600	\$9,600	\$9,600
In-process research and development	\$4,800	\$4,800	\$4,800	\$4,800	\$4,800	\$4,800	\$4,800	\$4,800	\$4,800	\$4,800	\$4,800	\$4,800	\$4,800	\$4,800	\$4,800	\$4,800
Property and equipment, net	\$46	\$40	\$36	\$31	\$31	\$31	\$31	\$31	\$31	\$31	\$31	\$31	\$31	\$31	\$31	\$31
Right-of-use asset	\$575	\$519	\$443	\$404	\$404	\$404	\$404	\$404	\$404	\$404	\$404	\$404	\$404	\$404	\$404	\$404
Other non-current assets	\$74	\$70	\$19	\$19	\$19	\$19	\$19	\$19	\$19	\$19	\$19	\$19	\$19	\$19	\$19	\$19
Total Assets	\$66,270	\$62,894	\$60,404	\$58,119	\$71,219	\$71,219	\$41,546	\$11,406	(\$22,634)	(\$60,644)	(\$65,996)	\$17,688	\$382,709	\$952,020	\$1,578,356	\$2,255,887
Current Liabilities					\$1,800											
Accounts Payable	\$1,004	\$805	\$668	\$708	\$708	\$708	\$708	\$708	\$708	\$708	\$708	\$708	\$708	\$708	\$708	\$708
Accrued Expenses and other current liabilities	\$2,059	\$1,488	\$1,637	\$1,687	\$1,500	\$1,500	\$1,500	\$1,500	\$1,500	\$1,500	\$1,500	\$1,500	\$1,500	\$1,500	\$1,500	\$1,500
Operating Lease	\$216	\$218	\$190	\$202	\$202	\$202	\$202	\$202	\$202	\$202	\$202	\$202	\$202	\$202	\$202	\$202
Total Current Liabilities	\$3,279	\$2,510	\$2,494	\$2,597	\$2,410	\$2,410	\$2,410	\$2,410	\$2,410	\$2,410	\$2,410	\$2,410	\$2,410	\$2,410	\$2,410	\$2,410
Deferred tax liability	\$202	\$202	\$202	\$202	\$202	\$202	\$202	\$202	\$202	\$202	\$202	\$202	\$202	\$202	\$202	\$202
Other non-current liabilities	\$411	\$351	\$302	\$255	\$255	\$255	\$255	\$255	\$255	\$255	\$255	\$255	\$255	\$255	\$255	\$255
Total liabilities	\$3,892	\$3,063	\$2,999	\$3,054	\$2,867	\$2,867	\$2,867	\$2,867	\$2,867	\$2,867	\$2,867	\$2,867	\$2,867	\$2,867	\$2,867	\$2,867
Stockholders' equity:																
Common Stock	\$49	\$49	\$49	\$49	\$49	\$49	\$49	\$49	\$49	\$49	\$49	\$49	\$49	\$49	\$49	\$49
Addional Paid-In Capital	\$478,149	\$478,365	\$478,572	\$479,077	\$479,077	\$479,077	\$479,077	\$479,077	\$479,077	\$479,077	\$479,077	\$479,077	\$479,077	\$479,077	\$479,077	\$479,077
Accumulated Deficit	(\$415,702)	(\$418,456)	(\$421,084)	(\$423,937)	(\$426,730)	(\$426,730)	(\$456,403)	(\$486,543)	(\$520,583)	(\$558,593)	(\$563,944)	(\$480,261)	(\$115,239)	\$454,072	\$1,080,407	\$1,757,939
Accumulated Other	(\$118)	(\$127)	(\$132)	(\$124)	(\$124)	(\$124)	(\$124)	(\$124)	(\$124)	(\$124)	(\$124)	(\$124)	(\$124)	(\$124)	(\$124)	(\$124)
Total Equity	\$62,378	\$59,830	\$57,405	\$55,066	\$52,273	\$52,273	\$22,600	(\$7,540)	(\$41,580)	(\$79,590)	(\$84,942)	(\$1,258)	\$363,763	\$933,074	\$1,559,409	\$2,236,941
Total Liab & Equity	\$66,270	\$62,894	\$60,404	\$58,119	\$55,140	\$55,140	\$25,467	(\$4,673)	(\$38,713)	(\$76,723)	(\$82,075)	\$1,609	\$366,630	\$935,941	\$1,562,277	\$2,239,808
Shares Iss'd (000)	49,046	8,145	49,046	49,046	59,095	\$51,559	\$59,243	\$71,987	\$84,806	\$85,146	\$85,487	\$85,830	\$86,174	\$86,519	\$86,865	\$87,213
Shares Out (000)	49,046	8,145	49,046	49,046	59,537	\$51,669	\$59,644	\$85,008	\$85,381	\$85,723	\$86,066	\$86,411	\$86,757	\$87,105	\$87,454	\$87,804

Source: DBoralCapital & Company reports



MedicNova, Inc. Cash Flow Statement (\$000)	2023A	1Q24A	2Q24A	3Q24E	4Q24E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E	2034
Cash Flows From Operating Activities:																
Net Loss	(23,964)	(3,668)	(5,922)	(8,774)	(11,574)	(11,574)	(29,673)	(30,140)	(34,040)	(38,010)	(5,352)	83,684	365,021	569,311	626,335	677,531
Acquired in Process R&D	1,077	240	397	14,750	14,750	14,750										
Stock-based compensation expense	1,077	240	397	610	610	610										
Depreciation and amortization expense	12	3	5	8	8	8										
Reduction in the carrying amount of operating lease right-of-use asset	52			17	17	17										
Other Assets																
Changes in assets and liabilities:																
Prepaid expenses and other current assets	759	648	436	328	328	328										
Other assets	33			0	0	0										
Accounts payable	1,447	(338)	(1,816)	(1,354)	(1,354)	(1,354)										
Accrued expenses and other current liabilities	(407)	(1,246)	(816)	(609)	(609)	(609)										
Operating lease liability	(55)			(16)	(16)	(16)										
Net Cash Used in Operating Activities	(19,971)	(4,121)	(7,319)	4,958	1,800	1,800	(29,673)	(30,140)	(34,040)	(38,010)	(5,352)	83,684	365,021	569,311	626,335	677,531
Cash Flows From Investing Activities:																
Acquired in-process research and development				(14,750)	1,500	1,500										
Purchase of property and equipment				(7)												
Net cash provided by investing activities	0		0	(14,757)	1,500	1,500	0	0	0	0	0	0	0	0	0	0
Cash flows from financing activities:																
Proceeds from Sale of Common Stock			94,803	94,759	94,759	94,759	0	0	0	0	0	0	0	0	0	0
Net cash provided by financing activities	0	0	94,803	94,759	94,759	94,759	0	0	0	0	0	0	0	0	0	C
Increase (decrease) in Cash and Cash Equivilents	(19,971)	(4,121)	87.484	84.959	98.059	98,059	(29,673)	(30,140)	(34,040)	(38,010)	(5,352)	83,684	365,021	569,311	626,335	677.531
Cash and Cash Equivilents - Beginning Of Period	35,497	15,527	14,450	14,450	14,450	14,450	112,509	82,836	52,696	18,656	(19,354)	(24,706)	58,978	423,999	993,310	1,619,645
Exchange Differences on Cash and Cash Equivilents		,-	,	0	0	0	,	. ,	. ,	-,	, .,,	. , ,	.,.	.,	.,.	
Cash and Cash Equivilents - End of Period	15.527	11.406	101,934	99,409	112,509	112.509	82.836	52.696	18.656	(19.354)	(24,706)	58.978	423,999	993.310	1.619.645	2.297.177
Source: DBoralCapital & Company reports		,,,,,	. ,	,	_,	1-,000	,	4-,444		(10,000.)	,,	,	2,000	,	,, 0,0.0	. , . , ,



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SELL (S) - Total return expected to underperform S&P 500 by at least 10%

# Distribution of Ratings/IB Services D. Boral

		_	ID SEI V./ Fa	131 12 1103.
Rating	Count	Percent	Count	Percent



### MediciNova, Inc. Rating History as of 11/29/2024

