2026年1月6日

Lucid Capital Markets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1月5日、米国ニューヨークに本拠を置く投資銀行Lucid Capital Marketsのアナリストであるる Elemer Piros 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。

【Lucid Capital Markets 公式 web サイト】
https://www.lucidcapitalmarkets.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。

MediciNova, Inc.（メディシノバ・インク）
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Rating	Buy
Price (01/02/2026)	$1.33
Price Target	$11.00

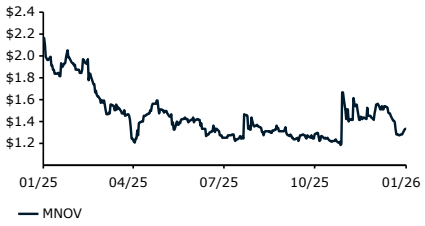
Market Data

% to Target	727.1%
52-Week High	$2.20
52-Week Low	$1.13
Market Cap (mil)	$65.2
Cash & Equivalents	$33.0
Total Debt	$0.0
Enterprise Value	$32.2
Cash per Share	$0.67
Shares Outstanding (mil)	49.0
3-Month ADTV	955,354
Short Interest (% of Float)	0.7%
Short interest (mil)	0.3
Float	43.4
Fiscal Year-End	Dec

Estimates

EPS Diluted	**2024A**	**2025E**	**2026E**
Q1	-	(0.06)A	(0.07)
Q2	-	(0.07)A	(0.07)
Q3	-	(0.06)A	(0.06)
Q4	-	(0.07)	(0.06)
FY	(0.23)	(0.26)	(0.26)
Revenue ($M)	**2024A**	**2025E**	**2026E**
Q1	-	0.0A	0.0
Q2	-	0.1A	0.0
Q3	-	0.1A	0.0
Q4	-	0.0	0.0
FY	0.0	0.3	0.0

Performance Chart



Medicinova Inc (MNOV)

Pivotal ALS Trial Meets Validated Commercial Opportunity; Initiating with a Buy Rating and an $11 Price Target

KEY POINTS

Initiating coverage of MediciNova (MNOV) with a Buy rating and an $11/share 12-month price target. MediciNova is in a pivotal trial with an anti-inflammatory and neuroprotective agent for ALS.

Our Buy thesis on the shares of MediciNova is based on the following:

Progressive Neurological Disease: Amyotrophic lateral sclerosis (ALS), or Lou Gehrig's disease, is a progressive, fatal neurological disorder affecting about 16,000 Americans, with roughly 5,000 new US cases each year. It causes worsening loss of motor control, speech, swallowing, and breathing, along with fatigue and muscle twitching or cramping. ALS typically begins in mid-life, leads to significant medical and care costs, and is usually fatal within five years. Its exact causes remain unclear.

Addressing Inflammation and Neuronal Damage: MediciNova's lead drug ibudilast MN-166 reduces harmful neuroinflammation and supports neuronal resilience through multiple interconnected mechanisms. It inhibits several phosphodiesterases increasing intracellular cAMP and cGMP levels that shift immune cells away from pro-inflammatory states while promoting neurotrophic and survival signaling. Concurrently, it suppresses key inflammatory mediators such as TNF-α, MIF, and TLR-4, limiting microglial and astrocyte activation and reducing chronic neuroinflammation. Beyond inflammation control, ibudilast also influences mitochondrial function, oxidative stress, apoptosis, and protein-clearance pathways, supporting overall cellular homeostasis and neuroprotection.

Precedent Transaction: In December 2025, Shionogi (4507.T; Not Rated) announced plans to acquire global rights to RADICAVA, one of the approved drugs in ALS, from Tanabe Pharma (Private) for an upfront $2.5B, adding approximately $700M in expected F2026 sales and establishing a dedicated rare-disease commercial platform under a wholly owned subsidiary. The deal, which includes potential future royalties, highlights continued strategic and commercial commitment to ALS therapies and serves as positive industry validation that ALS remains a viable market despite clinical and regulatory challenges.

Blockbuster Potential: If approved by regulators (2028 in the US), we estimate that MN-166 could generate sales of ~$1B by 2035 in the US and key European markets.

Valuation & Risks: We arrive at our 12-month price target of $11/share by assessing the after-tax, risk-adjusted NPV of potential future cash flows from the company's MN-166 program. The probability-adjusted, fully taxed (21%) NPV (15% discount rate) of potential cash flows through 2042 is ~$600M or $11/share, corresponding to our 12-month price target. Factors that could impede shares from reaching our price target include failure of MN-166 to demonstrate significant efficacy benefit or found to be unsafe, leading to the discontinuation of the clinical programs and commercial launch. In addition, the company may not be able to raise additional funds to complete development.

BACKGROUND

Amyotrophic Lateral Sclerosis

Amyotrophic lateral sclerosis (ALS), also called Lou Gehrig's disease, is a progressive, fatal neurological disease affecting as many as 16,000 Americans with 5,000 new cases occurring in the United States each year[1]. Related medical care, equipment, and home health care costs can be significant, especially in the later stages of the disease. Symptoms may include loss of equilibrium and/or motor control in hands and arms, difficulty speaking, swallowing and/or breathing, persistent fatigue, and twitching and cramping, which can sometimes be severe. ALS strikes in mid-life and is usually fatal within five years of diagnosis. The causes for ALS are not clearly understood; more work is needed to conclusively determine what factors contribute to its development.[2]

There are two primary types of ALS: sporadic and familial. Sporadic ALS, where there are no other cases known in the patient's family, is the most common form of ALS in the United States, representing 90 to 95% of all cases. Conversely, familial ALS suggests a hereditary basis for the disorder. Only about 5 to 10% of all ALS patients appear to have the genetic or inherited form of ALS. In those families, there is a 50% chance each offspring will inherit gene mutation and may therefore develop the disease[3].

The disorder belongs to a class of maladies known as motor neuron diseases. ALS occurs when specific nerve cells in the brain and spinal cord that control voluntary movement gradually degenerate. The loss of these motor neurons causes the muscles under their control to weaken and atrophy, inevitably leading to paralysis. ALS manifests itself in different ways, depending on which muscles weaken first[4].

Even through the exact pathogenic pathway of ALS is not clear, multiple mechanisms that may be responsible for ALS have been proposed: neuroinflammation, mitochondria dysfunction, glutamate excitotoxicity, oxidative stress, Impaired protein homeostasis, Impaired axonal transport, dysregulated nucleocytoplasmic transport, and cytoskeletal abnormalities, as illustrated in Figure 2[5]. Simply put, ALS reflects disturbances in the microtubule-associated tau protein metabolism. The motor neuron ultimately is significantly disrupted. The microenvironment of the neuron becomes a complex milieu in which high levels of glutamate provide a source of chronic neurotoxicity, and the contribution of activated microglial cells leads to further damage and eventually to motor neuron death.

Neuroinflammation is the best represented therapeutic target covered by a variety of approaches, including modulation of regulatory immune T cells (Tregs). It was discovered in pathological studies that there are immune abnormalities in the CNS, as well as in the blood and cerebrospinal fluid of individuals affected by ALS[6]. Those abnormalities include T cell abnormalities, increased levels of circulating chemokines and cytokines and elevated systemic inflammation. Additionally, the SOD1 animal model of ALS also exhibits signs of inflammation and immune abnormalities suggesting that the immune system may play a role in the development of the disease. The immune and inflammatory changes observed in ALS might be one of the primary contributors to the disease, that further damages the neurons and exacerbates injury. On the other hand, neuroinflammation and T cell infiltration could be a secondary response to the tissue damage that occurs in ALS, similar to other types of nervous system injuries. Once present, inflammation and immune changes could either enhance damage or have a protective effect. The protective aspects of inflammation include the removal of debris by microglia, which is essential for repair, and interaction with T cells. Brain-specific T cells at the site of injury can also contribute to repairing damaged or inflamed tissues, which are known as "protective immunity." This process is probably due to the cytokines and growth factors delivered by T cells to the injury site. Protective immunity appears to be a general and homeostatic phenomenon.

[1] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6735526/
[2] http://www.nih.gov
[3] http://www.als.org
[4] Xiong ZQ *et al*., Neuron 2002 (35): 1011
[5] Mead, R.J., Shan, N., Reiser, H.J. et al. Amyotrophic lateral sclerosis: a neurodegenerative disorder poised for successful therapeutic translation. Nat *Rev Drug Discov* 22, 185–212 (2023). https://doi.org/10.1038/s41573-022-00612-2
[6] McCombe PA, Henderson RD. The Role of immune and inflammatory mechanisms in ALS. *Curr Mol Med.* 2011 Apr;11(3):246-54. doi: 10.2174/156652411795243450. PMID: 21375489; PMCID: PMC3182412

Standard of Care in ALS

Currently, there is no cure for ALS, nor is there a proven therapy that prevents or reverses the course of the disease. The natural history of disease progression demonstrated in the PRO-ACT database, the largest ALS data repository, showed that the average rate of patient decline is 1 point/month on the ALSFRS-R functional rating score (Figure 3, left panel). There are only three FDA-approved drugs for ALS: Rilutek, RADICAVA and RELYVIRO.

Rilutek (riluzole, oral pill) can prolong survival modestly of ALS patients but will not help patients regain muscle strength[7]. Using the Wilcoxon test, the treatment groups gained 90 and 60 days of median survival in two pivotal Phase 3 trials, with 95% confidence intervals. There was no statistically significant difference in mortality at the end of the study[8].

RADICAVA (edaravone). In a registration trial, RADICAVA (edaravone), chronically administered via an intravenous infusion, was shown to improve the ALSFRS-R scale[9] by 2.5 points (scale from 0-48) at 24 weeks[10]. Treated patients declined by 5 points, while placebo patients experienced a 7.5-point decrease (Figure 3, right panel). Ninety percent of patients enrolled in the trial were also taking oral Rilutek. Neither of these drugs alters the course of the disease significantly. The mechanism by which Rilutek and RADICAVA function has not been elucidated.

RELYVRIO. The latest drug to be approved is RELYVRIO (sodium phenylbutyrate and taurursidol combined) provided a 3.3-point benefit on the ALSFRS-R, when compared to placebo at 24 weeks (Figure 3, middle panel).[11] In a post-hoc long-term survival analysis of the RELYVRIO trial indicated that while there is no difference in terms survival between the drug and placebo up to 12 months, there is a separation between the curves between 18 and 32 months, providing a median survival benefit of ~4 months. This information is not included in the prescription information for RELYVRIO.

Amylyx (AMLX; Not Rated) announced in April 2024 that it had initiated the voluntary withdrawal process for RELYVRIO from the market due to its failure to demonstrate efficacy in a significant clinical trial. Relyvrio would not be accessible for new patients. However, for patients currently undergoing treatment in the U.S. and Canada who, in consultation with their healthcare provider, choose to continue therapy can transition to a complimentary drug program. The decision was followed by the findings from a large-scale Phase 3 clinical trial that was disclosed in early March, revealed that RELYVRIO provided a benefit similar to placebo measured by the ALS functional scale (evaluating breathing, swallowing, and speech abilities over a 48-week period). Additionally, it did not notably enhance patient-reported quality of life, overall survival, or respiratory function.

QALSODY. In April 2023, the FDA approved QALSODY (tofersen) as a treatment for individuals suffering from ALS linked to a mutation in the superoxide dismutase 1 (SOD1) gene, known as SOD1-ALS. Mutations in the SOD1 gene are the second-most common cause of familial ALS, found in about 10-20% of familial cases and 1-2% of sporadic cases of ALS. Qalsody, an antisense oligonucleotide, targets SOD1 mRNA to diminish the production of the SOD1 protein. The approval decision was based on measurements of plasma neurofilament light (NFL), which serves as a blood-based indicator for nerve damage and the progression of neurodegeneration. The trial failed to achieve a significant improvement over placebo, when measured by the ALSFRS-R (NCT02623699). However, based on trends observed on multiple secondary endpoints, including NFL, Biogen (BIIB; Not Rated) submitted an NDA to the FDA. Following an advisory panel review, the drug was approved on an accelerated basis in April 2023. We consider tofersen not a directly competing drug against COYA-302 due to its narrow applicability for the overall ALS population.

[7] http://www.mdausa.org
[8] http://aventispharma-us.com/Pls/riluteck_TXT.html
[9] The ALSFRS-R scale consists of 12 questions that evaluate the fine motor, gross motor, bulbar, and respiratory function of patients with ALS (speech, salivation, swallowing, handwriting, cutting food, dressing/hygiene, turning in bed, walking, climbing stairs, dyspnea, orthopnea, and respiratory insufficiency). Each item is scored from 0-4, with higher scores representing greater functional ability
[10] https://www.radicavahcp.com/assets/dist/pdfs/radicava-prescribing-information.pdf
[11] https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/216660s000lbledt.pdf

Figure 1: Glossary of Terms - ALS

ALSFRS: Amyotrophic Lateral Sclerosis Functional Rating Scale. It is a measure of disability in ALS patients

ALSFRS-R: Amyotrophic Lateral Sclerosis Functional Rating Scale – Revised. It includes more functional assessments than ALSFRS

Amyotrophic Lateral Sclerosis (ALS): A chronic, progressive disease marked by gradual degeneration of the nerve cells in the central nervous system that control voluntary muscle movement. The disorder causes muscle weakness and atrophy

Antigen-Presenting Cells (APCs): A group of immune cells that are capable of processing and presenting antigens for recognition by T cells to initiate the adaptive cellular immune responses

Blood–Brain Barrier (BBB): A highly selective semipermeable border of endothelial cells that prevents solutes in the circulating blood from non-selectively crossing into the extracellular fluid of the central nervous system where neurons reside

Cell Adhesion Molecules (CAMs): A subset of cell surface proteins that are involved in the binding of cells with other cells or with the extracellular matrix

Cerebrospinal Fluid (CSF): Clear, colorless body fluid found within the tissue that surrounds the brain and spinal cord

CTLA-4: Also known as CD152, is a protein receptor that functions as an immune checkpoint and downregulates immune responses

Effector T Cells (Teffs): Functional cells for executing immune functions

Excitotoxicity: Overstimulation of neurons that can lead to neuronal death overtime

Forced Vital Capacity (FVC): Lung function tests that measure total amount of air exhaled

FOXP3: A fork head / winged-helix transcription factor localized on the X chromosome (Xp11.23)

Frontotemporal Dementia (FTD): Result of damage to neurons in the frontal and temporal lobes of the brain. Many possible symptoms can result, including unusual behaviors, emotional problems, trouble communicating, difficulty with work, or difficulty with walking

Interleukin-2 (IL-2): An interleukin, a type of cytokine signaling molecule in the immune system

Oxidized Low-Density Lipoprotein (oxLDL): A product of lipid oxidation, is considered as a marker of oxidative stress

Motor Neuron: Nerve cells that conveys impulses initiating muscle contraction or glandular secretion

Natural Killer Cells (NK Cells): A type of immune cell that has granules (small particles) with enzymes that can kill tumor cells or cells infected with a virus

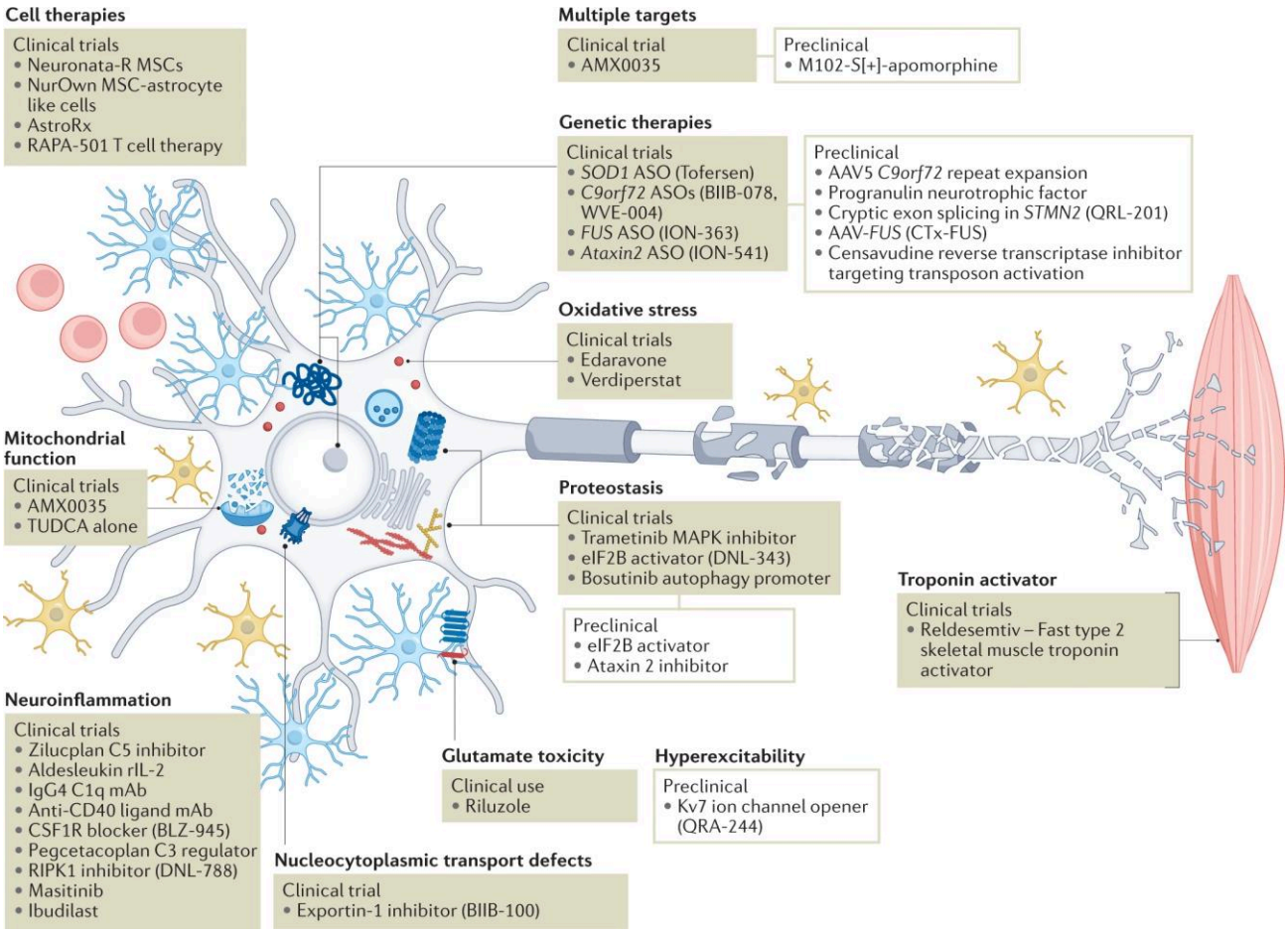
Oxidized Low-Density Lipoprotein (oxLDL): Measures protein damage due to oxidative. modification of the apolipoprotein B (ApoB) subunit on low- density lipoprotein cholesterol (LDL-C)

Primary Progressive Aphasia (PPA): A type of dementia, caused by damage to parts of the brain that control our language, personality, emotions, and behavior

Regulatory Immune T cells (Tregs): A specialized subpopulation of T cells that act to suppress immune response, thereby maintaining homeostasis and self-tolerance

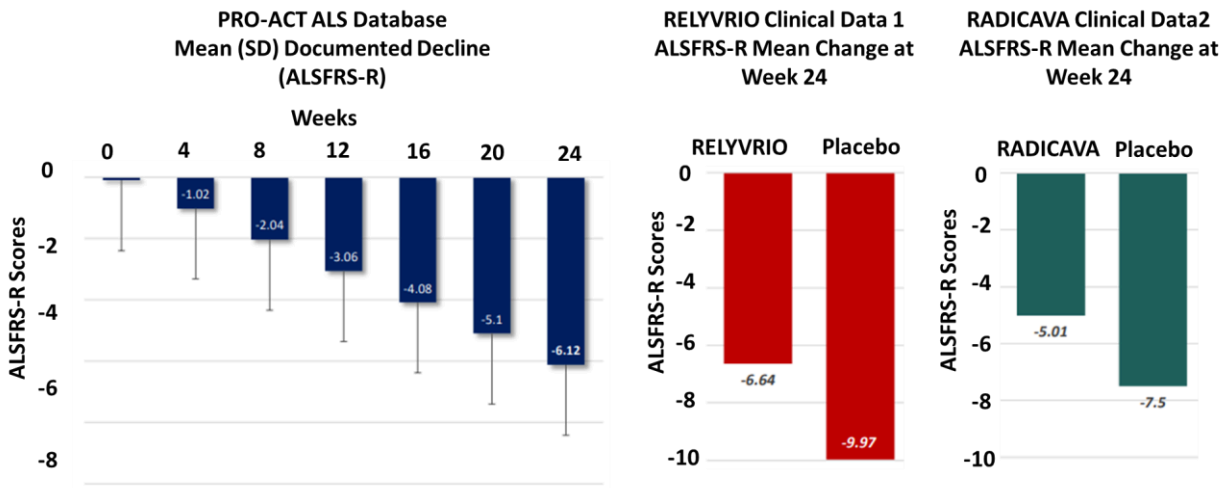
Selective Serotonin Reuptake Inhibitors (SSRIs): The most commonly prescribed antidepressants. They can ease symptoms of moderate to severe depression, are relatively safe and typically cause fewer side effects, by increasing levels of serotonin in the brain through blocking the reabsorption of serotonin into neurons

Figure 2: Biochemical Mechanisms Potentially Involved in ALS



Source: Mead, R.J., Shan, N., & Reiser, H.J. et al. Nat Rev Drug Discov. 2023. 22, 185–212.

Figure 3: Efficacy of Current Standard of Care for ALS



Source: Coya Therapeutics Corporate Presentation, April 2024.

Neurodegeneration: Glial Activation, Cytokine Signaling, and Immune Dysregulation

Neurodegeneration is now understood as a process driven not only by neuronal vulnerability, but by persistent activation of inflammatory signaling pathways within the central nervous system, particularly those mediated by glial cells[12]. Several molecular mechanisms repeatedly implicated across neurodegenerative diseases converge on immune amplification, failure of resolution, and toxic glial–neuron interactions.

Glial Activation

In ALS, chronic neuroinflammation is tightly interwoven with the core processes that damage motor neurons and drive disease progression[13]. In ALS, misfolded proteins such as TDP-43 and mutant SOD1 accumulate in motor neurons due to genetic and environmental factors. These protein aggregates directly stress neurons, mutant SOD1 increases oxidative stress, and TDP-43 aggregates can infiltrate mitochondria and trigger release of mitochondrial DNA, which activates innate immune sensors like the cGAS-STING pathway. This intracellular stress not only harms neurons but also leads to the release of danger signals (DAMPs) and pro-inflammatory cytokines into the surrounding tissue.

Once released, these inflammatory mediators activate microglia and other glial and immune cells in the central nervous system. Rather than resolving damage, these cells enter a sustained pro-inflammatory state that further injures motor neurons. Persistent immune activation creates a vicious cycle: neuronal injury fuels inflammation, and inflammation accelerates neuronal degeneration. Genetic susceptibility and environmental influences can also directly enhance immune cell activation, reinforcing this self-perpetuating pathological loop. The mechanisms highlighted in Figure 4 visually map how protein pathology, mitochondrial dysfunction, and innate immune signaling converge to maintain chronic inflammation as a core driver of ALS pathology.

Cytokine Signaling

A central pathway involves pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-6. These cytokines are released primarily by activated microglia and astrocytes in response to injury, protein aggregation, or metabolic stress. While short-term cytokine signaling supports repair, chronic elevation leads to synaptic dysfunction, mitochondrial impairment, oxidative stress, and ultimately neuronal death[14]. Sustained cytokine exposure also alters neurotransmission and disrupts neuronal homeostasis, accelerating disease progression.

Another key driver is macrophage migration inhibitory factor (MIF), an upstream immune regulator that sustains inflammatory signaling[15]. MIF acts as a molecular “brake” on immune resolution, keeping glial cells locked in an activated state. Elevated MIF activity has been linked to prolonged microglial activation, increased cytokine production, and impaired cellular stress responses. By perpetuating inflammation, MIF contributes to the transition from protective immune surveillance to chronic neurotoxicity.

Immune Dysregulation

Phosphodiesterase (PDE)–regulated cyclic nucleotide signaling is also central to neuroinflammatory control[16]. Cyclic AMP (cAMP) and cyclic GMP (cGMP) are intracellular messengers that normally suppress inflammatory gene expression and promote cell survival pathways. Excessive PDE activity reduces these cyclic nucleotides, removing an important anti-inflammatory restraint. Low cAMP levels favor glial activation, cytokine release, and reduced neurotrophic support, tipping the balance toward degeneration. Taken together, the mechanisms commonly inhibited in neuroinflammatory modulation—pro-inflammatory cytokines, upstream immune regulators like MIF, excessive PDE activity, and sustained glial activation—represent core biological drivers of neurodegeneration. Targeting these pathways aims not to silence the immune system, but to restore balance, allowing glial cells to return to supportive, neuroprotective roles rather than perpetuating neuronal injury.

[12] Kempuraj D, Thangavel R, Natteru PA, Selvakumar GP, Saeed D, Zahoor H, Zaheer S, Iyer SS, Zaheer A. Neuroinflammation Induces Neurodegeneration. *J Neurol Neurosurg Spine.* 2016;1(1):1003. Epub 2016 Nov 18. PMID: 28127589; PMCID: PMC5260818.
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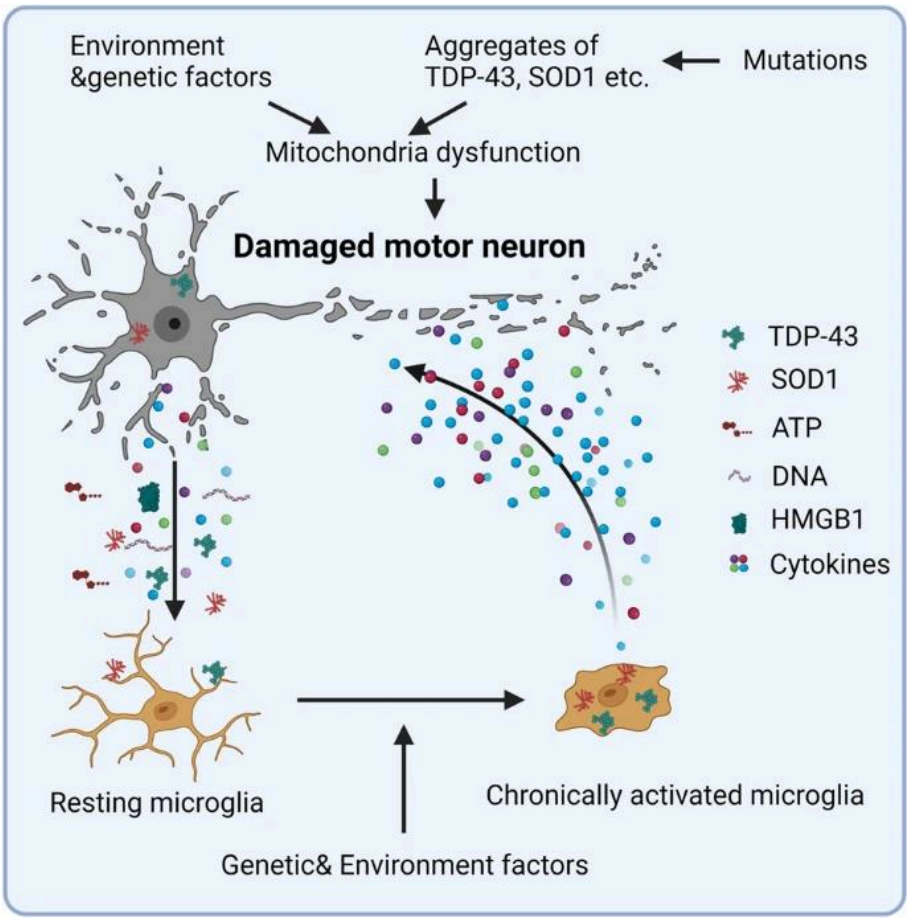
[15] Alfahel L, Gschwendtberger T, Kozareva V, Dumas L, Gibbs R, Kertser A, Baruch K, Zaccai S, Kahn J, Thau-Habermann N, Eggenschwiler R, Sterneckert J, Hermann A, Sundararaman N, Vaibhav V, Van Eyk JE, Rafuse VF, Fraenkel E, Cantz T, Petri S, Israelson A. Targeting low levels of MIF expression as a potential therapeutic strategy for ALS. *Cell Rep Med.* 2024 May 21;5(5):101546. doi: 10.1016/j.xcrm.2024.101546. Epub 2024 May 3. PMID: 38703766; PMCID: PMC11148722.
[16] Baillie GS, Tejeda GS, Kelly MP. Therapeutic targeting of 3',5'-cyclic nucleotide phosphodiesterases: inhibition and beyond. *Nat Rev Drug Discov.* 2019 Oct;18(10):770-796. doi: 10.1038/s41573-019-0033-4. Epub 2019 Aug 6. PMID: 31388135; PMCID: PMC6773486.

Figure 4: Inflammation in ALS



Source: Kempuraj et al., 2016

LEAD PRODUCT CANDIDATE IBUDILAST

Overview

Ibudilast is a small-molecule, orally available anti-inflammatory and neuroimmune modulator that has been investigated across a range of neurological and neuropsychiatric disorders[17]. Originally approved in Japan for the treatment of asthma and post-stroke dizziness, ibudilast has gained interest in Western drug development for its potential to target neuroinflammation, a process increasingly recognized as a key driver of neurodegeneration and chronic neuropsychiatric disease.

Mechanistically, ibudilast acts primarily as a phosphodiesterase (PDE) inhibitor, with activity against PDE-4 and PDE-10, and also inhibits macrophage migration inhibitory factor (MIF). Through these actions, it suppresses pro-inflammatory cytokine signaling and shifts glial cells, particularly microglia and astrocytes, away from a neurotoxic, inflammatory state. This results in reduced neuroinflammation and potential protection of neurons from progressive damage.

Clinically, ibudilast has been studied in conditions such as ALS, multiple sclerosis (MS), progressive neurological disorders, and substance use disorders, including alcohol and methamphetamine dependence. In ALS and MS, its therapeutic rationale is based on slowing disease progression by dampening immune-mediated neuronal injury rather than directly targeting neurotransmission. In addiction research, ibudilast has shown potential to reduce cravings and relapse by modulating neuroimmune pathways implicated in reward and stress responses.

Ibudilast is generally well tolerated, with a safety profile established through decades of use in Japan. Reported side effects are typically mild to moderate and may include gastrointestinal discomfort, headache, and fatigue. Because it does not act directly on classic neurotransmitter receptors, ibudilast is not associated with abuse potential. Overall, ibudilast represents a neuroimmune-focused therapeutic approach, aiming to modify disease biology by reducing inflammation in the central nervous system rather than providing symptomatic relief alone.

History of Ibudilast Approval in Japan

Ibudilast was developed in Japan in the 1980s and received its first regulatory approvals there in the late 1980s to early 1990s. It was approved for the treatment of bronchial asthma and later for post-stroke dizziness, conditions in which inflammation and vascular dysfunction were believed to play important roles. At the time, Japanese regulatory standards placed a strong emphasis on demonstrated clinical benefit and safety in domestic populations, and ibudilast's favorable tolerability profile supported its approval. Since then, it has been prescribed in Japan for several decades, generating extensive real-world safety data across large patient populations. This long clinical history has helped establish ibudilast as a well-characterized and generally safe anti-inflammatory agent.

Despite its long-standing use in Japan, ibudilast has never been approved by the FDA, largely for strategic and regulatory reasons rather than safety concerns. Ibudilast was approved in Japan for indications, such as asthma and post-stroke dizziness, that are crowded, generic-dominated markets in the US, making the commercial rationale for pursuing FDA approval weak. Ibudilast's original patents expired long ago, reducing incentives for the original developers to invest in US regulatory filings.

Therefore, recently ibudilast has been repurposed and reformulated for novel neurological and neuropsychiatric indications such as ALS, multiple sclerosis, and substance use disorders. In these programs, ibudilast is being evaluated as an investigational new drug (IND) under modern FDA standards, in modified formulations, doses, or combinations.

[17] Ramezani A, Varshosaz J, Darash S, Ebne-Ali-Heydari Y. A comprehensive systematic review of Ibudilast as a neuroprotective therapy for progressive multiple sclerosis. *Mult Scler Relat Disord.* 2025 Dec;104:106807. doi: 10.1016/j.msard.2025.106807. Epub 2025 Oct 19. PMID: 41135262.

Ibudilast: From Respiratory Therapy to Neuroprotection

Early observations that helped justify ibudilast's transition from a respiratory drug to a CNS-focused therapy originated from small Japanese studies in stroke and chronic cerebrovascular disease, rather than from large, definitive efficacy trials. These studies suggested that ibudilast exerted direct, measurable effects in the brain, providing an early clinical signal that its pharmacology extended well beyond the lungs.

In a small PET imaging study in ischemic stroke patients, investigators observed a rapid increase in cerebral blood flow (CBF) following oral administration of ibudilast. Although the study involved only a handful of patients and was not designed to assess functional recovery, it demonstrated that ibudilast could quickly modify cerebral perfusion in both affected and unaffected hemispheres. This finding was important because it showed that the drug crosses into the CNS and alters brain physiology in a way that could plausibly influence neurological symptoms[18].

Additional studies in patients with chronic cerebrovascular disease, including individuals experiencing post-stroke dizziness and depressive symptoms, reported symptomatic improvements after ibudilast treatment[19] [20]. These patient-reported benefits were accompanied by regional increases in cerebral blood flow, particularly in frontal and occipital cortical areas. While these studies were small and often open label, the pairing of subjective improvement with objective imaging changes strengthened the perception among clinicians that ibudilast had meaningful CNS activity.

Importantly, ibudilast was already used in Japan for post-stroke dizziness and chronic cerebral ischemic symptoms, which positioned it at the boundary between peripheral and central indications[21]. This real-world clinical use, combined with early imaging and symptom data, provided practical evidence that ibudilast was not merely an anti-asthmatic drug but one capable of modulating brain-related processes relevant to neurological disease.

Taken together, these early strokes and cerebrovascular studies did not prove that ibudilast improves long-term neurological recovery. However, they did establish three critical points that justified its transition into CNS development: central nervous system penetration, measurable effects on brain physiology (especially cerebral blood flow), and signals of neurological symptom improvement. These findings laid the groundwork for later, more rigorous investigations of ibudilast in neuroinflammatory and neurodegenerative disorders such as multiple sclerosis, ALS, and substance use disorders.

License Agreement for Ibudilast with MediciNova in 2004

KYORIN Pharmaceutical entered into a global licensing agreement with MediciNova, under which KYORIN granted MediciNova the rights to develop, manufacture, and sell ibudilast for the treatment of multiple sclerosis outside of Japan, China, South Korea, and Taiwan.

Under the agreement, KYORIN was to receive an up-front payment, development milestone payments, and future royalties on ibudilast sales. MediciNova's interest in developing an oral treatment for MS was driven by the need for non-injectable therapies that could improve quality of life for patients, especially given the high prevalence of MS in the U.S. and Europe compared with Japan. Interest in ALS emerged much later in the mid-2010s, as growing scientific evidence linked ibudilast's anti-inflammatory and glial-modulating properties to mechanisms relevant to ALS. During this period, MediciNova began exploratory research and early development planning for ALS, made possible by subsequent rights expansion or renegotiation beyond the original MS-only license.

Early clinical data for ibudilast (MN-166) in ALS was first reported in 2017[22]. This marked the effective start of ALS as a formal indication for the drug. The program advanced further in 2019–2020 with the launch of the COMBAT-ALS Phase 2b/3 clinical trial[23], establishing ALS as a major, independent development pathway for ibudilast separate from the earlier MS focus.

[18] Fukuyama H, Kimura J, Yamaguchi S, Yamauchi H, Ogawa M, Doi T, Yonekura Y, Konishi J. Pharmacological effects of ibudilast on cerebral circulation: a PET study. *Neurol Res.* 1993 Jun;15(3):169-73. doi: 10.1080/01616412.1993.11740130. PMID: 8103582.
[19] Inoue N, Harada M. Effect of ibudilast on non-specific symptoms in patients with chronic cerebral ischemia. Analysis of cerebral blood flow. *Arzneimittelforschung.* 2008;58(6):277-82. doi: 10.1055/s-0031-1296507. PMID: 18677969.
[20] Inoue N, Fukuda S, Inada T, Sameshima E, Tokushima Y, Harada M. Effect of ibudilast on the reciprocal inhibitory visual-vestibular interaction closely related to dizziness after cerebral ischemia. *J Stroke Cerebrovasc Dis.* 2014 Jan;23(1):51-5. doi: 10.1016/j.jstrokecerebrovasdis.2012.09.007. Epub 2012 Oct 22. PMID: 23085301.
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[22] https://investors.medicinova.com/news-releases/news-release-details/medicinova-announces-mn-166-ibudilast-als-abstract-accepted-1
[23] https://www.clinicaltrials.gov/study/NCT04057898

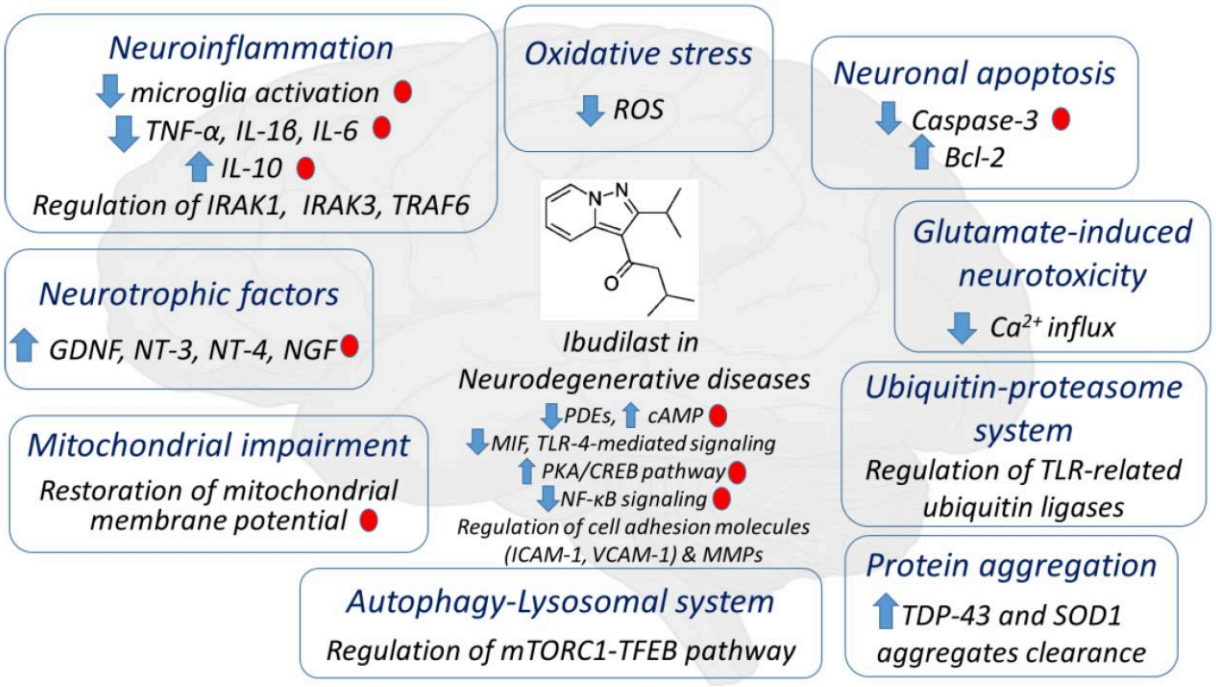
Ibudilast - Mechanism of Action in Neuroinflammation

Ibudilast works through multiple interconnected molecular mechanisms that converge on reducing harmful neuroinflammation and promoting cellular resilience [24] (Figure 5). A central aspect of its action is inhibition of cyclic nucleotide phosphodiesterases (PDEs), particularly PDE-3, PDE-4, PDE-10, and PDE-11. By blocking these enzymes, ibudilast raises intracellular levels of cyclic adenosine monophosphate (cAMP) and cyclic guanosine monophosphate (cGMP), which are key secondary messengers in many signaling pathways. Elevated cyclic nucleotides help shift immune cells away from a pro-inflammatory state and support processes such as neurotrophic factor expression and cellular survival signaling.

At the same time, ibudilast inhibits pro-inflammatory mediators such as TNF-α, macrophage migration inhibitory factor (MIF), and Toll-like receptor 4 (TLR-4). Suppressing these molecules dampens activation of microglia and astrocytes, the brain's resident immune cells, reducing the production of inflammatory cytokines and mitigating chronic neuroinflammation—a key driver of neuronal injury in many CNS disorders.

In addition to its anti-inflammatory effects, ibudilast influences other cellular processes implicated in neuronal health. By increasing cAMP/cGMP signaling, it can help regulate mitochondrial function and oxidative stress pathways, modulate apoptosis (programmed cell death), and impact proteostasis systems such as the ubiquitin–proteasome and autophagosome–lysosome pathways that clear damaged proteins and organelles. These broader actions support cellular homeostasis and may contribute to neuroprotection beyond simple inflammation suppression.

Figure 5: Effects of Ibudilast Related to Neurodegenerative Diseases



Source: Angelopoulou et al., 2022

[24] Angelopoulou E, Pyrgelis ES, Piperi C. Emerging Potential of the Phosphodiesterase (PDE) Inhibitor Ibudilast for Neurodegenerative Diseases: An Update on Preclinical and Clinical Evidence. *Molecules.* 2022 Dec 2;27(23):8448. doi: 10.3390/molecules27238448. PMID: 36500540; PMCID: PMC9737612.

CLINICAL DEVELOPMENT OF IBUDILAST IN ALS

Exploratory Phase 1b Biomarker Study

Study Design. A Phase 1b, open-label biomarker trial designed to evaluate whether high-dose ibudilast (MN-166) engages key biological targets implicated in ALS[25]. The rationale for the study was based on evidence that neuroinflammation - particularly microglial activation - and axonal injury play central roles in ALS progression.

A total of 35 participants with ALS were enrolled and treated with ibudilast for up to 36–40 weeks, with dose escalation targeting 100 mg/day. The primary endpoints were biological rather than clinical and focused on microglial activation, measured using PBR28 PET imaging in the motor cortex, and axonal damage, assessed via serum neurofilament light (NfL) levels. Secondary and exploratory outcomes included clinical measures such as ALSFRS-R and survival, as well as safety and tolerability.

Safety and Tolerability. Although ibudilast could be administered to ALS patients, high-dose treatment was difficult to sustain. Approximately 37% of participants required dose reductions, and 31% discontinued treatment early due to adverse events. The most common issues included gastrointestinal symptoms, fatigue, and other dose-related side effects, indicating that 100 mg/day may be near or beyond the tolerability threshold for many ALS patients.

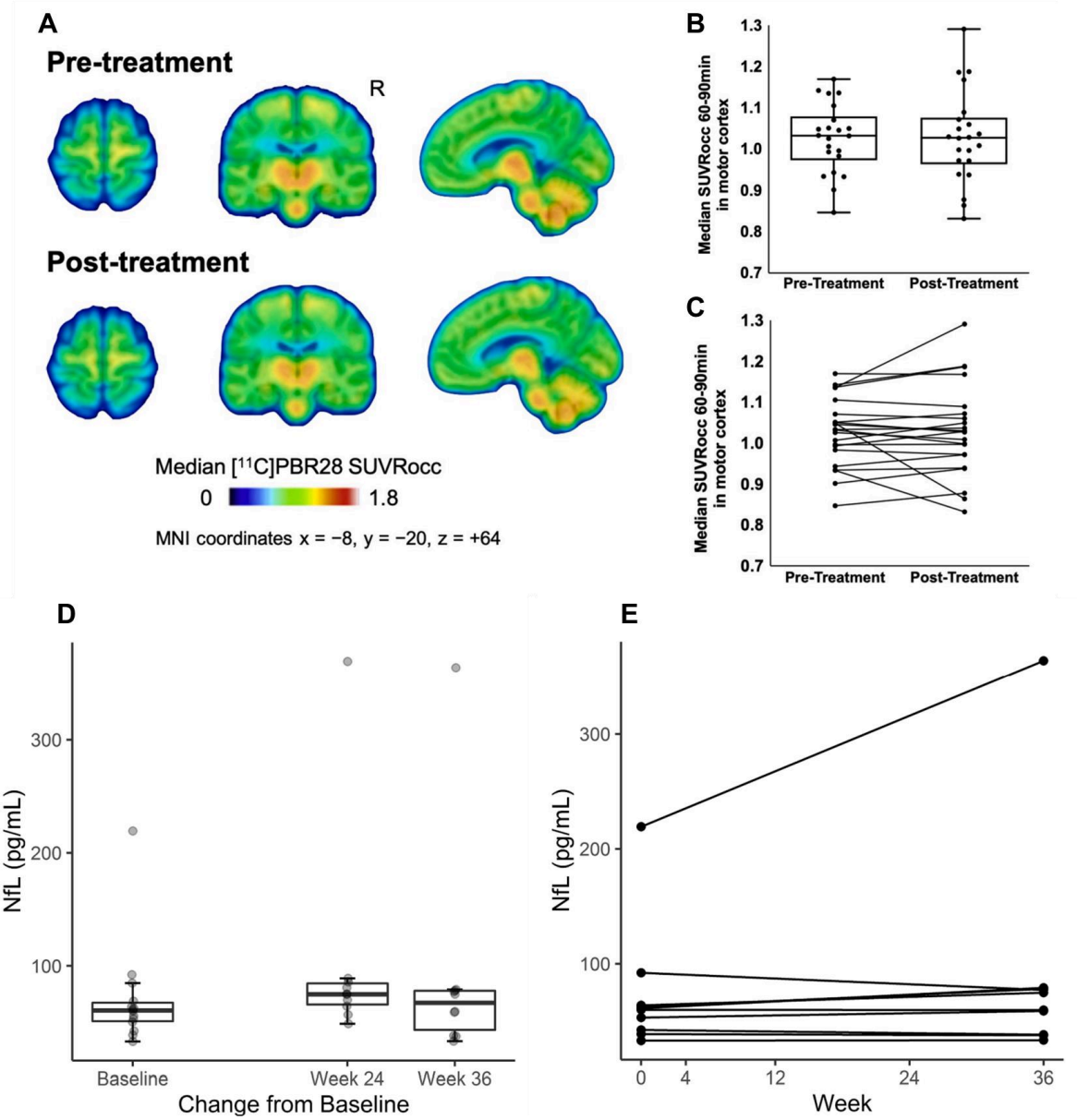
Biomarker & Efficacy Data. On the primary biomarker endpoints, ibudilast did not produce statistically significant reductions in either PBR28 PET signal (Figure 6A, B & C) or serum NfL (Figure 6D & E) over the treatment period. While baseline PET measures correlated with disease severity, indicating biological relevance of the imaging marker, treatment-related changes were small and variable. Similarly, serum NfL levels did not show a consistent or meaningful decline across participants, suggesting limited evidence of neuroprotective target engagement at the group level.

Exploratory clinical outcomes showed heterogeneous disease trajectories, with some individuals exhibiting slower functional decline, but the study was not powered to assess efficacy. Any apparent clinical stabilization or correlations between biomarkers and outcomes were considered hypothesis-generating rather than conclusive.

Conclusion. The study demonstrated that while high dose ibudilast is feasible in ALS, it did not clearly engage the intended neuroinflammatory or neurodegenerative biomarkers and posed tolerability challenges at the highest doses. The findings highlighted the importance of dose optimization, better patient stratification, and careful biomarker selection in future ALS trials targeting neuroinflammation.

[25] Babu S, Hightower BG, Chan J, Zürcher NR, Kivisäkk P, Tseng CJ, Sanders DL, Robichaud A, Banno H, Evora A, Ashokkumar A, Pothier L, Paganoni S, Chew S, Dojillo J, Matsuda K, Gudesblatt M, Berry JD, Cudkowicz ME, Hooker JM, Atassi N. Ibudilast (MN-166) in amyotrophic lateral sclerosis- an open label, safety and pharmacodynamic trial. *Neuroimage Clin.* 2021;30:102672. doi: 10.1016/j.nicl.2021.102672. Epub 2021 Apr 15. PMID: 34016561; PMCID: PMC8102622.

Figure 6: Exploratory Phase 1b Biomarker Study



Source: Fox et al., 2018

Phase 2a Study IBU-ALS-1201

Study Design. The Phase 1b/2a ALS study of MN-166 (ibudilast) was designed to evaluate both safety and early signs of efficacy in patients with amyotrophic lateral sclerosis. The trial enrolled 51 ALS patients who were not using non-invasive ventilation and assessed ibudilast as an add-on to riluzole. Participants were randomized in a double-blind manner to receive ibudilast or placebo for six months, followed by a six-month open-label extension in which all patients could receive active treatment. The primary endpoint was safety and tolerability, with exploratory efficacy endpoints including functional decline measured by the ALSFRS-R and survival outcomes.

Safety Data. The study met its primary endpoint, demonstrating a favorable safety and tolerability profile for ibudilast. Seven serious adverse events were reported, but none were attributed to the study drug. All treatment-related adverse events were mild to moderate, with the most common being nausea, anorexia, and loss of appetite, consistent with known effects of ibudilast and riluzole. Importantly, there were no severe or life-threatening treatment-related adverse events, supporting continued clinical development.

Efficacy Results. Exploratory efficacy analyses focused on responder definition based on ALSFRS-R outcomes. A responder was defined as a patient whose ALSFRS-R total score improved, remained stable, or declined by no more than one point over six months. During the double-blind phase, 29.4% of patients receiving ibudilast were responders, compared with 17.6% in the placebo group, indicating a trend toward slower functional decline (Figure 7A). When placebo patients crossed over to ibudilast in the open-label extension, 35.3% met the responder criteria, suggesting consistency of effect after treatment initiation.

Longitudinal analyses further showed that responders experienced less functional decline over time compared with non-responders, as reflected in ALSFRS-R trajectories (Figure 7B). In addition, responder status was associated with improved survival probability, with survival analyses showing a clear separation between responders and non-responders over extended follow-up (Figure 7C). While these findings were exploratory and not powered for definitive statistical conclusions, they provided converging functional and survival signals.

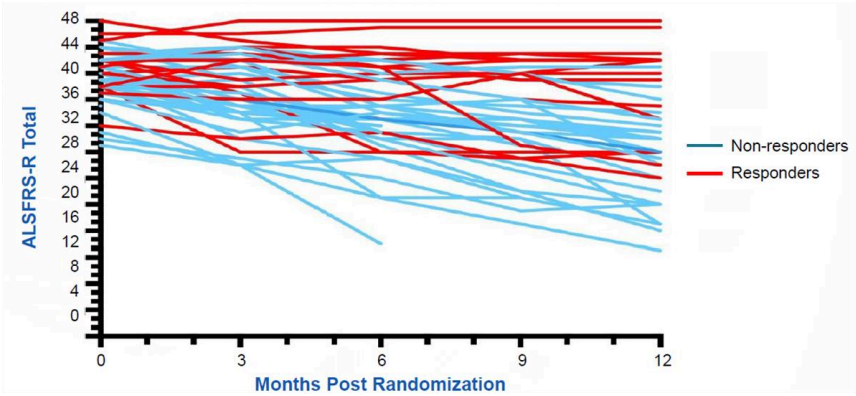
Taken together, the Phase 2a study demonstrated that MN-166 (ibudilast) is safe and well tolerated in ALS patients and showed consistent trends toward functional stabilization and improved survival in a subset of patients. These results, combined with the observed responder patterns, directly informed the design of subsequent Phase 3 trials, including higher dosing, longer treatment duration, and enrollment of earlier-stage ALS patients.

Figure 7: Phase 2a Study IBU-ALS-1201

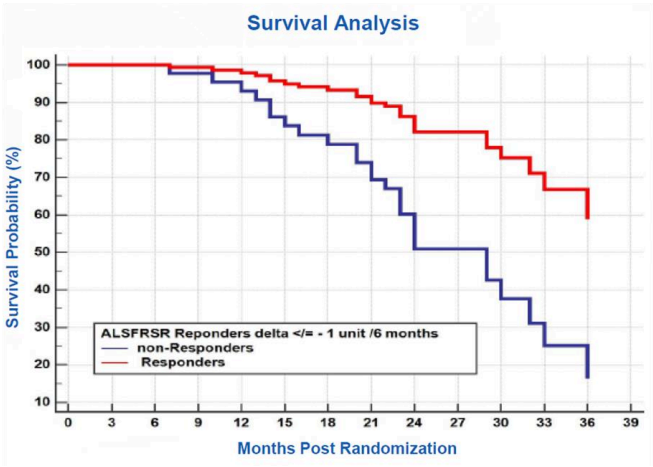
A

Responder Analysis			
Outcome	**Responder Category**	**Placebo (n=16)** +Riluzole	**MN-166 (n=33)** +Riluzole
ALSFRS-R	Stable or improved from baseline	2/16 (12.5%)	7/33 (21.2%)
ALSAQ-5 (QOL)		4/16 (25%)	17/33 (51.5%)
MMT (muscle strength)		4/16 (25%)	11/33 (33.3%)

B



C



Source: MediciNova Corporate Presentation, December 2025

COMBAT-ALS Phase 2b/3 Clinical Trial of Ibudilast in ALS

Study Design. The COMBAT-ALS trial is a Phase 2b/3, multicenter, randomized, double-blind, placebo-controlled study designed to evaluate the efficacy and safety of ibudilast in patients with ALS. The study enrolls patients across 17 sites in the US and Canada, reflecting an effort to capture a representative ALS population while maintaining consistency in trial execution. Patients are randomized to receive either MN-166 or placebo during a 12-month double-blind treatment phase, followed by a six-month open-label extension, allowing all participants access to active treatment.

The trial population is carefully defined to balance early disease intervention with measurable progression. Eligible patients must have a diagnosis of familial or sporadic ALS according to El Escorial–Revised criteria, with symptom onset within 18 months prior to screening. Functional requirements include a baseline ALSFRS-R score of at least 35, limits on severely impaired subscores, and a documented pulmonary function of ≥70% predicted. Additionally, patients must demonstrate a moderate disease progression rate (0.3–1.0 ALSFRS-R points per month), ensuring sufficient decline to detect a treatment effect while avoiding overly rapid progression that could obscure therapeutic benefit.

From a treatment standpoint, the study reflects real-world ALS care, as patients are enrolled while receiving standard therapy with riluzole, and edaravone use is permitted with appropriate wash-in requirements. MN-166 is administered orally and was selected based on prior evidence of central nervous system penetration, glial cell modulation, and anti-inflammatory and neuroprotective effects, as well as a favorable safety profile in more than 900 exposed subjects.

The primary objective of COMBAT-ALS is to assess the effect of MN-166 on functional decline and survival, using the ALS Functional Rating Scale–Revised (ALSFRS-R) and survival-based composite measures. Key secondary objectives include evaluation of muscle strength via hand-held dynamometry, quality of life using ALSAQ-5, and overall safety and tolerability. This combination of endpoints is intended to capture both clinically meaningful functional outcomes and broader patient-centered measures.

A notable feature of the study design is the inclusion of a pre-specified interim analysis, not to assess efficacy, but to evaluate whether outcomes measured at six months reliably predict 12-month outcomes. Correlation analyses using CAFS, modified CAFS, and ALSFRS-R scores were conducted in a defined subset of patients. The observation of strong correlations between the 6- and 12-month timepoints supported the internal validity of the chosen endpoints and confirmed the appropriateness of the 12-month double-blind duration.

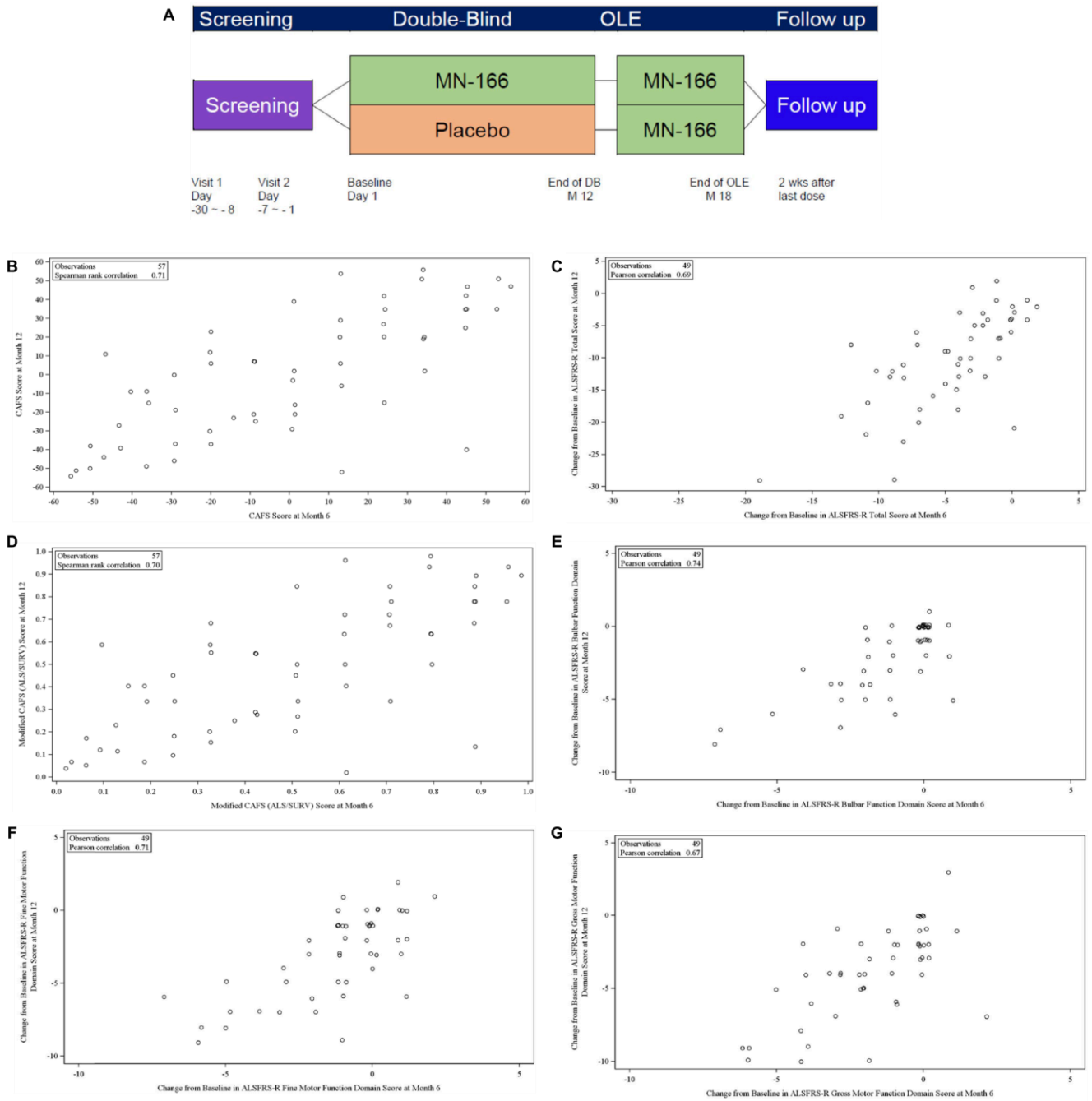
Importantly, although shortening the double-blind phase to six months could accelerate recruitment and readouts, the study team concluded—based on statistical considerations and guidance from an independent Data Safety Monitoring Board (DSMB) - that maintaining the 12-month design preserves statistical power, face validity, and regulatory credibility. The DSMB reviewed the interim data and recommended that the trial continue unchanged, reinforcing confidence in the study's structure.

Overall, the COMBAT-ALS study design reflects a deliberate balance between scientific rigor, clinical relevance, and regulatory expectations. By targeting an early but progressing ALS population, incorporating robust functional and survival endpoints, and maintaining a sufficiently long blinded treatment period, the trial is positioned to meaningfully assess whether MN-166 can slow disease progression in ALS.

Interim Analysis. The company has presented an update and interim analysis from its ongoing COMBAT-ALS Phase 2b/3 clinical trial. As of December 2025, The study has achieved the milestone of patient enrollment (n=234). Results demonstrated strong positive correlations between six- and 12-month outcomes across multiple measures (Figure 8B to G), including the Combined Assessment of Function and Survival (CAFS) score (Spearman correlation 0.71), modified CAFS (0.70), and ALSFRS-R (0.69). Subscale analyses showed similarly strong correlations for bulbar, fine motor, and gross motor function, though not for respiratory function.

The DSMB recommended that the study continue without modification. Based on these findings, MediciNova elected to maintain the current study design and treatment duration. The company expects top-line results anticipated in 2026.

Figure 8: COMBAT-ALS Phase 2b/3 Clinical Trial Study Design & Interim Analysis



Source: MediciNova Corporate Poster, ALS / MND Meeting 2024

CLINICAL DEVELOPMENT OF IBUDILAST FOR OTHER INDICATIONS

Ibudilast in Progressive Multiple Sclerosis

Study Design. This was a Phase 2, multicenter, randomized, double-blind, placebo-controlled trial (NN102/SPRINT-MS) conducted across 28 US sites[26]. A total of 255 patients with either primary progressive MS or secondary progressive MS were randomized 1:1 to receive oral ibudilast (up to 100mg daily) or placebo for 96 weeks. The primary endpoint was the rate of brain atrophy, measured by the brain parenchymal fraction on MRI. Major secondary endpoints included advanced imaging measures of tissue damage (diffusion tensor imaging of pyramidal tracts, magnetization transfer ratio, cortical thickness), retinal nerve fiber layer thickness, and disability progression measured by the EDSS.

Safety and Tolerability. Ibudilast was generally well tolerated, but adverse events were more frequent than with placebo. The most common side effects included gastrointestinal symptoms (nausea, diarrhea, abdominal pain, vomiting), headache, and depression. Serious adverse events occurred at similar rates in the ibudilast and placebo groups, and there were no deaths or opportunistic infections. Discontinuation rates due to adverse events were modestly higher with ibudilast.

Key Results. Ibudilast met the primary endpoint, demonstrating a statistically significant reduction in the rate of brain atrophy compared with placebo (Figure 9A). The annualized decline in brain parenchymal fraction was −0.0010 per year with ibudilast versus −0.0019 per year with placebo, corresponding to an absolute difference of 0.0009 per year (P=0.04) (Figure 9B). Over 96 weeks, this translated to approximately 2.5mL less brain tissue loss and a 48% relative slowing of brain atrophy.

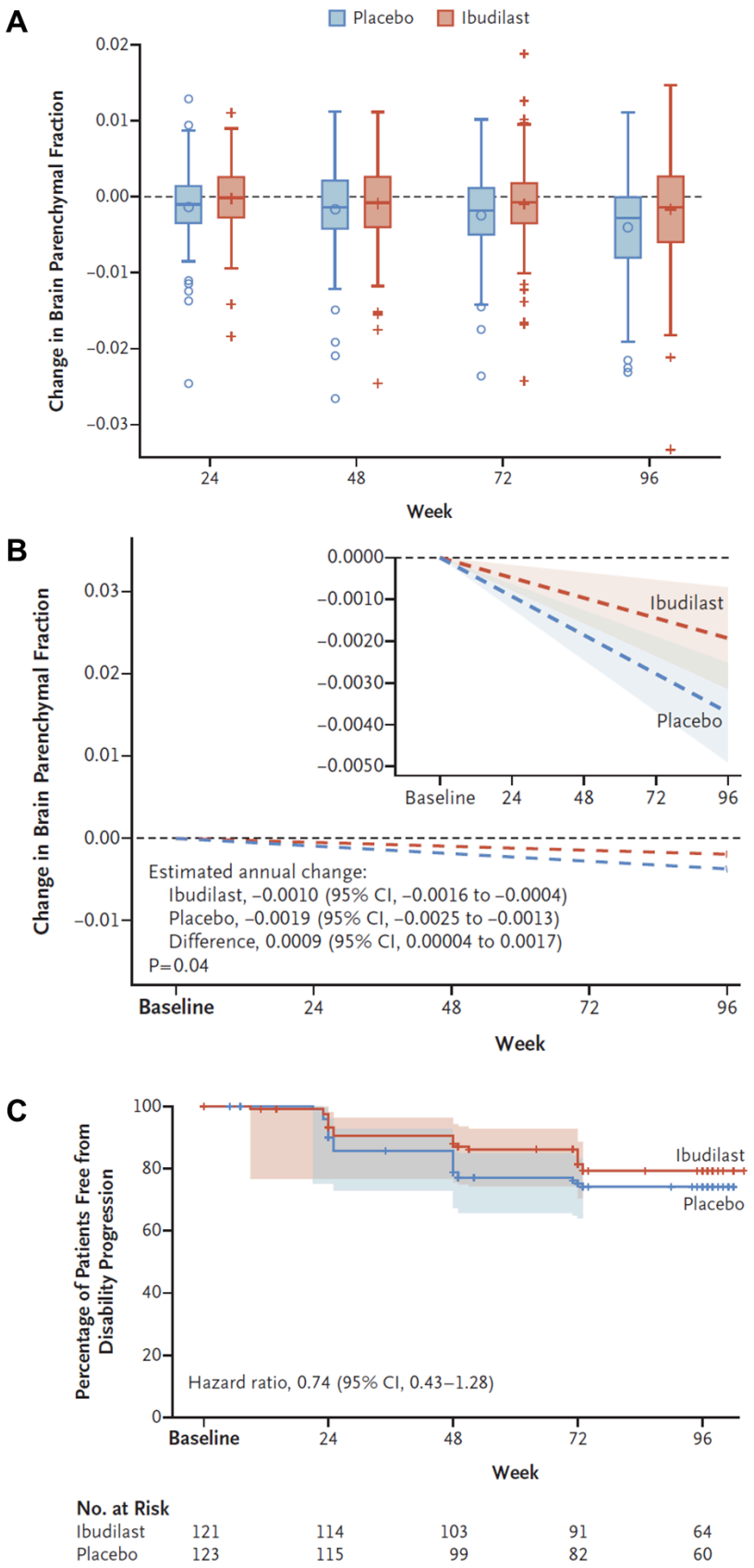
For secondary endpoints, results were mixed. Imaging measures of cortical thickness and magnetization transfer ratio favored ibudilast, suggesting potential neuroprotective effects, but these analyses were not adjusted for multiple comparisons and therefore were considered exploratory. Disability progression was evaluated as a key secondary outcome in the study using established clinical measures, most notably the Expanded Disability Status Scale (EDSS). Over the 96-week treatment period, there was no statistically significant difference between patients treated with ibudilast and those receiving placebo in terms of confirmed disability progression (Figure 9C). This indicated that, despite evidence of biological activity, ibudilast did not demonstrate a measurable impact on physical disability within the timeframe of the trial.

Progressive multiple sclerosis is characterized by slow and gradual functional decline, making short- to medium-term changes in disability difficult to detect, particularly in a Phase 2 study. They also highlighted limitations of the EDSS, which is weighted toward ambulation and may lack sensitivity to subtle neurological changes or early neuroprotective effects that do not immediately translate into observable functional improvement. As a result, the absence of an effect on disability progression was not interpreted as definitive evidence of clinical inefficacy, but rather as a reflection of the challenges inherent in measuring functional outcomes in progressive MS over relatively short durations.

Conclusions and Implications. The study demonstrated that ibudilast significantly slowed the progression of brain atrophy in patients with progressive MS over 96 weeks, supporting its potential neuroprotective effects. However, the clinical significance of reduced brain atrophy remains uncertain, as this benefit did not translate into a clear reduction in disability progression during the trial period. Overall, the trial provided proof of biological activity and justified further investigation, while highlighting the need for larger and longer studies to determine whether slowing brain atrophy with ibudilast leads to meaningful functional benefits for patients with progressive MS.

[26] Fox RJ, Coffey CS, Conwit R, Cudkowicz ME, Gleason T, Goodman A, Klawiter EC, Matsuda K, McGovern M, Naismith RT, Ashokkumar A, Barnes J, Ecklund D, Klingner E, Koepp M, Long JD, Natarajan S, Thornell B, Yankey J, Bermel RA, Debbins JP, Huang X, Jagodnik P, Lowe MJ, Nakamura K, Narayanan S, Sakaie KE, Thoomukuntla B, Zhou X, Krieger S, Alvarez E, Apperson M, Bashir K, Cohen BA, Coyle PK, Delgado S, Dewitt LD, Flores A, Giesser BS, Goldman MD, Jubelt B, Lava N, Lynch SG, Moses H, Ontaneda D, Perumal JS, Racke M, Repovic P, Riley CS, Severson C, Shinnar S, Suski V, Weinstock-Guttman B, Yadav V, Zabeti A; NN102/SPRINT-MS Trial Investigators. Phase 2 Trial of Ibudilast in Progressive Multiple Sclerosis. *N Engl J Med.* 2018 Aug 30;379(9):846-855. doi: 10.1056/NEJMoa1803583. PMID: 30157388; PMCID: PMC6172944.

Figure 9: Phase 2 Trial of Ibudilast in Progressive Multiple Sclerosis



Source: Fox et al., 2018

Phase 1/2 Glioblastoma (GBM) Study

Study Design. The study was a single-center, open-label, dose-escalation Phase 1b/2a trial that evaluated the safety, tolerability, and initial efficacy of ibudilast plus standard temozolomide chemotherapy in patients with both newly diagnosed (nGBM) and recurrent glioblastoma (rGBM)[27]. Daily ibudilast (starting at 30mg twice daily and escalating to 50mg twice daily) was administered alongside monthly cycles of temozolomide. The primary objectives were to determine the recommended Phase 2 dose (R2PD) of ibudilast and assess 6-month progression-free survival (PFS-6) as an efficacy signal. A standard 3 + 3 design was used for dose escalation.

A total of 62 GBM patients were enrolled (36 newly diagnosed and 26 recurrent). The study found that 50mg twice daily was the recommended Phase 2 dose (R2PD) of ibudilast in this combination, and the combination was generally safe and well tolerated, with most treatment-related adverse events (e.g., lymphopenia, leukopenia, neutropenia, thrombocytopenia) consistent with expected toxicities from temozolomide and not unexpected for the regimen.

Efficacy Results. PFS-6 was 44 % in newly diagnosed GBM and 31 % in recurrent GBM, with the recurrent GBM rate higher than historical controls (Figure 10A). Median progression-free survival was 8.7 months in newly diagnosed and 2.4 months in recurrent patients, while median overall survival was 21.0 months and 8.6 months (Figure 10B & C), respectively. Although median survival outcomes were not markedly higher than historical benchmarks, the PFS-6 findings in recurrent GBM met the study's primary efficacy signal criteria.

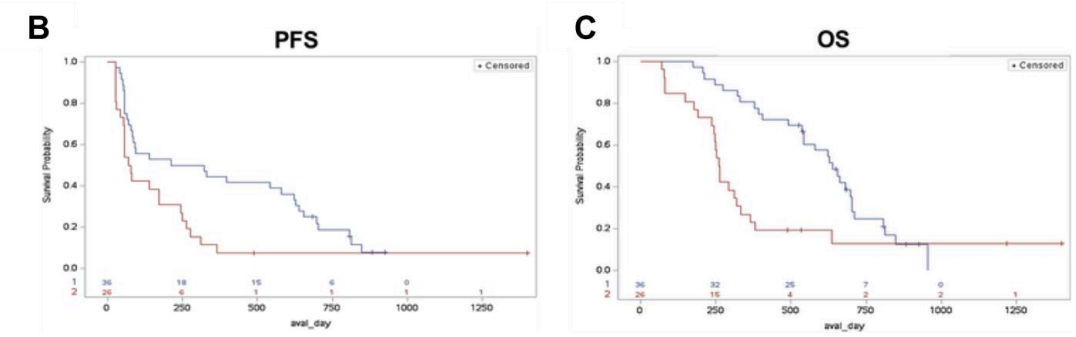
Exploratory immunohistochemistry analyses indicated that higher intratumoral CD3 expression at baseline was associated with earlier progression within five months, suggesting that immune microenvironment markers may correlate with response. Preclinical data presented alongside the clinical results also suggested potential synergy when ibudilast is combined with immune checkpoint blockade agents, pointing to future avenues for combination immunotherapy strategies in GBM.

Conclusion. The Phase 1b/2a study showed that the ibudilast + temozolomide combination is safe and tolerable in GBM patients and produced encouraging progression-free survival signals, particularly in recurrent disease, supporting further exploration of this approach.

Figure 10: Phase 1/2 GBM Study

A

	nGBM (N = 36)	rGBM (N =26)
Progression-Free Survival		
PFS6 rate	16 (44.4%)	8 (30.8%)
Median PFS (95% CI)	8.7 months (2.6, 20.5)	2.4 months (1.8, 5.7)
Overall Survival		
OS-6 months	35 (97.2%)	21 (80.8%)
OS-12 months	29 (80.6%)	7 (26.9%)
Median OS (95% CI)	21 months (17.7, 23.0)	8.6 months (7.8, 10.5)



Source: MediciNova Corporate Presentation, December 2025

[27] MediciNova, Inc. (2024). Phase 1b/2a study evaluating the combination of MN-166 (ibudilast) and temozolomide in patients with newly diagnosed and recurrent glioblastoma. *Journal of Clinical Oncology*, 42(16_suppl), 2016. https://doi.org/10.1200/JCO.2024.42.16_suppl.2016

Phase 2b Study in Chemotherapy-Induced Peripheral Neuropathy (CIPN)

Peripheral neuropathy refers to a group of symptoms resulting from damage to nerves located outside the brain and spinal cord, known as peripheral nerves. Certain chemotherapy agents and other cancer treatments can injure these nerves, particularly those responsible for sensation in the hands and feet, leading to chemotherapy-induced peripheral neuropathy (CIPN). CIPN is a common adverse effect of cancer treatment and is frequently described by patients as sensations of tingling or “pins and needles” in the fingers and toes.

CIPN can significantly affect cancer treatment outcomes by necessitating dose reductions or early discontinuation of chemotherapy, and it often has a substantial negative impact on patients’ quality of life and long-term survivorship. A meta-analysis of more than 4,000 patients reported that CIPN prevalence was approximately 68% within the first month after chemotherapy, declining to 60% at three months and 30% at six months or longer following treatment. Long-term neurotoxicity remains a major concern for the growing population of cancer survivors, particularly among individuals treated for breast and colorectal cancers.

Study Design. This Phase 2b, multicenter, randomized, double-blind, placebo-controlled study is designed to evaluate whether ibudilast can reduce acute neurotoxicity symptoms and CIPN, as well as assess whether treatment with ibudilast leads to fewer neurotoxicity-related chemotherapy dose reductions in patients with metastatic colorectal cancer receiving oxaliplatin for up to six months. The study enrolled 100 patients, randomized in a 1:1 ratio to receive either ibudilast or placebo. Study treatment (ibudilast 60mg/day or matching placebo) begins two days prior to the first oxaliplatin cycle and continue throughout the course of oxaliplatin chemotherapy.

The clinical trial is being conducted through a collaboration between MediciNova, the University of Sydney, and the Australasian Gastro-Intestinal Trials Group (AGITG). Dr. Janette Vardy, Professor of Cancer Medicine at the University of Sydney, will serve as the lead principal investigator. The study is designed to assess ibudilast as a potential therapy to reduce the severity of acute neurotoxicity and CIPN in patients with metastatic colorectal cancer. AGITG will fund the study, while MediciNova will supply the study drug and provide regulatory support.

Plan Forward. In December 2025, MediciNova announced the successful completion of patient enrollment for the Phase 2 OXTOX clinical trial (Oxaliplatin Neurotoxicity study in patients with metastatic colorectal cancer). A total of 100 patients has been randomized into two treatment groups across 11 clinical sites in Australia, and enrollment has now formally closed.

Participants will continue receiving chemotherapy in combination with the assigned study medication (ibudilast or placebo) until disease progression or the development of unacceptable adverse effects. The trial is expected to conclude once the final participant reaches six months following completion of chemotherapy. Although the precise completion date has not yet been established, top-line results are anticipated to be available in late 2026.

CLINICAL DEVELOPMENT OF NON-CORE ASSETS MN-001

MN-001 Overview

MN-001, also known by its chemical name tipelukast, is an orally administered small-molecule drug developed by MediciNova. It is designed as a multi-mechanism agent targeting inflammatory, fibrotic, and metabolic pathways, distinguishing it from single-target anti-inflammatory therapies. Its oral route of administration supports chronic use in systemic diseases.

The mechanism of action of MN-001 is multimodal, combining inhibition of leukotriene signaling and phosphodiesterase activity. Specifically, tipelukast inhibits the leukotriene and 5-lipoxygenase (5-LO) pathways, reducing the synthesis of pro-inflammatory lipid mediators derived from arachidonic acid. In parallel, it acts as a phosphodiesterase (PDE) 3 and PDE4 inhibitor, increasing intracellular cyclic nucleotide levels and thereby suppressing inflammatory cell activation. MN-001 also exhibits leukotriene receptor antagonism, further dampening leukotriene-driven inflammatory responses.

These combined molecular actions translate into several clinically relevant biological effects. MN-001 demonstrates anti-inflammatory and anti-fibrotic activity, reducing pathways associated with tissue remodeling and fibrosis. In metabolic tissues, it shows lipid-lowering properties, including the ability to reduce serum triglyceride levels. Mechanistically, this effect is partly mediated through downregulation of CD36 expression, a fatty-acid transporter, which in turn inhibits the uptake of arachidonic acid into hepatocytes and limits downstream inflammatory lipid production.

Overall, MN-001 (tipelukast) is positioned as a systemic, multi-pathway modulator with potential utility across inflammatory, fibrotic, and metabolic diseases. Its ability to simultaneously target leukotriene signaling, phosphodiesterase activity, lipid metabolism, and fibrotic processes underpins its development in indications such as pulmonary fibrosis, liver disease, and metabolic disorders, where complex inflammatory and lipid-driven mechanisms intersect.

Clinical Development of MN-001

The first Phase 2 study of MN-001 (MN-001-NATG-201) evaluated its effects in patients with NAFLD/NASH and hypertriglyceridemia (HyperTG) in a multi-center, open-label trial in the United States. Nineteen patients were enrolled and treated with 250 mg/day for 4 weeks followed by 500 mg/day for 8 weeks. The study demonstrated a meaningful improvement in lipid parameters, particularly in patients with type 2 diabetes mellitus (T2DM). Across all subjects, serum triglycerides declined by approximately 40% by Week 8. In the T2DM subgroup, triglycerides fell by ~51%, alongside a statistically significant increase in HDL-cholesterol (+15.8%, $p<0.0002$) (Figure 11A). These findings suggested MN-001 has clinically relevant lipid-lowering effects, especially in metabolically high-risk patients.

Building on these results, an ongoing randomized Phase 2 study (MN-001-NATG-202) was initiated in patients with HyperTG, T2DM, and NAFLD (Figure 11B). This trial is a randomized (1:1), placebo-controlled, double-blind study conducted at two U.S. centers, enrolling 40 patients. Participants receive MN-001 at 500 mg/day or placebo for 24 weeks, following a screening period of up to eight weeks. Target enrollment has been completed. The next key catalysts for MN-001 are expected by the summer of 2026, led by the Phase 2 randomized data readout, followed by regulatory and partnering discussions contingent on study results.

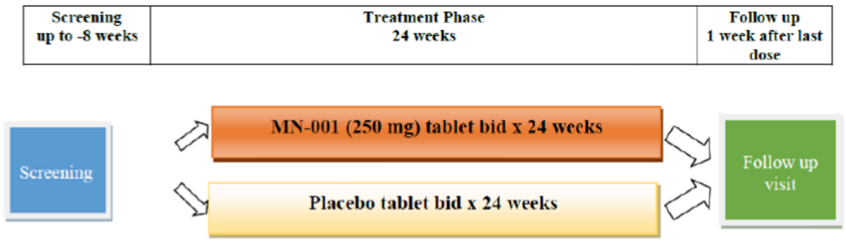
The primary endpoints of the ongoing study are change from baseline in liver fat content, measured by FibroScan controlled attenuation parameter (CAP), and change in fasting serum triglyceride levels at Week 24. Secondary objectives include evaluation of safety and tolerability and broader effects on the lipid profile, including HDL-C, LDL-C, and total cholesterol. Together, these studies position MN-001 as a potential therapy addressing both metabolic dyslipidemia and liver fat accumulation in patients with NAFLD/NASH and cardiometabolic comorbidities.

Figure 11: Clinical Development of MN-001

A

	Serum TG level (mg/dL)			Serum HDL-C level (mg/dL)		
Timepoints	All subjects (n=19)	**With T2DM (n=10)**	w/o T2DM (n=9)	All subjects (n=19)	**With T2DM (n=10)**	w/o T2DM (n=9)
Baseline	345.7	444.7	235.7	38.7	36	41.8
Week 8	206.9	218.8	193.8	41.9	41.7	42.2
Mean % change from Baseline (p-value)	- 40.2%	-50.8% (p=0.098)	-17.8%	+ 8.3%	+15.8% (p<0.0002)	+0.9%

B



Source: MediciNova Corporate Presentation, December 2025

COMPETITIVE LANDSCAPE OF ALS

Besides the therapies approved for ALS (Figure 12), there are several drugs in development (Figure 13), which can be grouped in the following categories.

Radicava Acquisition Reinforces ALS Market Interest

Radicava is a free-radical scavenger originally developed in Japan in the late 1980s and first used for stroke before being studied in ALS. It was approved by the FDA for ALS in 2017, making it one of the few disease-modifying treatments available for this progressive neurodegenerative condition and offering the first new option in more than two decades. The drug is thought to act by reducing oxidative stress in motor neurons, though its precise mechanism in ALS is not fully understood. Clinical trial data showed that edaravone slowed functional decline in a selected early-stage ALS population over six months, and real-world and cohort analyses have suggested modest benefits on survival in some settings, but its overall impact remains limited and context-specific rather than transformative.

In December 2025, Shionogi (4507.T; Not Rated) announced a planned acquisition of global rights to both intravenous and oral formulations of RADICAVA (edaravone) from Tanabe Pharma (Private), creating a dedicated rare disease commercial platform and adding approximately $700M in annual sales in F2026. Under the agreement, Shionogi will make an upfront payment of $2.5B to Tanabe Pharma via Shionogi Inc. upon completion of the transaction. The deal also includes potential royalty payments on future sales, subject to specified terms. Following the closing, the RADICAVA ORS® and IV RADICAVA business will operate as a wholly owned subsidiary of Shionogi Inc. This kind of major pharma investment in a rare disease treatment signal that even difficult-to-serve indications like ALS continue to attract strategic interest and commercial commitment.

This deal can be viewed as positive industry validation of ALS as a viable commercial category, suggesting that large pharmaceutical companies see ongoing value in therapies for ALS patients despite clinical and regulatory challenges.

Assets Under Clinical Development

ALS Mutations

AP-101 is a human monoclonal antibody designed to selectively target the misfolded form of the SOD1 protein, a pathogenic species implicated in both familial and sporadic ALS. In Phase 2, randomized, double-blind, placebo-controlled trial (NCT05039099), AP-101 is being evaluated for safety, tolerability, pharmacokinetics, and pharmacodynamics in ALS patients receiving standard of care. AL-S Pharma has reported positive topline Phase 2 results, with AP-101 meeting its primary safety and tolerability endpoint. Exploratory analyses showed clinically meaningful signals across outcomes related to survival, respiratory support, disease progression staging, and stabilization of neurofilament biomarkers, supporting biological activity and potential disease-modifying effects. The development of AP-101 to human proof-of-concept is being led by AL-S Pharma AG (private), a private company formed through a partnership between Neurimmune (private) and TVM Capital Life Science. The program is being executed in collaboration with Chorus, an independent clinical development unit of Eli Lilly and Company (LLY; Not Rated), leveraging a global network of ALS experts and an efficient, adaptive clinical development strategy as the program advances toward later-stage trials.

ION363 is an antisense medicine developed by Ionis (IONS; Not Rated) that is designed to decrease the production of the fused in sarcoma (FUS) protein. It aims to treat ALS in individuals with mutations in the FUS gene. Currently it is in Phase 3 development (NCT04768972). Current treatment options for FUS-ALS are limited, and no medications exist to significantly slow the disease's progression. The estimated number of FUS-ALS patients in G7 countries is around 350[28]. In preclinical trials, a reduction in mutant FUS protein using antisense-mediated therapy prevented motor neuron loss in a FUS-ALS mouse model. The hypothesis is that reducing FUS protein levels could reverse or halt disease progression in FUS-ALS patients.

LAM-002 is a PIKfyve kinase inhibitor developed by AI Therapeutics (private) which triggers the activation of transcription factor EB (TFEB), the chief regulator of lysosomal biogenesis. By activating TFEB, LAM-002 eliminates toxic aggregates that

[28] Lai SL, Abramzon Y, Schymick JC, Stephan DA, Dunckley T, Dillman A, Cookson M, Calvo A, Battistini S, Giannini F, Caponnetto C, Mancardi GL, Spataro R, Monsurro MR, Tedeschi G, Marinou K, Sabatelli M, Conte A, Mandrioli J, Sola P, Salvi F, Bartolomei I, Lombardo F; ITALSGEN Consortium; Mora G, Restagno G, Chiò A, Traynor BJ. FUS mutations in sporadic amyotrophic lateral sclerosis. *Neurobiol Aging.* 2011 Mar;32(3):550.e1-4. doi: 10.1016/j.neurobiolaging.2009.12.020. Epub 2010 Feb 6. PMID: 20138404; PMCID: PMC2891336.

contribute to various neurodegenerative conditions, including ALS[29].The Phase 2a trial (NCT05163886) of LAM-002 demonstrated the drug's target engagement in 14 patients with C9ORF72-associated ALS. During the trial, AIT-101 met its primary objective of safety, reduced the protein aggregate poly (GP) by 73%, which is a biomarker for neurodegeneration in C9ORF72-associated ALS.

Oxidative Stress

EPI-589 is an orally available, brain-penetrant small molecule designed to reduce oxidative stress in ALS. It aims to boost processes involved in controlling oxidative stress and enhance energy metabolism in cells' mitochondria[30]. Its exploratory Phase 2 clinical trial[31] by Sumitomo (TYO: 4506; Not Rated) for ALS is ongoing.

PTC857 is an orally available small molecule being developed by PTC Therapeutics (PTCT; Not Rated) as a treatment for ALS. It works by inhibiting 15-LO, which reduces oxidative stress and prevents the depletion of reduced glutathione, making it a redox-active inhibitor of ferroptosis[32]. Its pharmacological action is expected to slow or prevent neurodegeneration in ALS by preventing ferroptosis. The ongoing Phase 2 study, called CARDINALS, is investigating whether PTC857 outperforms a placebo at slowing progression in ALS patients (NCT05349721).

Mitochondrial Dysfunction

CNM-Au8. Clene (CLNN; Not Rated) is developing gold nanoparticles for treating ALS. CNM-Au8 is a concentrated, aqueous suspension of clean surfaced, faceted nanocrystalline gold. The nanocrystals are aggregated into various shapes, with an average diameter of 13nm. Each crystal contains 30,000 to 70,000 gold atoms. As opposed to directly interacting with proteins or other macromolecules, the electron cloud surrounding the crystals is utilized as a catalyst for chemical reactions in the brain. By directly donating or receiving electrons, CNM-Au8 enhances intracellular bioenergetic reaction rates, without requiring energy input from cells, therefore increasing the cell's net energetic capacity. Bioenergetic deficit is observed in neurodegenerative disorders, such as ALS, MS and PD. Restoring the deficit is a key therapeutic objective to reverse the course of these diseases. In parallel to the Phase 2 trial, the company initiated a Phase 3 trial, as part of a consortium that is conducting the Healey ALS Platform Trial, which is a multi-center, multi-regimen clinical trial evaluating various drugs with a shared placebo arm, CNM-Au8 was amongst the first four drugs to be selected by Healey Center Science Advisory Committee from among the 30 applications from 10 different countries. Placebo patient data is pooled from studies arms to serve as the control for CNM-Au8 and other investigational agents explored in the trial. While the primary endpoint wasn't met, similarly to the earlier trial (RESCUE-ALS), a significant survival benefit was observed in the Healy trial as well (Figure 14). Complementing earlier results from the same trial, new analyses revealed that extended treatment with CNM-Au8 in the HEALEY ALS platform trial, spanning up to approximately 2.5 years, significantly decreased the mortality risk among ALS patients when compared to a historical placebo cohort from previous ALS trials.

RNS60 is designed by Revalesio (private) to address chronic neurodegenerative illnesses by mitochondrial dysfunction, including ALS. It has a distinct ability to activate intracellular signaling pathways that have anti-inflammatory impacts and encourage mitochondrial biogenesis, cell survival, and differentiation. RNS60 safeguards neurons and oligodendrocytes in the CNS, while regulating immune cell function to restore cellular homeostasis[33]. It is currently being evaluated in a Phase 2 clinical trial for ALS (NCT02988297).

Protein Homeostasis

SLS-005 (trehalose) is a type of disaccharide that has the ability to cross blood brain barrier. It can stabilize proteins and activate autophagy through the activation of TFEB, which is responsible for controlling the expression of genes involved in the breakdown of waste material in lysosomes. SLS-005 has shown promise as a potential treatment for various diseases characterized by abnormal accumulation of waste material in cells, such as neurodegenerative diseases. In animal models, SLS-005 has been found to decrease the buildup of harmful waste material and reduce the aggregation of misfolded

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[33] Vallarola A, Sironi F, Tortarolo M, Gatto N, De Gioia R, Pasetto L, De Paola M, Mariani A, Ghosh S, Watson R, Kalmes A, Bonetto V, Bendotti C. RNS60 exerts therapeutic effects in the SOD1 ALS mouse model through protective glia and peripheral nerve rescue. *J Neuroinflammation*. 2018 Mar 1;15(1):65. doi: 10.1186/s12974-018-1101-0. PMID: 29495962; PMCID: PMC5833072

proteins[34]. A Phase 2/3 randomized, double-blind, placebo-controlled study evaluated SLS-005 in 160 patients over 24 weeks and Seelos (SEEL – not rated). Although the research did not achieve statistical significance in both the primary and secondary outcome measures within the Full Analysis Set, it did demonstrate a 13% enhancement in Function and Mortality, with an 88% probability of success, compared to the pre-specified 98%. This suggests a potential indication of efficacy in a pre-defined subgroup.

Neuroinflammation

Albutein is a plasma exchange (PE) procedure aiming to modify the metabolic profile of plasma and cerebrospinal fluid in patients with ALS, by eliminating harmful substances associated with the disease[35]. With some efficacy signal showing in an open-label study by Grifols (GRF; Not Rated), further evaluation of PE-A in controlled studies involving more patients is warranted[36].

ALZT-OP1a is company's proprietary inhaled formulation of cromolyn, engineered to improve blood brain barrier permeability and bioavailability. Cromolyn is a mast-cell stabilizer that acts as an anti-inflammatory compound by suppressing cytokine release[37]. Currently it is under development by AZTherapies (Private) in a Phase 2a randomized, open-label, multi-center, multi-dose clinical trial in subjects with mild to moderate-stage ALS patients (NCT04428775).

ANX-005 is a humanized immunoglobulin G4 recombinant antibody against C1q[38] being developed by Annexon (ANNX; Not Rated). According to preliminary data from eight patients taking part in a Phase 2a clinical study, it showed a slowing of disease progression in adults with ALS (NCT04569435). Recruitment of up to 24 patients is underway at a number of locations across the US and Canada.

BLZ945 is an orally active, potent, and selective CSF-1R inhibitor, with potential effect on regulating microglia activity[39]. It is currently in Phase 2 open-label study for ALS (NCT04066244), run by Novartis (NVS; Not Rated).

Masitinib is a tyrosine kinase inhibitor that is in the late stage of development for ALS. Its unique characteristic is that it provides neuroprotection in both the CNS and PNS[40]. Following its positive Phase 2B/3 results, AB Science (AB; Not Rated) has launched a confirmatory Phase 3 study, with an optimized design that includes enrolment of patients at an earlier stage of their disease (NCT03127267). In 2022, the company applied for conditional Marketing Authorization to the EMA for masitinib for the treatment of ALS. In January 2024, EMA delayed issuing an opinion on whether to grant conditional approval or not. Ab-Science received approval from health authorities to proceed with a Phase 3 clinical trial of masitinib in ALS, advancing the tyrosine kinase inhibitor into a pivotal study to evaluate its potential to slow disease progression.

Tegoprubart is a humanized monoclonal antibody under investigation that targets CD40 Ligand (CD40L)[41], a membrane protein associated with enhanced peripheral immune reactions and neuroinflammation in individuals with ALS. In May 2022, a Phase 2a clinical trial was completed by Eledon (ELDN; Not Rated) for Tegoprubart (NCT04322149) with positive topline trial results indicating target engagement and a decrease in significant inflammatory biomarkers among patients with ALS.

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[41] Michels M, Danieslki LG, Vieira A, Florentino D, Dall'Igna D, Galant L, Sonai B, Vuolo F, Mina F, Pescador B, Dominguini D, Barichello T, Quevedo J, Dal-Pizzol F, Petronilho F. CD40-CD40 Ligand Pathway is a Major Component of Acute Neuroinflammation and Contributes to Long-term Cognitive Dysfunction after Sepsis. *Mol Med.* 2015 Mar 26;21(1):219-26. doi: 10.2119/molmed.2015.00070. PMID: 25822797; PMCID: PMC4503652.

COYA 302, developed by Coya Therapeutics (COYA; Buy) is an investigational immunomodulatory biologic combination therapy designed to enhance regulatory T-cell (Treg) function while suppressing pro-inflammatory monocytes and macrophages. COYA 302 combines proprietary low-dose interleukin-2 with CTLA-4 Ig and is being developed for subcutaneous administration in ALS and other neurodegenerative diseases. In 2025, COYA 302 reached several important regulatory and operational milestones. The FDA accepted the IND for COYA 302 in ALS in mid-2025, enabling the initiation of a multicenter Phase 2 clinical program. The trial was subsequently accepted as a NEALS-affiliated study, facilitating site activation and execution across leading ALS centers in the United States. In parallel, Health Canada issued a No Objection Letter, allowing the trial to expand into Canadian clinical sites and supporting broader patient recruitment.

The ALSTARS Trial, a Phase 2, randomized, double-blind, placebo-controlled study, was formally launched in the second half of 2025, and patient dosing began by December 2025. The study is designed to evaluate the safety and efficacy of COYA 302 over a 24-week treatment period, with clinical and biomarker endpoints relevant to ALS disease progression. Based on the trial design top-line Phase 2 data are expected after completion of enrollment and the 24-week treatment period, placing the anticipated readout in 2026, subject to enrollment pace and operational execution. This Phase 2 readout represents the next major value-inflection catalyst for Coya’s ALS program.

Cell Therapy

NurOwn employs mesenchymal stem cells derived from the patient's bone marrow, which are treated in a laboratory and then administered through intrathecal injection. The objective of this therapy is to offer neuroprotection, stimulate the development of new motor neurons, and enhance nerve-muscle interactions. In 2019, NurOwn failed to meet the primary endpoint of a Phase 3 trial (NCT03280056), causing specialists to question the effectiveness of the therapy. Following that, the FDA declined NurOwn's approval application in November 2022, but a sudden reversal took place when FDA planned to hold an Advisory Committee (AdCom) meeting to discuss BrainStorm Cell Therapeutics’ NurOwn. In April 2024, the company announced a Phase 3b confirmatory trial of NurOwn, after consultations with the FDA after an earlier Phase 3 setback. The company disclosed that the FDA has granted a written agreement under a special protocol assessment (SPA), outlining the design for the trial of NurOwn intended for ALS (BCLI; Not Rated).

Figure 12: Marketed Drugs for ALS

Drug	Company	Target(s)	Modality	Route of Administration	US Approval Year
Rilutek (Riluzole)	ADVANZ PHARMA	Glutamine	Small Molecule	Oral	1995
Radicava (Edaravone)	Mitsubishi Tanabe	Mitochondria	Small Molecule	Oral / Intravenous	2017
Exservan (Riluzole Oral Film)	Mitsubishi Tanabe	Glutamine	Small Molecule	Sublingual Oral Transmucosal	2019
Relyvrio (Tauroursodeoxycholic Acid & Sodium Phenylbutyrate)	Amylyx	Mitochondria	Small Molecule	Oral	2022 (Withdrawn in 2024)
Qalsody (Tofersen)	Biogen	SOD1	Antisense	Intrathecal	2023
NEURONATA-R (Lenzumestrocel)	CORESTEM	Stem cells	Cell Therapy	Intrathecal	N/A (Approved in Korea only)

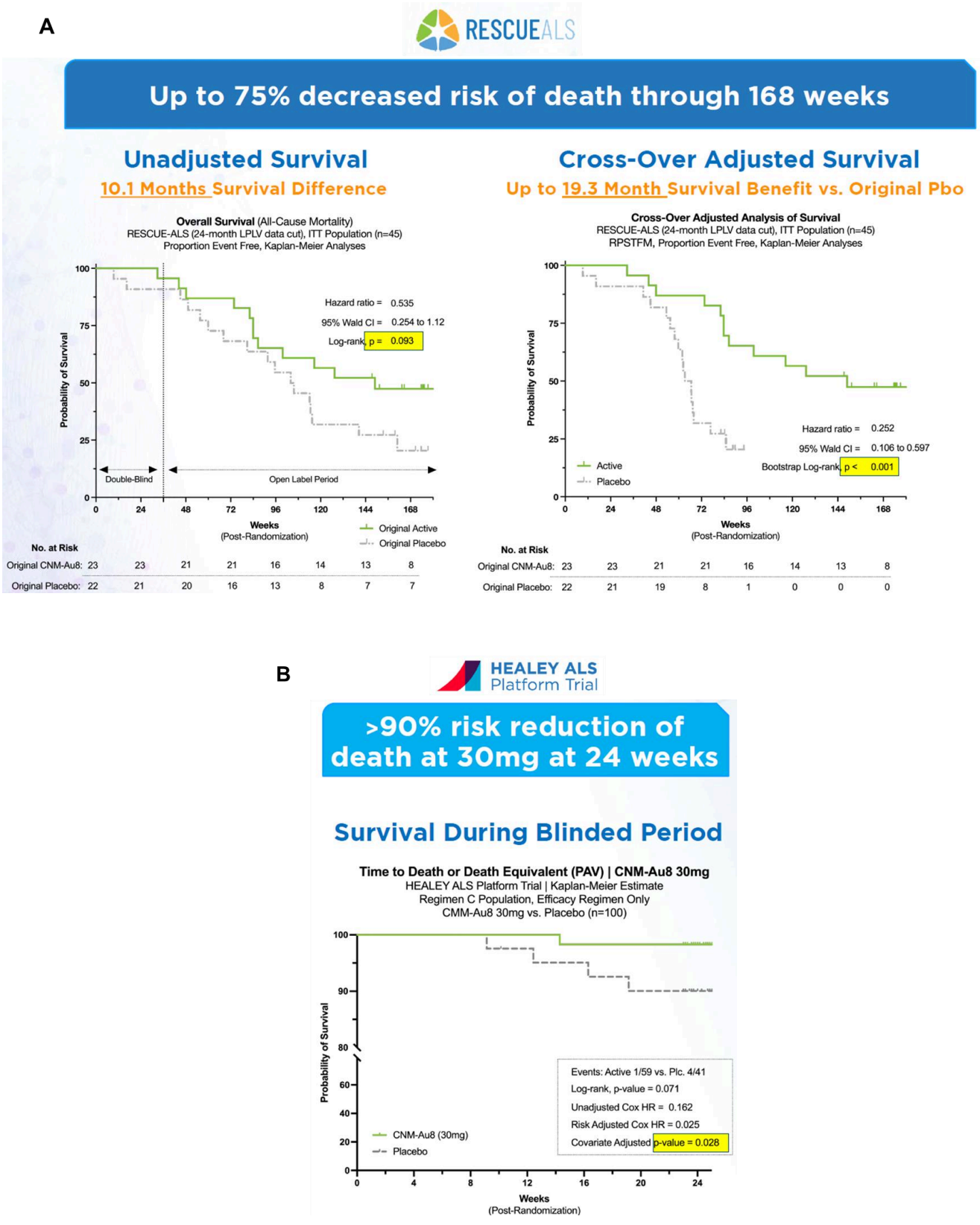
Source: BioMedTracker

Figure 13: Other Pipeline Drugs for ALS

Drug	Company	Addressable Patients	Target(s)	Modality	Phase
NurOwn	BrainStorm Cell Therapeutics	Familial & Sporadic ALS	Stem cells	Cell therapy	Phase IIIb
ION363	Ionis	Familial ALS (FUS mutation)	FUS	Antisense oligonucleotide	Phase III
Masitinib	AB Science	Familial & Sporadic ALS	Tyrosine kinase	Small molecule	Phase III
SLS-005	Seelos Therapeutics	Familial & Sporadic ALS	TFEB	Small molecule	Phase II/III
CNM-Au8	Clene	Familial & Sporadic ALS	Mitochondrial electron transport chain	Small molecule	Phase II/III
Albutein	Grifols	Familial & Sporadic ALS	Albumin	Protein therapy	Phase II
ALZT-OP1a	AZTherapies	Familial & Sporadic ALS	Mast cells	Small molecule	Phase II
ANX-005	Annexon	Familial & Sporadic ALS	C1q / complement pathway	Monoclonal antibody	Phase II
AP-101	Neurimmune / AL-S Pharma	Familial & Sporadic ALS	Misfolded SOD1	Monoclonal antibody	Phase II
BLZ945	Novartis	Familial & Sporadic ALS	CSF-1R	Small molecule	Phase II
COYA 302	COYA	Familial & Sporadic ALS	IL-2 & Treg Cells	Small molecule	Phase II
EPI-589	Sumitomo	Familial & Sporadic ALS	Mitochondrial electron transport chain	Small molecule	Phase II
LAM-002	AI Therapeutics	Familial ALS (C9orf72 mutation)	PIKFYVE	Small molecule	Phase II
PTC857	PTC Therapeutics	Familial & Sporadic ALS	15-Lipoxygenase	Small molecule	Phase II
RNS60	Revalesio	Familial & Sporadic ALS	PI3K-Akt-BAD pathway	Oxygenated nanobubbles	Phase II
Tegoprubart	Eledon	Familial & Sporadic ALS	CD40 / gp39, Fc receptors	Monoclonal antibody	Phase II

Source: BioMedTracker

Figure 14: Survival Benefit in Two Different Studies for CNM-Au8



Source: Clene Company Presentation, March 2024

PRICING, MARKET POTENTIAL, NPV

ALS patients currently have only three treatment options: riluzole, a generic oral pill, RADICAVA, an IV infusion and RELYVRIO all of which showed a very modest benefit on the ALSFRS-R scale in pivotal studies. Following a failure in a confirmatory trial, Amylyx (AMLX; Not Rated) initiated the voluntary withdrawal process for RELYVRIO from the market. RELYVRIO would not be accessible for new patients. For patients currently undergoing treatment in the US and Canada who choose to continue therapy can transition to a complimentary drug program.

The annual cost of RADICAVA and RELYVRIO is ~$160,000 in the US, which doesn't include cost of administration, such as nursing services and supplies.[42] We assume, that if successful, ibudilast can be priced, conservatively, at least at par with these drugs in the US. If MediciNova obtains approval following a pivotal trial, the drug could be launched in 2028 in the US and in 2029 in EU5 countries. We assume that five years following launch, in 2042, the drug could achieve ~$335M in sales in the US (10% market share; Figure 15) and ~$230M in EU5 (10% market share; Figure 15), where the drug would be sold at a price 2/3 of the U.S. list price, in our calculation.

The combined risk-adjusted (40% probability of success) NPV for ibudilast is ~$600M ($11/share), according to our model (Figure 16).

[42] https://www.ajmc.com/view/als-managed-care-considerations

Figure 15: Market Model (US + EU5)

ALS Market - US			2024A	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E	2034E	2035E	2036E	2037E	2038E	2039E	2040E	2041E	2042E
($ in thousands)																					
ALS prevalence*			16,338	16,453	16,568	16,684	16,801	16,918	17,037	17,156	17,276	17,397	17,519	17,641	17,765	17,889	18,014	18,141	18,268	18,395	18,524
Market Penetration							1%	3%	5%	8%	10%	13%	15%	15%	15%	15%	15%	15%	15%	15%	15%
Patients treated							168	508	852	1,372	1,728	2,175	2,628	2,646	2,665	2,683	2,702	2,721	2,740	2,759	2,779
Treatment cost**							$160	$168	$176	$185	$194	$204	$214	$225	$236	$248	$261	$274	$287	$302	$317
Total US sales							**$26,881**	**$85,268**	**$150,264**	**$254,210**	**$335,986**	**$444,069**	**$563,443**	**$595,757**	**$629,923**	**$666,049**	**$704,247**	**$744,636**	**$787,341**	**$832,495**	**$880,238**
COGS							($1,344)	($4,263)	($7,513)	($12,710)	($16,799)	($22,203)	($28,172)	($29,788)	($31,496)	($33,302)	($35,212)	($37,232)	($39,367)	($41,625)	($44,012)
R&D			($3,597)	($3,741)	($3,741)	($3,741)	($3,741)	($3,741)	($3,741)	($3,741)	($3,741)	($3,741)	($3,741)	($3,741)	($3,741)	($3,741)	($3,741)	($3,741)	($3,741)	($3,741)	($3,741)
SG&A			($2,740)	($3,206)	($3,612)	($3,612)	($26,881)	($42,634)	($45,079)	($45,079)	($45,079)	($45,079)	($45,079)	($45,079)	($45,079)	($45,079)	($45,079)	($45,079)	($45,079)	($45,079)	($45,079)
Operating expenses			($6,338)	($6,947)	($7,353)	($7,353)	($31,966)	($50,638)	($56,333)	($61,531)	($65,619)	($71,023)	($76,992)	($78,608)	($80,316)	($82,123)	($84,032)	($86,052)	($88,187)	($90,445)	($92,832)
EBT			**($6,338)**	**($6,947)**	**($7,353)**	**($7,353)**	**($5,085)**	**$34,630**	**$93,930**	**$192,679**	**$270,367**	**$373,045**	**$486,451**	**$517,149**	**$549,607**	**$583,927**	**$620,215**	**$658,584**	**$699,154**	**$742,050**	**$787,406**
Probability of success	40%		*40%*	*40%*	*90%*	*90%*	*90%*	*100%*	*100%*	*100%*	*100%*	*100%*	*100%*	*100%*	*100%*	*100%*	*100%*	*100%*	*100%*	*100%*	*100%*
Probability-adjusted EBT			**($6,338)**	**($6,947)**	**($7,353)**	**($7,353)**	**($5,085)**	**$13,852**	**$37,572**	**$77,072**	**$108,147**	**$149,218**	**$194,580**	**$206,860**	**$219,843**	**$233,571**	**$248,086**	**$263,434**	**$279,661**	**$296,820**	**$314,963**
Discount rate	15%																				
NPV of EBT		**$504,321**																			

*Prevalence: 5 out of 100,000 people; https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6735526/

**The annual cost of treatment with edaravone is $160,000 in the US: https://www.ajmc.com/view/als-managed-care-considerations.

Source: MediciNova SEC filings, Lucid Capital Markets estimates

ALS Market - EU5			2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E	2034E	2035E	2036E	2037E	2038E	2039E	2040E	2041E	2042E
($ in thousands)																					
ALS prevalence*			16,338	16,453	16,568	16,684	16,801	16,918	17,037	17,156	17,276	17,397	17,519	17,641	17,765	17,889	18,014	18,141	18,268	18,395	18,524
Market Penetration								1%	3%	5%	8%	10%	13%	15%	15%	15%	15%	15%	15%	15%	15%
Patients treated								169	511	858	1,382	1,740	2,190	2,646	2,665	2,683	2,702	2,721	2,740	2,759	2,779
Treatment cost**								$109	$115	$120	$126	$133	$139	$146	$154	$161	$169	$178	$187	$196	$206
Total EU5 sales								**$18,475**	**$58,603**	**$103,273**	**$174,713**	**$230,916**	**$305,198**	**$387,242**	**$409,450**	**$432,932**	**$457,761**	**$484,013**	**$511,772**	**$541,122**	**$572,155**
COGS								($924)	($2,930)	($5,164)	($8,736)	($11,546)	($15,260)	($19,362)	($20,473)	($21,647)	($22,888)	($24,201)	($25,589)	($27,056)	($28,608)
R&D			($3,597)	($3,741)	($3,741)	($3,741)	($3,741)	($3,741)	($3,741)	($3,741)	($3,741)	($3,741)	($3,741)	($3,741)	($3,741)	($3,741)	($3,741)	($3,741)	($3,741)	($3,741)	($3,741)
SG&A			($2,740)	($3,206)	($3,612)	($3,612)	($3,612)	($18,475)	($29,301)	($30,982)	($30,982)	($30,982)	($30,982)	($30,982)	($30,982)	($30,982)	($30,982)	($30,982)	($30,982)	($30,982)	($30,982)
Operating expenses			($6,338)	($6,947)	($7,353)	($7,353)	($7,353)	($23,139)	($35,972)	($39,886)	($43,458)	($46,269)	($49,983)	($54,085)	($55,195)	($56,369)	($57,611)	($58,923)	($60,311)	($61,779)	($63,331)
EBT			**($6,338)**	**($6,947)**	**($7,353)**	**($7,353)**	**($7,353)**	**($4,665)**	**$22,630**	**$63,386**	**$131,254**	**$184,647**	**$255,216**	**$333,157**	**$354,255**	**$376,563**	**$400,150**	**$425,090**	**$451,460**	**$479,343**	**$508,824**
Probability of success	40%		*40%*	*40%*	*90%*	*90%*	*90%*	*100%*	*100%*	*100%*	*100%*	*100%*	*100%*	*100%*	*100%*	*100%*	*100%*	*100%*	*100%*	*100%*	*100%*
Probability-adjusted EBT			**($6,338)**	**($6,947)**	**($7,353)**	**($7,353)**	**($7,353)**	**($4,665)**	**$9,052**	**$25,355**	**$52,502**	**$73,859**	**$102,086**	**$133,263**	**$141,702**	**$150,625**	**$160,060**	**$170,036**	**$180,584**	**$191,737**	**$203,530**
Discount rate	15%																				
NPV of EBT		**$272,100**																			

*We assume a similar prevalence to the US market

**We assume 66% of the treatment cost in the US

Source: MediciNova SEC filings, Lucid Capital Markets estimates

Figure 16: NPV Model

NPV Model (in thousands)			2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E	2032E	2033E	2034E	2035E	2036E	2037E	2038E	2039E	2040E	2041E	2042E
Probability-adjusted EBT																					
US			($6,338)	($6,947)	($7,353)	($7,353)	($5,085)	$13,852	$37,572	$77,072	$108,147	$149,218	$194,580	$206,860	$219,843	$233,571	$248,086	$263,434	$279,661	$296,820	$314,963
EU5			($6,338)	($6,947)	($7,353)	($7,353)	($7,353)	($4,665)	$9,052	$25,355	$52,502	$73,859	$102,086	$133,263	$141,702	$150,625	$160,060	$170,036	$180,584	$191,737	$203,530
Total probability-adjusted EBT			**($12,675)**	**($13,893)**	**($14,706)**	**($14,706)**	**($12,438)**	**$9,187**	**$46,624**	**$102,426**	**$160,648**	**$223,077**	**$296,667**	**$340,122**	**$361,545**	**$384,196**	**$408,146**	**$433,470**	**$460,246**	**$488,557**	**$518,492**
Taxes (21%)										($21,510)	($33,736)	($46,846)	($62,300)	($71,426)	($75,924)	($80,681)	($85,711)	($91,029)	($96,652)	($102,597)	($108,883)
Probability-adjusted EAT**			**($12,675)**	**($13,893)**	**($14,706)**	**($14,706)**	**($12,438)**	**$9,187**	**$46,624**	**$80,917**	**$126,912**	**$176,231**	**$234,367**	**$268,697**	**$285,620**	**$303,515**	**$322,435**	**$342,441**	**$363,594**	**$385,960**	**$409,609**
Discount rate	15%																				
NPV of probability-adjusted EAT		**$612,605**																			
Number of shares outstanding		54,046																			
NPV of probability-adjusted EAT/sh		**$11**																			

*EBT=earnings before taxes

**EAT=earnings after taxes

*** By 2031E, tax was adjusted based on NOL carryforward

Source: Lucid Capital Markets estimates

In thousands except per share values

MANAGEMENT

Yuichi Iwaki, M.D., Ph.D. – President and Chief Executive Officer, and Founder

Dr. Iwaki holds three professorships at the University of Southern California School of Medicine in the Departments of Urology, Surgery and Pathology and has been Director of the Transplantation Immunology and Immunogenetic Laboratory since 1992. He is also a visiting professor at the Nihon University School of Medicine, Kyushu University and Toho University, School of Medicine in Japan. Prior to joining the faculty at the University of Southern California School of Medicine, Dr. Iwaki held professorships at the University of Pittsburgh School of Medicine in the Departments of Surgery and Pathology from 1989 through 1991. He received both his M.D. and Ph.D. degrees from Sapporo Medical School in Sapporo, Japan. Dr. Iwaki is the author of 200 peer-reviewed publications and more than 40 books. He has been advising pharmaceutical companies and venture capital funds regarding research and investment strategies for over 30 years and is a board member of several biotechnology companies.

Kazuko Matsuda, M.D., Ph.D, MPH – Chief Medical Officer

Dr. Matsuda has served as Chief Medical Officer and previously as Vice President of Clinical Development for MediciNova since 2010 and is responsible for all clinical development. Previously, Dr. Matsuda was a clinical advisor to MediciNova for its MN-221 and MN-166 development programs. Prior to joining MediciNova, Dr. Matsuda was assistant professor, University of Southern California, Keck School of Medicine after an appointment at the Children's Hospital Los Angeles. Dr. Matsuda commenced her residency in internal medicine/pediatrics at Michigan State University and completed a pediatric residency at Loma Linda University. She is a board certified pediatrician in both the United States and Japan. Dr. Matsuda received her M.D. and Ph.D. from Sapporo Medical School and MPH from Harvard University, School of Public Health.

David H. Crean, Ph.D. – Chief Business Officer

Dr. Crean has served as Chief Business Officer since May 2021. Dr. Crean is President and CEO of Coast BioVentures LLC, an emerging life sciences venture fund with a focus on the biopharmaceutical industry. In parallel, he is a managing partner with Cardiff Advisory LLC, a strategic and financial advisory firm focused on mergers, acquisitions and partnering transactions with life science and healthcare companies. Previously, Dr. Crean served as Managing Director for Objective Capital Partners, LLC driving its practice in the same practice domains, and currently serves in a senior advisory capacity with his former firm. Dr. Crean currently serves in leading roles on the Boards of Directors for Histogen, Inc. as Board Chairman and the former Chairman of the Audit Committee, and the California Life Sciences Association ("CLSA") as a member of the Executive Committee. He is a limited partner with a leading life sciences venture fund, Mesa Verde Venture Partners, and a member of Corporate Directors Forum and BIOCOM. Dr. Crean is also a contributing author for PharmaBoardroom.com and Forbes.com through his work with Forbes Los Angeles Business Council. Dr. Crean holds FINRA Series 79 and Series 63 licenses and is a Registered Investment Banking Representative of BA Securities LLC, Member FINRA SIPC. He has an M.B.A. with a finance concentration from Pepperdine University, a Ph.D. in Biophysics and a M.S. in Oncology from the State University of New York at Buffalo, and a B.S. in Biology/ Pre-Med from Canisius College.

RISKS

MediciNova is a development-stage company, and investment in it carries inherent risks.

Clinical Trial Risk

Ibudilast is currently being evaluated in Phase 2b/3 study (COMBAT-ALS). While early data is encouraging and supports further clinical development, Ibudilast may ultimately not be deemed safe or effective in ongoing and upcoming trials. So far, interim safety analyses of Ibudilast have not identified any significant safety concerns.

Regulatory Risk

The FDA and European regulators may require additional clinical trials beyond those currently anticipated by MediciNova.

Competition Risk

Ibudilast faces competition from other treatment for ALS.

Financing Risk

As of September 2025, the company's cash position was approximately $33M. We estimate the company will use around $12M in 2026. MediciNova may need to raise additional equity capital to support its clinical development unless it can secure licensing deals for its development-stage assets. However, financing may not be available on favorable terms, if at all.

Income Statements

MediciNova												Elemer Piros, Ph.D. 646-350-1528 epiros@lucidcm.com
			2025E					2026E				
($ In thousands, except per share data)	**2023A**	**2024A**	**1QA**	**2QA**	**3QA**	**4QE**	**2025E**	**1QE**	**2QE**	**3QE**	**4QE**	**2026E**
Revenue	$1,000	-	-	$135	$123	-	$258	-	-	-	-	**-**
Operating expenses:												
Cost of Service	**-**	**-**	-	($116)	($115)	-	($232)	-	-	-	-	**-**
Research and development	($5,658)	($7,195)	($1,840)	($2,189)	($1,583)	($1,870)	($7,482)	($1,870)	($1,870)	($1,870)	($1,870)	($7,482)
General and administrative	($5,242)	($5,481)	($1,363)	($1,437)	($1,806)	($1,806)	($6,412)	($1,806)	($1,806)	($1,806)	($1,806)	($7,224)
Operating Loss	**($9,900)**	**($12,675)**	**($3,203)**	**($3,607)**	**($3,381)**	**($3,677)**	**($13,867)**	**($3,677)**	**($3,677)**	**($3,677)**	**($3,677)**	**($14,706)**
Interest Income	$1,835	$1,671	$336	$325	$341	$334	$1,336	$334	$334	$334	$334	$1,336
Other Income (Expense)	($503)	($39)	$2	$1	($10)	-	($7)	-	-	-	-	**-**
Net Loss	**($8,568)**	**($11,044)**	**($2,864)**	**($3,281)**	**($3,050)**	**($3,343)**	**($12,538)**	(3,343)	(3,343)	(3,343)	(3,343)	**(13,370)**
Basic and diluted loss per share	($0.17)	($0.23)	($0.06)	($0.07)	($0.06)	($0.07)	($0.26)	($0.07)	($0.07)	($0.06)	($0.06)	($0.26)
Weighted average number of shares outstanding	49,046	49,046	49,046	49,046	49,046	49,046	**49,046**	49,046	49,046	54,046	54,046	**51,546**

Source: MediciNova SEC filings, Lucid Capital Markets estimates

Risks for: Medicinova Inc (MNOV)

MediciNova is a development-stage company, and investment in it carries inherent risks.

Clinical Trial Risk

Ibudilast is currently being evaluated in Phase 2b/3 study (COMBAT-ALS). While early data is encouraging and supports further clinical development, Ibudilast may ultimately not be deemed safe or effective in ongoing and upcoming trials. So far, interim safety analyses of Ibudilast have not identified any significant safety concerns.

Regulatory Risk

The FDA and European regulators may require additional clinical trials beyond those currently anticipated by MediciNova.

Competition Risk

Ibudilast faces competition from other treatments for ALS.

Financing Risk

As of September 2025, the company's cash position was approximately $33M. We estimate the company will use around $12M in 2026. MediciNova may need to raise additional equity capital to support its clinical development unless it can secure licensing deals for its development-stage assets. However, financing may not be available on favorable terms, if at all.

Valuation for: Medicinova Inc (MNOV)

We arrive at our 12-month price target of $11/share by assessing the after-tax, risk-adjusted NPV of potential future cash flows from the company's MN-166 program. The probability-adjusted, fully taxed (21%) NPV (15% discount rate) of potential cash flows through 2042 is ~ $600M or $11/share, corresponding to our 12-month price target.

Company Description for: Medicinova Inc (MNOV)

MediciNova, Inc., a biopharmaceutical company, focuses on developing novel and small molecule therapeutics for the treatment of serious diseases with unmet medical needs in the United States. The company develops MN-166 (ibudilast), an oral anti-inflammatory and neuroprotective agent in Phase 2b/3 clinical trial for treating neurological and other disorders, such as progressive multiple sclerosis, amyotrophic lateral sclerosis, chemotherapy-induced peripheral neuropathy, degenerative cervical myelopathy, glioblastoma, and substance dependence and addiction, as well as prevention of acute respiratory distress syndrome, and long COVID. It is also developing MN-001 (tipelukast), an orally bioavailable small molecule compound in Phase 2 clinical trial to treat fibrotic and other metabolic disorders, including nonalcoholic fatty liver disease and hypertriglycedemia. The company has a license agreement with Kyorin Pharmaceuticals for the development and commercialization of MN-166 and MN-001.

Appendix

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Neutral: We generally believe “Neutral” rated stocks will have an average risk-adjusted total return over the next 12 months.

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Buy: 79.8%	Buy: 82.1%
Neutral: 20.2%	Neutral: 17.9%
Sell: 0.0%	Sell: 0.0%
Not Rated: 0.0%	Not Rated: 0.0%

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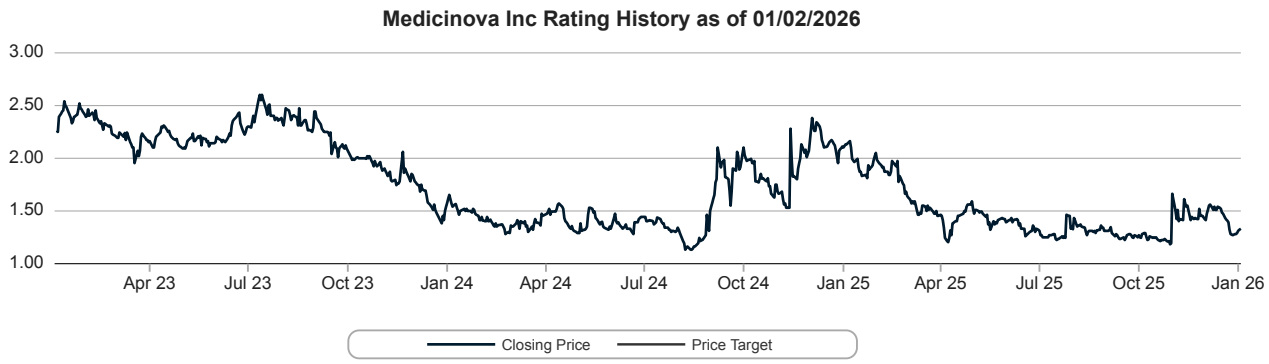
Medicinova Inc Rating History as of 01/02/2026
3.00
2.50
2.00
1.50
1.00
Apr 23
Jul 23
Oct 23
Jan 24
Apr 24
Jul 24
Oct 24
Jan 25
Apr 25
Jul 25
Oct 25
Jan 26
Closing Price
Price Target