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MediciNova Corporate Presentation

Forward-Looking Statements

Statements in this presentation that are not historical in nature constitute forward-looking statements within the meaning of the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. These forward-looking statements include statements regarding MediciNova's clinical trials supporting the safety and efficacy of its product candidates and the potential novelty of such product candidates as treatments for disease, plans and objectives for clinical trials and product development, strategies, future performance, expectations, assumptions, financial condition, liquidity and capital resources. These forward-looking statements include, without limitation, statements regarding the future development and efficacy of MN-166, MN-221, MN-001, and MN-029. These forward-looking statements may be preceded by, followed by or otherwise include the words "believes," "expects," "anticipates," "intends," "estimates," "projects," "can," "could," "may," "will," "would," "considering," "planning" or similar expressions. These forward-looking statements involve a number of risks and uncertainties that may cause actual results or events to differ materially from those expressed or implied by such forward-looking statements. Factors that may cause actual results or events to differ materially from those expressed or implied by these forward-looking statements include, but are not limited to, risks of obtaining future partner or grant funding for development of MN-166, MN-221, MN-001, and MN-029 and risks of raising sufficient capital when needed to fund MediciNova's operations and contribution to clinical development, risks and uncertainties inherent in clinical trials, including the potential cost, expected timing and risks associated with clinical trials designed to meet FDA guidance and the viability of further development considering these factors, product development and commercialization risks, risks related to MediciNova's reliance on the success of its MN-166 and MN-001 product candidates, the uncertainty of whether the results of clinical trials will be predictive of results in later stages of product development, the risk of delays or failure to obtain or maintain regulatory approval, risks associated with the reliance on third parties to sponsor and fund clinical trials, risks regarding intellectual property rights in product candidates and the ability to defend and enforce such intellectual property rights, the risk of failure of the third parties upon whom MediciNova relies to conduct its clinical trials and manufacture its product candidates to perform as expected, the risk of increased cost and delays due to delays in the commencement, enrollment, completion or analysis of clinical trials or significant issues regarding the adequacy of clinical trial designs or the execution of clinical trials, and the timing of expected filings with the regulatory authorities, MediciNova's collaborations with third parties, the availability of funds to complete product development plans and MediciNova's ability to obtain third party funding for programs and raise sufficient capital when needed, and the other risks and uncertainties described in MediciNova's filings with the Securities and Exchange Commission, including its annual report on Form 10-K for the year ended December 31, 2023 and its subsequent periodic reports on Forms 10-Q and 8-K. Undue reliance should not be placed on these forward-looking statements, which speak only as of March 15, 2024. MediciNova disclaims any intent or obligation to revise or update these forward-looking statements.

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MediciNova's mission is to develop promising **new therapeutics** for the treatment of diseases with **high unmet medical needs**.

MediciNova Overview

Late-stage biopharma company developing oral, anti-inflammatory candidates with well-established safety and efficacy profiles

- Differentiated product profiles have potential to meet needs of patients across a wide range of indications
- Targeting large, underserved, markets

Robust pipeline focused on neurological, fibrotic, and other diseases with no or inadequate treatment options

- MN-166 (ibudilast): targeting CNS disorders with high unmet needs, including Phase 3 programs in ALS and DCM
  - Progressive MS program is Phase 3 ready
  - Other programs in ARDS, glioblastoma, CIPN, substance dependence, and Long COVID
- MN-001 (tipelukast): Phase 2 for NAFLD

Well-funded with capital efficient business model

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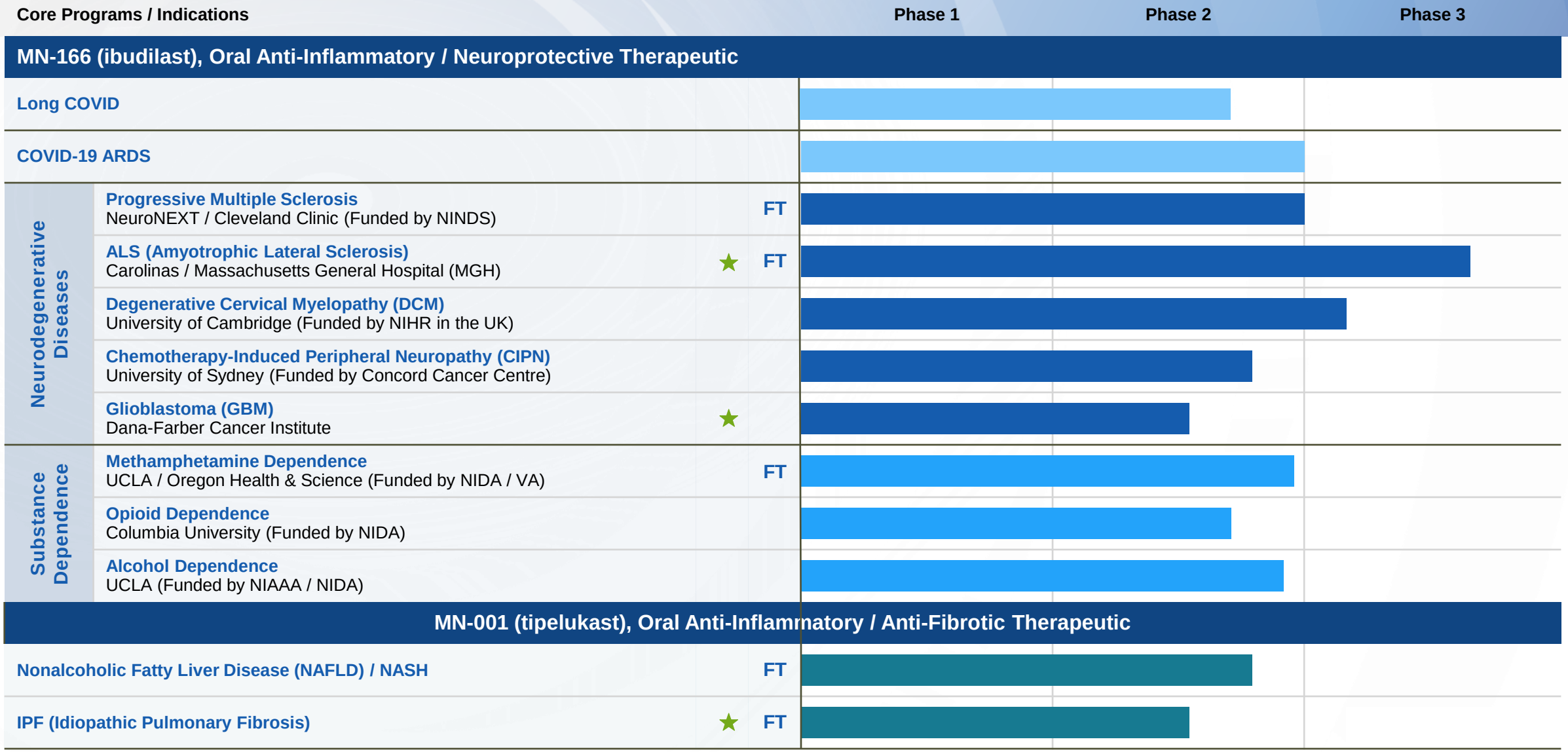
Robust Pipeline Targeting High Unmet Needs



MN-166

Ibudilast

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MN-166 (ibudilast) Overview

Oral, anti-inflammatory neuroprotective candidate

- Well established safety and tolerability profile
- Approved in Japan for post-stroke dizziness / asthma (~3 MM patients)

Late-stage development across major indications

- Phase 3 trials in Amyotrophic Lateral Sclerosis (ALS) and Degenerative Cervical Myelopathy (DCM) are ongoing
- Phase 3 ready in progressive multiple sclerosis (MS)
  - Phase 2 data shows potential for strong efficacy in Secondary Progressive MS without Relapse for which there are no approved drugs
- Completed Phase 2 trial in COVID-19 ARDS with positive results

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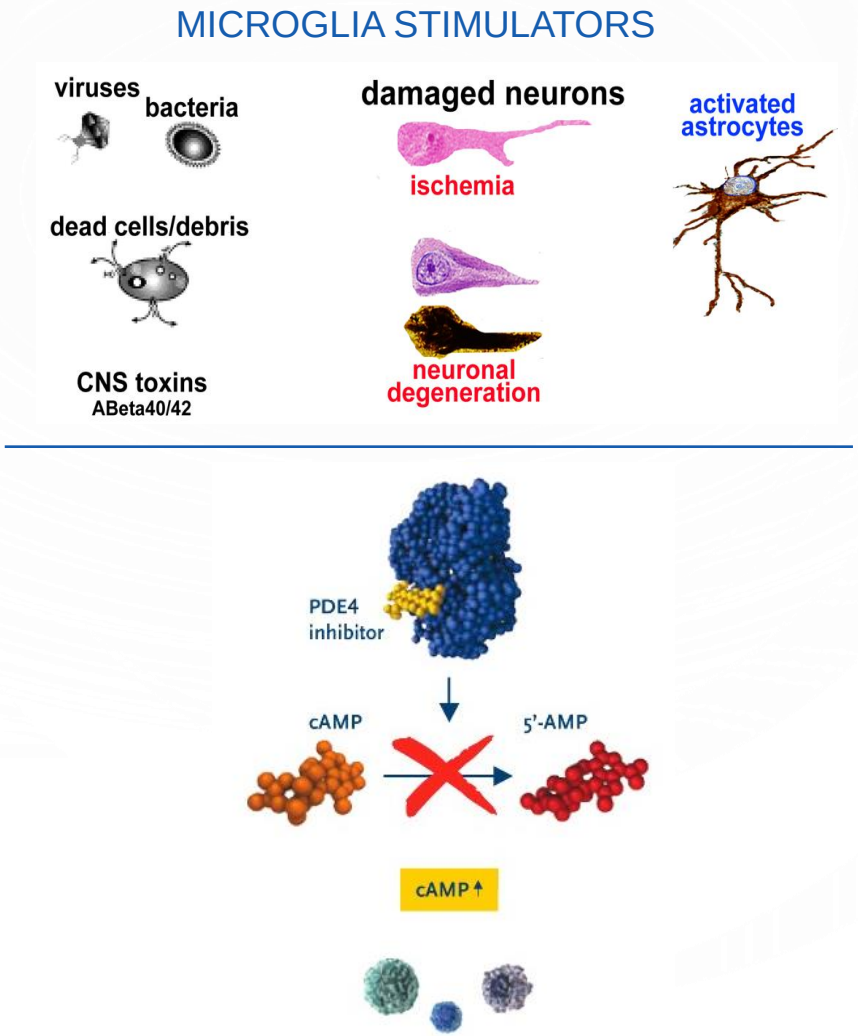
MN-166 (ibudilast): Multiple Mechanisms of Action



MIF Inhibition

- Linked to attenuated disease progression in animal models of MS

PDE 4 Inhibition

- Increases cAMP
- Reduces pro-inflammatory cytokines (i.e. IL-1, TNF-α, IL-6)
- Neuroprotection

Glial Cell Attenuation

- Role of Glia:
  - Type of macrophage
  - Activated during brain damage
  - **Glial activation leads to neurodegeneration**

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Amyotrophic Lateral Sclerosis (ALS) Landscape

ALS AFFECTS

~16K

People in United States[1]

ORPHAN INDICATION

LIFE EXPECTANCY

2-5

Years[1]

FATAL

An effective new drug for ALS could generate sales of

$1B+[2]

EXPECTED MARKET OPPORTUNITY

APPROVED DRUGS

RILUZOLE
Increases survival by ONLY 2-3 months[3]

RADICAVA
No survival benefit on label[4]

RELYVRIO
Limited efficacy data[5]
No Phase 3 data

QALSODY
Approved for SOD_1-ALS[6] which affects 2% of ALS patients

MN-166 (ibudilast) Advantages:

- Potential to improve survival compared to standard of care
- No serious safety issues (other ALS drugs have Warnings on the labels)

1. Source: ALS Association; 2. Source: Cowen & Co. estimate; 3. Cochrane Database of Systematic Reviews; 4. Radicava prescribing information; 5. Relyvrio prescribing information; 6. Qalsody prescribing information.

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Positive Phase 2 Results in ALS

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

*Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised (ALSFRS-R) total score measures the functional activity of an ALS subject. ALS subjects decline on the ALSFRS-R total score over time as the disease progresses and their symptoms worsen.

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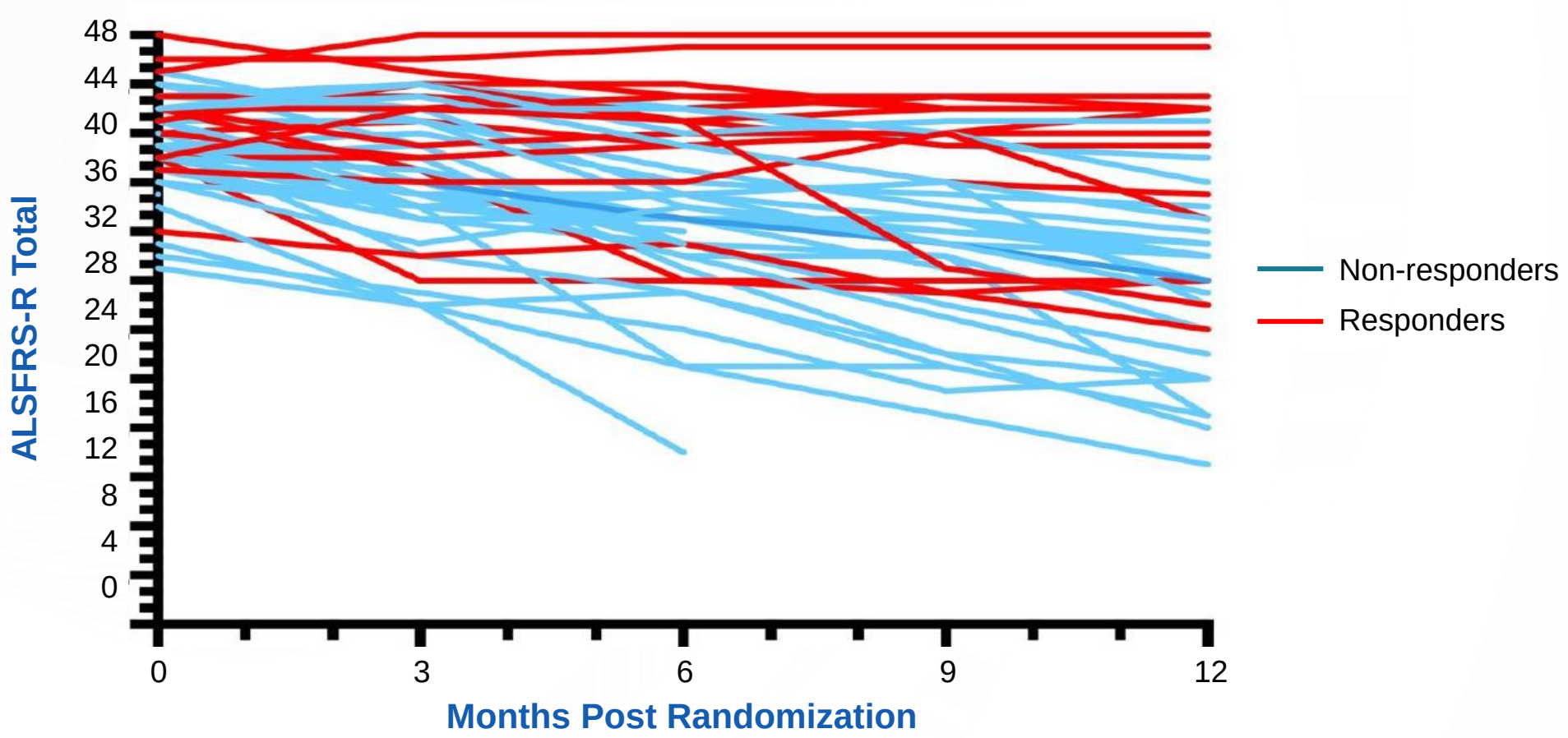
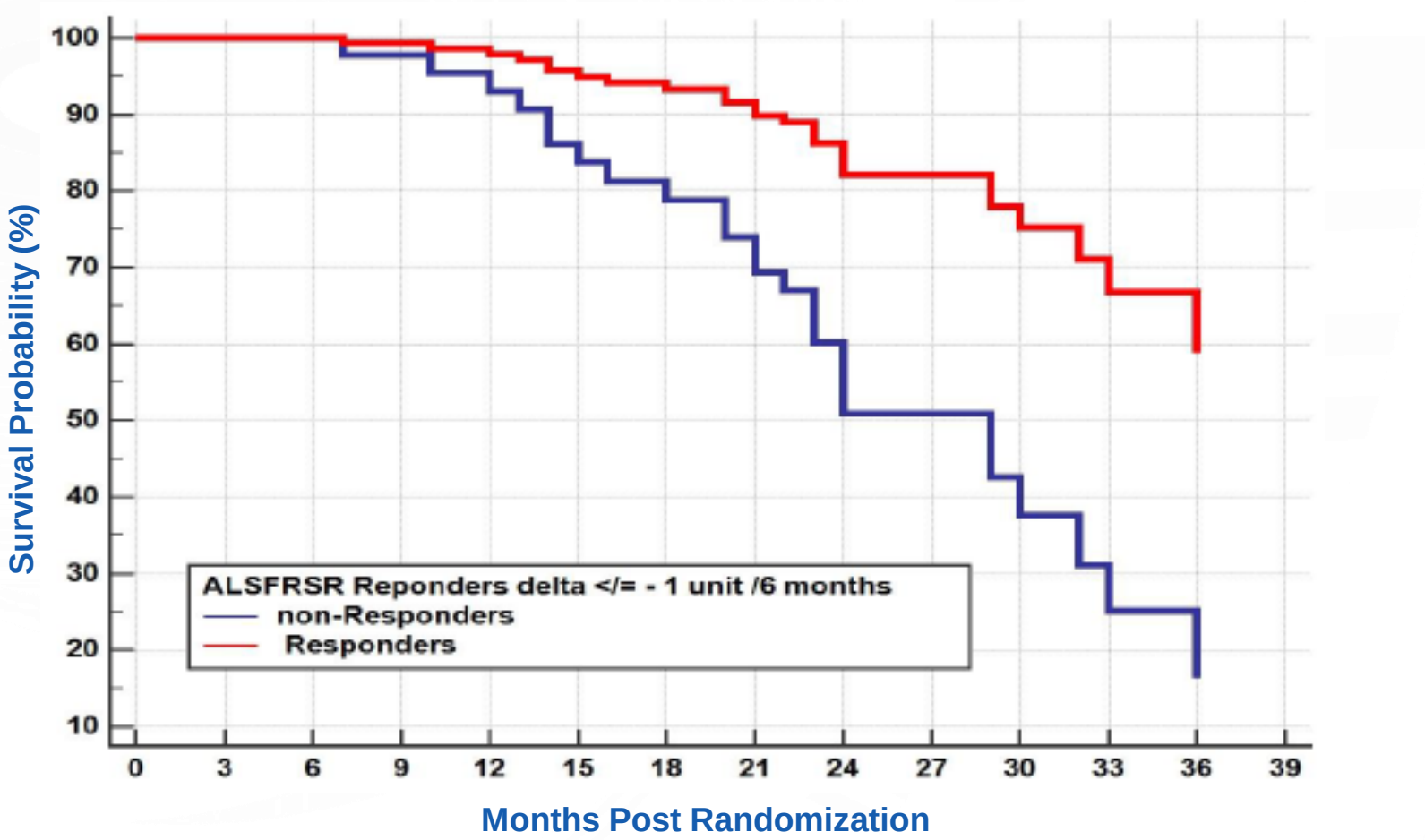
Responders Showed Less Functional Decline



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

Responders Showed Improved Survival

Survival Analysis



Phase 3 ALS Trial Ongoing

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

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Phase 3 ALS Trial: Study Design Optimization

Higher Dose

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

Longer Treatment Period

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

Early Stage of Disease

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

No Slow Progressors

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

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Progressive Multiple Sclerosis (MS)

MS AFFECTS

2.8M

Worldwide[1]

Diminished Quality of Life

(e.g. fatigue, walking difficulties, weakness, pain, cognitive changes, depression)[1]

CURRENT MS MARKET

$20.4B

Worldwide

SPMS w/o RELAPSE

NO APPROVED DRUGS

for long-term treatment

SPMS w/ RELAPSE

MAYZENT (siponimod)

MAVENCLAD (cladribine)[2]

VUMERITY (diroximel fumarate)

ZEPOSIA (ozanimod)

+ OTHER DRUGS

PPMS

OCREVUS (ocrelizumab)

for Primary Progressive MS

Large Market Opportunity for Secondary Progressive MS (SPMS) without Relapses

- The vast majority of secondary progressive MS patients do not have relapses
- Only 10.0% of placebo-treated SPMS subjects had a relapse during the Phase 2b trial of MN-166 (ibudilast) over 96 weeks of treatment
- Only 18.7% of placebo-treated SPMS subjects had a relapse during the Phase 3 trial of MAYZENT (siponimod) with a median study duration of 21 months

1. Source: National Multiple Sclerosis Society; 2. MAVENCLAD's Prescribing Information has a Boxed Warning for an increased risk of malignancy and fetal harm. It is generally recommended for patients who have had an inadequate response to, or are unable to tolerate, an alternate MS drug.

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Overview of Completed Phase 2b Progressive MS Trial

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

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MN-166 (ibudilast) Achieved Both Primary Endpoints in Phase 2b Study

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

Results published in the New England Journal of Medicine; Top-line data presented at ECTRIMS conference; Disability data was presented at ACTRIMS conference

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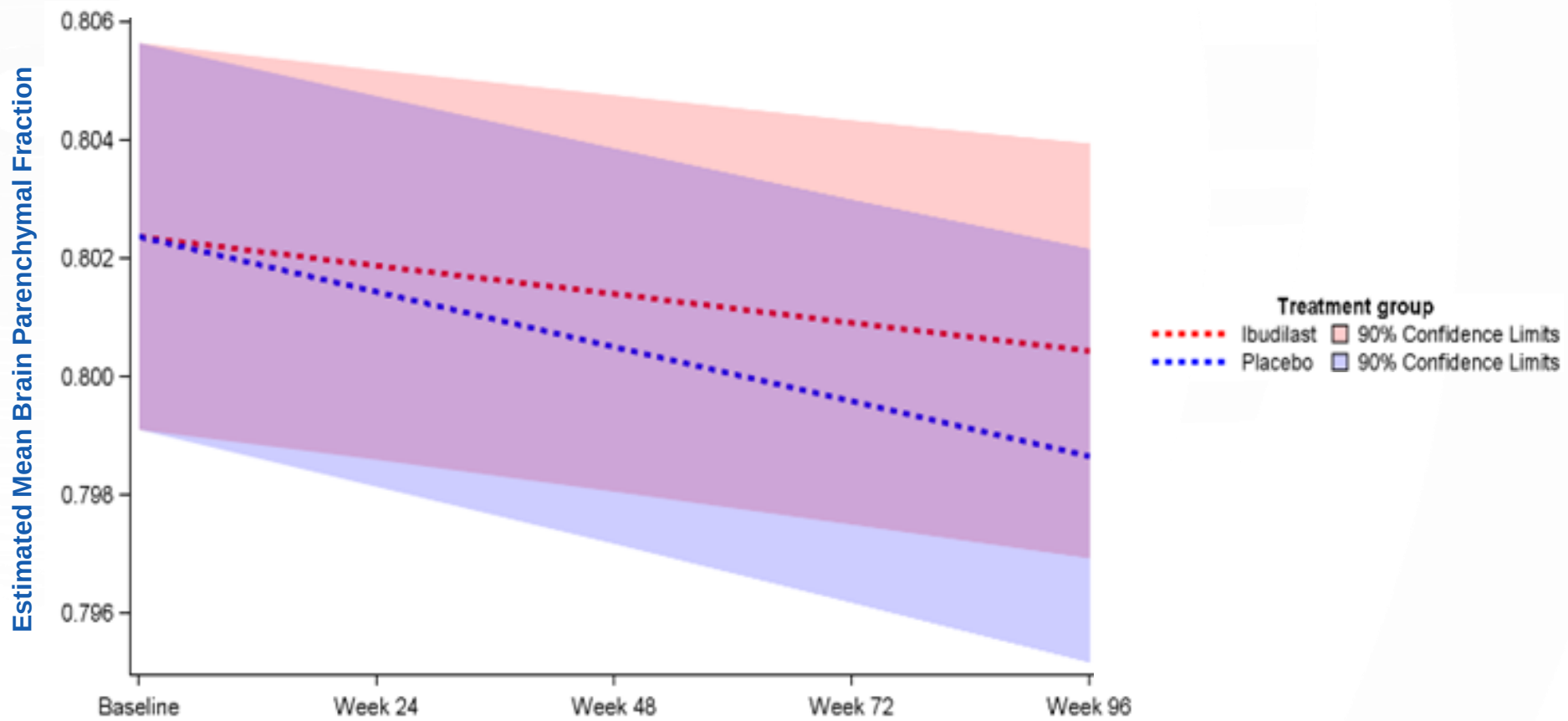
MN-166 (ibudilast) Reduced Brain Atrophy Progression by 48% (p=0.04)



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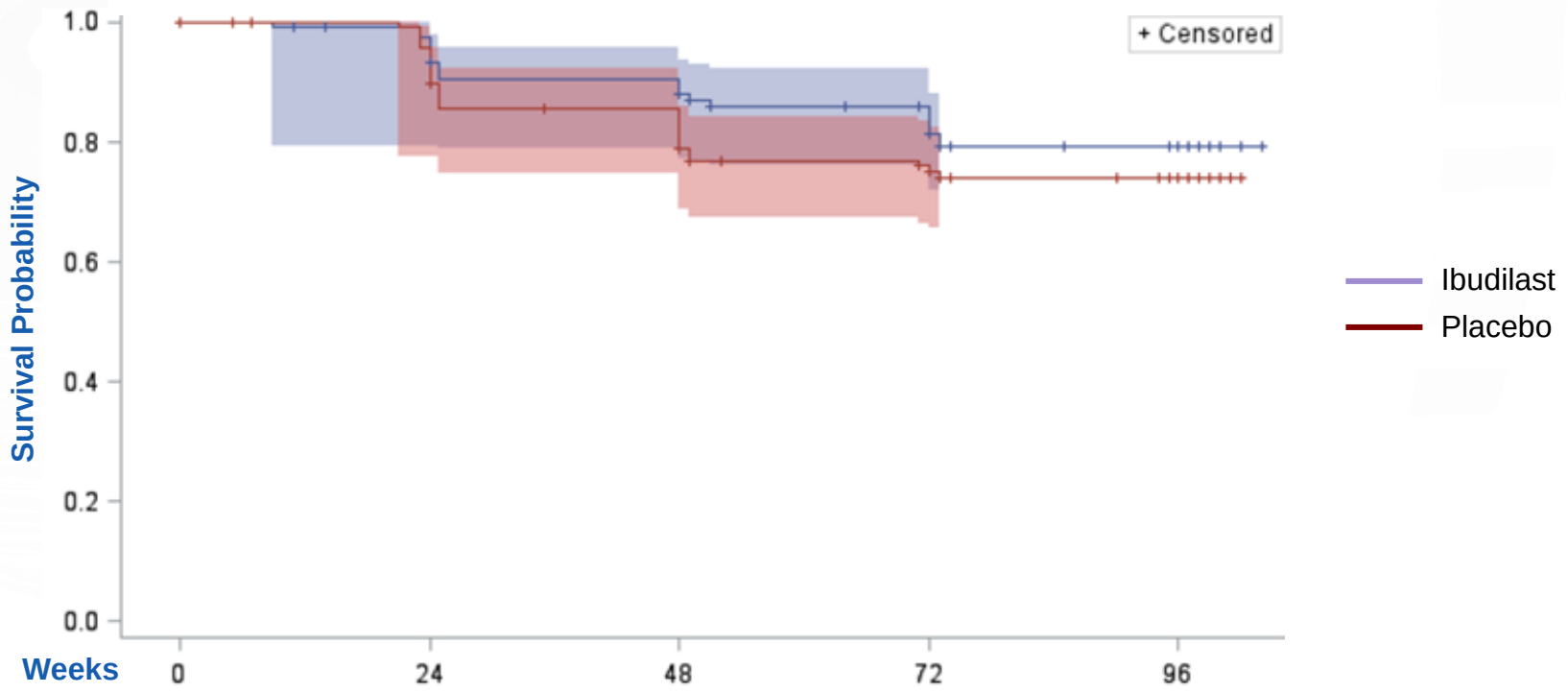
MN-166 (ibudilast) Reduced the Risk of Confirmed Disability Progression by 26%*

Approvable endpoint for Progressive MS

Product-Limit Survival Estimates

With Number of Subjects at Risk and 90% Half-Wellner Bands



Weeks	0	24	48	72	96
Ibudilast	121	114	103	91	64
Placebo	123	115	99	82	60

* Hazard ratio = 0.74, Confirmed disability progression was measured using EDSS

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MN-166 (ibudilast) Shows Greatest Efficacy in SPMS without Relapse

Risk of Confirmed Disability Progression by Subgroup

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

*MN-166 (ibudilast) vs. Placebo

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Phase 2b Results Demonstrated Differentiated Potential in Both PPMS and SPMS

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

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

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Superior Safety Profile

Safety drives market share in MS (e.g. Copaxone peak sales were much higher than Tysabri)

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

* MAYZENT requires 7 assessments prior to first dose: CYP2C9 Genotype Determination, Complete Blood Count, Ophthalmic Evaluation, Cardiac Evaluation, Current or Prior Medications, Vaccinations, and Liver Function Tests.

MN-166 (ibudilast): Phase 3 Ready in Progressive MS

Discussions Ongoing with Potential Partners

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

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Overview of Degenerative Cervical Myelopathy (DCM)

- Degenerative cervical myelopathy (DCM), also known as cervical spondylotic myelopathy, involves spinal cord dysfunction from compression in the neck
- DCM is the most common form of spinal cord impairment in adults and results in disability and reduced quality of life
- Patients report neurological symptoms such as pain and numbness in limbs, poor coordination, imbalance, and bladder problems
- According to the American Association of Neurological Surgeons, more than 200,000 cervical procedures are performed each year to relieve compression on the spinal cord or nerve roots
- There are no pharmaceuticals approved for the treatment of DCM

Phase 3 Trial in DCM Ongoing

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

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Potential for MN-166 (ibudilast) in Acute Respiratory Distress Syndrome (ARDS)

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

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

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

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

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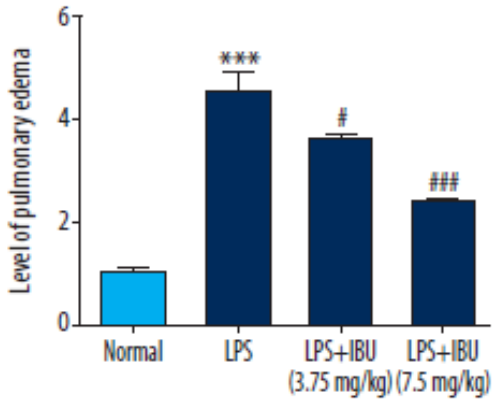
Preclinical Model of ARDS Shows Reduction in Key Inflammatory Cytokines

MN-166 (ibudilast) treatment significantly reduced pulmonary edema (p<0.001)

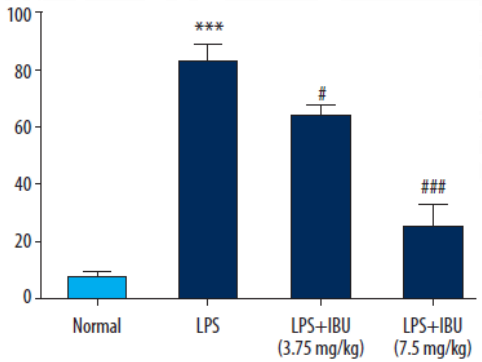
– Pulmonary edema was measured by the pulmonary edema score



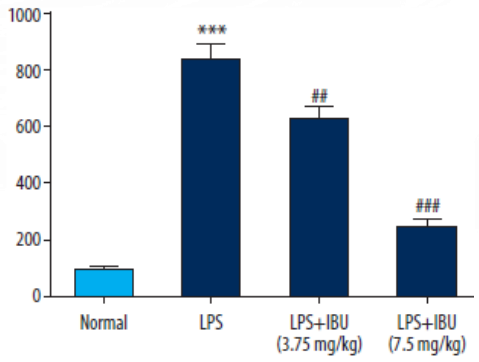
MN-166 (ibudilast) treatment significantly reduced serum inflammatory cytokines

– TNF-α, IL-1β, IL-6, and MCP-1 (all p<0.001)

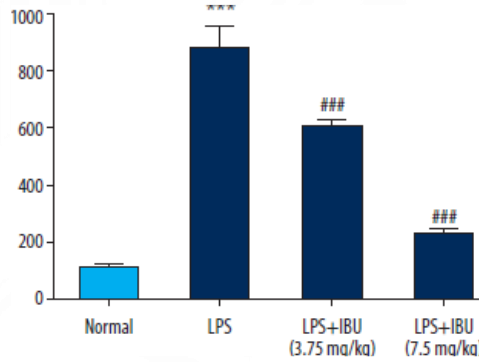
TNF-α



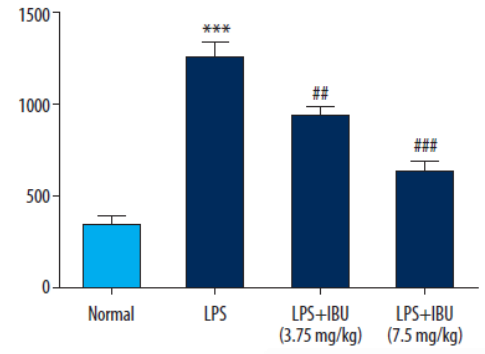
IL-1β



IL-6



MCP-1



Med Sci Monit, 2020; 26: e922281, Yang et al. 2020; *** P<0.001 vs. Normal; # P<0.05; ## P<0.01; ### P<0.001 vs. LPS.

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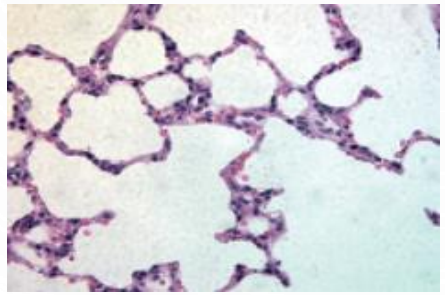
MN-166 (ibudilast) Demonstrates Improvements in ARDS Preclinical Model

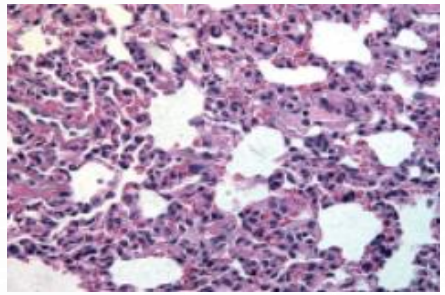
MN-166 (ibudilast) reversed histological changes in lung tissue

- inflammation, hemorrhage, alveolar congestion, and alveolar wall edema

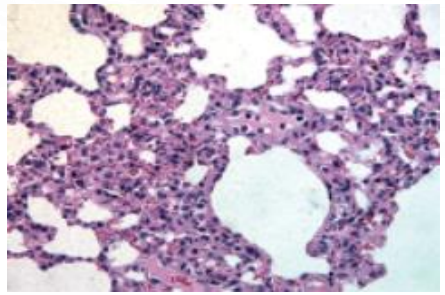
Normal



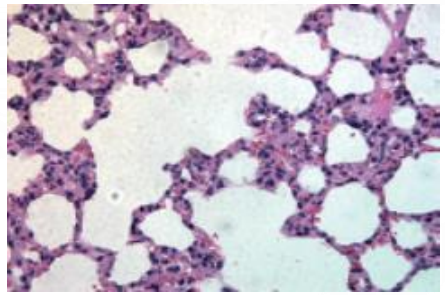
LPS



LPS+IBU (3.75 mg/kg)



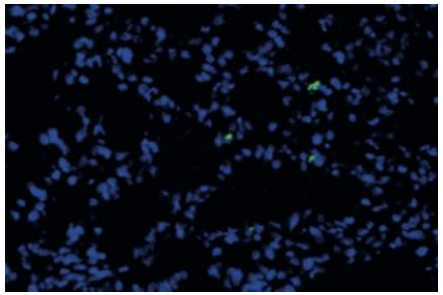
LPS+IBU (7.5 mg/kg)



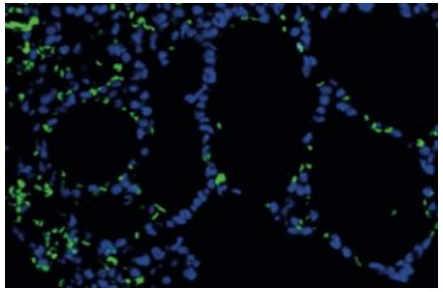
MN-166 (ibudilast) protects against pulmonary injury by attenuating cell apoptosis

- TUNEL staining assay showed MN-166 (ibudilast) reduced lung tissue cell apoptosis (bright green)

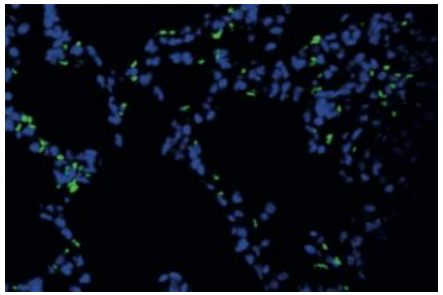
Normal



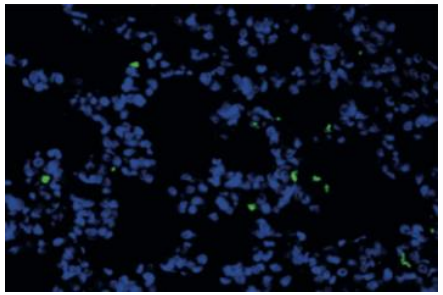
LPS



LPS+IBU (3.75 mg/kg)



LPS+IBU (7.5 mg/kg)



Med Sci Monit, 2020; 26: e922281, Yang et al. 2020

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Positive Phase 2 Results in COVID-19 ARDS

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

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BARDA Partnership

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

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

FDA approval does not require human clinical studies for this indication

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

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Phase 2 Trial in Glioblastoma (GBM): Results

Disease Overview	• Glioblastoma is an aggressive brain tumor that develops from glial cells • ~ 12,000 cases of glioblastoma are diagnosed each year in the U.S. • Median survival is ~11-15 months for more aggressive glioblastoma (IDH-wildtype) who receive standard treatment (surgery, temozolomide, and radiation therapy)
Trial Design	• **Part 1:** 15 subjects • **Part 2:** 62 subjects (36 newly diagnosed GBM patients and 26 recurrent GBM patients)
	• Open-label clinical study at Dana-Farber Cancer Institute (DFCI) in Boston • **Principal Investigator:** Patrick Wen, M.D., Harvard Medical School / DFCI
	• **Duration:** 28 days for Part 1; 6 months for Part 2
	• **Dosing Part 1:** MN-166 (ibudilast) dose-escalation 60-100 mg/day + temozolomide • **Dosing Part 2:** MN-166 (ibudilast) fixed-dose + temozolomide
Results	• **Primary Objective – Part 1:** Safety and tolerability • **Part 1 Safety Review:** No serious adverse events related to MN-166 (ibudilast). No concerning safety signals. • **Primary Objective – Part 2:** Proportion of patients who are progression-free at 6 months (PFS6) • **Part 2 Efficacy:** PFS6 was 44% for newly diagnosed GBM and 31% for recurrent GBM

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Positive Chemotherapy-Induced Peripheral Neuropathy (CIPN) Trial Results

Disease Overview	• Chemotherapy can damage peripheral nerves, resulting in pain, burning, tingling, loss of feeling, coordination/balance problems, muscle weakness, trouble swallowing and passing urine, constipation, and blood pressure changes • CIPN prevalence is ~60% at 3 months, and 30% at 6 months or more
Trial Design	• N=16 subjects with metastatic gastrointestinal cancer (colorectal cancer and upper gastrointestinal cancers) who are receiving oxaliplatin • Open-label, sequential cross-over clinical study at the University of Sydney Concord Cancer Centre in Australia • **Principal Investigator:** Dr. Janette Vardy • **Dosing #1:** One cycle of chemotherapy without MN-166 (ibudilast), followed by • **Dosing #2:** One cycle of chemotherapy with 30 mg MN-166 (ibudilast) twice daily
Phase 1 Study Results	• MN-166 (ibudilast) improved or stabilized neurotoxicity in the majority of participants (expected to worsen in patients with continued chemotherapy) • Oxaliplatin-Specific Neurotoxicity Scale (OSNS): 12 out of 14 participants reported acute neurotoxicity (Grade 1 or 2) in both cycles – Of those, 10 out of 12 participants were unchanged and 2 participants had improved symptoms from Grade 2 to Grade 1 with MN-166 (ibudilast) treatment • No effect of MN-166 (ibudilast) on systemic exposure of oxaliplatin

Results published in *Cancer Chemotherapy and Pharmacology* (9/2020)

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Phase 2b Trial in CIPN Ongoing

Trial Design	• N=100 subjects with metastatic colorectal cancer receiving oxaliplatin
	• Multi-center, randomized, double-blind, placebo-controlled Phase 2b trial • **Principal Investigator:** Dr. Janette Vardy, University of Sydney in Australia
	• **Duration:** Start treatment two days prior to first cycle of oxaliplatin chemotherapy and it continues for the duration of the chemotherapy
	• **Dosing:** 60 mg/day of MN-166 (ibudilast) or placebo (1:1 randomization)
Objectives	• **Primary Objective:** acute neurotoxicity severity (Oxaliplatin Acute Symptom Questionnaire)
	• **Secondary Objective:** Chemotherapy-induced peripheral neuropathy (CIPN) severity; treatment adherence including dose reductions of oxaliplatin; safety

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MN-001

Tipelukast

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MN-001 (tipelukast) Overview

Oral, anti-inflammatory and anti-fibrotic candidate

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

Strong safety profile, with >600 human subjects exposed

- Prior asthma studies established safety and tolerability

Positive Phase 2 data in NASH / NAFLD

Completed Phase 2 trial in IPF

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

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MN-001(tipelukast): Differentiated through Multiple Mechanisms of Action

Anti-Fibrotic Activity

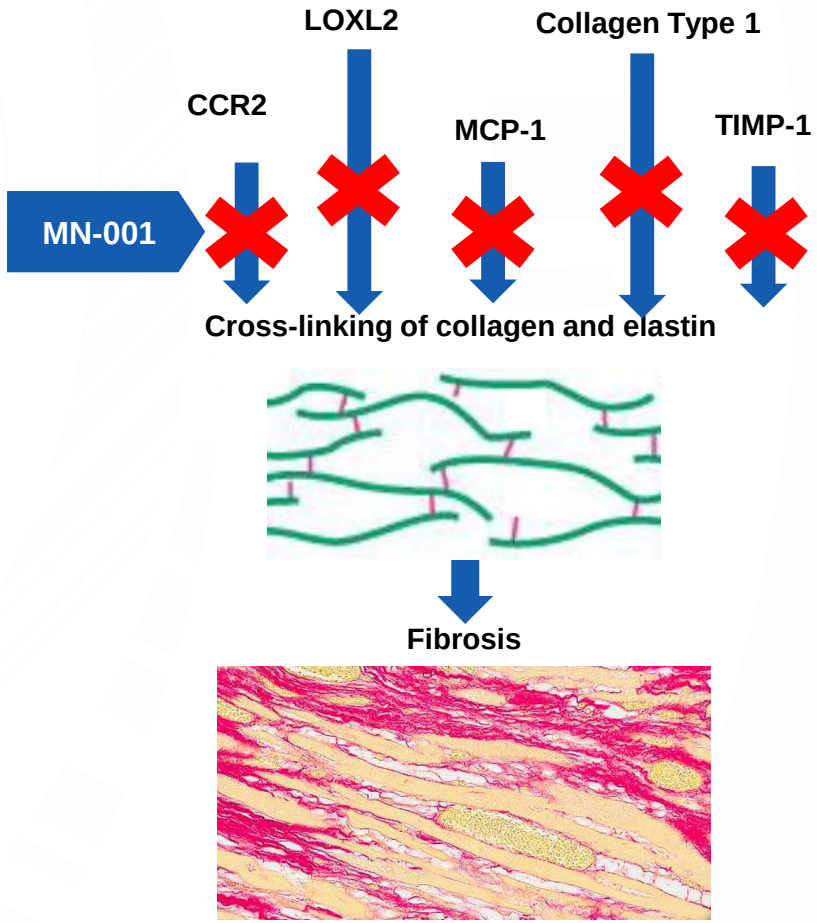
- MN-001 (tipelukast) reduces mRNA expression of genes that are known to promote fibrosis (e.g. LOXL2, Collagen Type 1, TIMP-1)
- MN-001 (tipelukast) inhibits 5-lipoxygenase (5-LO)

Anti-Inflammatory Activity

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

Reduces Triglycerides

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



Idiopathic Pulmonary Fibrosis (IPF)

IPF PREVALENCE

~100K

People in United States[1]

ORPHAN INDICATION

LIFE EXPECTANCY

3-5

Years[1]

FATAL

IPF MARKET FORECAST

$3B+

By 2025[2]

APPROVED DRUGS

ESBRIET (pirfenidone)

- Approved in October 2014
- Phase 3 studies enrolled mild to moderate IPF

No survival benefit shown[3]

OFEV (nintedanib)

- Approved in October 2014
- Phase 3 studies enrolled mild to moderate IPF

No survival benefit shown[4]

1. U.S. National Library of Medicine; 2. GlobalData; 3. Esbriet prescribing information; 4. OFEV prescribing information

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IPF Phase 2 Trial Completed

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

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Nonalcoholic Steatohepatitis (NASH) and Nonalcoholic Fatty Liver Disease (NAFLD)

NASH AFFECTS

1.5-6.5%

of Adults in the U.S.[1]

PREVALENCE

24%

of Adults in the U.S.[1] have

NAFLD

OVERWEIGHT OR OBESE

NASH MARKET FORECAST

$20B

By 2027[2]

APPROVED DRUGS

REZDIFFRA
(resmetirom)

- Approved in March 2024 for noncirrhotic NASH with moderate to advanced liver fibrosis
- Continued approval may be contingent upon verification and description of clinical benefit in ongoing confirmatory trials

1. National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK); 2. iHealthcareAnalyst, Inc.

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Phase 2 NASH / NAFLD Trial

MN-001 (tipelukast) reduced serum triglycerides (primary endpoint)

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

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Phase 2 Trial in NAFLD, Type 2 Diabetes and Hypertriglyceridemia Ongoing

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

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Financial Summary

- Cash Position: $51 million as of 12/31/2023
- Capital Efficient: Operating cash burn of only $12.9 million in 2022 and $7.4 million in 2023 despite late-stage development programs

Upcoming Milestones

MN-166 (ibudilast)

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

MN-001 (tipelukast)

- Phase 2 update in NAFLD, Type 2 diabetes and hypertriglyceridemia

Thank You

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Appendix

MN-166 (ibudilast): ALS Biomarker Trial *Completed*

Study evaluated the effects of MN-166 (ibudilast) on reducing brain microglial activation in ALS subjects measured by uptake of a positron emission tomography (PET) biomarker

No significant effect on mean PBR28-PET uptake

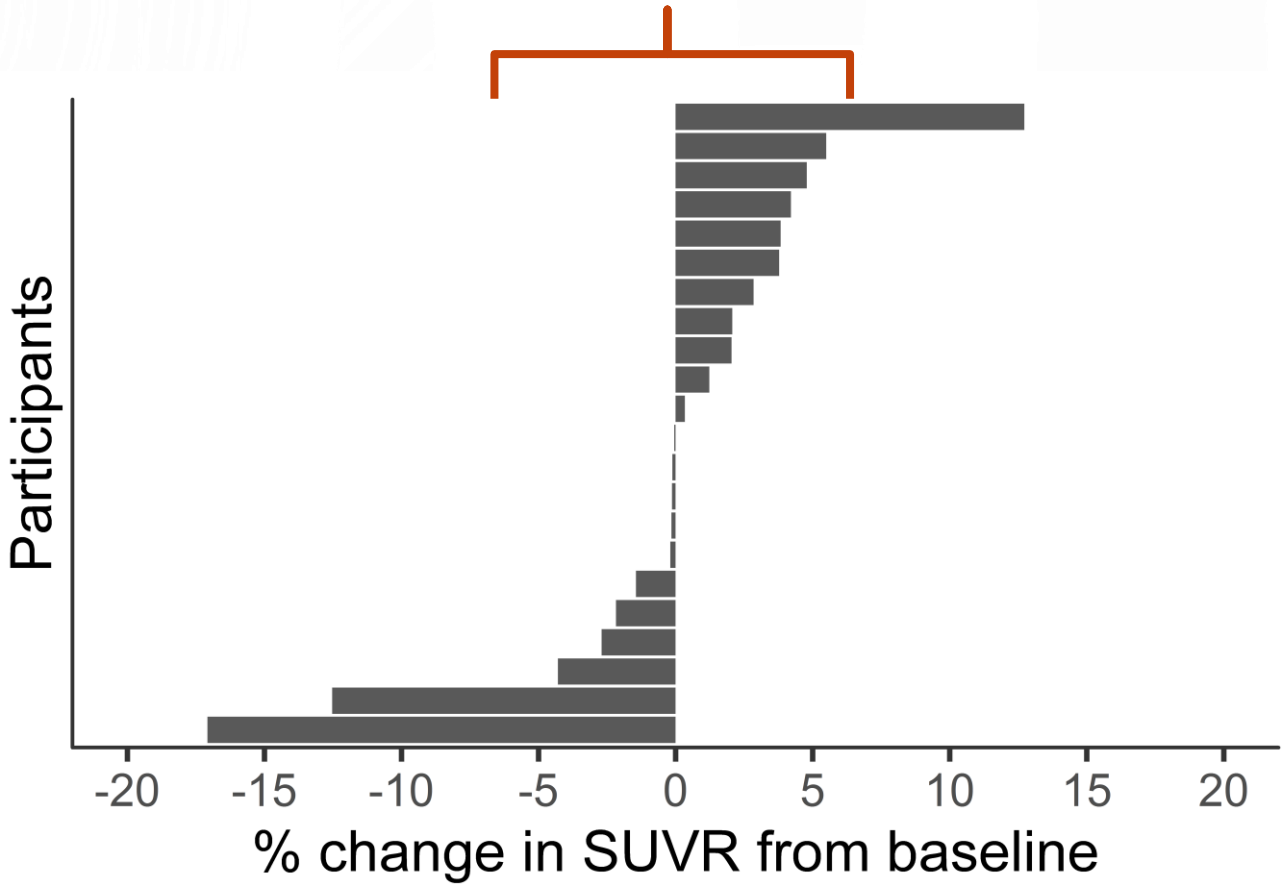
- Open label design: no placebo group, so we cannot draw any definitive conclusions
- Placebo patients are expected to have an increase in microglial activation over time as the disease progresses: MN-166 may have shown a significant decrease vs. placebo in a double-blind design

More patients had a significant decrease in PBR28-PET of >10% than a significant increase

- Most patients showed an increase or decrease of <5% which is within the margin of error for measurement
- Two patients had a decrease in microglial activation of >10% vs. one had an increase in microglial activation of >10%

Delta PBR-PET Uptake (SUVR)

Test-retest variability of PBR-PET SUVR is ~7% in motor cortices ALS imaging biomarker cohort (Alshikho et al, 2018)



MN-166 (ibudilast) Phase 2 ALS Trial

Completed

Trial Design	• N = 51 ALS subjects not using non-invasive ventilation • Phase 2 randomized, double-blind trial at Carolinas Neuromuscular/ALS-MDA Center • Principal Investigator: Dr. Benjamin Rix Brooks • Duration: 6 months of double-blind treatment + open label extension (6 months) • Dosing: 60 mg/day of MN-166 (ibudilast) or placebo (2:1 randomization) with riluzole
Objectives	• **Primary endpoint**: safety and tolerability • Other endpoints: functional activity (ALSFRS-R), respiratory function, muscle strength, quality of life, Clinical Global Impression of Change, serum creatinine as a biomarker, and pharmacokinetics
Status	• **Completed** • Top-line data presented at the International Symposium on ALS/MND • Received FDA feedback on pivotal trial design in September 2018

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MN-166 (ibudilast) Phase 2b Progressive MS Trial

Completed

Funding	Funded by NIH grant through NINDS
Priority	**MN-166 (ibudilast) was the first drug chosen by NINDS for an interventional clinical trial in the NeuroNEXT program**
Principal Investigator	**Robert Fox, M.D.** Cleveland Clinic
Clinical Coordinating Center	Massachusetts General Hospital
Data Coordinating Center	University of Iowa
Sites	28 academic medical centers in the NeuroNEXT network
Additional Funding	National Multiple Sclerosis Society provided patient advocate input and trial enrollment awareness and also provided additional funding

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MN-166 (ibudilast) Phase 2b Progressive MS Trial *Completed*

- All OCT measures showed less loss of retinal tissue for MN-166 (ibudilast) compared to placebo

Macular Measures: Optical Coherence Tomography (OCT) Analysis

Ibudilast reduced macular volume loss:

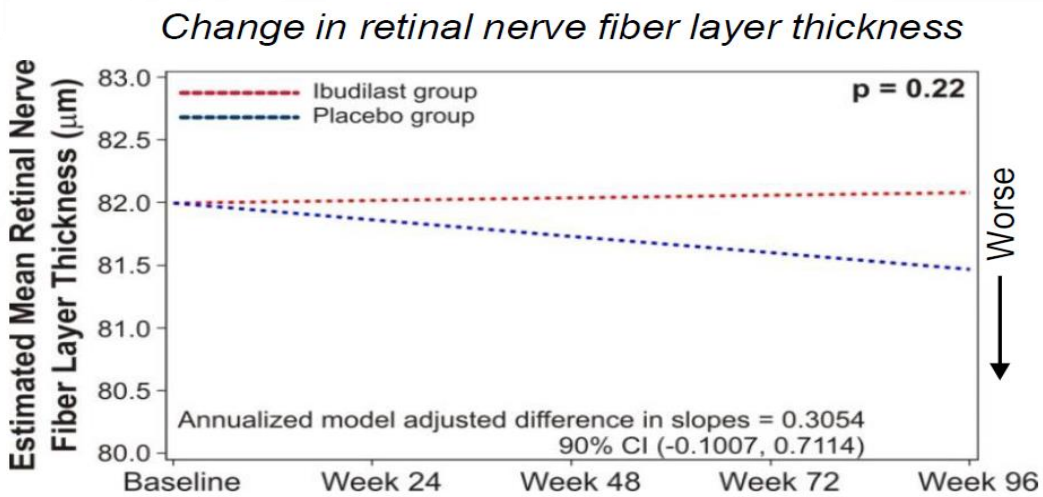
MACULAR VOLUME CHANGE - SPECTRALIS SITES		
Treatment group	**Estimated annual rate of MV change (95% CI)**	**P-value for difference in rate of change**
Ibudilast	-0.005 (-0.027, 0.017)	**0.044**
Placebo	-0.037 (-0.058, -0.015)	

MACULAR VOLUME CHANGE - CIRRUS SITES		
Treatment group	**Estimated annual rate of MV change (95% CI)**	**P-value for difference in rate of change**
Ibudilast	-0.000 (-0.022, 0.021)	0.173
Placebo	-0.021 (-0.041, -0.000)	

Ibudilast reduced thinning of GCIP (ganglion cell and inner plexiform layer):

GCIP THICKNESS – CIRRUS SITES		
Treatment group	**Estimated annual rate of GCIP change (95% CI)**	**P-value for difference in rate of change**
Ibudilast	-0.489 (-0.913, -0.065)	0.118
Placebo	-0.959 (-1.368, -0.550)	

Ibudilast reduced thinning of RNFL:



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MN-166 (ibudilast) Reduced Opioid Withdrawal and Craving

Phase 1b / 2a Trial Results	**MN-166 (ibudilast) reduced Subjective Opioid Withdrawal Scale (SOWS)** • MN-166 (ibudilast) significantly reduced perspiring ($p<0.05$) and hot flashes ($p<0.05$), two components of SOWS • Principal Investigator: Dr. Sandra Comer, Columbia University
Phase 2 Self-Administration Trial Results	MN-166 (ibudilast) significantly **decreased the craving** for • heroin ($p<0.01$), • cocaine ($p<0.01$) • tobacco ($p<0.05$)
	MN-166 (ibudilast) significantly **decreased the reinforcing effects of oxycodone** ($p<0.05$)
	MN-166 (ibudilast) significantly **enhanced the analgesic effects of oxycodone** ($p<0.05$)
	Principal Investigator: Dr. Sandra Comer, Columbia University

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MN-166 (ibudilast) Improved Attention in Methamphetamine Dependence

Phase 1b Trial Results	• MN-166 (ibudilast) significantly reduced perseverations (p=0.01) and variability in response times (p=0.006), suggesting a protective effect on sustained attention • Principal Investigators: Dr. Steven Shoptaw and Dr. Keith Heinzerling, **University of California, Los Angeles (**UCLA)
Phase 2 Trial Design	• Ongoing Phase 2 randomized, double-blind, placebo-controlled study in recently-abstinent methamphetamine users • Endpoints include effects of MN-166 (ibudilast) on neuroinflammation, brain function, and methamphetamine craving • Principal Investigator: Dr. Milky Kohno, Oregon Health & Science University
Phase 2 Trial Results	• Phase 2 randomized, double-blind, placebo-controlled outpatient study in methamphetamine-dependent subjects • Did not achieve the primary endpoint of abstinence during the final two weeks of treatment • Principal Investigator: Dr. Keith Heinzerling, UCLA

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MN-166 (ibudilast) Trials in Alcohol Dependence

Results shows statistically significant reduction in cravings compared to placebo

Phase 2a Trial Results	• MN-166 (ibudilast) significantly decreased basal, daily alcohol craving over the course of the study ($p<0.05$) • Principal Investigator: Dr. Lara Ray, UCLA
Phase 2 Trial Results	• Phase 2, randomized, double-blind, placebo-controlled, outpatient trial in 52 non-treatment-seeking subjects with alcohol use disorder • MN-166 (ibudilast) significantly reduced the odds of heavy drinking across time by 45% ($p=0.04$) (OR=0.55; 95% CI: 0.30, 0.98) • MN-166 (ibudilast) significantly reduced alcohol cue-elicited activation in the ventral striatum (reward response) evaluated by fMRI ($p=0.01$) and reduced alcohol craving on non-drinking days ($p=0.02$) • Results were published in Nature's *Translational Psychiatry* • Principal Investigator: Dr. Lara Ray, UCLA
Phase 2b Trial Results	• Phase 2b randomized, double-blind, placebo-controlled, outpatient trial in 102 treatment-seeking individuals with moderate or severe alcohol use disorder • Primary Endpoint: MN-166 (ibudilast) was not superior to placebo at reducing percent heavy drinking days (≥ 5 drinks for men / ≥ 4 drinks for women). There was a placebo effect in which both the placebo and MN-166 (ibudilast) decreased heavy drinking. • Principal Investigator: Dr. Lara Ray, UCLA

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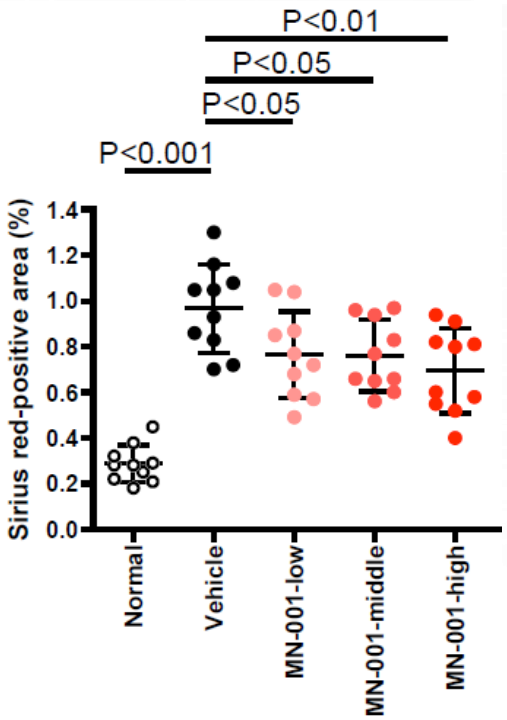
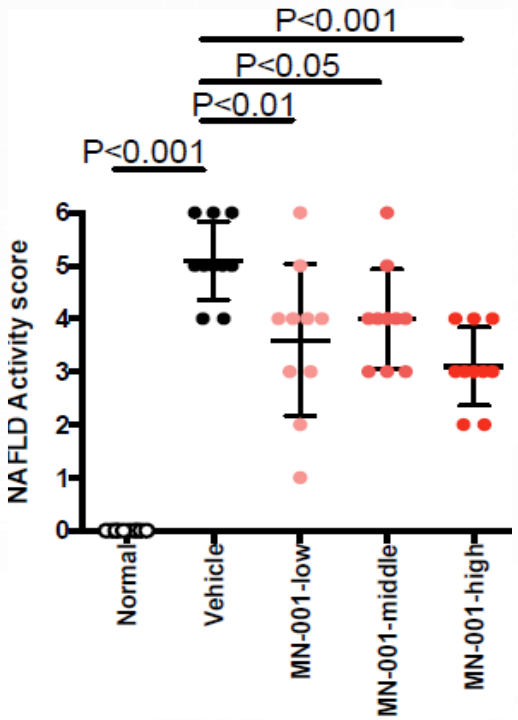
MN-001 (tipelukast) Data

NASH & NAFLD Animal Model Studies

% of Fibrosis Area



NAFLD Activity Score (NAS)



Animal model studies shows MN-001 (tipelukast) significantly reduced fibrosis in a dose-dependent manner

- Improved NAFLD Activity Score (NAS) via a reduction in hepatocyte ballooning
- Reduced fibrosis area in every preclinical model tested (NASH, Advanced NASH)

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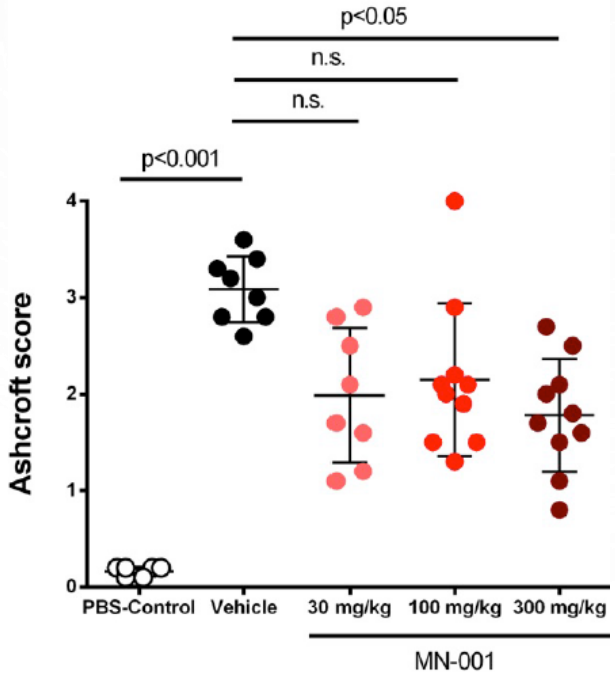
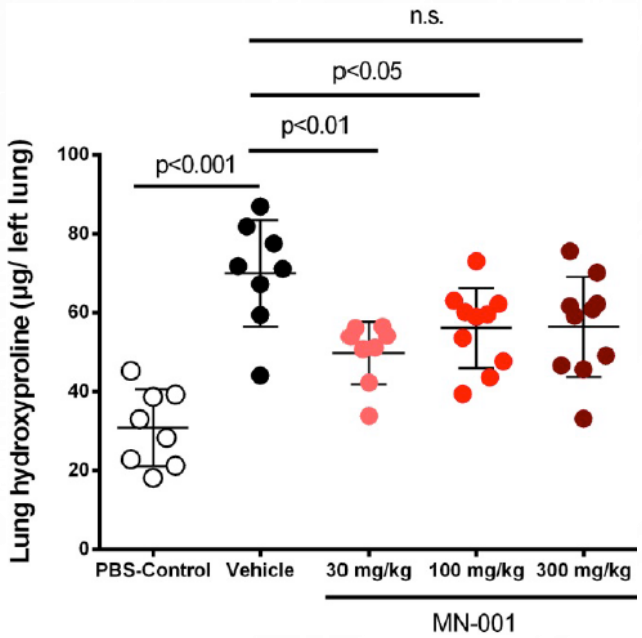
MN-001 (tipelukast) Data

IPF Animal Model Study

Ashcroft Score



Lung Hydroxyproline



Animal model study shows MN-001 (tipelukast) significantly reduced the Ashcroft Score

- Ashcroft Score measures pulmonary fibrosis based on histopathological staining

MN-001 (tipelukast) significantly reduced lung hydroxyproline content

- Hydroxyproline content is an indicator of fibrosis or storage of collagen in tissue

MN-166 (ibudilast): Patents

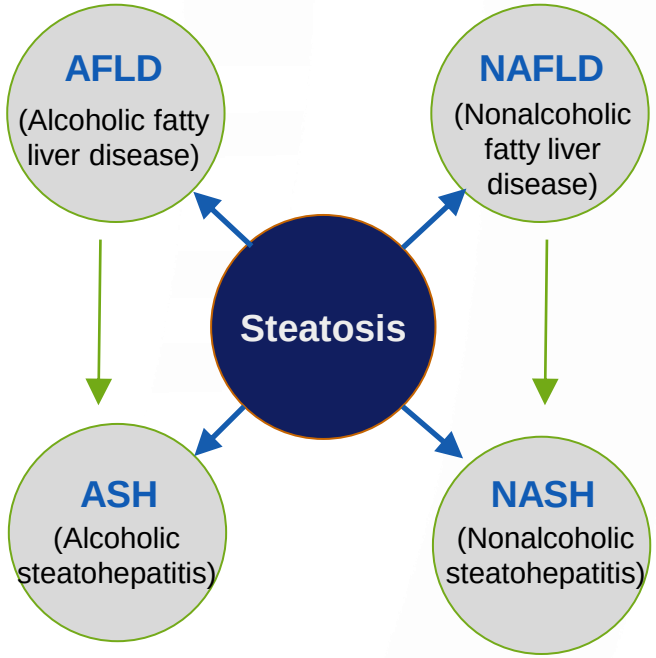
Progressive Multiple Sclerosis (U.S. Patent 8,138,201)	• Method of treating PPMS or SPMS with ibudilast • Expires no earlier than November 26, 2029 • Foreign patents based on the U.S. patent have been granted in Canada, China, Japan, European Patent Office, Switzerland, Germany, Denmark, Spain, France, United Kingdom, Hungary, Italy, Netherlands, and Sweden
Progressive Multiple Sclerosis (U.S. Patent 8,338,453)	• Method of lessening a conversion of a brain lesion to a persistent black hole in progressive MS using ibudilast • Expires no earlier than July 8, 2028
Progressive Multiple Sclerosis (U.S. Patent 9,114,136)	• Method of reducing brain volume loss in progressive MS using ibudilast • Expires no earlier than July 8, 2028
Progressive Multiple Sclerosis (U.S. Patent 10,946,071)	• Method of treating progressive MS with ibudilast + interferon-beta • Expires no earlier than October 8, 2039
Amyotrophic Lateral Sclerosis (ALS) (U.S. Patent 9,314,452), Canada	• Method of treating amyotrophic lateral sclerosis (ALS) with ibudilast • Expires no earlier than January 23, 2029
ALS and Neurodegenerative Diseases (U.S. Patent 10,258,611), Europe, Japan	• Method of treating ALS and neurodegenerative diseases with ibudilast + riluzole • Expires no earlier than November 24, 2035
Glioblastoma (U.S. Patent 10,744,123)	• Method of treating glioblastoma with ibudilast + other drugs (temozolomide, carmustine, bevacizumab, procarbazine, hydroxyurea, irinotecan, lomustine, nimotuzumab, sirolimus, etc.) • Expires no earlier than February 11, 2039
Drug Addiction (U.S. Patent 7,915,285)	• Method of treating drug addiction or drug dependence with ibudilast • Expires no earlier than January 27, 2030 • Foreign patents based on the U.S. patent have been granted in Japan, European Patent Office, Germany, Spain, France, United Kingdom, and Italy
Neuropathic Pain (U.S. Patent 7,534,806)	• Method of treating neuropathic pain with ibudilast • Expires no earlier than December 6, 2025
Ophthalmic Disease (U.S. Patent 11,154,540)	• Method of treating an ophthalmic disease/disorder or injury associated with a neurodegenerative disease/disorder or a neuro-ophthalmologic disorder with ibudilast • Expires no earlier than October 18, 2039

Note: Expiration dates listed above do not include patent term restoration which would add up to 5 years extension.

MN-001 (tipelukast): 6 New Patents

6 New Patents cover MN-001 (tipelukast) and MN-002 (a major metabolite of MN-001)

NASH	• Treatment of nonalcoholic steatohepatitis (NASH) • Expires no earlier than Dec 2032
Advanced NASH	• Treatment of advanced NASH with fibrosis • Expires no earlier than Sep 2034
NAFLD	• Treatment of nonalcoholic fatty liver disease (NAFLD) • Expires no earlier than Dec 2032
Liver Disorders	• Treatment of steatosis, lobular inflammation, hepatic ballooning, hepatic scarring, and elevated liver hydroxyproline levels • Expires no earlier than Dec 2032
Lipid Disorders	• Treatment of hypertriglyceridemia, hypercholesterolemia, and hyperlipoproteinemia • Expires no earlier than July 2034
Fibrosis	• Treatment of fibrosis in a broad range of organs • Expires no earlier than June 2035



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