2026年3月17日

H.C. Wainwright & Co.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3月16日、米国ニューヨークに本拠を置く投資銀行H.C. Wainwright & Co.のアナリストであるLander Egaña Gorroño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。

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MediciNova, Inc.（メディシノバ・インク）
東京事務所 IR担当
E-mail　infojapan@medicinova.com
URL　https://medicinova.jp/

MediciNova, Inc. (MNOV)
Rating: Buy

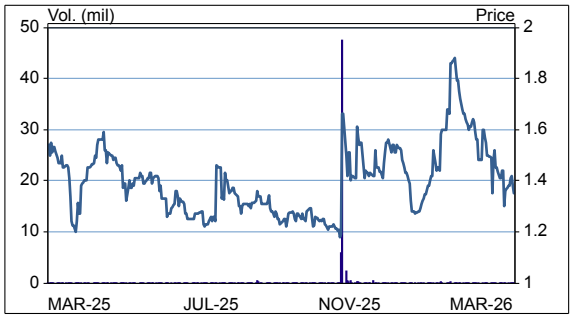
Lander Egaña Gorroño, Ph.D.
212-916-3977
legana@hcwresearch.com
Joseph Pantginis, Ph.D.
646-975-6968
jpantginis@hcwresearch.com

A Novo Approach to Multi-Target Medicine; Initiating at Buy and $10 PT

Stock Data	3/13/2026
Price	$1.35
Exchange	NASDAQ
Price Target	$10.00
52-Week High	$1.96
52-Week Low	$1.13
Enterprise Value (M)	$36
Market Cap (M)	$66
Shares Outstanding (M)	49.2
3 Month Avg Volume	74,619
Short Interest (M)	0.19
Balance Sheet Metrics	
Cash (M)	$30.8
Total Debt (M)	$0.0
Total Cash/Share	$0.63

EPS ($) Diluted			
Full Year - Dec	2025E	2026E	2027E
1Q	(0.06)A	(0.06)	--
2Q	(0.07)A	(0.06)	--
3Q	(0.06)A	(0.06)	--
4Q	(0.06)A	(0.08)	--
FY	(0.24)	(0.26)	(0.43)

Revenue ($M)			
Full Year - Dec	2025E	2026E	2027E
1Q	0.0A	0.0	--
2Q	0.1A	0.1	--
3Q	0.1A	0.1	--
4Q	0.2A	0.2	--
FY	0.4A	0.5	0.7



(Multi)targeting converging pathways in complex diseases. We are initiating coverage of MediciNova with a Buy rating and $10 price target. MediciNova is a clinical-stage biotechnology company developing multi-target small molecule therapies across a broad pipeline, primarily focused on neurodegenerative and metabolic/fibrotic diseases with significant unmet medical need. Core pipeline assets include ibudilast (MN-166), currently in Phase 2b/3 studies for amyotrophic lateral sclerosis (ALS), and tipelukast (MN-001), under Phase 2 evaluation for the treatment of hypertriglyceridemia (HTG) and nonalcoholic fatty liver disease (NAFLD) in patients with type 2 diabetes (T2D). Both candidates leverage multi-modal MoA intended to enhance efficacy relative to single-target therapies by simultaneously modulating multiple biological pathways, promoting synergistic activity, and potentially addressing comorbid conditions with a single therapy. Ibudilast demonstrated stabilization or improvement in several functional ALS scores and prolonged survival in Phase 2 studies. The Phase 2b/3 COMBAT-ALS trial aims to validate ibudilast's longer-term efficacy in a larger ALS population, and inform next regulatory/clinical steps (topline data by YE26). For tipelukast, following preclinical data demonstrating significant anti-fibrotic effects, and clinically meaningful triglyceride reductions in NAFLD patients with HTG, which were greater in those with concomitant T2D, results from the ongoing Phase 2 NATG-202 trial (topline data in mid-2026) aim to support a registrational trial in T2D patients with HTG and NAFLD. Current cash position should provide runway through ibudilast (Phase 2b/3) and tipelukast (Phase 2) readouts and, if results are positive, the initiation of later-stage trials. With the support of MediciNova's disciplined operational strategy and strong focus on execution, ongoing programs are well-positioned to achieve favorable data-driven clinical milestones and progress in their respective indications, in our belief.

Expanding optionality; diversified upside with limited spend. MediciNova structures its pipeline around internally-funded core programs (strategic priority; ALS and HTG/NAFLD/T2D) and capital-efficient, non-core ibudilast programs supported primarily through non-dilutive government grant funding. By modulating neuroprotective and immunosuppressive pathways implicated across neurodegenerative, neurological, and immunologically active disorders, ibudilast holds potential for broad multi-indication applicability rooted in a shared biological mechanism. This model enables focused investment in priority indications (ALS) while expanding the clinical reach of ibudilast through external collaborations. We view the non-core portfolio (more below) as a meaningful value driver for the company, offering: 1) capital-efficient development with minimal internal R&D spend; 2) diversified clinical risk for ibudilast beyond ALS; and 3) a strategic pathway to potential partnerships for late-stage development and commercialization. Collectively, this framework enhances both downside protection and long-term optionality across indications, in our belief.

Early functional and survival signals meet ibudilast's late-stage validation; Phase 2b/3 COMBAT-ALS data by YE26. MediciNova in-licensed ibudilast from Kyorin Pharmaceutical (TSE:4569; OTC:KYRNF) in 2004, following approval in Japan and South Korea for the treatment of asthma and post-stroke complications (i.e. dizziness) in the late 1980s. Ibudilast is a multi-target, oral small molecule inhibitor of phosphodiesterase (PDE), macrophage migration inhibitory factor (MIF), and toll-like receptor (TLR)-mediated pathways, that presents a multi-modal anti-inflammatory and neuroprotective MoA. The responder analysis from the Phase 2 ALS-1201 clinical trial evaluating ibudilast, in combination with riluzole SoC, in 49 ALS patients showed higher rates of stable or improved ALS Functional Rating Scale-Revised (ALSFRS-R), manual muscle testing (MMT), and five-item ALS Assessment Questionnaire (ALSAQ-5) scores at month six compared to the placebo + riluzole group. In addition, subjects who completed six or 12 months of treatment exhibited improved survival (p=0.0025) of up to 30 months following treatment. Ibudilast was generally safe and tolerable when administered with riluzole. While we acknowledge ALS-1201's single-site risk and the potential confounding effect of riluzole combination, our positive view is primarily driven by the favorable ALSFRS-R outcomes. Notably, prior late-stage ALS trials have shown that investigational therapies often struggle to sustain long-term functional ALSFRS-R improvements and meet clinical endpoints. We expect the ongoing Phase 2b/3 COMBAT-ALS trial to validate prior efficacy (functional and survival) and safety signals in a larger population in the longer-term (12 months), and inform next steps for ibudilast, including potential progression to regulatory filing or a confirmatory pivotal trial. Enrollment in COMBAT-ALS has been completed with a total of 234 randomized patients, and topline data are anticipated by YE26. While COMBAT-ALS does not incorporate prespecified biomarker endpoints, the ongoing NIH-supported SEANOBI Expanded Access Program (EAP) aims to generate meaningful neurofilament light chain (NfL) and clinical outcome (ALSFRS-R) data from the real-world ALS population. We believe that its broad, genotype-agnostic, and multi-modal approach, together with Phase 2 evidence of favorable safety and efficacy, support the clinical and regulatory advancement of ibudilast as a novel treatment to delay ALS disease progression.

Tipelukast set to reshape the HTG-NAFLD-T2D axis; Phase 2 NATG-202 data in mid-2026. Tipelukast was in-licensed from Kyorin in 2002 as an orally bioavailable small molecule with multiple MoA targeting inflammation (5-lipoxygenase (5-LO)/ leukotriene (LTs), PDE, and CD36 pathways), fibrosis, and lipid metabolism. Preclinical studies demonstrated anti-fibrotic effects in livers from NAFLD animal models, and inhibition of triglyceride (TG) biosynthesis and lipid-modifying activity in hepatotoxic and monocytic human cell lines, respectively. Of note, HTG, NAFLD, and T2D are pathophysiologically interconnected through systemic insulin resistance, dysregulated lipid metabolism, and chronic inflammation, forming a self-reinforcing metabolic axis. An open-label Phase 2 trial in patients with NAFLD and HTG (n=14) showed that tipelukast treatment led to early serum TG reductions (28.8%; p=0.00006) at week eight. Interestingly, subgroup analyses demonstrated that compared to participants without T2D (n=9), T2D patients (n=10) showed greater TG reductions at week eight (50.8% vs. 17.8% reduction in non-T2D), and a greater high-density lipoprotein cholesterol (HDL-C) increases (15.8% vs. 1.0% in non-T2D; p<0.0002), strengthening the case for prioritizing T2D patients in further clinical evaluation. There were no clinically significant safety and tolerability issues related to tipelukast. The Phase 2 NATG-202 trial is evaluating tipelukast in T2D patients with HTG and NAFLD over 24 weeks. Enrollment has been completed, and topline data are anticipated in mid-2026. We believe these results could mark a key inflection point supporting tipelukast's advancement into Phase 3 studies. Although multiple agents are in development for NAFLD, tipelukast is uniquely positioned in targeting both HTG and NAFLD driven by T2D, offering a more holistic therapeutic approach.

Broad indication optionality strengthens strategic collaboration prospects for ibudilast. MediciNova's non-core pipeline strategy is characterized by a differentiated "platform-in-a-molecule" approach focused on ibudilast. The likelihood of ibudilast's multi-indication potential is reinforced by its multi-modal MoA and extensive human safety data pre- and post-approval in Japan and South Korea. Non-core programs include clinical development in progressive multiple sclerosis (MS; Phase 2b completed), substance dependence (Phase 2 ongoing in methamphetamine dependence), chemotherapy-induced peripheral neuropathy (CPIN; Phase 2b ongoing), degenerative cervical myelopathy (DCM; Phase 3 ongoing), glioblastoma (Phase 1/2 completed), acute respiratory distress syndrome (ARDS; Phase 2 completed), and Long COVID (Phase 2/3 ongoing). On top of ALS, the FDA granted Fast Track designations to ibudilast for the treatment of progressive MS and methamphetamine dependence. With respect to the lead, non-core MS program, ibudilast showed ability to significantly reduce the rate of whole-brain atrophy (48% reduction) vs. placebo (p=0.04) in these patients. Ibudilast also demonstrated a 26% reduction (HR=0.74) in the risk of confirmed disability progression, with the greatest benefits observed in secondary progressive MS patients without relapse (46% risk reduction; HR=0.538). MediciNova finalized the design of a future registrational trial, and the progressive MS program is Phase 3-ready pending potential collaborators and/or partnerships.

Valuation and Risks. We are instituting a Buy rating and $10 price target. Our valuation is based on our clinical net present value (NPV) model, which allows us to flex multiple assumptions affecting a drug's profile. We currently value MediciNova based on the contribution of its core clinical-stage assets, ibudilast (MN-166) in ALS (15% PoS; 33% contribution) and tipelukast (MN-001) for the treatment of HTG and NAFLD due to T2D (20% PoS; 67% contribution) in the U.S. Moving forward, we believe significant upside potential exists based on: (1) attaining higher market penetration than currently projected in the above-mentioned indications; (2) augmenting projected chances of success based on the progress of the clinical candidates; (3) adding additional commercial geographies; and (4) progress of non-core programs through licensing deals and/or collaboration agreements. Factors that could impede reaching our PT include failed or inconclusive clinical trials, the inability of the company to secure adequate funding to progress its drugs through the development pathway or the occurrence of dilutive capital raises.

Company Background and Summary

MediciNova Inc., is a clinical-stage biotechnology company developing novel, multi-target small molecule therapies across a broad pipeline, primarily focused on neurodegenerative and metabolic/fibrotic diseases with significant unmet medical need. Following formation in 2000 and listing on the Hercules Market of the Osaka Securities Exchange/Standard Market of the Tokyo Stock Exchange (Code: 4875) in 2005, MediciNova began trading on the NASDAQ Global Market (dual listing) on December 7, 2006, with net proceeds from the U.S. IPO totaling approximately $10.64 million. The company acquired exclusive rights to its lead clinical-stage assets, ibudilast (MN-166) and tipelukast (MN-001) through licensing agreements with Kyorin Pharmaceutical Co. (TSE:4569; OTC:KYRNF), and utilized prior preclinical and early clinical data to prepare IND applications and advance the programs in the U.S. MediciNova categorizes its pipeline into internally funded core programs (strategic priority) and non-dilutive, partnered, non-core programs typically funded by third parties (investigator-initiated studies (ISS)). Core programs include ibudilast, currently in Phase 2b/3 studies for amyotrophic lateral sclerosis (ALS), and tipelukast, under Phase 2 evaluation for the treatment of hypertriglyceridemia (HTG) and nonalcoholic fatty liver disease (NAFLD) in type 2 diabetic (T2D) patients.

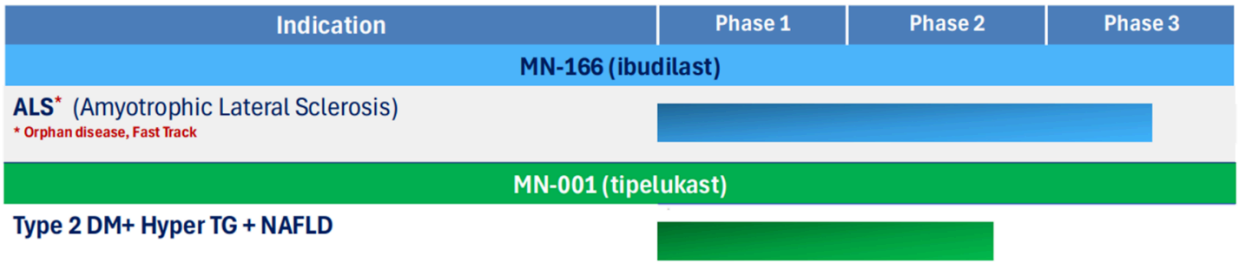
Ibudilast is a multi-target, oral small molecule inhibitor of phosphodiesterase (PDE), macrophage migration inhibitory factor (MIF), and toll-like receptor (TLR)-mediated pathways, that presents a multi-modal anti-inflammatory and neuroprotective MoA. The ALS-1201 Phase 2 study of ibudilast + riluzole SoC demonstrated stable or improved functional (ALS Functional Rating Scale-Revised (ALSFRS-R) and manual muscle testing (MMT)) and QoL (five-item ALS Assessment Questionnaire (ALSAQ-5)) scores at six months vs. placebo + riluzole. In addition, subjects who completed six or 12 months of treatment exhibited improved survival (p=0.0025) of up to 30 months following treatment. Ibudilast was generally safe and tolerable when administered with riluzole. The ongoing Phase 2b/3 COMBAT-ALS trials aims to validate prior efficacy and safety signals over 12 months in a larger population, and inform potential progression into regulatory filing or a confirmatory pivotal trial. Enrollment in COMBAT-ALS has been completed with a total of 234 randomized patients, and topline data are anticipated by YE26. We believe that its broad, genotype-agnostic, and multi-modal approach, together with Phase 2 evidence of favorable safety and efficacy support ibudilast's clinical and regulatory progress in ALS.

Tipelukast is an orally bioavailable small molecule with multiple MoA targeting inflammation (5-lipoxygenase (5-LO)/ leukotriene (LTs), PDE, and CD36 pathways), fibrosis, and lipid metabolism. An open-label Phase 2 trial in patients with NAFLD and HTG (n=14) showed that treatment was associated with significant, early serum triglyceride (TG) level reductions (28.8% reduction; p=0.00006) at week eight. Interestingly, subgroup analyses demonstrated that compared to participants without T2D (n=9), T2D patients (n=10) showed a greater reduction in serum TG levels at week eight (50.8% vs. 17.8% reduction in non-T2D), and a greater high-density lipoprotein cholesterol (HDL-C) increase (15.8% vs. 1.0% in non-T2D; p<0.0002), strengthening the case for prioritizing T2D patients in further clinical evaluation. There were no clinically significant safety and tolerability issues related to tipelukast. The ongoing NATG-202 Phase 2 trial is evaluating safety and efficacy in T2D patients with HTG and NAFLD over 24 weeks. Enrollment has been completed, and topline data are anticipated mid-2026. We believe these results represent a key inflection point in justifying a larger Phase 3 trial. While several agents are in clinical development for the treatment of NAFLD, tipelukast is the only investigational asset targeting HTG and NAFLD due to T2D, representing a more holistic therapeutic approach, in our belief.

MediciNova's non-core programs are led by the development of ibudilast in progressive multiple sclerosis (MS; Phase 2b completed), substance dependence (Phase 2 ongoing in methamphetamine dependence), chemotherapy-induced peripheral neuropathy (CPIN; Phase 2b ongoing), degenerative cervical

myelopathy (DCM; Phase 3 ongoing), glioblastoma (Phase 1/2 completed), acute respiratory distress syndrome (ARDS; Phase 2 completed), and Long COVID (Phase 2/3 ongoing). We believe the non-core programs are important longer-term value drivers for the company, representing: 1) a capital-efficient model with minimal internal R&D spend that leverages non-dilutive funding; 2) diversified clinical risk for ibudilast if the lead indication (ALS) fails; and 3) a path for potential strategic alliances with leading pharmaceutical companies who seek to complete ibudilast product development and commercialization.

MediciNova Core Pipeline



Source: Adapted from company materials.

Upcoming Company Catalysts

Candidate	Indication	Timeline	Milestone	Impact*
Ibudilast (MN-166)	ALS	YE26	Topline Phase 2b/3 COMBAT-ALS data	***
Tipelukast (MN-001)	HTG+NAFLD+T2D	mid-2026	Topline Phase 2 NATG-202 data	**

*Source: Company documents. *HCW assessment of milestone's potential to represent a meaningful stock catalyst.*

We Are Bullish on the Shares of MediciNova Based on the Following Three Factors:

1. Ibudilast's multi-target strategy represents a potential breakthrough for ALS.

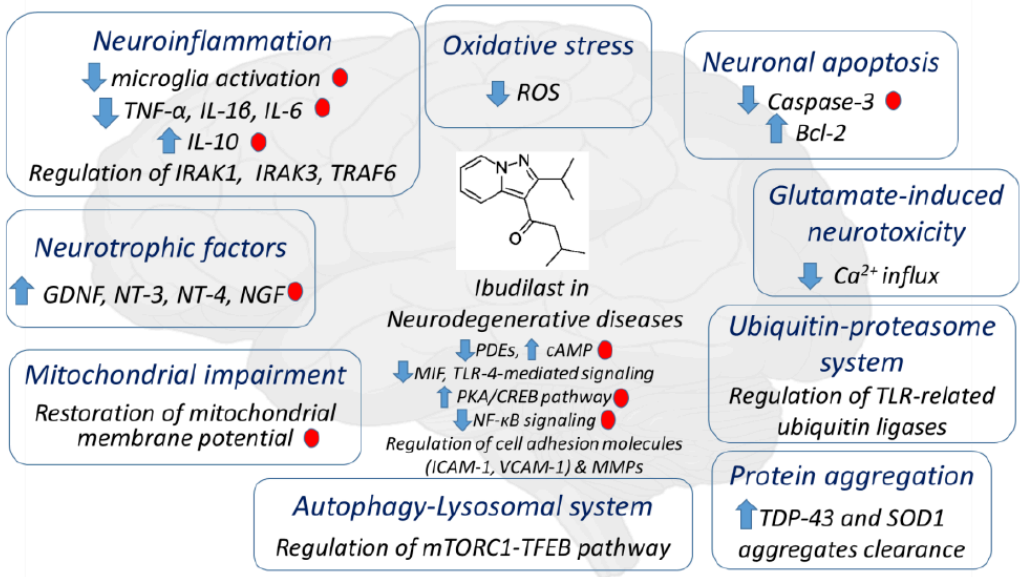
ALS remains a debilitating disease with significant unmet needs and scarce therapeutic options. Amyotrophic lateral sclerosis (ALS), also known as Lou Gehrig's disease, is a progressive neurodegenerative disease that affects the brain and spinal cord neurons. While the specific cause of ALS is still unknown, epidemiological studies suggest that ALS arises from a combination of genetic and environmental factors. Once diagnosed disease progression causes the apoptosis of neurons, resulting in muscle weakness and the loss of voluntary muscle control. In the disease, both upper and lower motor neurons are affected, and clinical manifestations include fatigue, weakness, and impaired daily functions including speaking, swallowing, walking and breathing. Progression to respiratory failure generally occurs within three to five years from disease onset and diagnosis, and the mean survival time of an ALS patient is estimated at two to five years. The ALS Association indicates that approximately 5,000 individuals are diagnosed in the U.S. annually, with a U.S prevalence of ~20,000-30,000 cases (Hardiman O., et al. *Nature*. 2017). There are currently three commercial treatments approved by the FDA for the treatment of ALS: 1) Radicava (edaravone) (intravenous or oral), a free radical scavenger that reduces oxidative stress and favors neuroprotection and disease progression by capturing unstable reactive oxygen species (ROS); 2) Rilutek (riluzole) (oral), a glutamate blocker capable of delaying the onset of ventilator-dependence or tracheostomy in some patients and prolonging survival by two to three months; and 3) QALSODY (tofersen) (intrathecal injection), a superoxide dismutase 1 (SOD1) targeting antisense oligonucleotide (ASO) for adult ALS patients with a mutation in the SOD1 gene. These drugs have only modest effects on disease progression, and the search for novel and effective ALS drugs is an active sector of research, development, and commercialization though remains quite risky.

The current ALS drug development landscape is highly diverse, encompassing gene therapies (i.e., ASOs), cell therapies, small molecules, and nanotherapeutic approaches. Together, these programs highlight a rich landscape of therapeutic strategies designed to slow neurodegeneration, preserve motor neuron function, and ultimately modify ALS disease progression. We summarize selected companies and programs next. QRL-201 by QurAlis (private) is an ASO designed to restore stathmin-2 (STMN2) protein expression (in Phase 1 dose-finding studies). ION363 by Ionis Pharmaceuticals (IONS; Buy; Kapoor), is an ASO targeting the production of the neurotoxic form of the fused in sarcoma (FUS) protein (in Phase 3). NurOwn (debamestrocel) by BrainStorm Cell Therapeutics (BCLI; not rated) is an autologous stem cell therapy (MSC-NTF) designed to support secretion of neurotrophic and immunomodulatory factors (in confirmatory Phase 3b). Pridopidine by Prilenia Therapeutics (private) and Ferrer (private) is a sigma-1 receptor agonist (RA) aimed at neuroprotection and modulation of cellular stress (in Phase 3). Masitinib by AB Science (EPA:AB; not rated) is a tyrosine kinase inhibitor (TKI) aimed at reducing neuroinflammation (in Phase 3). Zhimeng Biopharma (private) is developing CB03-154 (in Phase 2/3), a potassium channel (KCNQ2/3) opener designed to stabilize neuronal membranes by reducing excessive excitation and inhibiting neuronal firing. RNS60 by Revalesio (private) uses charge-stabilized nanostructures to modulate neuroinflammation, support mitochondrial function, and modulate immune cell activation and homeostasis (in Phase 2). Clene (CLNN; Buy) is developing CNM-Au8, a suspension of clean-surfaced gold nanocrystals designed to enhance neuronal bioenergetics (ongoing discussions for potential regulatory submission via accelerated approval). Finally, MediciNova is developing ibudilast (MN-166), a multi-target, anti-inflammatory, and neuroprotective small molecule, currently in Phase 2b/3 evaluation in the COMBAT-ALS clinical trial.

Exploring ibudilast's multi-modal neuroprotective potential for ALS. In October 2004, MediciNova entered into an exclusive license agreement with Kyorin for the development and commercialization of ibudilast, an oral, anti-inflammatory, and neuroprotective agent that has been in use for over 20 years in Japan and South Korea for the treatment of asthma and post-stroke complications (i.e., dizziness). MediciNova obtained exclusive, worldwide rights (excluding Japan, China, South Korea, and Taiwan) to the patents for broader uses (except ophthalmic solution formulations), including neurological indications. Under the terms of the license agreement, MediciNova is obligated to make payments of up to $5.0 million based on the achievement of certain clinical and regulatory milestones, and tiered royalties (mid-single-digit to low-double-digit percentage) on net sales of the licensed products.

Ibudilast is a central nervous system (CNS)-penetrant, small molecule neuroimmune modulator with several complementary mechanisms targeting ALS pathophysiology, which together provide a strong biological rationale for its therapeutic potential. According to its mechanistic profile, ibudilast inhibits the macrophage migration inhibitory factor (MIF), certain phosphodiesterases (PDEs; primarily PDE-3, -4, and also -10, -11), as well as toll-like receptor 4 (TLR4). Collectively, these actions converge on neuroimmune modulation, and activation of downstream neuroprotective pathways. At the molecular level, preclinical evidence indicates that ibudilast suppresses neuroinflammation by: 1) inhibiting microglia activation (a major contributor to ALS neurodegeneration); 2) downregulating pro-inflammatory cytokines (TNF-α, IL-1β and IL-6); and 3) upregulating anti-inflammatory modulators (IL-10). In addition, ibudilast upregulates neurotrophic factors (GDNF, NT-3, NT-4 and NGF), and prevent mitochondrial impairment by restoring the mitochondrial membrane potential. It can also affect the autophagy-lysosomal system pathway (mTORC1-TFEB) and promote abnormal protein aggregate clearance (TDP-43 and SOD1), thereby supporting motor neuron survival (Chen Y., et al. *Biochem Biophys Res Commun*. 2020). Ibudilast may also protect against neuronal apoptosis by downregulating caspase-3 and upregulating Bcl-20, and suppressing the production of ROS. On top of PDE inhibition, ibudilast can also inhibit the intracellular form of MIF and TLR-4. MIF inhibition results in decreased inflammation and immune cell exhaustion. TLR-4 blocking may lead to additional reduction of pro-inflammatory cytokines via independent signaling pathways (NF-κB, IRAK1 and TRAF6). The figure below summarizes ibudilast-mediated molecular effects (red circles indicate specific mechanisms derived, at least partially, from PDE inhibition).

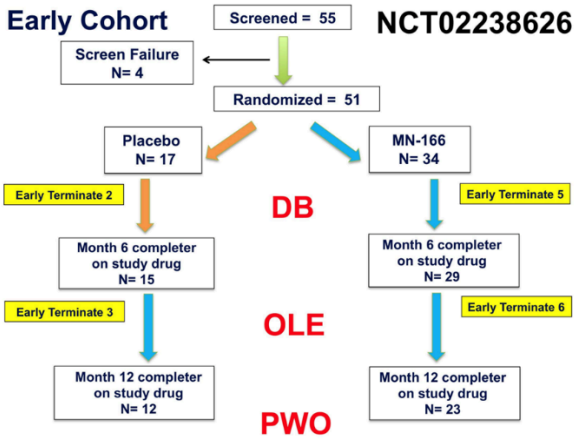
Ibudilast-mediated Orchestration of Molecular Pathways



Source: Angelopoulou E., et al. Molecules. 2022.

Encouraging Phase 2 results unveil functional ALS improvements, and potentially de-risk ongoing Phase 2b/3 trial. The Phase 2 ALS-1201 trial was conducted at The Carolinas Neuromuscular/ALS MDA Center, which is part of the Carolinas HealthCare System Neurosciences Institute-Neurology, an internationally recognized program of clinical care, research, and education for degenerative neuromuscular diseases, and one of the most comprehensive ALS and muscular dystrophy facilities in the U.S. ALS-1201 was a randomized, double-blind, placebo-controlled study that included a six-month treatment period followed by a six-month open-label extension (OLE) study after two weeks of wash-out. The Phase 2 trial evaluated the safety, tolerability, and initial efficacy of 60 mg/day ibudilast or placebo (2:1), in combination with 100 mg/day riluzole in 51 ALS patients (NCT02238626). Primary endpoint was safety, and secondary endpoints included, among others, the mean change in ALS Functional Rating Scale-Revised (ALSFRS-R) total score, QoL (five-item ALS Assessment Questionnaire (ALSAQ-5)), respiratory function (slow vital capacity (SVC)), and muscle strength (manual muscle testing (MMT), and instrumented hand-held dynamometry (HHD)), from baseline to month six. Subject trajectory and baseline characteristics of the early cohort (EC; six-month treatment period) are summarized in the figure below. Patients were diagnosed with familial or sporadic ALS, with disease onset of ≤5 years, currently on a stable dose of riluzole, and SVC ≥60% within one month prior to treatment initiation. The FDA granted Fast Track (2015) and Orphan-Drug (2016) designations to ibudilast for the treatment of ALS. The European Commission (EC) also granted Orphan Medicinal Product Designation (2016).

Subject Trajectory and Baseline Characteristics of ALS-1201 Study Participants



	Placebo (N=17)	Ibudilast (N=34)
Age	57.5	59.2
Female	5 (29.4%)	11 (32.4%)
Ethnicity •Caucasian •African American •Asian •Unknown	 15 (88.2%) 2 (11.8%) 0% 0%	 31 (91.2%) 1 (2.9%) 1 (2.9%) 1 (2.9%)
Baseline ALSFRS-R	39.0	39.3
Baseline SVC	97.2	92.0
Baseline MIP/NIF	-98.1	-86.0
Baseline MMT (Right)	4.08	4.16
Baseline MMT (Left)	3.97	4.15
Baseline ALSAQ-5	6.4	6.4

Source: Brooks BR., et al. American Academy of Neurology (AAN) annual meeting '18. DB, double-blinded; OLE, open label extension; PWO, post-wash out.

Ibudilast (60 mg, daily) was generally safe and tolerable when administered with riluzole in ALS-1201 participants (intention-to-treat (ITT) population; placebo, n=17; ibudilast, n=34). Interim analyses did not show major safety issues or tolerability concerns compared to placebo during the first three months. Treatment-emergent adverse events (TEAEs) exhibited a similar pattern between ibudilast and placebo arms (below, left table), with most events being mild to moderate, and no treatment withdrawals reported. Commonly reported AEs included gastrointestinal (GI) symptoms (nausea, vomiting, diarrhea, abdominal pain), fatigue, headache, and insomnia (below, right table).

Ibudilast Safety and Tolerability Profile in ALS Patients

	# of Subjects or # of Events	
	Placebo N=17	Ibudilast N=34
# of Subject with at Least one TRAEs	n= 3	n= 4
Total events # of TRAEs	5	8
Severe or Life-threatening TRAEs	0	0
Serious TRAEs	0	0

System Organ Code	# of Events	
	Placebo (n=3)	Ibudilast (n=4)
Gastrointestinal system	1	2
Nervous system disorder	3	0
Metabolism and Nutrition	0	4
Investigation	1	1
Injury	0	1

Source: Brooks BR., et al. AAN '17.

Responder analyses (n=49) of stable or improved ALSFRS-R, ALSAQ-5, and MMT scores at month six vs. baseline, showed higher rates in the ibudilast group (n=33) compared to the placebo group (n=16) in all three clinical outcomes (see below). Responders were defined as: 1) <12 units (<1 unit per month) decrease in ALSFRS-R total score; 2) not losing one MMT unit in neck and leg muscles; and 3) zero unit loss or any unit gain in ALSAQ-5 per six-month change in the DB and OLE portions of the study.

Higher Responder Rates in Ibudilast Arm

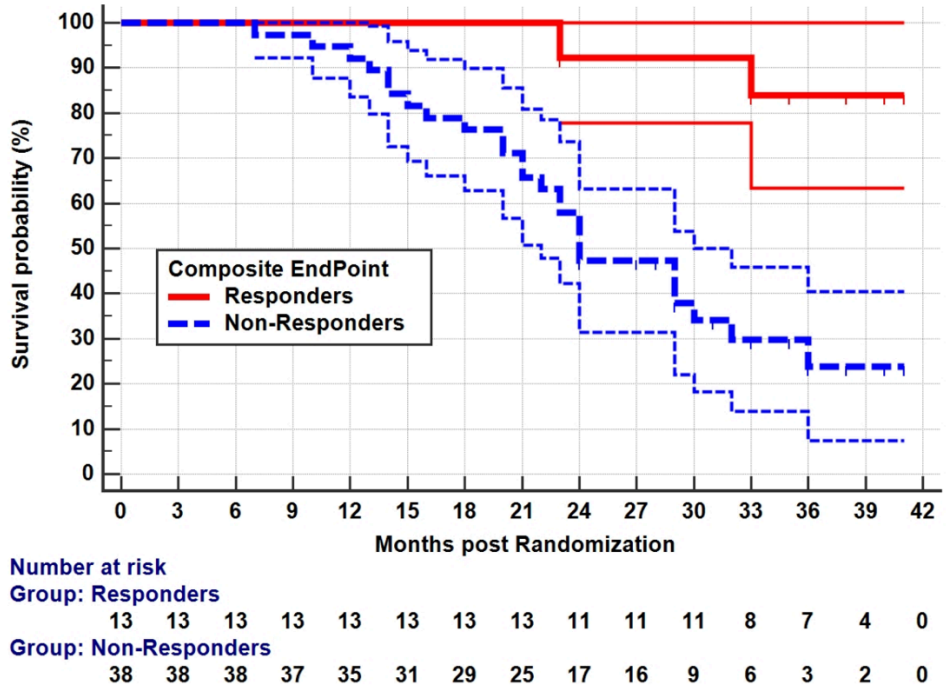
Parameter	Responder Category	Placebo (+ riluzole) (N=16)	MN-166 (+ riluzole) (N=33)
ALSFRS-R Total Score	Stable or Improved	2/16 (12.5%)	7/33 (21.2%)
ALSAQ-5		4/16 (25.0%)	17/33 (51.5%)
MMT (muscle strength)		4/16 (25.0%)	11/33 (33.3%)

ALSFRS-R: Amyotrophic lateral sclerosis functional rating scale – revised;
ALSAQ-5: Amyotrophic Lateral Sclerosis Assessment Questionnaire-5;
MMT: Manual muscle testing

Source: Brooks BR., et al. AAN '18.

In line with responder rates, ibudilast exhibited improved survival in participants from the double-blind and OLE portions of the study. This was clinically meaningful in patients who could not complete the protocol (not per protocol (PP); median survival ~24 months; blue line) and in those who completed the full protocol (PP; median survival ~36 months; red line). Ibudilast-treated subjects (ITT) who showed no ALS progression at six or 12 months, showed improved survival (p=0.001) at month 30 post-treatment. Subjects who completed six or 12 months of ibudilast treatment (PP) showed improved survival (p=0.0025) of up to 30 months post-treatment. Of note, in randomized controlled trials and systematic reviews, riluzole has consistently shown a modest survival benefit of ~2-3 months in ALS patients (Miller RG., et al. *Cochrane Database of Systematic Reviews*. 2021), and median survival from ALS diagnosis in population-based studies tends to be ~1.5-2.5 years (Jordan H., et al. *Neuroepidemiology*. 2015).

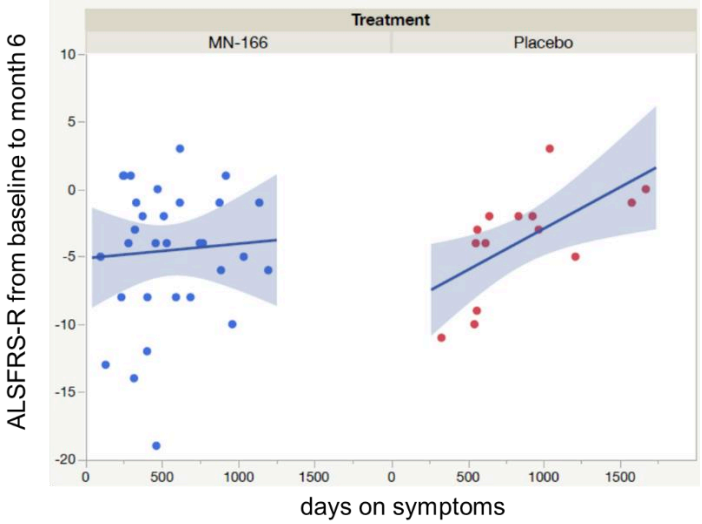
Improved Survival in Ibudilast Arm



Source: Brooks BR., et al. AAN '18.

Further analyses using ALS history data (i.e. days from first onset of symptom) identified a negative correlation between longer ALS history and ALSFRS-R score progression after ibudilast treatment. As observed below, a significant positive correlation (r=0.63; p<0.05) was observed between ALS history and ALS disease progression in the placebo group (red dots), suggesting greater disease progression in short ALS history patients. In contrast, no correlation (r estimate=0.06; p=0.73) was observed between ALS history and ALS disease progression in the ibudilast group, indicating that ibudilast efficacy is expected to be more robust in patients with a shorter ALS history.

Improved Ibudilast-Mediated Functional Benefits in Patients with Short ALS History

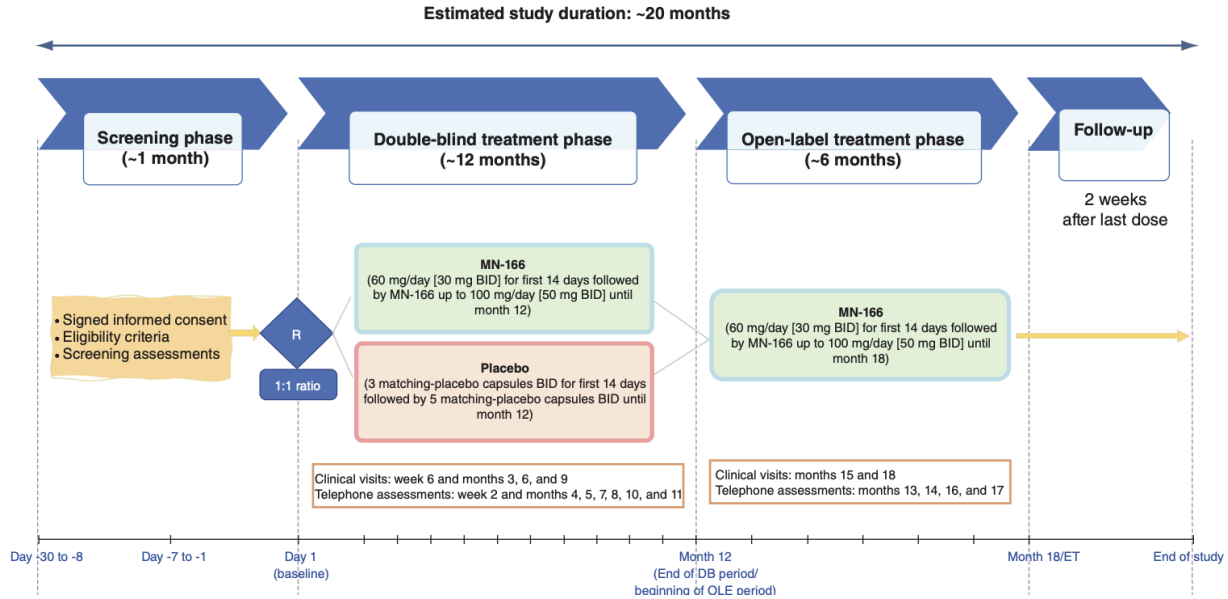


Source: Matsuda K., et al. AAN '19.

While we acknowledge ALS-1201's single-site risk and the potential confounding effect of riluzole combination, our positive view is primarily driven by the favorable ALSFRS-R outcomes reported in the trial. We believe these results validate the potential of ibudilast to delay disease progression, improve functional outcomes, and prolong survival in ALS patients, and support further evaluation in the ongoing, larger Phase 2b/3 COMBAT-ALS clinical trial.

COMBAT-ALS poised unlock ibudilast's regulatory and clinical paths in ALS; topline data by YE26. COMBAT-ALS is a multicenter (U.S. and Canada), double-blind, placebo-controlled Phase 2b/3 trial evaluating the efficacy and safety of ibudilast in ALS patients over 12 months. Upon completion of the double-blind phase, subjects may continue to the OLE portion of the study for an additional six months (~20 months in total, including a one-month screening phase and a two-week end-of-study period) (NCT04057898; study design below). The study expects to enroll ~230 patients, diagnosed with familial or sporadic ALS, with disease onset of ≤18 months from initial clinical signs of weakness before screening, ALSFRS-R score ≥35 at screening, and pulmonary function test ≥70%. Patients are expected to be randomized (1:1) to ibudilast or matching placebo (up to 100 mg/day (50 mg BID)). The dual primary endpoint includes the change from baseline in ALSFRS-R score at 12 months, and overall survival (individual endpoints may achieve statistical significance independently to be considered indicative of a successful trial). Secondary endpoints include, muscle strength (HHD), QoL (ALSAQ-5), responder analysis (ALSFRS-R), safety, and tolerability.

Phase 2b/3 COMBAT-ALS Study Design



Source: Oskarsson B., et al. Neurodegener Dis Manag. 2021.

In September 2025, MediciNova announced enrollment completion with a total of 234 randomized patients. Baseline characteristics are summarized in the table below. Note that based on Phase 2 ALS-1201 ALS history data, COMBAT-ALS targets patients with shorter ALS history (disease onset of ≤18 months). As opposed to ALS-1201, COMBAT-ALS participants are allowed to use SoC during the study, including riluzole and edaravone, but ibudilast is being evaluated independently vs. placebo.

Baseline Characteristics of COMBAT-ALS Study Participants

- **Baseline Characteristics:**
  - Total randomized patients: 234 (Female: 86 [36.8%], Male: 148 [63.2%])
  - Mean age at screening: 60.6 years
  - Racial distribution: Caucasian (90.2%), Asian (5.1%), African American (1.3%), Native Hawaiian or Other Pacific Islander (0.4%), American Indian or Alaskan Native (0.4%), Other (2.6%)
  - ALS onset type: Upper limb (46.2%), Lower limb (32.5%), Bulbar (20.9%), Unknown (0.4%)
  - Mean ALSFRS-R score at screening: 40.6
  - Mean disease duration from first symptom: 12.5 months
  - These demographics and clinical profiles are consistent with other Phase 2 and Phase 3 ALS trials, supporting the generalizability of the study findings.

Source: Company materials, December 2025.

We highlight a recent pre-specified interim analysis in the COMBAT-ALS study protocol. Results indicated a positive correlation between month six- and 12-month data, supporting the reliability of the measurement tools used across these timepoints (Oskarsson B., et al. Poster presentation. International Symposium on ALS/MND '24). While shortening the double-blind phase to six months could improve recruitment and accelerate data readout, it would reduce statistical power, weaken face validity, and potentially lower the likelihood of regulatory approval if outcomes are positive. The external Data and Safety Monitoring Board (DSMB) reviewed these results and recommended that the trial should continue as originally planned (12-month double-blind period). Topline efficacy and safety data are anticipated by the end of 2026. If positive, Phase 2b/3 results are expected to inform next steps for ibudilast, including discussions with regulators, potential progression to regulatory filing, and/or a confirmatory pivotal Phase 3 trial.

We believe ibudilast is differentiated by several key mechanistic and clinical attributes:

- ✓ **Broad, multi-modal MoA** driving anti-inflammatory and neuroimmune modulation, rather than a single target mechanistic approach
- ✓ **Genotype-agnostic therapeutic approach** with potential applicability across the broader ALS population rather than limited genetically defined subsets
- ✓ **Phase 2 evidence** of favorable safety, functional stabilization or improvement (ALSFRS-R), and prolonged survival
- ✓ **Ongoing late-stage Phase 2b/3 trial** evaluating combined assessment of function and survival (CAFS) endpoints over ~12 months

Functional vs. survival vs. biomarker endpoints; none can be ignored. We believe that both functional and survival outcomes should ideally be favorable for the potential approvals of novel therapeutic ALS candidates. In addition, favorable surrogate biomarker data (i.e. neurofilament light chain (NfL)) are critical for potential accelerated approvals. However, prior late-stage ALS trials taught us that while investigational candidates seem to struggle with maintaining long-term functional ALS improvements (ALSFRS-R); robust survival benefits may be seen as a success for this population with high unmet needs, and regulators, with the support of physicians and patient advocates, should consider adjusting ALSFRS-R endpoint criteria for these trials, and contemplate potential new approvals also based on survival benefits. Interestingly, in 2024, Congress expressed the need for regulatory flexibility for accelerated approval treatments for rare diseases and put pressure on the FDA in terms of modifying approval guidelines, and re-evaluating the use of survival data as a clinical endpoint in ALS. For ibudilast, while COMBAT-ALS captures both functional and survival

endpoints, it lacks NfL as a prespecified endpoint, which may limit its ability to support a regulatory filing and raises the possibility that the FDA could request a confirmatory Phase 3 trial.

Expanding access to ibudilast via NIH-supported EAP. With support from a $22 million National Institute of Neurological Disorders and Stroke (NINDS/NIH) grant, the multicenter, open label SEANOBI EAP offers access to ibudilast treatment to ALS patients who are not eligible to participate in the COMBAT-ALS randomized clinical trial, while also generating important biomarker (NfL) and clinical outcome (ALSFRS-R) data from a real-world ALS population (NCT06743776). As of January 2026, 12 U.S. sites have been activated, and 100 patients have been enrolled, representing 50% of the planned study participants (n~200). These combined data, together with Orphan Drug Designation from the FDA and EMA, and Fast Track Designation from the FDA, support advancing ibudilast closer to becoming an approved treatment option for people living with ALS.

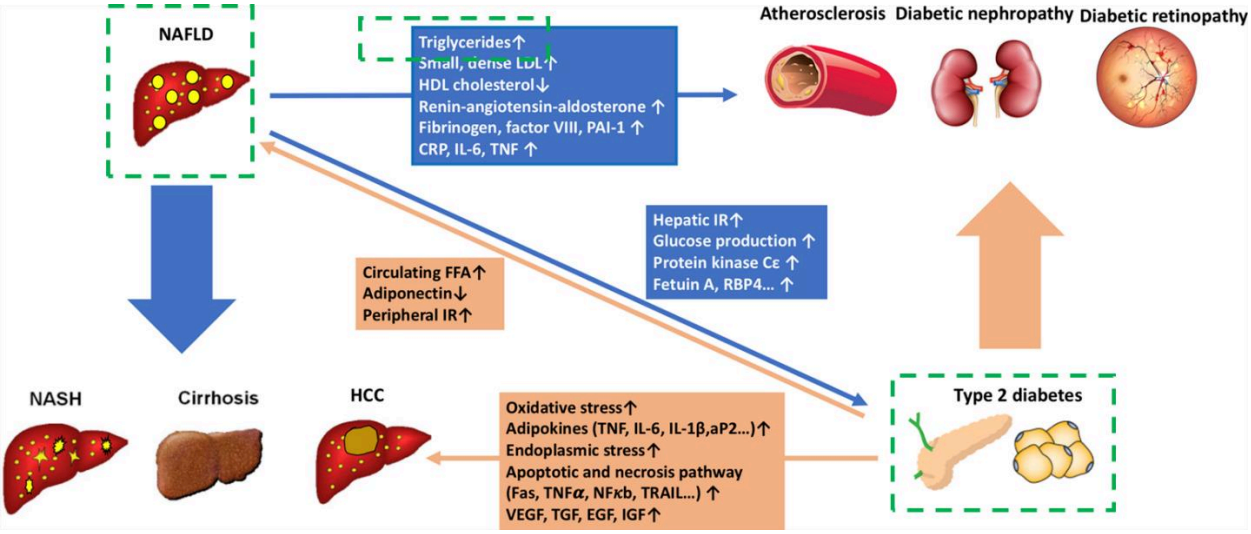
2. Tipelukast is well-positioned to tackle key manifestations of metabolic syndromes.

The metabolic vicious cycle: linking NAFLD, HTG, and T2D. Nonalcoholic fatty liver disease (NAFLD), now frequently referred to as metabolic dysfunction-associated steatotic liver disease (MASLD), is defined as the presence fat accumulation in the liver (not caused by alcohol), and is the most frequent reason for liver transplantation in the U.S. This excessive lipid deposition in hepatocytes can progress into nonalcoholic steatohepatitis (NASH), now often called metabolic dysfunction-associated steatohepatitis (MASH), a severe form of fatty liver disease characterized by fat buildup, inflammation, and damage to liver cells, and even more severe diseases, including cirrhosis and hepatocellular carcinoma (HCC), which are also characterized by liver injury and fibrosis (Hou X., et al. *Lipids Health Dis*. 2021; Marušić M., et al. *Can J Gastroenterol Hepatol*. 2021). The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK/NIH) estimates that ~25% of U.S. adults have some level of NAFLD.

Although the pathogenesis of NAFLD is not fully understood, multiple factors such as insulin resistance, nutritional factors, and genetic predisposition have some level of impact on its development. In type 2 diabetes (T2D), the insulin-induced suppression of adipose tissue lipolysis is impaired, and the influx of free-fatty acids (FFAs) into the liver increases (Buzzetti E., et al. *Metabolism*. 2016). The main source of fat accumulation in the livers of NAFLD patients comes from triglycerides (TG), which increase alongside lipotoxicity and liver injury. NAFLD also associates with a highly atherogenic lipoprotein profile, characterized by high serum TG, low-density lipoprotein (LDL-C), and apolipoprotein B (ApoB) concentrations, and reduced high-density lipoprotein (HDL-C) levels (Loria P., et al. *Atherosclerosis*. 2014). Interestingly, prior studies have shown that hypertriglyceridemia (HTG) is one of the risk factors for NAFLD (Lonardo A., et al. *Dig Liver Dis*. 2002), and the degree of HTG significantly correlates with the severity of NAFLD (Hsiao PJ., et al. *J Gastroenterol Hepatol*. 2007; Tutunchi H., et al. *BMC Res Notes*. 2020).

It is considered that NAFLD affects 55-70% of patients living with type 2 diabetes (T2D). Global NAFLD prevalence in T2D, according to a meta-analysis including ~50,000 patients from 80 studies, was found to be as high as ~55% (Ciardullo S., et al. *J Clin Med*. 2023). Other research showed a prevalence of NAFLD in T2D of up to ~59%, and ~77% in obese T2D patients (Dai W., et al. *Medicine*. 2017). Remarkably, the risk of developing T2D is 5-fold higher in patients with NAFLD (Jäger S., et al. *PLoS One*. 2015). The pathophysiological connections between NAFLD and type T2D are depicted in the figure below.

Interconnection Between HTG, NAFLD and T2D



Source: Xia MF., et al. Front. Pharmacol. 2019.

There are currently no pharmaceuticals approved specifically for the treatment of NAFLD/MASLD. Management centers on reversing liver fat accumulation through lifestyle modifications and weight loss. In the case of NAFLD + T2D, proper management of insulin resistance and hyperglycemia is essential for reducing liver disease progression. For NASH/MASH with moderate to advanced fibrosis, FDA-approved treatments include Rezdiffra (resmetirom; partial agonist of the thyroid hormone receptor-beta (THR-β)) and Wegovy (semaglutide; glucagon-like peptide-1 (GLP-1) RA). These therapies target liver fat reduction and fibrosis to prevent progression to cirrhosis. Meta-analyses of multiple resmetirom studies show mean TG reductions of ~23-24 mg/dL vs. placebo, representing a modest but statistically significant decrease in serum TG levels (Mazhar S., at al. *Ann Med Surg (Lond).* 2024). In the Phase 3 ESSENCE trial in patients with biopsy-confirmed MASH and liver fibrosis, semaglutide exhibited mean TG reductions of ~16.8 mg/dL vs. ~0.3 mg/dL with placebo (Petta s., et al. *Liver Int*. 2025). MASH approval labels for both resmetirom and semaglutide are not limited to non-diabetic patients and can be used in clinical practice in patients with concurrent T2D.

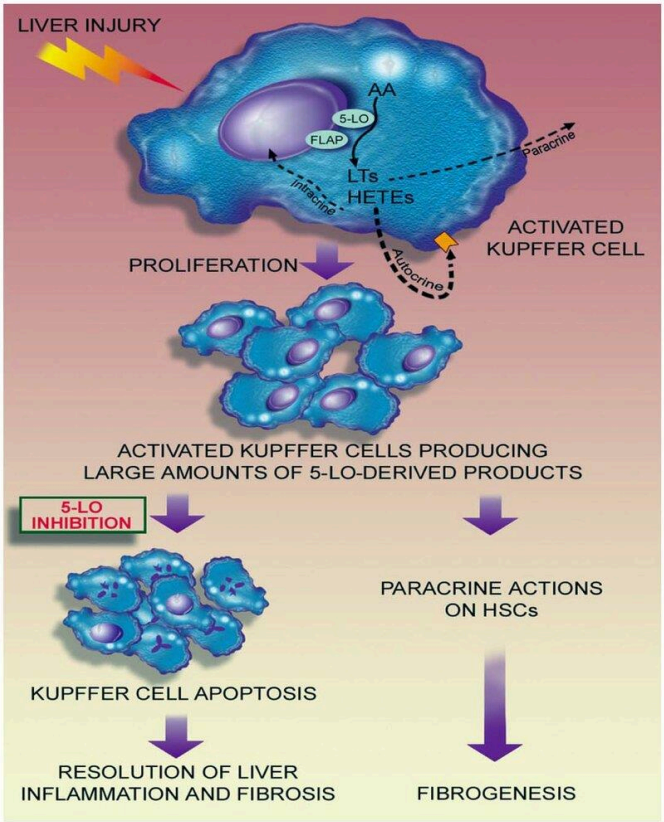
While several investigational agents are in clinical development for the treatment of NAFLD and NASH, to our knowledge MediciNova's anti-inflammatory and anti-fibrotic small molecule candidate, tipelukast (MN-001), is the only investigational asset targeting HTG and NAFLD due to T2D. Whereas resmetirom primarily targets hepatic lipid metabolism and semaglutide is weight-centric, we believe tipelukast may offer a more holistic therapeutic approach, and/or serve as an add-on strategy to currently approved and developmental therapies.

Preclinical studies highlight robust anti-fibrotic and lipid-modifying activity. In March 2002, MediciNova entered into an exclusive license agreement with Kyorin for the development and commercialization of tipelukast, an oral, anti-fibrotic, and anti-inflammatory small molecule compound. MediciNova obtained exclusive, worldwide rights (excluding Japan, China, South Korea, and Taiwan) to the patents and know-how related to tipelukast and its active metabolite, MN-002, in all indications, including NASH, advanced NASH with fibrosis, NAFLD, steatosis, HTG, hypercholesterolemia (HC), hyperlipoproteinemia (HL), fibrosis, ulcerative colitis (UC), interstitial cystitis, and irritable bowel syndrome, and excluding ophthalmic solution formulations. Under the terms of the license agreement, MediciNova is obligated to make payments of up to $5.0 million ($4.0 million already paid) based on the achievement of

certain clinical and regulatory milestones, and tiered royalties (mid-single-digit to low-double-digit percentage) on net sales of the licensed products.

Tipelukast is a novel, orally bioavailable small molecule compound, that exerts its effects through several mechanisms to produce its anti-fibrotic and anti-inflammatory activity, including leukotriene (LT) receptor antagonism, inhibition of PDEs (primarily -3 and -4), and inhibition of the 5-lipoxygenase(5-LO)/LT pathway. The 5-LO/LT pathway is a pro-inflammatory mechanism that drives liver fibrosis by promoting Kupffer cell survival and activating hepatic stellate cells (HSCs). The figure below illustrates the possible mechanism by which 5-LO inhibition attenuates liver fibrosis. In Kupffer cells, 5-LO translocates from the cytosol to the nuclear membrane to generate arachidonic acid (AA) metabolites such as LTs. The presence of a metabolically active 5-LO pathway in these macrophages is vital for their growth and survival. In the early stages of liver inflammation and fibrosis, Kupffer cells proliferate and produce large amounts of 5-LO-derived products. These, in turn, exert their paracrine actions on HSCs, thus promoting fibrogenesis. Inhibition of the 5-LO pathway induces apoptosis and inactivates Kupffer cells, thereby reducing liver inflammation and fibrosis.

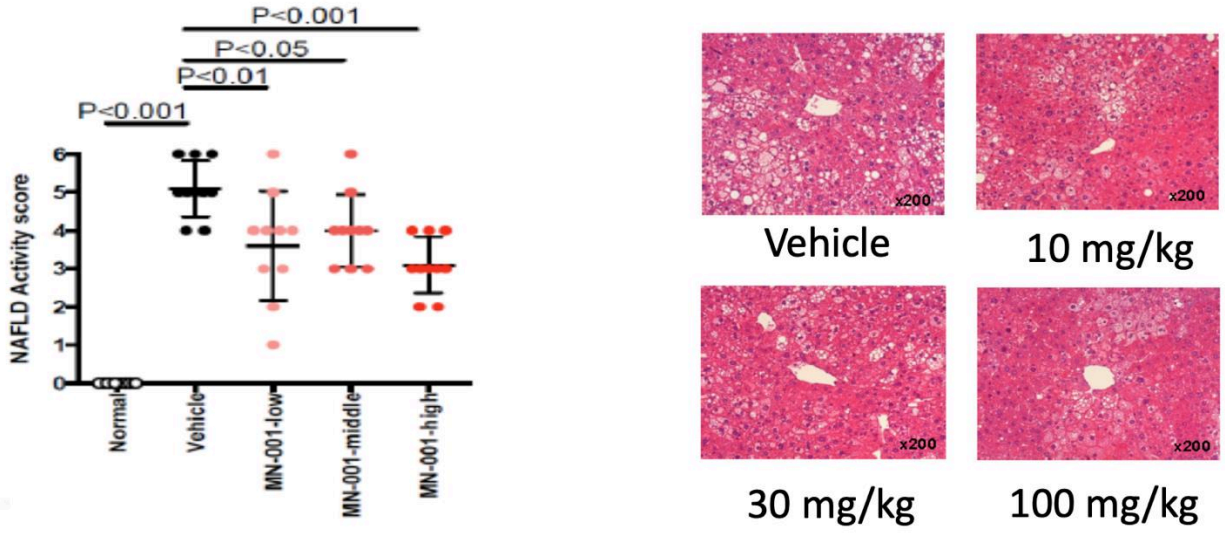
5-LO/LT Pathway in the Progression of Liver Fibrosis



Source: *Titos E., et a. FASEB J. 2003.*

In preclinical studies evaluating the potential efficacy of tipelukast in a STAM mouse model of advanced NASH, tipelukast was administered orally once daily (10, 30, and 100 mg/kg) for four weeks. NAFLD activity score (NAS) was significantly reduced in the tipelukast-treated group compared to the non-treated group ($p<0.001$; see below).

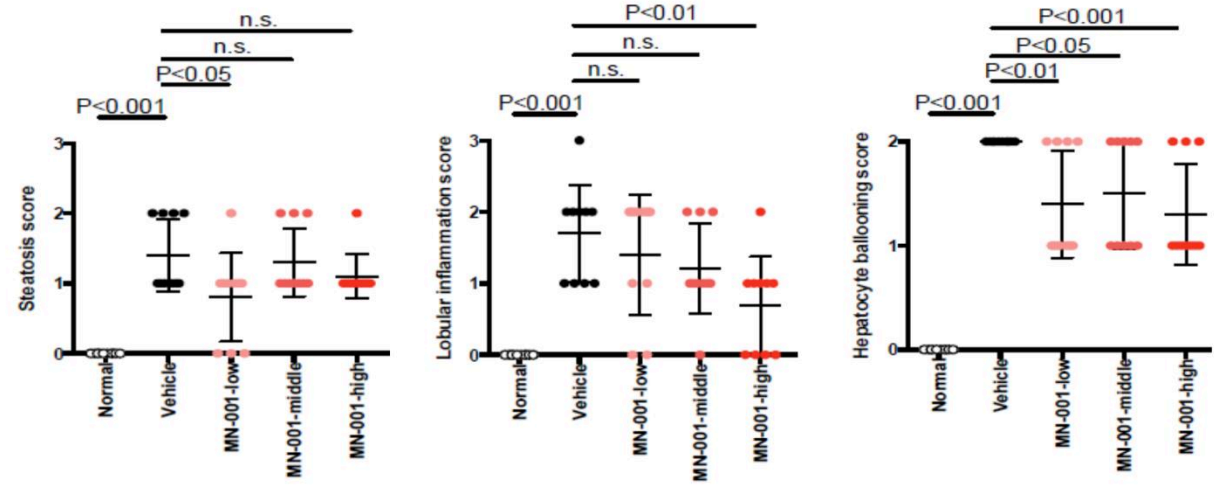
Tipelukast-Mediated NAFLD Improvement *In Vivo*



Source: *Matsuda K., et a. American Association for the Study of Liver Disease (AASLD) '17.*

The reduction was observed consistently in all NAS components, including steatosis score ($p<0.05$), lobular inflammation score ($p<0.01$), and hepatocyte ballooning score ($p<0.001$) (see below).

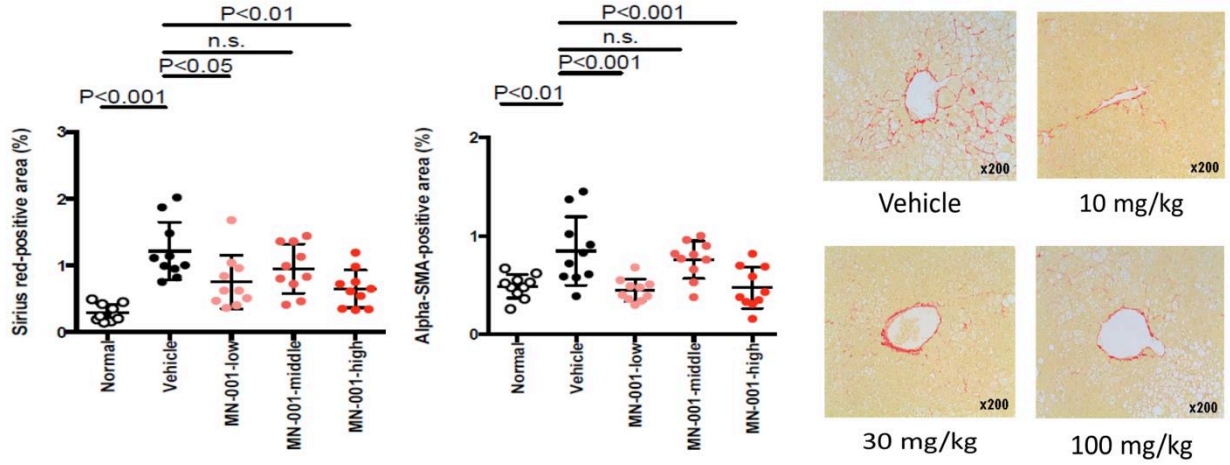
Consistent Reduction in all NAS Components



Source: *Matsuda K., et al. AASLD '17.*

Both collagen fibers (sirius red staining; $p<0.01$; below, left panel) and alpha-smooth muscle actin (SMA staining; activated fibroblasts; $p<0.001$; below, right panel) fibrotic histologic areas were significantly reduced in the tipelukast-treated group, supporting a direct anti-fibrotic effect.

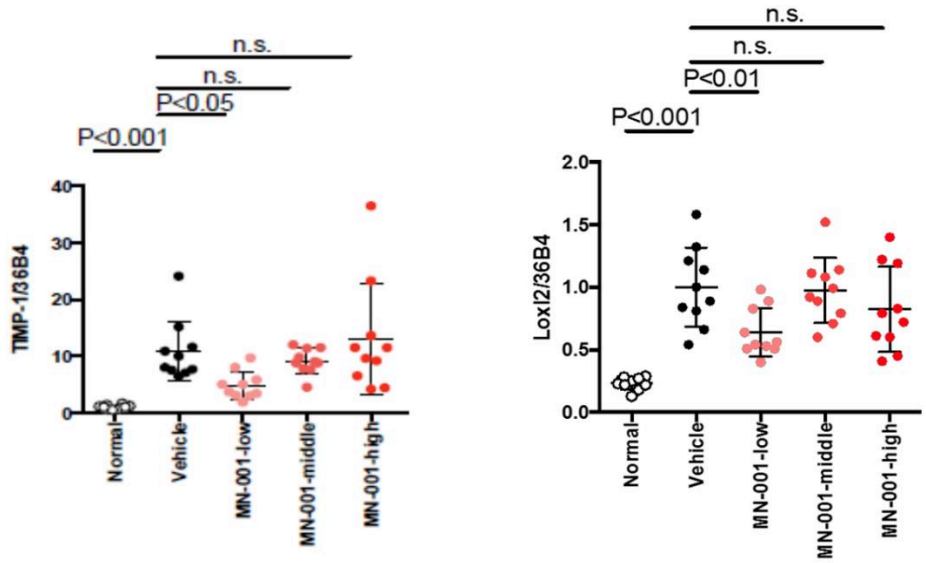
Tipelukast Limits Progression of Fibrosis *In Vivo*



Source: *Matsuda K., et a. AASLD '17.*

Histological observations were validated via gene expression studies demonstrating that tipelukast-mediated downregulation of pro-fibrotic genes (see below), including lysyl oxidase-like 2 (LOXL2) and tissue inhibitor of metalloproteinases 1 (TIMP-1).

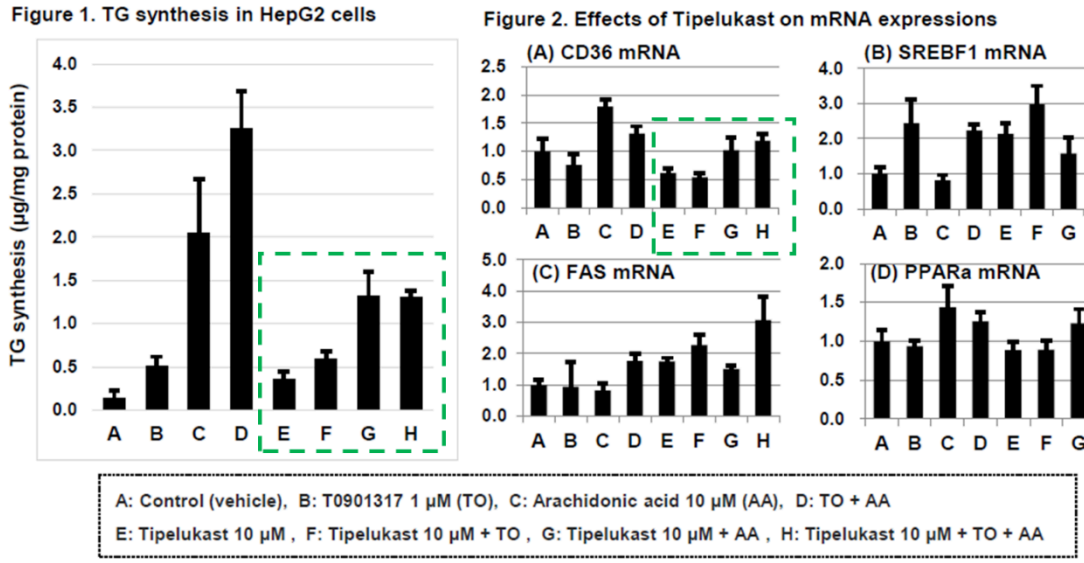
Downregulation of Pro-Fibrotic Genes *In Vivo*



Source: *Matsuda K., et a. AASLD '17.*

In vitro tipelukast exhibited an inhibitory effect on TG synthesis in HepG2 cells derived from human HCC samples (below, left panel). The expression of CD36 mRNA, a crucial membrane-bound translocase that facilitates the uptake of long-chain FFAs, including AA, into hepatocytes, was suppressed in tipelukast-treated cells (below, right panel). CD36 drives hepatic TG accumulation and lipotoxicity by promoting the uptake and esterification of FFAs, and its expression is upregulated in NAFLD (Rada P., et al. *Cell Death Dis*. 2020). These observations suggest that tipelukast reduces TG biosynthesis by inhibiting AA uptake into hepatocytes. In addition, the 5-LO/LT pathway is directly linked to AA, acting as the primary enzyme in converting it into pro-inflammatory LTs (Silverstein RL., et al. *Sci Signal*. 2010).

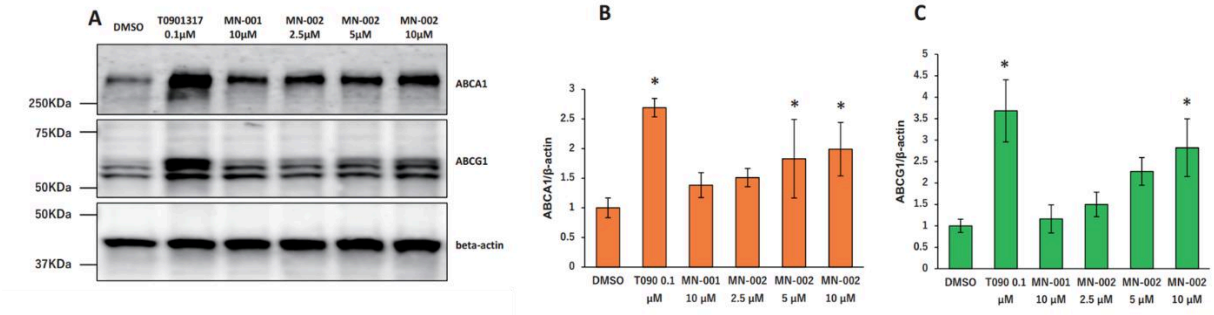
Inhibition of TG Synthesis *In Vitro*



Source: Ogura M., et a. AASLD '21

Additional lipid-modifying effects were reported in a recent study demonstrating that tipelukast's active metabolite, MN-002, significantly enhances cholesterol efflux in macrophages by upregulating the ATP-binding cassette transporter A1 (ABCA1) and ATP-binding cassette sub-family G member 1 (ABCG1) cholesterol transport proteins, thereby potentially reducing foam cell formation and limiting early atherogenesis. Cholesterol efflux was assessed *in vitro* in THP-1 macrophages in the presence of apolipoprotein A-I (ApoA-I) or HDL-C. MN-002 treatment upregulated ABCA1 and ABCG1 protein expression (see below).

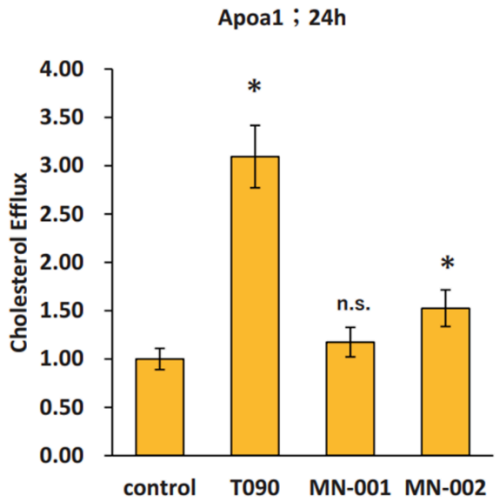
Upregulation of Key Cholesterol Transport Proteins



Source: *Qi H., et al. J Atheroscler Thromb. 2026.*

Accordingly, MN-002 significantly improved ApoA-I-mediated cholesterol efflux (p=0.0377; see below), supporting tipelukast-mediated improvements in lipid metabolism, and potentially opening doors for additional metabolic indications, including dyslipidemia and atherosclerotic cardiovascular disease (ASCVD).

Improved Cholesterol Efflux *In Vitro*



Source: *Qi H., et al. J Atheroscler Thromb. 2026.*

In summary, preclinical observations demonstrate that tipelukast ameliorates the overall metabolic profile in the context of NAFLD/NASH (fibrosis, TG, and lipid profile) and support clinical evaluation for the treatment of fatty liver disease and associated complications.

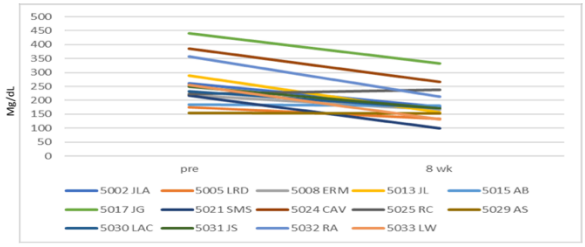
Early Phase 2 data exceeded expectations for TG reduction, and support T2D as a key target population. Following encouraging preclinical results NASH mouse models and cell lines, the FDA cleared the IND application (three different Phase 2 clinical trial protocols in NASH and NAFLD) and granted Fast Track designation to tipelukast for the treatment of NASH patients with fibrosis. MediciNova initiated the open-label, NATG-201 Phase 2 PoC clinical trial investigating tipelukast for the treatment of HTG in NASH and NAFLD patients (NCT02681055). Study participants had: 1) fasting serum TG level >150 mg/dL at screening; and 2) histologically proven NASH based on liver biopsies performed within the last 36 months, or abdominal ultrasound confirmation of NAFLD. Anti-diabetic medications or statins were allowed during the study. Patients were randomized to 250 mg/day tipelukast for four weeks and 500 mg/day for eight weeks (total study period 12 weeks). The trial was terminated early after positive results from an interim analysis (n=14) in which tipelukast significantly reduced mean serum TG levels (primary endpoint). After 8 weeks of treatment, TG levels were reduced in 13 out of 14 subjects. Pre-treatment TG level was 260.1 mg/dL vs. 185.2 mg/dL post-treatment. Tipelukast reduced mean TG by 74.9 mg/dL, resulting in a 28.8% reduction (p=0.00006) (see below). There were no clinically significant safety and tolerability issues related to tipelukast. Of note, the safety of tipelukast has been evaluated in >600 subjects in prior asthma and interstitial cystitis clinical trials conducted by Kyorin, without relevant concerns.

Tipelukast-Mediated Early TG Reductions

Table 3: Effects of Tipelukast on Mean Triglyceride Levels after 8 Weeks Treatment (t-test: Paired Two Sample for Means)

	pre-treatment	Week 8	Change
Mean serum TG level (mg/dL)	260.1	185.2	- 74.9 (- 28.8 %)
Variance	6796.7	3613.7	
Observations	14	14	
Pearson Correlation		0.77	
Hypothesized Mean Difference		0	
df		13	
t Stat		5.36	
P-value		0.00006	

Figure 5: Changes in Individual Subject Serum TG Levels after 8 weeks MN-001 Treatment



Source: Matsuda K., et al. European Association for the Study of the Liver (EASL) '18.

Interestingly, a post-hoc, subgroup analysis (n=19) demonstrated that compared to participants without T2D (n=9), T2D patients (n=10) showed a greater reduction in serum TG levels at week eight (50.8% reduction in T2D vs. 17.8% reduction in non-T2D; p=0.098), and a greater HDL-C increase (15.8% increase in T2D vs. 1.0% in non-T2D; p<0.0002) (see below). LDL-C reductions at week eight also trended higher in T2D patients (15.4% vs. 6.7% in non-T2D). These observations strengthen the case for prioritizing T2D patients in further late-stage clinical evaluation.

Tipelukast-Mediated Improved Lipid Profile in T2D Patients

Mean TG (mg/dL)	Baseline	Week 8	Change	p-value
All Subjects (N=19)	345.7	206.9	-40.2 %	
With T2DM (n=10)	444.7	218.7	-50.8%	p=0.098
Without T2 DM (n=9)	235.7	193.8	-17.8%	

Mean serum HDL (mg/dL)	Baseline	Week 8	Change	p-value
All Subjects (N=19)	38.7	41.9	+ 8.26 %	
With T2 DM (n=10)	36	41.7	+15.8 %	p<0.0002
Without T2 DM (n=9)	41.8	42.2	+0.96 %	

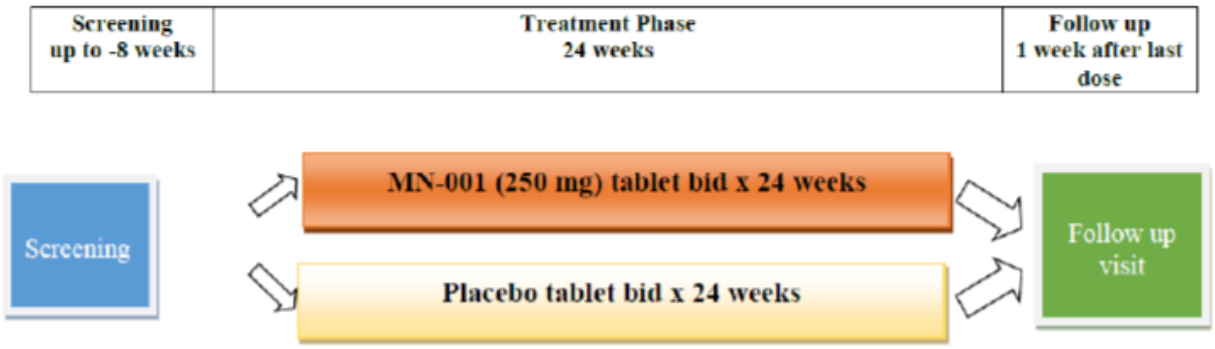
Mean T. cholesterol (mg/dL)	Baseline	Week 8	Change
All Subjects (N=19)	202.9	187.7	-7.5 %
With T2 DM (n=10)	210.2	192.8	-8.3 %
Without T2 DM (n=9)	194.8	182	-6.6 %

Mean serum LDL (mg/dL)	Baseline	Week 8	Change
All Subjects (N=19)	118.1	104.4	-11.6 %
With T2 DM (n=10)	126.9	107.4	-15.4 %
Without T2 DM (n=9)	108.3	101	-6.7 %

Source: Matsuda K., et al. International Diabetes Federation (IDF) World Diabetes Congress '22.

Ongoing NATG-202 trial is a key value inflection for tipelukast, in our belief; topline data in mid-2026. Considering that HTB and NAFLD are common metabolic conditions in T2D, and NATG-201 data showed greater TG reductions in these patient population, tipelukast is currently under Phase 2 evaluation in the NATG-202 clinical trial. This is a multi-center (U.S.), randomized, double-blind, placebo-controlled Phase 2 study evaluating the safety and efficacy of tipelukast in ~40 T2D patients with HTG and NAFLD (NCT05464784; see study design below). Participants (FibroScan score ≥ 248 dB/m within eight weeks of randomization, hemoglobin A1c (HbA1c) >6.5 and ≤10% at screening, stable dose of oral anti-diabetic therapy for ≥3 months prior to screening, fasting TG levels >150 mg/dL at screening) are being randomized (1:1) to receive either 500 mg/day of tipelukast or placebo for 24 weeks. The co-primary endpoints are change from baseline in liver fat content (FibroScan) and change from baseline in fasting serum TG levels at week 24. Secondary endpoints include safety and tolerability, and changes in lipid profile (HDL-C, LDL-C, and total-C).

Phase 2 NATG-202 Study Design



Source: Matsuda K., et al. European Atherosclerosis Society (EAS) '24.

Enrollment was completed in November 2025. Topline data are anticipated in mid-2026. We believe that NATG-202 represents a key inflection point in assessing whether the drug demonstrates sufficient clinical signal (TG and fibrosis improvements) and tolerability to justify a larger Phase 3 trial and eventual regulatory filing. In addition, the trial should define the optimal endpoints for the later-stage study design.

The promise and challenges of multi-target candidates; our thoughts. Polypharmacology agents, or drugs that act on multiple targets, as is the case for ibudilast and tipelukast, hold great promise for treating complex diseases, but they come with unique challenges. By simultaneously influencing several biological pathways, these drugs can be more effective than single-target therapies, particularly in complex indications like cancer, diabetes, and neurodegenerative disorders. Multi-target drugs also make it harder for diseases to develop resistance, and the combined mechanisms can produce synergistic effects, potentially allowing for lower doses and improving patient outcomes. In addition, they can simplify treatment regimens, improving patient compliance, offer more predictable pharmacokinetics than taking multiple separate drugs, and even address comorbid conditions with a single therapy. On the flip side, targeting multiple pathways increases the risk of side effects and can lead to complex or unpredictable interactions. Developing these drugs is scientifically challenging, as it requires designing a molecule that optimally balances potency, safety, and bioavailability across multiple targets. Finally, optimizing doses can be difficult, since each mechanism may require a different level of activity for the best therapeutic effect. In short, we highlight that multi-target drugs are a powerful tool in modern medicine, but their development requires careful balancing of benefits and risks.

3. Non-core ibudilast programs offer significant upside potential with minimal internal investment.

Multi-indication opportunities de-risk ibudilast clinical progress and strengthen potential partnerships. MediciNova's non-core pipeline strategy is characterized by a differentiated "platform-in-a-molecule" approach centered on ibudilast. Based on its multi-target MoA, ibudilast has the potential to address a broad spectrum of neurodegenerative, inflammatory, and addictive disorders through a shared mechanism targeting neuroinflammation. The likelihood of its multi-indication potential is also reinforced by its extensive human safety history in multiple clinical trials, as well as in the real-world, post-approval in Japan and South Korea. We believe that MediciNova's non-core programs are important valuation drivers for the company, representing: 1) a capital-efficient model with minimal internal R&D spend that leverages non-dilutive funding from government agencies; 2) a diversified clinical risk for ibudilast if the lead indication (ALS) fails; and 3) a path for potential strategic alliances with leading pharmaceutical companies who seek

to complete ibudilast product development and commercialization. We summarize the ibudilast non-core clinical pipeline in the table below, and detail the current status of the programs next:

Overview of Ibudilast Non-Core Programs

Indication	Clinical Stage	Primary Potential Benefit	Est. Internal Development Cost
Progressive MS	Phase 2b (Complete)	reduction in brain atrophy rate	low (NIH/NeuroNEXT funded)
Substance dependence	Phase 2 (ongoing)	reduction of methamphetamine-mediated neuroinflammation	low (grant-funded)
CIPN	Phase 2b (ongoing)	stabilizes/improves neurotoxicity in 71% of patients	low (funded by AGITG)
DCM	Phase 3 (ongoing)	adjuvant post-surgery recovery	low (NIHR UK grant)
GBM	Phase 1/2 (complete)	extension of PFS	moderate (Orphan Status exclusivity)
ARDS (COVID-19)	Phase 2 (complete)	higher rate of respiratory failure-free patients	low (federal funding)
Long COVID	Phase 2/3 (ongoing)	efficacy on COVID-19 lingering symptoms	low (grant-funded)

Source: H.C. Wainwright & Co. Research

- **Progressive Multiple Sclerosis (MS):** We view progressive MS as one of MediciNova's most relevant and attractive programs for potential partnerships, given the program's advanced stage of development, favorable Phase 2b data, the significant unmet medical need, and the relatively limited competitive landscape. MS is a chronic neurodegenerative disease of the CNS with a largely unknown etiology affecting ~2.8 to 2.9 million people worldwide. It is a leading cause of disability in young adults, frequently diagnosed between ages 20 and 50, and a 2-3x higher prevalence in women (Walton C., et al. *Mult Scler*. 2020). Approximately 85% of MS patients are initially diagnosed with relapsing-remitting MS (RRMS), characterized by acute attacks followed by partial or full recovery. Progressive MS involves a steady worsening of neurological function, with secondary progressive (SPMS) occurring after an initial RRMS phase, and primary progressive (PPMS) presenting as a gradual decline from the start with no early relapses. About 10–15% of RRMS individuals will eventually transition to SPMS, where disability progresses more steadily (McKay KA., et al. *Biomed Res Int*. 2015). Treatment options for progressive forms of MS (PPMS and SPMS) are limited, with Ocrevus (ocrelizumab; CD20-directed cytolytic antibody; IV infusion or subcutaneous injection) as the only approved therapy for PRMS (Albelo-Martínez. M, et al. *Neurotherapeutics*. 2025). Although several drugs are approved for PRMS with relapses (active form), there are no safe and effective therapies specifically for SRMS in the absence of relapses (non-active). Ibudilast was first evaluated in a Phase 2b trial in relapsing MS, demonstrating positive safety and neuroprotective signals, and suggesting potential for progressive MS. Subsequently, MediciNova partnered with investigators on the SPRINT-MS Phase 2b trial, a randomized, double-blind, placebo-controlled study in PRMS and SRMS, conducted by NeuroNEXT and funded by the National Institute of Neurological Diseases and Stroke (NINDS/NIH). Patients (n=255) were randomized to oral ibudilast (≤100 mg daily), or placebo, for 96 weeks. Baseline characteristics of study participants are summarized in the table below.

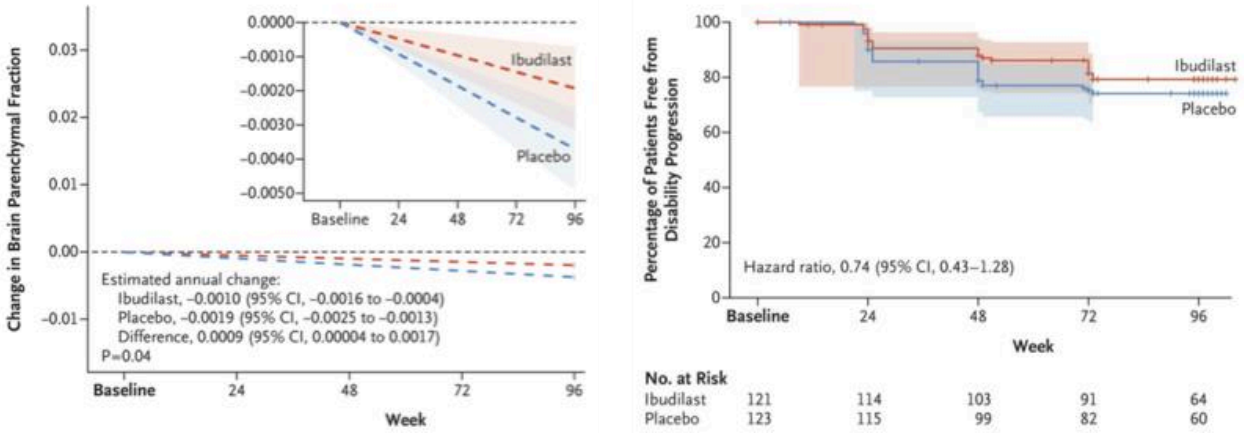
Baseline Characteristics of SPRINT-MS Phase 2b Study Participants

	Characteristic	Placebo (n = 126)	Ibudilast (n = 129)	P-value
Demographics	Age (yrs), mean (SD)	57 (6.5)	55 (7.8)	0.02
	Females, n (%)	69 (55%)	67 (52%)	0.65
	Race			
	Caucasian, n (%)	114 (91%)	122 (95%)	0.79
	Black / African American, n (%)	7 (6%)	4 (3%)	
	Other, n (%)	1 (1%)	3 (2%)	
	Unknown/Not Reported, n (%)	4 (3%)	0 (0%)	
	Hispanic/Latino, n (%)	3 (2%)	4 (3%)	1.00
Multiple Sclerosis	Primary Progressive, n (%)	66 (52%)	68 (53%)	0.96
	Use of Injection MS Therapy, n (%)	40 (32%)	40 (31%)	0.90
	Glatiramer Acetate, n (%)	24 (19%)	19 (15%)	
	Interferon-beta, n (%)	16 (13%)	21 (16%)	
	Disease Duration (yrs), median (min, max)	9 (0,36)	11 (0, 41)	0.64
	Expanded Disability Status Scale, median (min, max)	6.0 (3.0, 7.0)	6.0 (2.5, 6.5)	0.68
Imaging	Brain parenchymal fraction (unitless), mean (SD)	0.80 (0.0295)	0.80 (0.0298)	0.75
	T2 Lesion volume (cm^3), mean (SD)	10 (11.2)	10 (11.1)	0.99
	Magnetization transfer ratio in normal-appearing brain tissue (normalized units), mean (SD)	0.31 (0.31)	0.29 (0.25)	0.58
	Cortical thickness (mm), mean (SD)	3.03 (0.22)	3.04 (0.23)	0.72
	Longitudinal diffusivity (10^{-3} mm^2/sec), mean (SD)	1.24 (0.05)	1.25 (0.06)	0.15
	Transverse diffusivity (10^{-3} mm^2/sec), mean (SD)	0.56 (0.04)	0.55 (0.04)	0.04
	Retinal nerve fiber layer thickness (μm), mean (SD)	81.15 (13.15)	83.15 (10.81)	0.19

Source: Fox RJ., et al. N Engl J Med. 2019.

The trial met both primary endpoints of whole brain atrophy and safety and tolerability, demonstrating a statistically significant 48% reduction in the rate of whole brain atrophy with ibudilast vs. placebo (p=0.04), as measured by magnetic resonance imaging (MRI) analysis using brain parenchymal fraction (BPF) (below, left panel), without an increased rate of serious AEs (SAEs). Ibudilast also demonstrated a 26% reduction in the risk of confirmed disability progression (secondary endpoint) compared to placebo (hazard ratio (HR)=0.74), as measured by expanded disability status scale (EDSS) (below, right panel).

Change in Whole-Brain Atrophy and Risk of Disability



Source: Fox RJ., et al. N Engl J Med. 2019.

A subgroup analysis of the SPRINT-MS Phase 2b trial indicated that the greatest benefits were observed in SPMS patients without relapse, with a 46% risk reduction (HR=0.538).

Greater Risk Reduction in SPMS Without Relapse

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

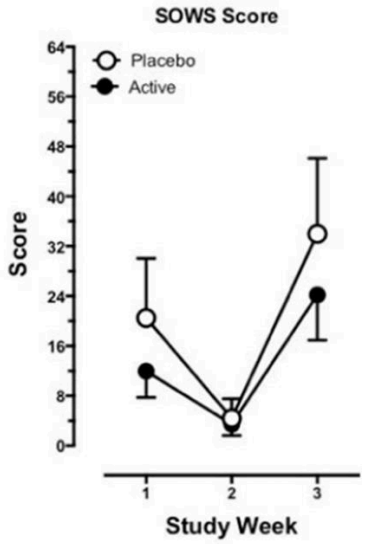
*MN-166 vs. Placebo

Source: Company presentation, April 2019.

The FDA granted Fast Track designation for the development of ibudilast for the treatment of patients with progressive MS. Based on SPRINT-MS data demonstrating the long-term efficacy potential of ibudilast for progressive MS patients, particularly those with SPMS without relapses, MediciNova finalized the design of a future registrational trial, and the progressive MS program is Phase 3-ready pending potential collaborators and/or partnerships.

- **Substance dependence:** According to the Substance Abuse and Mental Health Services Administration's (SAMHSA) 2023 National Survey on Drug Use and Health, there are ~1.8 million people with methamphetamine use disorder, ~5.6 million people with prescription pain reliever use disorder (~0.9 million people with heroin use disorder), and ~29.5 million people with alcohol use disorder (age ≥12 y.o) in the U.S. (U.S. Department of Health and Human Services 2024). Ibudilast is, or has been, under clinical evaluation in all three types of substance dependence:
  - Methamphetamine addiction: There is currently no pharmaceutical treatment approved for methamphetamine dependence. Following the receipt of Fast Track designation from the FDA for the treatment of methamphetamine dependence, MediciNova is currently collaborating with the Oregon Health & Science University on a biomarker study to evaluate ibudilast in methamphetamine use disorder. MediciNova continues to provide regulatory support and drug supply for the ongoing Phase 2 clinical trial (NCT03341078).
  - Opioid withdrawal and dependency: Current therapies for opioid withdrawal and dependence are largely based on opioid agonists or antagonists. These include narcotics such as methadone, buprenorphine, naloxone, and naltrexone. In contrast, there are very limited non-narcotic options for managing opioid withdrawal symptoms, including lofexidine, a central α-2 adrenergic agonist approved to mitigate opioid withdrawal symptoms and facilitate abrupt opioid discontinuation. Despite these options, there remains a significant and urgent unmet medical need for a safe, effective, non-addictive, non-opioid therapy for the treatment of prescription opioid and heroin addiction. To address this need, investigators at Columbia University and the New York State Psychiatric Institute (NYSPI) conducted a series of National Institute on Drug Abuse (NIDA/NIH)-funded clinical studies evaluating ibudilast. These included a randomized, double-blind, placebo-controlled Phase 1b/2a trial assessing its ability to reduce opioid withdrawal symptoms (NCT00723177), followed by a Phase 2a trial (NCT01740414) in patients with prescription opioid or heroin dependence (oxycodone self-administration). Positive Phase 2a results demonstrated, among other outcomes, ibudilast-mediated benefits on subjective craving for heroin effects (subjective opiate withdrawal scale (SOWS); $p<0.05$; see below), reinforcing the synergy with oxycodone.

Heroin-Craving Benefits Following Ibudilast Treatment



Source: Cooper ZD., et al. Addict Biol. 2017.

- Alcohol use disorder (AUD): Several pharmacotherapies are currently approved for the treatment of alcohol dependence, including disulfiram, naltrexone, and acamprosate. However, these agents have demonstrated modest efficacy and limited real-world uptake, and the development of a consistently safe and effective pharmacological treatment for AUD remains an unmet medical need. The clinical development of ibudilast for AUD is led by researchers at the University of California Los Angeles (UCLA) with a series of National Institute on Alcoholism and Alcohol Abuse (NIAAA/NIH)-funded studies. Although early clinical studies suggested favorable effects of ibudilast leading to decreased heavy drinking (i.e. reduced basal daily alcohol craving vs. placebo (n=24; $p<0.05$); 45% reduction in the odds of heavy drinking over time with vs. placebo (n=52; p=0.04); these signals did not translate into clear efficacy in a larger NIAAA-funded Phase 2b treatment-seeking population (n=102). Ibudilast failed to demonstrate superiority over placebo on the primary endpoint of percent heavy drinking days or on key secondary drinking outcomes, with both arms showing substantial improvements consistent with a strong placebo effect. While subsequent secondary and post-hoc analyses suggested potential mechanistic effects on cravings and possible benefit in biologically defined subgroups, such as patients with elevated baseline inflammatory markers, these findings remain exploratory and hypothesis-generating rather than confirmatory of clinical efficacy.

- **Chemotherapy-Induced Peripheral Neuropathy (CIPN):** Peripheral Neuropathy (PN) occurs when the nerves that are located outside of the brain and the spinal cord (peripheral nerves) are damaged. CINP is a common, debilitating, and often persistent combination of side effects (e.g., pain, burning, muscle weakness) associated with chemotherapeutic agents such as paclitaxel, oxaliplatin, and bortezomib. Underlying pathophysiology involves mitochondrial dysfunction, axonal degeneration, and neuroinflammation. It affects up to 68% of patients during treatment, and can severely impair QoL (Seretny M., et al. *Pain*. 2014). In 2018, MediciNova initiated a pilot clinical trial in Australia (ACTRN12618000232235), funded by the University of Sydney Concord Cancer Centre, evaluating ibudilast as a preventive therapy for CNIP. This was an open-label study that assessed acute neurotoxicity and drug-drug interactions (DDI) in patients with metastatic GI cancers, who were receiving oxaliplatin. Results showed that co-administration of ibudilast plus oxaliplatin, improved (2/14 participants) or stabilized (12/14 participants) oxaliplatin-induced neurotoxicity measured by the oxaliplatin-specific neurotoxicity

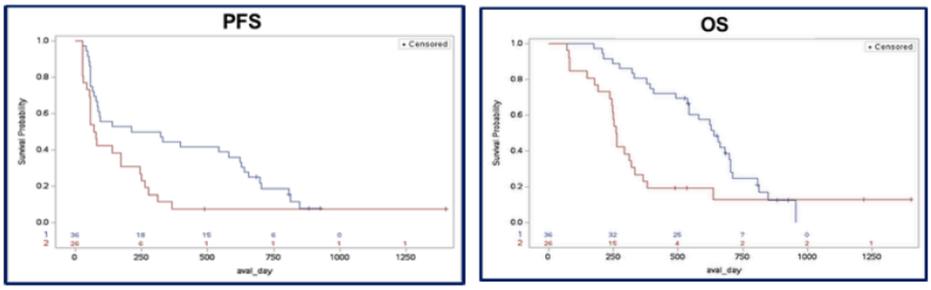
scale (OSNS) assessments on day three and at the end of the cycle. Pharmacokinetic analysis indicated no effect of ibudilast on systemic exposure of oxaliplatin (Teng C., et al. *Cancer Chemother Pharmacol*. 2020). The ongoing, multi-center, randomized OXTOX Phase 2b trial (NCT0405789), funded by the Australasian Gastro-Intestinal Trials Group (AGITG), is evaluating ibudilast over a 12-month period, and has recently completed enrollment of 100 metastatic colorectal cancer (CRC) patients. Participants will continue treatment until disease progression or other discontinuation criteria. Timing for results remains to be determined.

- **Degenerative Cervical Myelopathy (DCM):** DCM is a progressive condition where age-related deterioration of the cervical spine causes chronic compression of the spinal cord, leading to nerve dysfunction. Patients report neurological symptoms such as pain and numbness in limbs, poor coordination, imbalance, and bladder problems. Mechanistically, increased numbers of activated microglia and macrophages have been reported at the site of chronic spinal cord compression (Gharooni AA., et al. *Global Spine J*. 2022). There are no therapeutics approved, and it is estimated that ~150,000 cervical procedures are performed each year in the U.S. to relieve DCM (Ghogawala Z., et al. *Neurosurgery.* 2016). In collaboration with the University of Cambridge and funding from the National Institute for Health Research (NIHR) in the UK, in 2018 MediciNova initiated a Phase 3 clinical trial evaluating ibudilast as an adjuvant treatment for DCM following spinal surgery to determine whether ibudilast is more effective than placebo in improving outcomes after spinal surgery (co-primary endpoints: 1) the modified Japanese Orthopaedic Association (mJOA) score for motor dysfunction; and 2) Visual Analogue Scale (VAS) measure of neck pain, at six months after surgery). A Phase 3 kick-off meeting was held in 2019, and recruitment is underway in the RECEDE-Myelopathy trial (NCT04631471).

- **Glioblastoma (GBM):** GBM is a highly aggressive primary brain tumor arising from glial cells and is characterized by rapid growth and infiltration into surrounding brain tissues. It accounts for approximately 14% of all primary brain tumors, and it is estimated that approximately 12,000 new cases are diagnosed annually in the U.S. Prognosis remains poor, with a median survival of 12 to 15 months for treated patients, and approximately four months for those untreated (Singh S., et al. *Signal Transduct Target Ther*. 2025). The current SoC consists of surgical resection followed by radiation and temozolomide chemotherapy, with additional approved therapies including carmustine implants (biodegradable chemotherapy-loaded wafers) and bevacizumab (VEGF-A-targeting antibody); however, a significant unmet medical need remains. Early preclinical data evaluating ibudilast, in combination with temozolomide, in GBM mouse models demonstrated improved median survival compared to temozolomide alone (McDonald KL., et al. ASCO ’17). Additional findings identified MIF inhibition (Ha W., et al. *Sci Rep*. 2019) and modulation of immunosuppressive myeloid cell populations (Alban TJ., et al. *Front Immunol*. 2020) as a key mechanism. Following IND acceptance and the receipt of Orphan-Drug designation by the FDA in 2018, a Phase 1/2 clinical trial of ibudilast, in combination with temozolomide, was initiated at the Dana-Farber Cancer Institute (NCT03782415; enrollment completion in 2023). Phase 1/2 results demonstrated that the combination regimen was safe and well tolerated in 62 patients, including 36 newly diagnosed and 26 recurrent GBM patients, with six-month progression-free survival (PFS) rates of 44% and 31%, respectively (see below).

Favorable PFS Data Following Ibudilast + Temozolomide

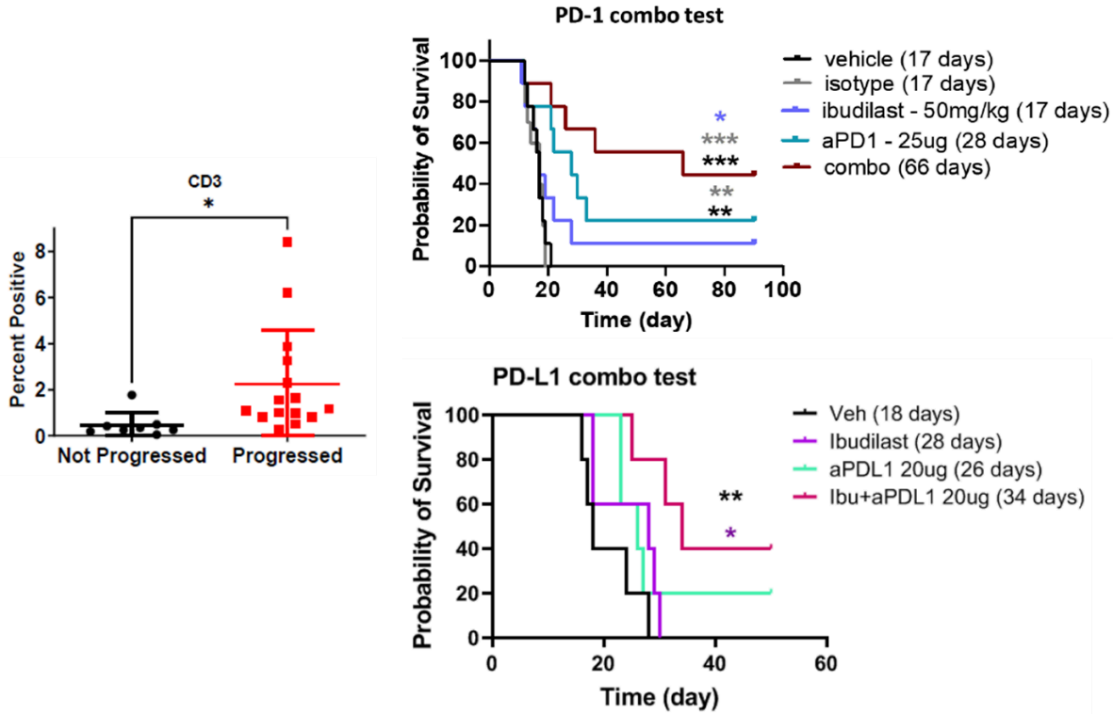
	nGBM (N = 36)	rGBM (N =26)
Progression-Free Survival		
PFS6 rate	16 (44.4%)	8 (30.8%)
Median PFS (95% CI)	8.7 months (2.6, 20.5)	2.4 months (1.8, 5.7)
Overall Survival		
OS-6 months	35 (97.2%)	21 (80.8%)
OS-12 months	29 (80.6%)	7 (26.9%)
Median OS (95% CI)	21 months (17.7, 23.0)	8.6 months (7.8, 10.5)



Source: Gilbert Y., et al. ASCO '24.

Immunohistochemistry analyses suggested CD3 expression as a potential predictor of tumor progression at five months in recurrent disease (below, left panel), and complementary preclinical studies showed significant survival benefits when ibudilast was combined with anti-PD-1 ($p<0.001$; below, top right panel) or anti-PD-L1 therapies ($p<0.05$; below, bottom right panel). Collectively, these findings support the continued development of ibudilast as a novel immunomodulatory adjunctive therapy for GBM.

Potential Biomarker and Combination Agents



Source: Lauko A., et al. Society for NeuroOncology (SNO) Annual Meeting '23.

- **Acute Respiratory Distress Syndrome (ARDS) in COVID-19 patients:** ARDS is a life-threatening, rapid-onset, lung condition where fluid fills the alveoli, severely lowering blood oxygen levels (hypoxemia). It typically develops in critically ill patients 24 to 48 hours after a potential injury, such as viral infections (coronavirus, pneumonia, or sepsis). According to the ARDS Foundation, there are an ~150,000 ARDS cases per year in the U.S., and the rate of death is ~40% (Diamond M., et al. *StatPearls*. 2024). Preclinical studies in ARDS animal models demonstrated that treatment with ibudilast reversed hemorrhage, alveolar congestion, and cell apoptosis in lung tissue, and also reduced the levels of inflammatory cytokines (Yang D., et al. *Med Sci Monit*. 2020). Results from the Phase 2 trial evaluating oral ibudilast in hospitalized COVID-19 patients at risk for developing ARDS (NCT04429555), demonstrated favorable improvements vs. placebo in several clinical endpoints analyzed, including: 1) proportion of patients free of respiratory failure at day seven (71% in treatment arm vs. 35% in placebo; p=0.02); 2) proportion of subjects discharged from the hospital at day seven (65% in treatment arm vs. 29% in placebo; p=0.02); and 3) proportion of patients with worsened clinical status at day seven (0% in treatment arm vs. 24% in placebo; p=0.05) (see below).

Clinical Improvement of COVID-19 Patients with ARDS

Outcome	MN-166 (n=17)	Placebo (n=17)	Difference
Recovered from Respiratory Failure by Day 7	12/17 (70.6%)	6/17 (35.3%)	35.3% (p=0.0196)
Improved NIAID8-point score by Day 7	12/17 (70.6%)	8/17 (47.1%)	23.5% (p=0.0817)
Discharged from hospital by Day 7	11/17 (64.7%)	5/17 (29.4%)	35.3 % (p=0.0196)
All cause mortality	0 /17 (0%)	2/17 (11.8%)	

Source: Company materials, January 2026.

- **Long COVID:** Long COVID is defined as a chronic condition that includes a wide range of symptoms (e.g., respiratory, neurologic, GI), and can last for weeks, months, or years following SARS-CoV-2 infection. The CDC's 2023 data reveal that 6.4% of U.S. adults report experiencing Long COVID, with 19.8% reporting significant limitations in daily activities (ND Ford., et al. *CDC MMWR Morb Mortal Wkly Rep*.2023). In 2022, MediciNova reached an agreement to collaborate with the University Health Network in Canada and participate in the Recovering from COVID-19 Lingering Symptoms Adaptive Integrative Medicine Trial (RECLAIM) trial. This is a grant-funded, multi-center, randomized clinical trial evaluating ibudilast, and other therapies, for the treatment of Long COVID and lingering symptoms of COVID-19. In 2023, Health Canada completed the review of the CTA and granted authorization to initiate the RECLAIM trial (NCT05513560), which is currently analyzing efficacy data.

Valuation

We are initiating coverage of MediciNova with a Buy rating and $10 price target. We base our valuation on our probability-weighted clinical net present value (NPV) valuation model. This is an independent, fully taxed snapshot of each drug's perceived value in both the U.S. and ex-U.S. We believe this method is appropriate in capturing the value of the clinical stage pipeline by allowing us to flex multiple assumptions, including chance of success, peak sales estimates, and year of commercial launch.

Our peak sales estimates are found by looking out approximately five to six years from projected drug launch. Per our market models below, and incorporating the vagaries, and timing of new drug launches, we believe a rough estimate of the market model sales in year five and year six best represent our view of peak. We believe a level of conservatism exists in our valuation model based on our assigned multiple of 17.0x, rather than the sometimes-inflated non-profitable biotech multiples in the 30-40x range. Our rationale for using Big Pharma multiples, plus a discount, is based on the potential acquisition metrics utilized by Big Pharma in valuing the smaller biotech as part of its overall portfolio. We are currently assigning a 15% discount rate, which is in line for the majority of our covered companies, except for those with higher perceived risks. Our valuation is also based on fully diluted share count.

Our clinical NPV valuation (see below) is based on the contribution of MediciNova's core clinical-stage assets, ibudilast (MN-166), currently in Phase 2b/3 evaluation for the treatment of ALS (15% PoS; 33% contribution), and tipelukast (MN-001), under Phase 2 evaluation for the treatment of HTG and NAFLD due to T2D (20% PoS; 67% contribution). We currently value the development of ibudilast and tipelukast only in the U.S. We believe ibudilast has the potential to receive regulatory green light to advance into registrational ALS studies and become the first genotype-agnostic, multi-target therapy approved for this indication. Note that for both programs, we project a relatively high degree of conservatism as we await: 1) Phase 2b/3 data and clinical/regulatory guidance for ibudilast; and 2) Phase 2 data for tipelukast, which should provide clearer insight into its efficacy and inform its potential commercial positioning as either a standalone therapy or an add-on strategy. While we assume higher market penetration for ibudilast, given the limited number of available ALS therapies and their modest efficacy, we apply a more conservative penetration assumption for tipelukast, reflecting the presence of already approved therapies for NASH/MASH. We still believe that tipelukast has the potential to be a blockbuster for MediciNova, attaining ~$1 billion peak sales, with only <1% market penetration in the U.S.

Based on the factors mentioned above, we believe significant upside potential exists to our valuation based on: (1) attaining higher market penetration than currently projected in the above-mentioned indications; (2) augmenting projected chances of success based on the progress of the clinical candidates; (3) adding additional commercial geographies; and (4) progress of non-core programs through licensing deals and/or collaboration agreements, which we believe investors fully currently discount from the company's valuation.

MediciNova NPV Valuation Model

Drug Name	Indication	Status	Launch	Success	Peak Sales (US$M)	Economics	Profitability	NPV (US$)
Ibudilast (MN-166)	ALS - U.S.	Phase 2b/3	2028	15%	675	100%	30%	3.28
Tipelukast (MN-001)	HTG and NAFLD in T2D - U.S.	Phase 2	2028	20%	1050	100%	30%	6.81
							Total	10.09

Source: H.C. Wainwright estimates.

Ibudilast ALS Market Model

U.S. ALS										
Ibudilast (MN-166)	**2026**	**2027**	**2028**	**2029**	**2030**	**2031**	**2032**	**2033**	**2034**	**2035**
Patients with ALS	25,000	26,250	27,563	28,941	30,388	31,907	33,502	35,178	36,936	38,783
Penetration	0.00%	0.00%	3.00%	4.50%	6.25%	7.30%	8.50%	10.50%	12.50%	9.25%
Number of patients treated	0	0	827	1,302	1,899	2,329	2,848	3,694	4,617	3,587
Cost of therapy ($K)*	$0.00	$0.00	$145.00	$149.35	$153.83	$158.45	$163.20	$168.09	$173.14	$178.33
Revenue ($M)	$0.00	$0.00	$119.90	$194.50	$292.16	$369.05	$464.74	$620.88	$799.38	$639.76
Royalties	0%	0%	7%	8%	9%	10%	12%	13%	13%	13%
Revenue to MediciNova ($M)	$0.00	$0.00	$111.50	$178.94	$265.86	$332.15	$408.97	**$540.17**	**$695.46**	$556.59
	Phase 2/3b readout	initiate Phase 3	potential approval U.S					peak sales		
*estimated annual cost for single course of treatment; based on other approved small molecules for ALS (i.e. edaravone brand version, Radicava)										

Source: H.C. Wainwright estimates.

Tipelukast HTG and NAFLD in T2D Market Model

U.S. HTG and NAFLD in T2D										
Tipelukast (MN-001)	**2026**	**2027**	**2028**	**2029**	**2030**	**2031**	**2032**	**2033**	**2034**	**2035**
Patients with T2D	35,000,000	35,700,000	36,414,000	37,142,280	37,885,126	38,642,828	39,415,685	40,203,998	41,008,078	41,828,240
T2D patients with HTG and/or NAFLD	17,500,000	17,850,000	18,207,000	18,571,140	18,942,563	19,321,414	19,707,842	20,101,999	20,504,039	20,914,120
Penetration	0.00%	0.00%	0.01%	0.03%	0.05%	0.07%	0.08%	0.10%	0.12%	0.11%
Number of patients treated	0	0	1,821	5,571	9,471	13,525	15,766	20,102	24,605	23,006
Cost of therapy ($K)*	$0.00	$0.00	$45.00	$46.35	$47.74	$49.17	$50.65	$52.17	$53.73	$55.34
Revenue ($M)	$0.00	$0.00	$81.93	$258.23	$452.16	$665.06	$798.53	$1,048.67	$1,322.08	$1,273.23
Royalties	0%	0%	7%	8%	9%	10%	12%	13%	13%	13%
Revenue to MediciNova ($M)	$0.00	$0.00	$76.20	$237.57	$411.47	$598.55	$702.71	**$912.34**	**$1,150.21**	$1,107.71
	Phase 2 readout	initiate Phase 3	potential approval U.S					peak sales		
*estimated annual cost for single course of treatment; based on other approved small molecules for similar indications (i.e.resmetirom brand version, Rezdiffra)										

Source: H.C. Wainwright estimates.

Risks

Clinical, regulatory, and market risk. The three primary risks for companies that are developing new therapeutic agents are: (1) regulatory risk including how the clinical data will be assessed by the FDA; (2) potential peers' competition; and (3) the risk of clinical trial failure. Additional regulatory challenges may be faced by the company, which could impede the potential success of a drug candidate. We value the competition and consider that potential comparable therapies may be developed from peers and could already be in later stages of development; however, we believe that MediciNova's multi-target small molecule therapeutic approach is one of its kind, and appears to be generating promising clinical-stage data in multiple indications with high unmet medical needs.

Financing risk. As with the majority of development stage biotechnology companies with no regulatory approved drug agents, maintaining funding is a critical necessity for the progression of the candidate pipeline. The company ended 2025 with $30.8 million in cash, which should provide runway through ibudilast (Phase 2b/3) and tipelukast (Phase 2) readouts and, if results are positive, the initiation of later-stage trials. However, cash burn could be significantly impacted based on increasing the number of development and commercial programs, which could be potentially offset by partner or collaborative milestone revenue payments. It is also likely that additional equity raises could come in the future based on pipeline and geographic expansions.

Commercial risk. Even if approval is obtained for a therapeutic candidate, MediciNova may not generate or sustain revenue from sales of the therapeutic product due to factors such as whether the therapeutic product can be sold at a competitive price and otherwise accepted in the market. Therefore, any revenue from sales of the therapeutic product may not offset the costs of development. The therapeutic candidate MediciNova is developing is derived from internal discovery platforms. Market participants with significant influence over acceptance of new treatments, such as physicians and third-party payers, may not adopt a treatment based on its therapeutic products, and the company may not be able to convince the medical community and third-party payers to accept and use, or to provide favorable coverage or reimbursement for, any therapeutic products developed by MediciNova or any future collaborators.

For additional risk considerations, please refer to the company's SEC filings.

($ in millions except per share data)

Profit & Loss	2022A	2023A	2024A	2025A	2026E	2027E	2028E	2029	2030
Licensing and R&D revenue	0.0	0.0	0.0	0.4	0.5	0.7	1.2	1.5	1.5
Milestone revenue	0.0	1.0	0.0	0.0	0.0	0.0	0.0	1.0	2.0
Product and Royalties	0.0	0.0	0.0	0.0	0.0	0.0	60.0	185.0	305.0
Other revenues	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.0	2.0
Revenues	**0.0**	**1.0**	**0.0**	**0.4**	**0.5**	**0.7**	**61.2**	**188.5**	**310.5**
CoGS	0.0	0.0	0.0	0.0	0.2	0.4	5.2	7.9	11.3
Gross Profit	**0.0**	**1.0**	**0.0**	**0.4**	**0.3**	**0.3**	**56.0**	**180.6**	**299.2**
Gross margin	*0%*	*100%*	*0%*	*100%*	*60%*	*43%*	*92%*	*96%*	*96%*
G&A	5.5	5.2	5.5	6.2	6.8	10.8	19.0	34.1	41.0
R&D	9.1	5.7	7.2	7.2	8.5	15.8	20.5	25.6	30.7
Other op ex	0.0	0.0	0.0	0.4	0.0	0.0	0.0	1.0	2.0
EBIT	**(14.6)**	**(9.9)**	**(12.7)**	**(13.3)**	**(15.0)**	**(26.3)**	**16.6**	**119.9**	**225.5**
EBIT margin	*nm*	*nm*	*nm*	*nm*	*nm*	*nm*	*27%*	*64%*	*73%*
Depreciation	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Amortization Intangibles	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
EBITDA	**(14.6)**	**(9.9)**	**(12.7)**	**(13.3)**	**(15.0)**	**(26.3)**	**16.6**	**119.9**	**225.5**
EBITDA margin	*nm*	*nm*	*nm*	*nm*	*nm*	*nm*	*27%*	*64%*	*73%*
Non operating expenses	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Net Interest Income/Other	0.6	1.3	1.6	1.3	1.5	1.6	1.7	2.1	2.4
Interest expense	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.2	0.3
EBT	**(14.1)**	**(8.6)**	**(11.0)**	**(12.0)**	**(13.5)**	**(24.7)**	**18.3**	**121.8**	**227.7**
EBT margin	*nm*	*nm*	*nm*	*nm*	*nm*	*nm*	*30%*	*65%*	*73%*
Provision for taxes	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	27.3
Net Income	**(14.1)**	**(8.6)**	**(11.0)**	**(12.0)**	**(13.5)**	**(24.7)**	**18.3**	**121.8**	**227.7**
Participation of preferred stock	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.0	2.0
Net Income to common	**(14.1)**	**(8.6)**	**(11.0)**	**(12.0)**	**(13.5)**	**(24.7)**	**18.3**	**122.8**	**202.3**
net margin	*nm*	*nm*	*nm*	*nm*	*nm*	*nm*	*30%*	*65%*	*65%*
Number of shares - basic	49.0	49.0	49.0	49.1	52.1	56.9	60.0	61.0	63.6
Number of shares - diluted	49.0	49.0	49.0	49.1	52.1	56.9	62.5	64.6	66.9
EPS - basic	**(0.29)**	**(0.17)**	**(0.23)**	**(0.24)**	**(0.26)**	**(0.43)**	**0.30**	**2.01**	**3.18**
EPS - diluted	**(0.29)**	**(0.17)**	**(0.23)**	**(0.24)**	**(0.26)**	**(0.43)**	**0.29**	**1.90**	**3.02**

Source: SEC filings and H.C. Wainwright estimates.

Lander Egaña Gorroño, Ph.D. legana@hcwco.com

Quarterly P&L

	Q1'25A	Q2'25A	H1'25A	Q3'25A	9M'25A	Q4'25A	FY'25A	Q1'26E	Q2'26E	H1'26E	Q3'26E	9M'26E	Q4'26E	FY'26E
Licensing and R&D revenue	0.00	0.13	0.13	0.12	0.26	0.15	0.4	0.00	0.13	0.13	0.12	0.26	0.24	0.5
Milestone revenue	0.00	0.00	0.00	0.00	0.00	0.00	0.0	0.00	0.00	0.00	0.00	0.00	0.00	0.0
Product and Royalties	0.00	0.00	0.00	0.00	0.00	0.00	0.0	0.00	0.00	0.00	0.00	0.00	0.00	0.0
Other revenues	0.00	0.00	0.00	0.00	0.00	0.00	0.0	0.00	0.00	0.00	0.00	0.00	0.00	0.0
Revenues	**0.00**	**0.13**	**0.13**	**0.12**	**0.26**	**0.15**	**0.4**	**0.00**	**0.13**	**0.13**	**0.12**	**0.26**	**0.24**	**0.5**
CoGS	0.00	0.12	0.12	0.12	0.23	-0.23	0.0	0.00	0.12	0.12	0.12	0.23	-0.03	0.2
Gross Profit	**0.00**	**0.02**	**0.02**	**0.01**	**0.03**	**0.38**	**0.4**	**0.00**	**0.02**	**0.02**	**0.01**	**0.03**	**0.27**	**0.3**
Gross margin	*nm*	*nm*	*nm*	*nm*	*nm*	*nm*	*100%*	*nm*	*nm*	*nm*	*nm*	*nm*	*nm*	*60%*
G&A	1.36	1.44	2.80	1.81	4.61	1.55	6.2	1.36	1.44	2.80	1.81	4.61	2.17	6.8
R&D	1.84	2.19	4.03	1.58	5.61	1.54	7.2	1.84	2.19	4.03	1.58	5.61	2.90	8.5
Other op ex	0.00	0.00	0.00	0.00	0.00	0.38	0.4	0.00	0.00	0.00	0.00	0.00	0.00	0.0
EBITDA	**(3.2)**	**(3.6)**	**(6.8)**	**(3.4)**	**(10.2)**	**(3.1)**	**(13.3)**	**(3.2)**	**(3.6)**	**(6.8)**	**(3.4)**	**(10.2)**	**(4.8)**	**(15.0)**
EBITDA margin							*nm*							*nm*
Non operating expenses	0.00	0.00	0.00	0.00	0.00	0.00	0.0	0.00	0.00	0.00	0.00	0.00	0.00	0.0
Net Interest Income/Other	0.34	0.33	0.66	0.33	0.99	0.30	1.3	0.34	0.33	0.66	0.33	0.99	0.51	1.5
Interest expense	0.00	0.00	0.00	0.00	0.00	0.00	0.0	0.00	0.00	0.00	0.00	0.00	0.00	0.0
EBT	**(2.9)**	**(3.3)**	**(6.1)**	**(3.1)**	**(9.2)**	**(2.8)**	**(12.0)**	**(2.9)**	**(3.3)**	**(6.1)**	**(3.1)**	**(9.2)**	**(4.3)**	**(13.5)**
EBT margin							*nm*							*nm*
Provision for taxes	0.00	0.00	0.00	0.00	0.00	0.01	0.0	0.00	0.00	0.00	0.00	0.00	0.00	0.0
Participation of preferred stock							0.0							0.0
Net Income to common	**(2.86)**	**(3.3)**	**(6.1)**	**(3.1)**	**(9.2)**	**(2.8)**	**(12.0)**	**(2.86)**	**(3.3)**	**(6.1)**	**(3.1)**	**(9.2)**	**(4.3)**	**(13.5)**
net margin							*nm*							*nm*
NoSH basic	49.05	49.05	49.05	49.05	8.34	49.12	49.06	49.88	51.95	50.91	52.59	8.34	54.11	52.13
NoSH diluted	49.05	49.05	49.05	49.05	8.34	49.12	49.06	49.88	51.05	50.46	52.59	8.34	54.11	52.13
EPS - basic	**(0.06)**	**(0.07)**	**(0.13)**	**(0.06)**	**(1.10)**	**(0.06)**	**(0.24)**	**(0.06)**	**(0.06)**	**(0.12)**	**(0.06)**	**(1.10)**	**(0.08)**	**(0.26)**
EPS - diluted	**(0.06)**	**(0.07)**	**(0.13)**	**(0.06)**	**(1.10)**	**(0.06)**	**(0.24)**	**(0.06)**	**(0.06)**	**(0.12)**	**(0.06)**	**(1.10)**	**(0.08)**	**(0.26)**

Source: SEC filings and H.C. Wainwright estimates.

Lander Egaña Gorroño, Ph.D. legana@hcwco.com

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Market Outperform (Buy): The common stock of the company is expected to outperform a passive index comprised of all the common stock of companies within the same sector.

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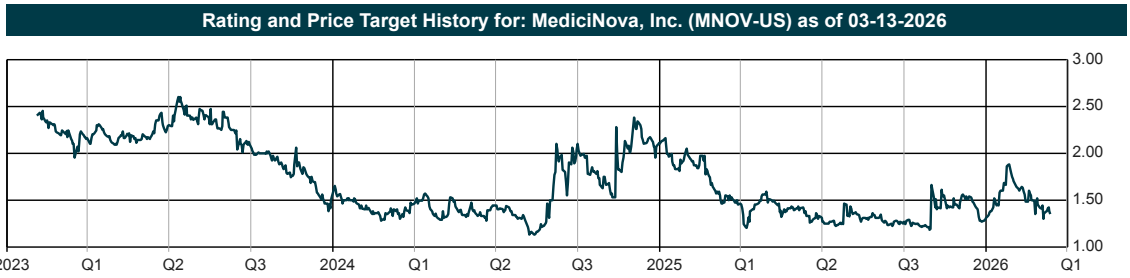

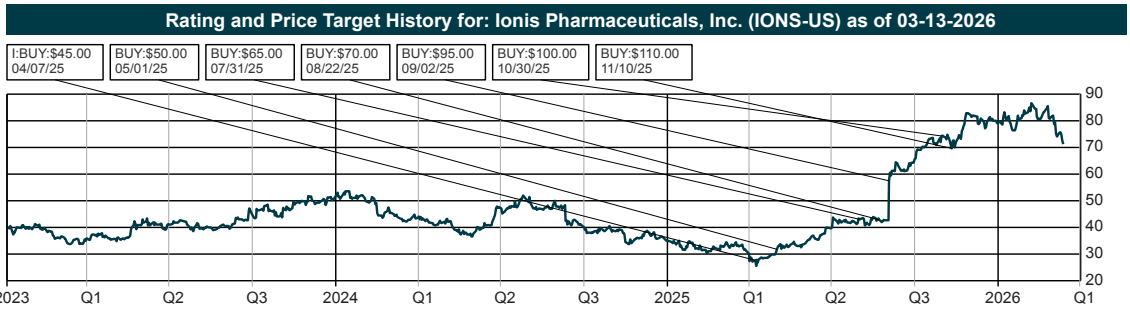

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Company	Ticker	H.C. Wainwright Rating	12 Month Price Target	Price	Market Cap
Ionis Pharmaceuticals, Inc.	IONS-US	Buy	$110.00	$71.19	$11760
Clene Inc.	CLNN-US	Buy	$31.00	$5.72	$67

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Distribution of Ratings Table as of March 13, 2026				
			IB Service/Past 12 Months	
Ratings	Count	Percent	Count	Percent
Buy	583	87.01%	158	27.10%
Neutral	62	9.25%	11	17.74%
Sell	1	0.15%	0	0.00%
Under Review	24	3.58%	4	16.67%

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