Athira PHARMA

Athira R&D Day

Enhancing the HGF/MET System to Fight Neurodegenerative Diseases

December 7, 2022

ADVANCING NEW THERAPIES FOR NEURONAL HEALTH

Disclaimer

This presentation and the accompanying oral commentary contain forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. These forward-looking statements are based on our management's beliefs and assumptions and on information currently available to our management. Forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified. In some cases, you can identify forward-looking statements by terminology such as "may," "will," "should," "could," "expect," "plan," anticipate," "believe," "estimate," "predict," "intend," "potential," "would," "continue," "ongoing" or the negative of these terms or other comparable terminology. Forward-looking statements include all statements other than statements of historical fact contained in this presentation, including information concerning our future financial performance, business plans and objectives, timing and success of our planned development activities, our ability to obtain regulatory approval, the potential therapeutic benefits and economic value of our product candidates, potential growth opportunities, competitive position, industry environment and potential market opportunities, and the impact of the COVID-19 pandemic on our business and operations.

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The ACT-AD trial was supported by a grant from the National Institute on Aging of the National Institutes of Health under Award Number R01AG06268. The information presented in this presentation is solely the responsibility of Athira and does not necessarily represent the official views of the National Institutes of Health.

This presentation concerns drug candidates that are under clinical investigation and which have not yet been approved for marketing by the U.S. Food and Drug Administration. The drug candidates are currently limited by federal law to investigational use, and no representation is made as to their safety or effectiveness for the purposes for which they are being investigated.

We announce material information to the public through a variety of means, including filings with the SEC, press releases, public conference calls, our website (www.athira.com/), our investor relations website (investors.athira.com), and our news site (investors.athira.com/news-and-events/press-releases). We use these channels, as well as social media, including our Twitter account (@athirapharma) and Facebook page (https://www.facebook.com/athirapharmainc), to communicate with investors and the public about Athira, our products, and other matters. Therefore, we encourage investors, the media, and others interested in Athira to review the information we make public in these locations, as such information could be deemed to be material information.

Agenda

- **Welcome and Introduction**
  Mark Litton, PhD, *President and Chief Executive Officer*
- **Fosgonimeton Preclinical Evidence**
  Kevin Church, PhD, *Executive Vice President, Research*
- **Fosgonimeton Development Program**
  Hans Moebius, MD, PhD, *Chief Medical Officer*
- **Alzheimer's Disease Landscape**
  Rachel Lenington, *Chief Operating Officer*
- **Preclinical Evidence of ATH-1105 in ALS**
  Kevin Church, PhD, *Executive Vice President, Research*
- **Closing remarks**
  Mark Litton, PhD, *President and Chief Executive Officer*
- **Q&A**

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ALS, amyotrophic lateral sclerosis.

OUR MISSION

To restore lives by advancing bold therapies for neuronal health, thoughtfully and urgently

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Enhancing the HGF/MET System to Fight Neurodegenerative Diseases

Preclinical Data

ASENT American Society for Experimental Neurotherapeutics

alzheimer's association AAIC 22

PNS Peripheral Nerve Society

Neuroscience 2022

mnda motor neurone disease association

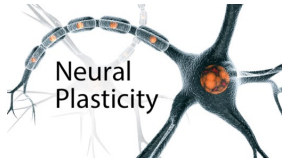
Neurotherapeutics

*In press

Translates to Clinical Data

CTAD

JAD Journal of Alzheimer's Disease



alzheimer's association AAIC 22

AD/PD™ 2022 ADVANCES IN SCIENCE & THERAPY

ActAD

LiftAD

Significant Market Opportunity

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Multifactorial Complex Pathologies Lead to Neurodegeneration

NEURODEGENERATIVE DISEASES

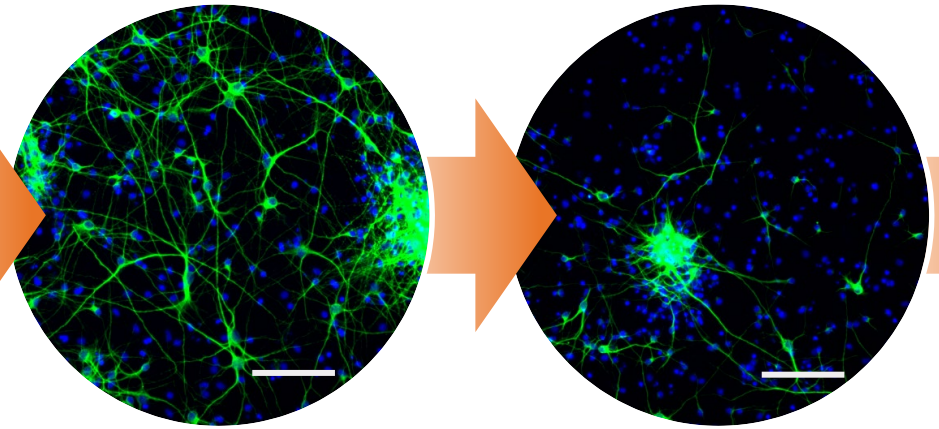
Inflammation

Oxidative stress

Protein pathology

Excitotoxicity

Synaptic dysfunction



HEALTHY **DISEASED**

= Neuron Marker

NEURODEGENERATION

Neuronal damage

Loss of network connectivity

Loss of function

Disease progression

Images are of primary cortical neuron cultures, showing healthy (untreated) cultures on the left, and cultures treated with glutamate (20 µM) on the right, demonstrating glutamate-mediated neuronal death and neurite degeneration.
Scale bar: 100 µm.
Neuron Marker=MAP2, microtubule associated protein 2

Positive Modulators of the HGF/MET Neurotrophic System

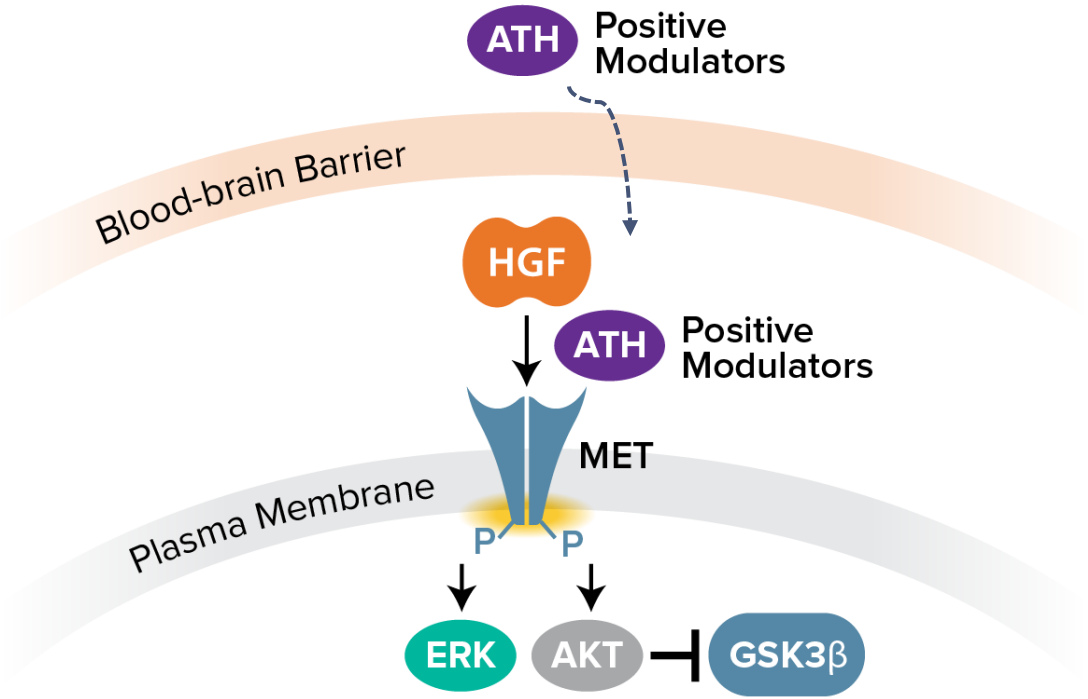
MULTIMODAL, PROTECTIVE, REGENERATIVE, DISEASE MODIFYING

Potential first-in-class small molecule drug candidates

- Cross the blood-brain barrier
- Positively modulate HGF/MET

Mechanism of Action

- Reduces inflammation
- Promotes regeneration
- Provides neuroprotection
- Potentially disease modifying



Neurotrophic

Neuroprotective

AKT, protein kinase B; ERK, extracellular-signal regulated kinase; GSK3b, glycogen synthase kinase-3 beta; HGF, hepatocyte growth factor.

Desole et al (2021). HGF and MET: From Brain Development to Neurological Disorders, *Frontiers in Cell and Dev Bio*.
Funakoshi and Nakamura (2011). Hepatocyte Growth Factor (HGF): Neurotrophic Functions and Therapeutic Implications for Neuronal Injury/Diseases, *Current Signal Transduction Therapy*.

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Fosgonimeton Preclinical Evidence

Kevin Church, PhD

Executive Vice President, Research

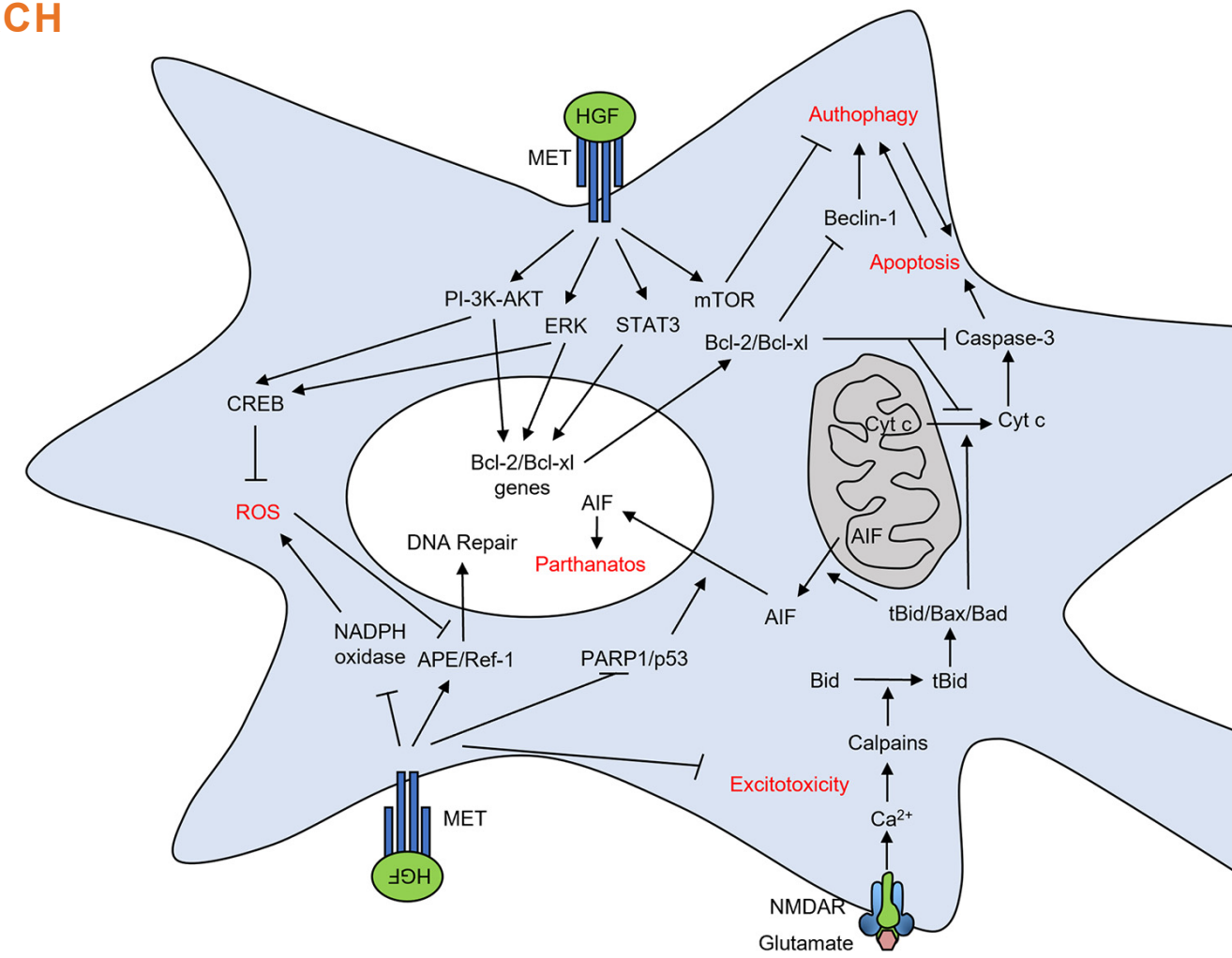
HGF/MET is a Critical Neuroprotective System

THE ACTIVITIES OF HGF/MET IN THE NERVOUS SYSTEM HAVE BEEN EXPLORED THROUGH 30 YEARS OF RESEARCH

HGF/MET activates signaling pathways to protect neurons from:

- Oxidative stress
- Excitotoxicity
- Apoptosis

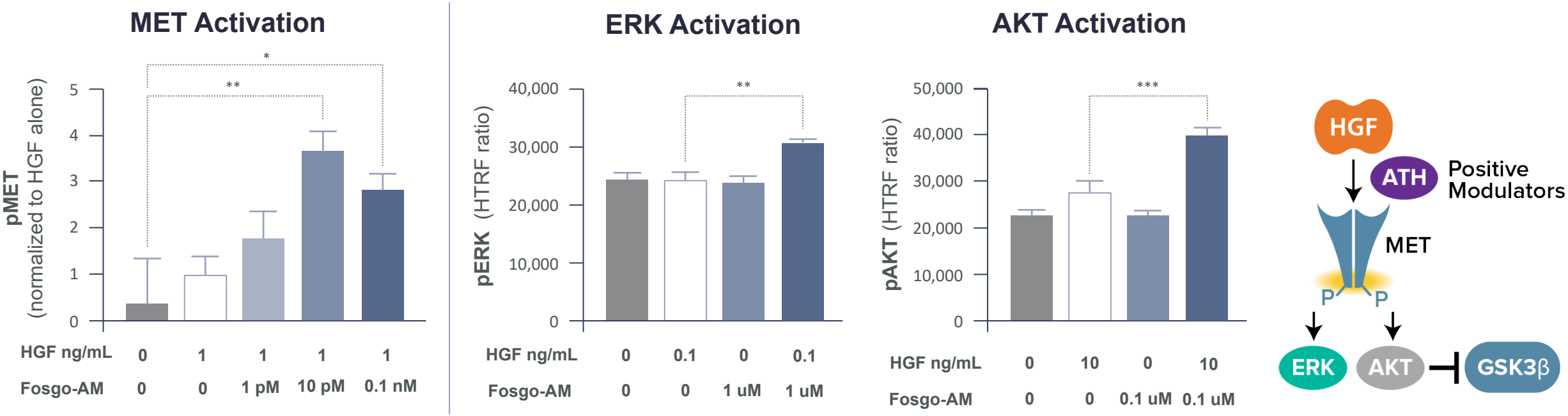
Adapted from Desole et al, 2021



Desole et al (2021). HGF and MET: From Brain Development to Neurological Disorders, *Frontiers in Cell and Developmental Biology*.

Fosgonimeton enhances the HGF/MET signaling pathway

Enhancement of HGF/MET stimulates a variety of intracellular signaling pathways, such as phospho-activation of ERK (pERK) and AKT (pAKT), that mediate neurotrophic and neuroprotective effects



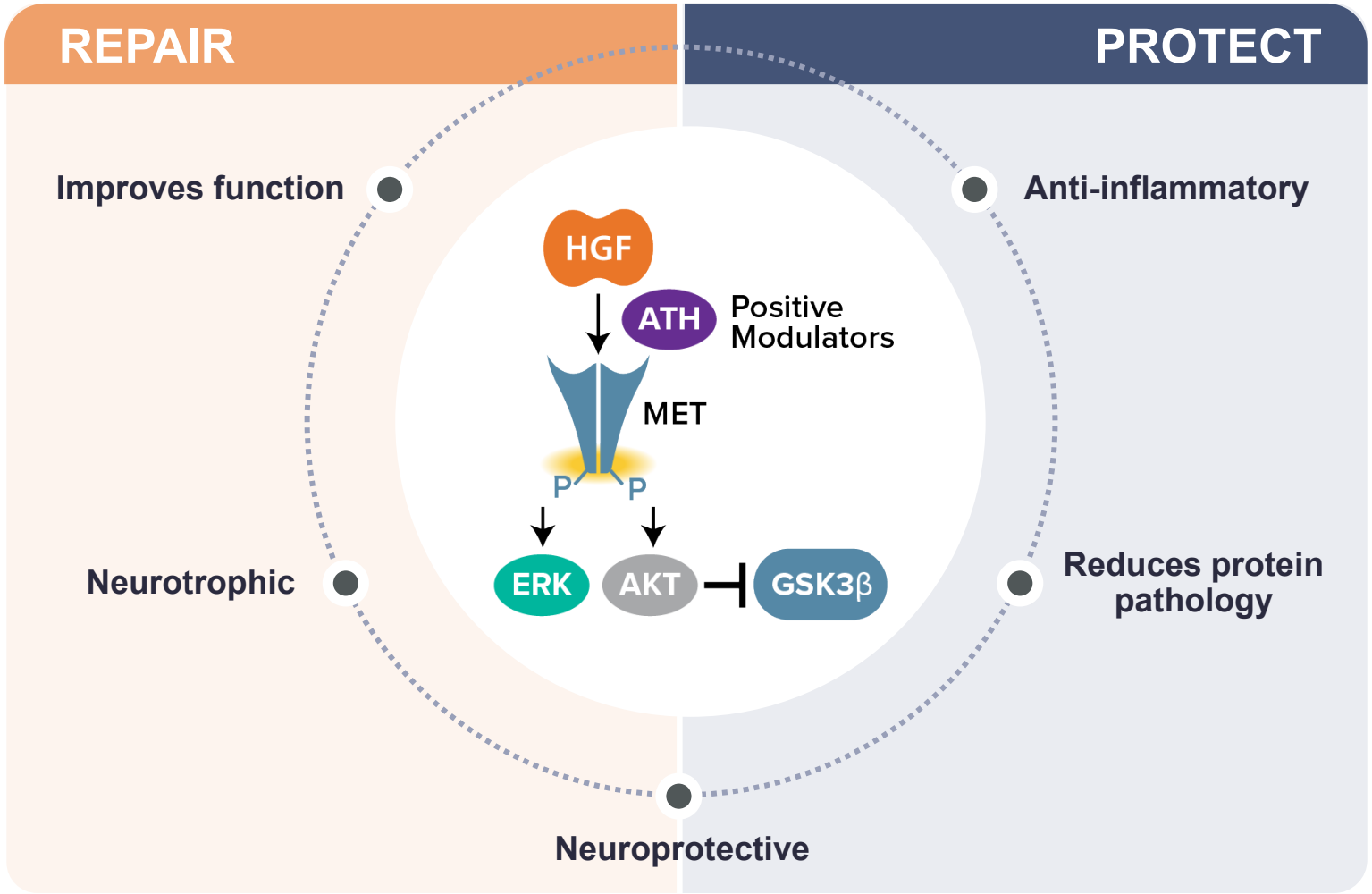
Primary MOA of ATH Molecules

Result in Downstream neurotrophic and neuroprotective pathway activation

HEK293 cell. Data presented as mean ± SEM. Statistics applied: One-way ANOVA with Tukey's multiple comparisons.
** p < 0.01, *** p < 0.001 vs. HGF only; n =3 for pMET; n = 3 for pERK; n = 4 for pAKT.
AKT, protein kinase B; ERK, extracellular-signal regulated kinase; Fosgo-AM, fosgonimeton active metabolite; GSK3b, glycogen synthase kinase-3 beta; HGF, hepatocyte growth factor.

ATH compounds protect and repair neural networks

PUBLISHED DATA DEMONSTRATE MULTIMODAL EFFECTS FOR NEURODEGENERATIVE DISEASES



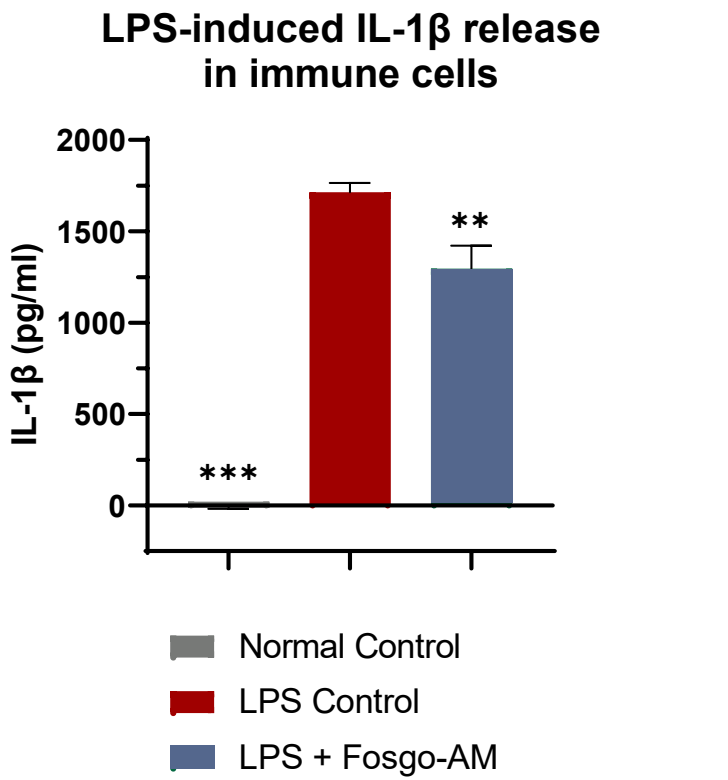
Growing preclinical evidence to support the potential therapeutic benefits of enhancing the HGF/MET system with ATH small molecules:

1. Johnston et al. (in press). Fosgonimeton, a Novel Positive Modulator of the HGF/MET System, Promotes Neurotrophic and Procognitive Effects in Models of Dementia. *Neurotherapeutics*
2. Setti et al. Fosgonimeton, a Small-Molecule Positive Modulator of HGF/MET, Protects Against Neuronal Damage and Motor Deficits in Preclinical Models of Parkinson's Disease. Presented at SfN 2022
3. Berthiaume et al. Small-Molecule Hepatocyte Growth Factor (HGF)/MET Positive Modulator ATH-1105 Is Neuroprotective in the TDP-43 Mouse Model of Amyotrophic Lateral Sclerosis. Presented at MNDA 2022
4. Reda et al. Fosgonimeton, a novel, small molecule positive modulator of the HGF/MET system is neuroprotective in primary neuron culture. Presented at AAIC 2022

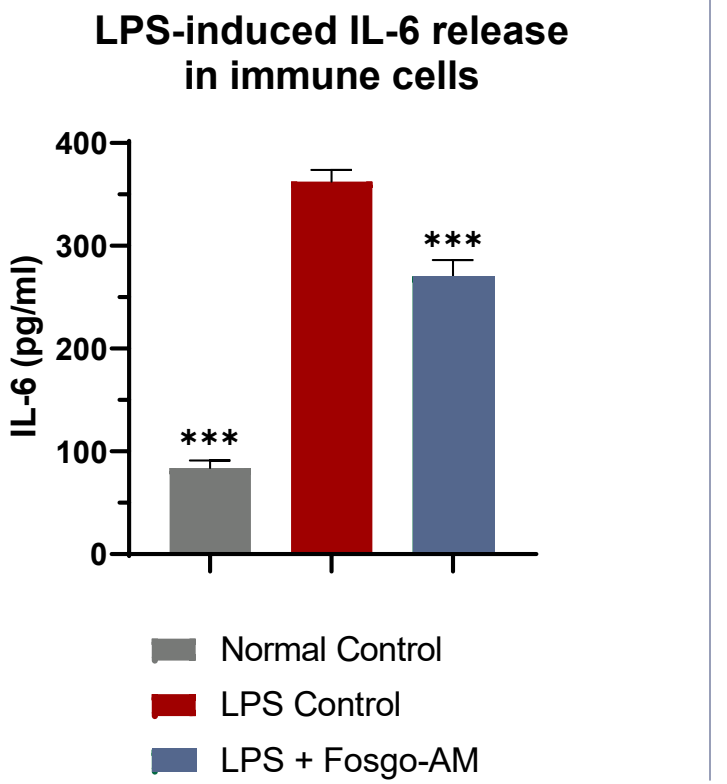
AKT, protein kinase B; ERK, extracellular-signal regulated kinase; GSK3b, glycogen synthase kinase-3 beta; HGF, hepatocyte growth factor.

Anti-inflammatory: Fosgonimeton significantly reduces inflammatory markers implicated in neurodegeneration

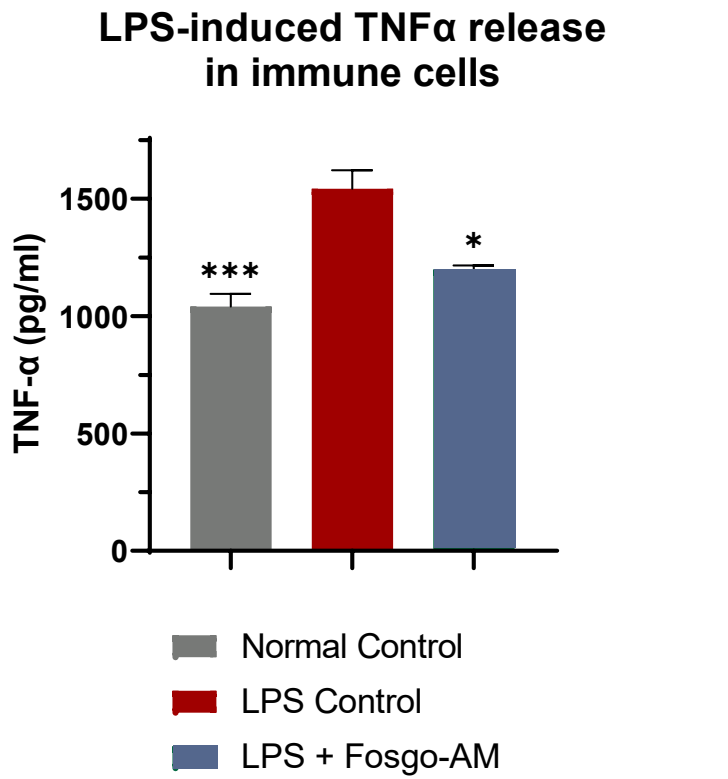
IL-1β



IL-6



TNF-α

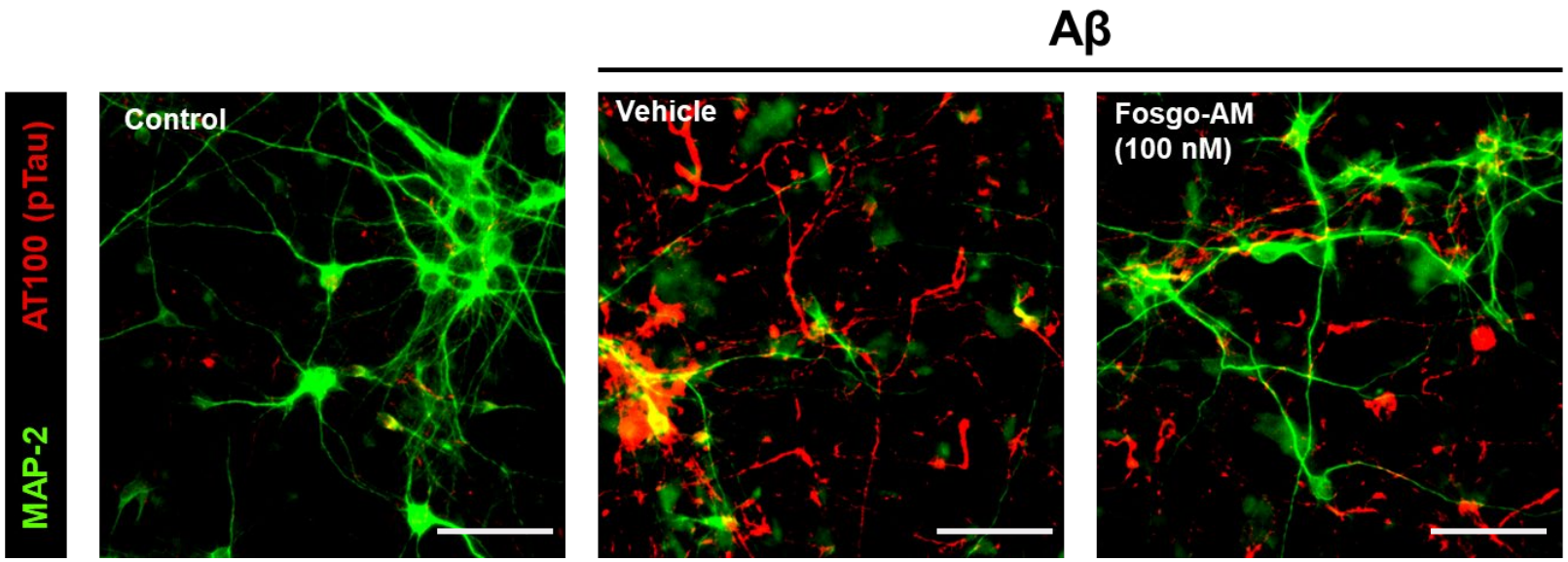


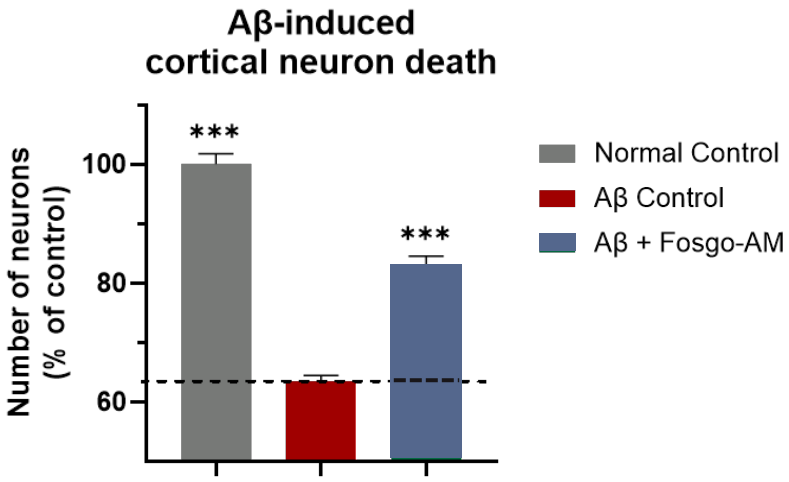
THP-1 cells. Data presented as mean ± SEM.

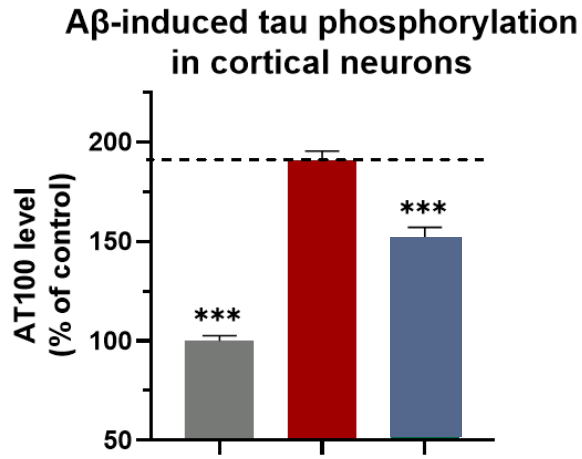
Statistics applied: 1-way ANOVA with Dunnett's test. *p<0.05, **p<0.01, ***p<0.001 vs. LPS Control; n = 3.

Fosgo-AM, fosgonimeton active metabolite; IL-1β, interleukin 1 beta; IL-6, interleukin 6; LPS, lipopolysaccharide; TNF-α, tumor necrosis factor alpha.

Alzheimer's Protein Pathology: Fosgonimeton reduces p-Tau protein pathology and protects neurons from degeneration-induced by Aβ





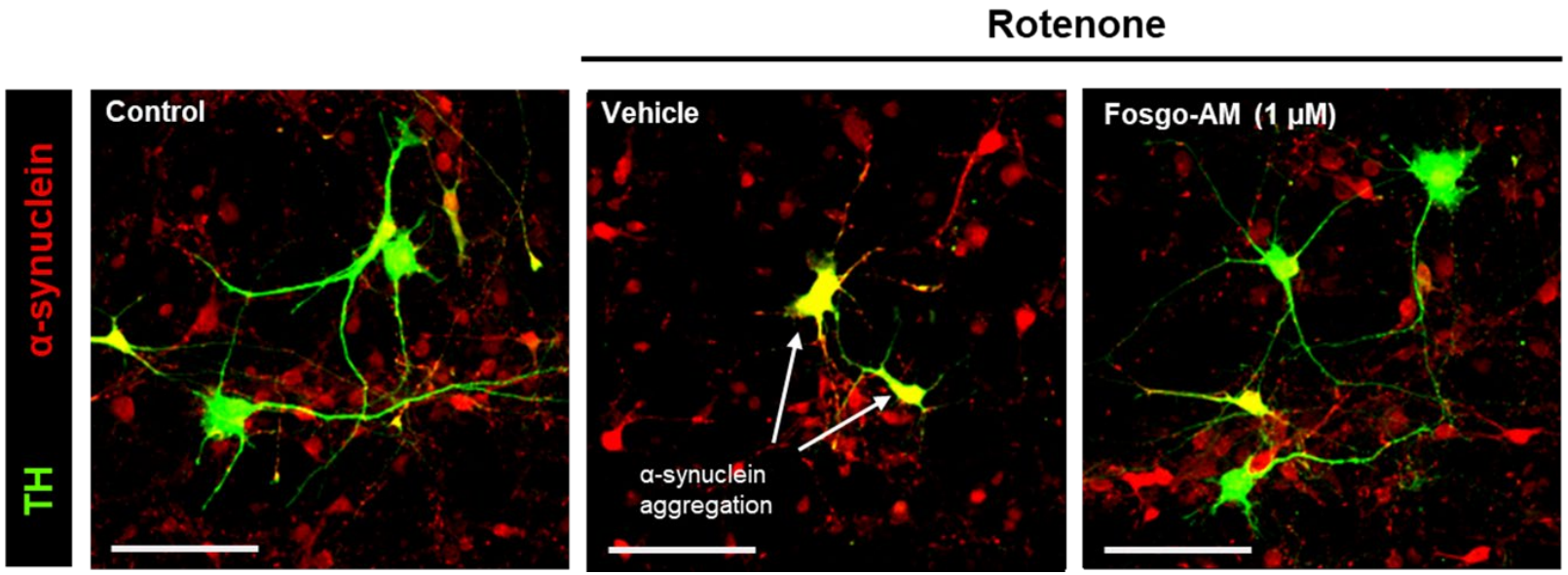


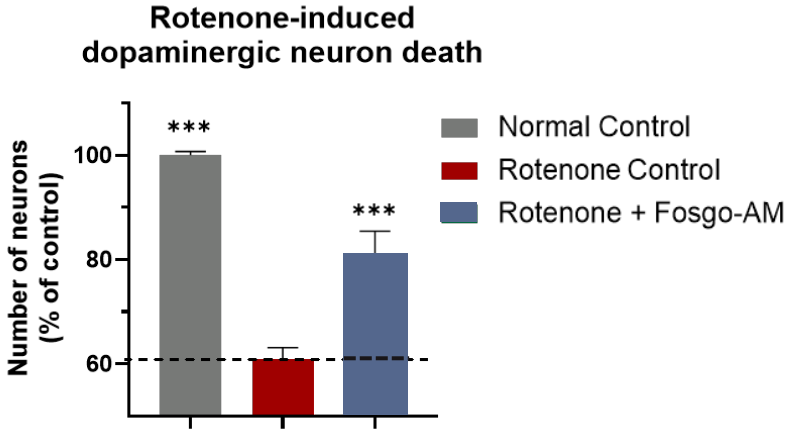
Primary rat cortical neurons. Cultures treated with vehicle control or 15 µM Aβ.

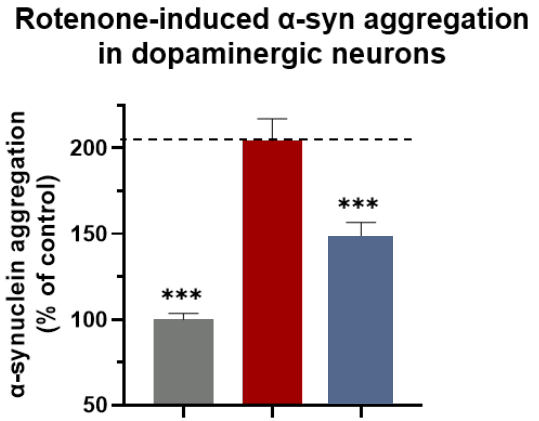
Data presented as mean ± SEM. Statistics applied: Aβ assay: One-way ANOVA with Dunnett's posttest. ***p<0.001 versus Aβ Control; n = 5-6. Scale bar: 100 µm.

Aβ, amyloid beta; AT100, hyperphospho-tau antibody; fosgo-AM; fosgonimeton active metabolite; MAP-2, microtubule-associated protein-2.

Parkinson's Protein Pathology: Fosgonimeton reduces α-synuclein aggregation and protects neurons from degeneration induced by the neurotoxin rotenone





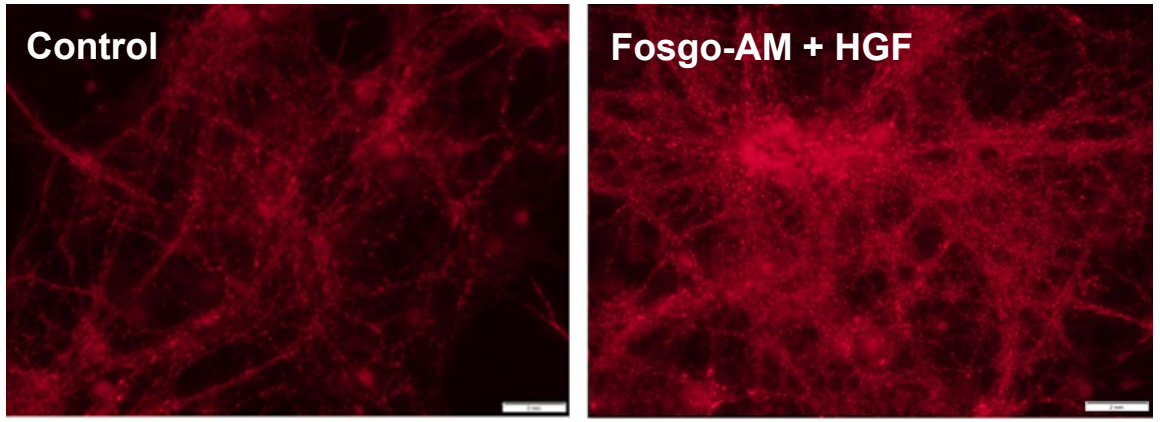


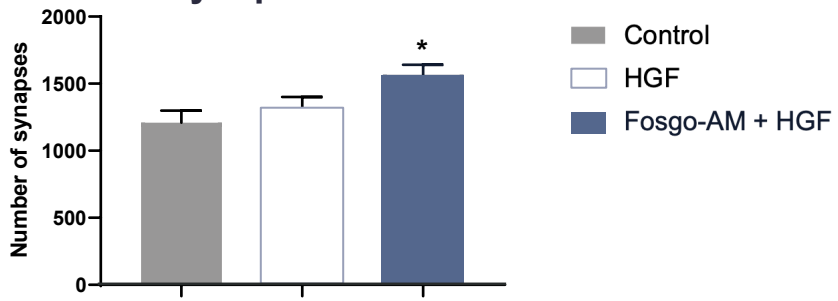
Primary mesencephalic neurons. Cultures treated with vehicle control or 10 nM rotenone.
Data presented as mean ± SEM. Statistics applied: 1-way ANOVA with Fisher least significant difference test. ***P < 0.001 versus Rotenone Control; n = 6.
Scale bar: 100 μm.
α-syn; alpha synuclein; fosgo-AM, fosgonimeton active metabolite; TH, tyrosine hydroxylase.

Neurotrophic: Enhancing HGF/MET promotes neurite outgrowth

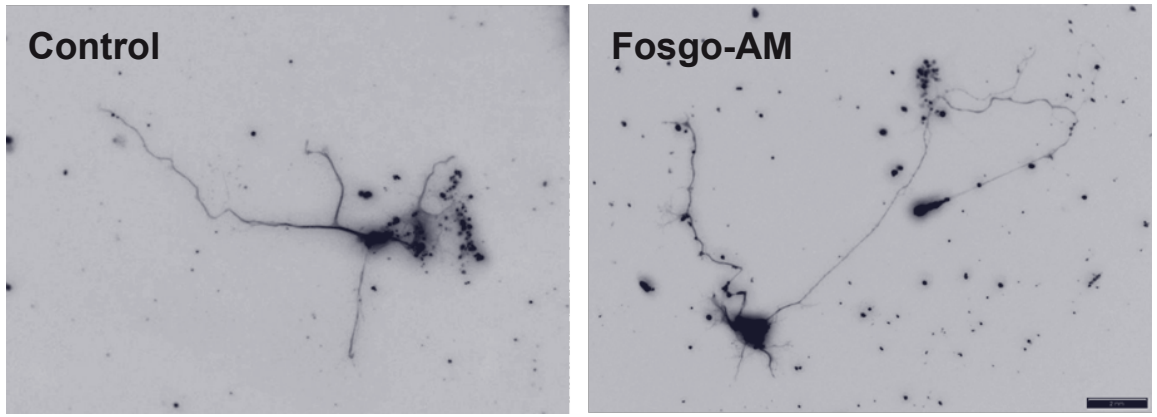
CULTURED HIPPOCAMPAL NEURONS TREATED WITH THE ACTIVE METABOLITE OF FOSGONIMETON SHOW INCREASED SYNAPTOGENESIS AND NEURITE OUTGROWTH

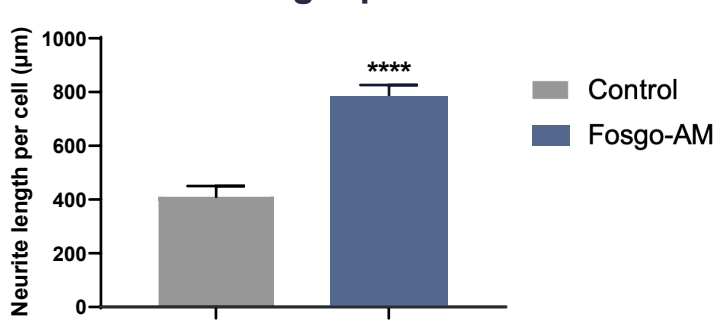
Synaptogenesis





Neurite outgrowth





Primary rat hippocampal neurons. Synaptogenesis assay immunostained with Synaptobrevin II; Neurite outgrowth cultures immunostained for β-tubulin III.

Data presented as mean ± SEM . Statistics applied – 1-way ANOVA with Dunnett posttest for synaptic count; Unpaired t-test for neurite outgrowth *p<0.05, ****p<0.0001 vs. Control; n = 10 images from 3 wells per treatment.

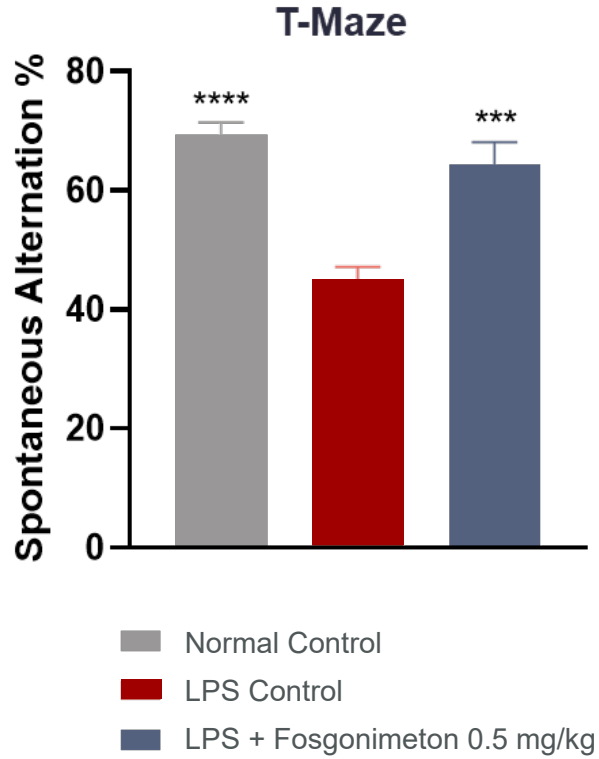
Scale bar = 20 µm.

Fosgo-AM, fosgonimeton active metabolite; HGF, hepatocyte growth factor.

Functional Improvements - Cognition:
Fosgonimeton reverses cognitive deficits caused by LPS

LPS TREATMENT CAUSES A SEVERE INFLAMMATORY RESPONSE LEADING TO COGNITIVE DEFICITS AND NEURODEGENERATION

- Cognitively normal mice have a natural drive to explore novelty, leading them to continuously alternate between each arm of the T-shaped maze.
- Cognitively impaired mice (such as those exposed to LPS) have poor working memory, leading them to repeatedly explore the same arm rather than alternating.
- LPS administration resulted in significant deficits in T-Maze spontaneous alternations compared to vehicle treated animals (LPS control)
- Treatment with Fosgonimeton attenuated these deficits, indicating procognitive activity

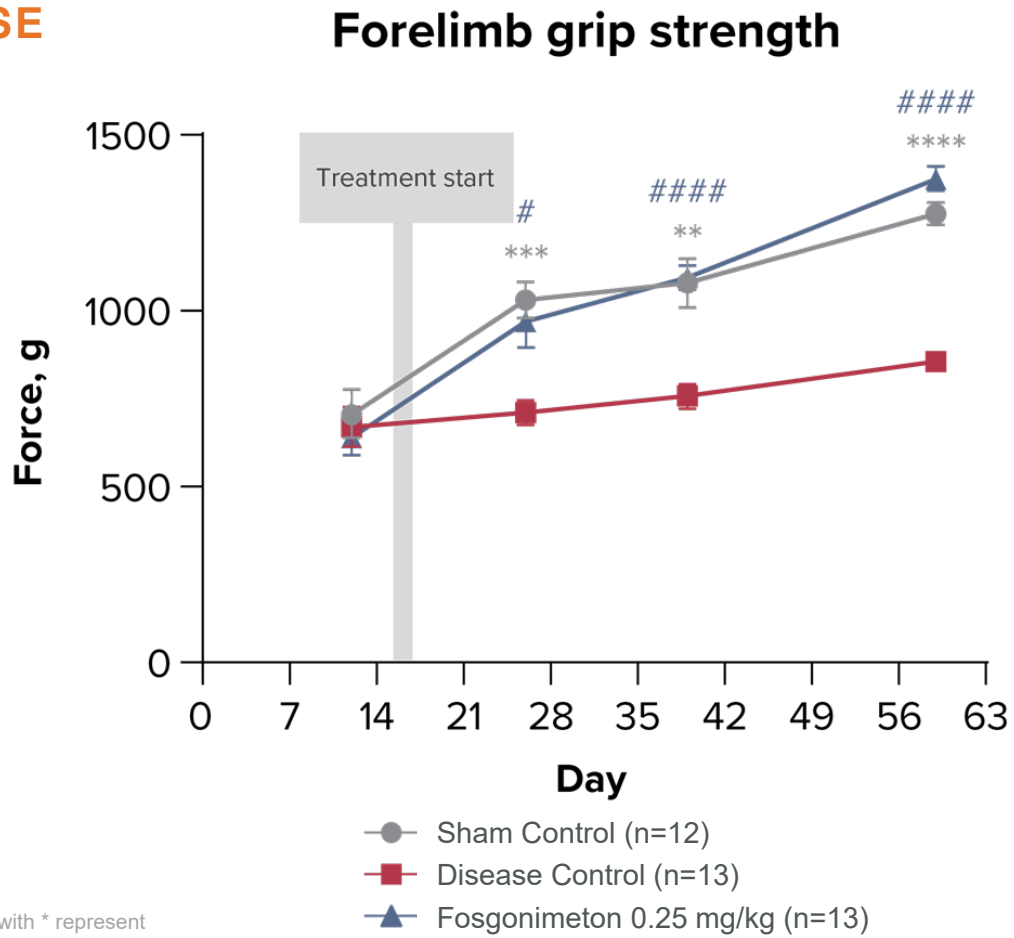


Data presented as means ± SEM. Statistics applied: One-way ANOVA with Dunnett's multiple comparisons.
*** p < 0.001, **** p < 0.0001 vs. LPS Control; n = 10 mice per group.
LPS, lipopolysaccharide.

Functional Improvements - Motor:
Fosgonimeton improves motor function

FOSGONIMETON TREATMENT RESCUES GRIP STRENGTH IN THE UNILATERAL 6-OHDA RAT MODEL OF PARKINSON'S DISEASE

- Rats have consistently weaker grip strength (ie, exert less pull force) following dopaminergic cell depleting surgery[1]
- After surgery, sham control animals initially had decreased grip strength, which recovered over time
- Fosgo treated animals were indistinguishable from the sham control
- Fosgo treatment also significantly improved performance in other motor assessments including the cylinder test and rotarod



Data presented as means ± SEM. Statistics applied: 2-way ANOVA with Dunnett test. Statistical significance indicated with * represent sham control versus disease control; # represent fosgonimeton versus disease control. For all symbols: *p < 0.05, **p < 0.01, ***p < 0.001, ****p< 0.0001 versus Disease control.

[1]Tiwari P et al. Pharmacological, Biochemical and Immunological Studies on Protective Effect of Mangiferin in 6-Hydroxydopamine (6-OHDA)-Induced Parkinson's Disease in RatsAnnals Neurosci. 2021;28:137-149.

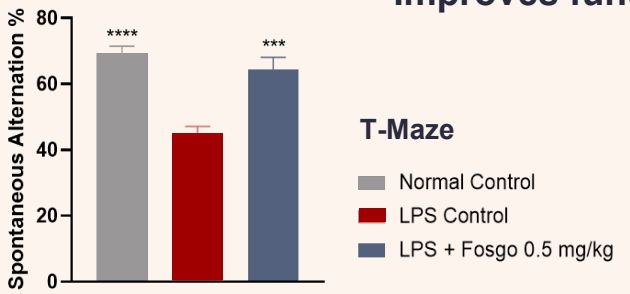
6-OHDA, 6-hydroxydopamine.

Fosgonimeton protects and repairs neural networks

MULTIMODAL APPROACH FOR MULTIMODAL DISEASES WITH POTENTIAL FOR DISEASE MODIFICATION

REPAIR | **PROTECT**

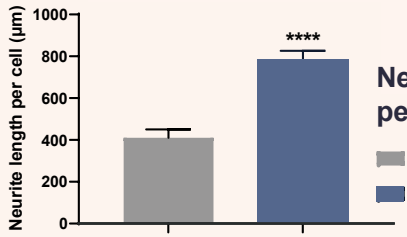
Improves function



T-Maze

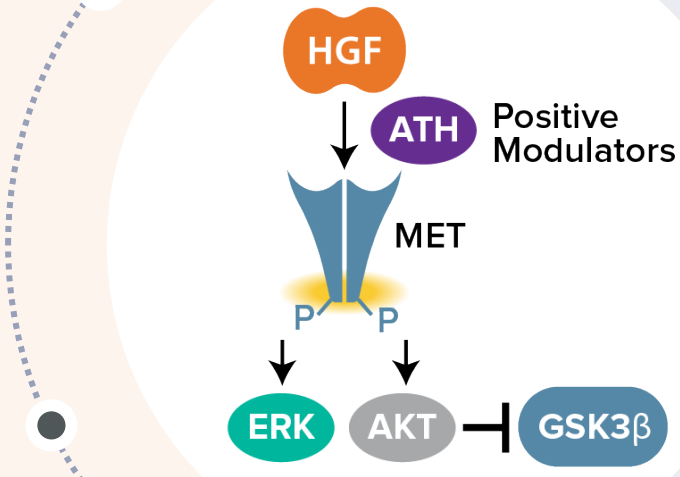
- Normal Control
- LPS Control
- LPS + Fosgo 0.5 mg/kg

Neurotrophic

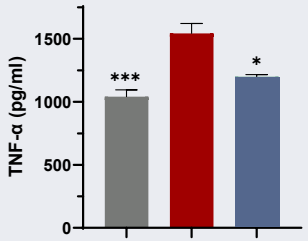


Neurite length per cell

- Control
- Fosgo-AM



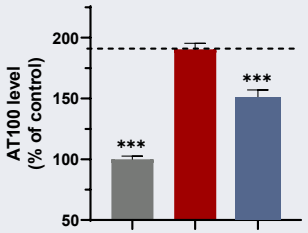
Anti-inflammatory



LPS-induced TNFα release in immune cells

- Normal Control
- LPS Control
- LPS + Fosgo-AM

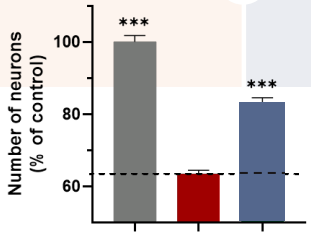
Reduces protein pathology



Aβ-induced tau phosphorylation in cortical neurons

- Normal Control
- Aβ Control
- Aβ + Fosgo-AM

Neuroprotective



Aβ-induced cortical neuron death

- Normal Control
- Aβ Control
- Aβ + Fosgo-AM

Aβ, amyloid beta; AKT, protein kinase B; ERK, extracellular-signal regulated kinase; fosgo-AM, fosgonimeton active metabolite; GSK3b, glycogen synthase kinase-3 beta; HGF, hepatocyte growth factor; LPS, lipopolysaccharide; TNF-α, tumor necrosis factor alpha.

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Fosgonimeton Development Program

Hans Moebius, MD, PhD
Chief Medical Officer

Significant progress in further characterizing fosgonimeton profile with completion of Phase 2 ACT-AD Study

CONSISTENT AND CONGRUENT IMPROVEMENTS IN BIOMARKER AND CLINICAL EFFECTS ACROSS DIVERSE MEASURES OF DISEASE PROGRESSION WITH A FAVORABLE SAFETY PROFILE

	PHASE 1*	PHASE 2*
AD Patient Population	Mild-to-Moderate	Mild-to-Moderate
Study Design	Double-blind, placebo-controlled	Double-blind, placebo-controlled
Duration	8 days	6 months + up to 18-month OLEX
N	11	77
Background AChEI Therapy	No	Allowed; potential efficacy interaction observed between fosgo and AChEI
Biomarkers analyzed to-date	ERP P300 latency	ERP P300 latency, NfL, GFAP, YKL40, Aβ 42/40 ratio, and p-Tau181
Cognition	Not measured	ADAS-Cog11
Function	Not measured	ADCS-ADL23
Biomarker Correlation to Clinical Endpoints	Unknown	Supportive
Safety	Favorable	Favorable

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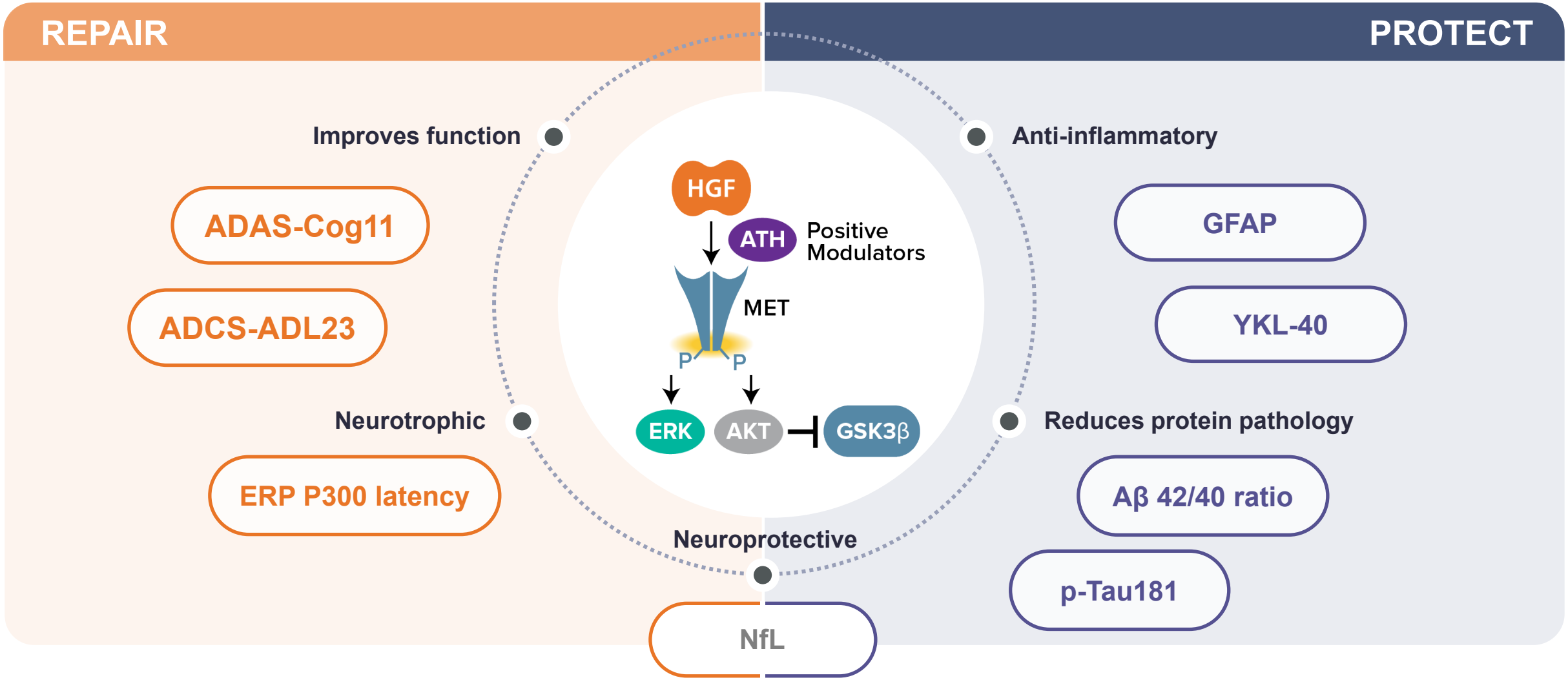
*Effects are compared against placebo control.

Aβ, amyloid beta; AD, Alzheimer's disease; ADAS-Cog11, Alzheimer's Disease Assessment Scale–Cognitive Subscale; ADCS-ADL23, Alzheimer's Disease Cooperative Study–Activities of Daily Living, 23-item version; ERP, event-related potential; GFAP, glial fibrillary acidic protein; NfL, neurofilament light chain; p-Tau181, tau phosphorylated at threonine-181; YKL-40, chitinase-3–like protein 1.

Clinical biomarker and functional measures enable translation of preclinical findings

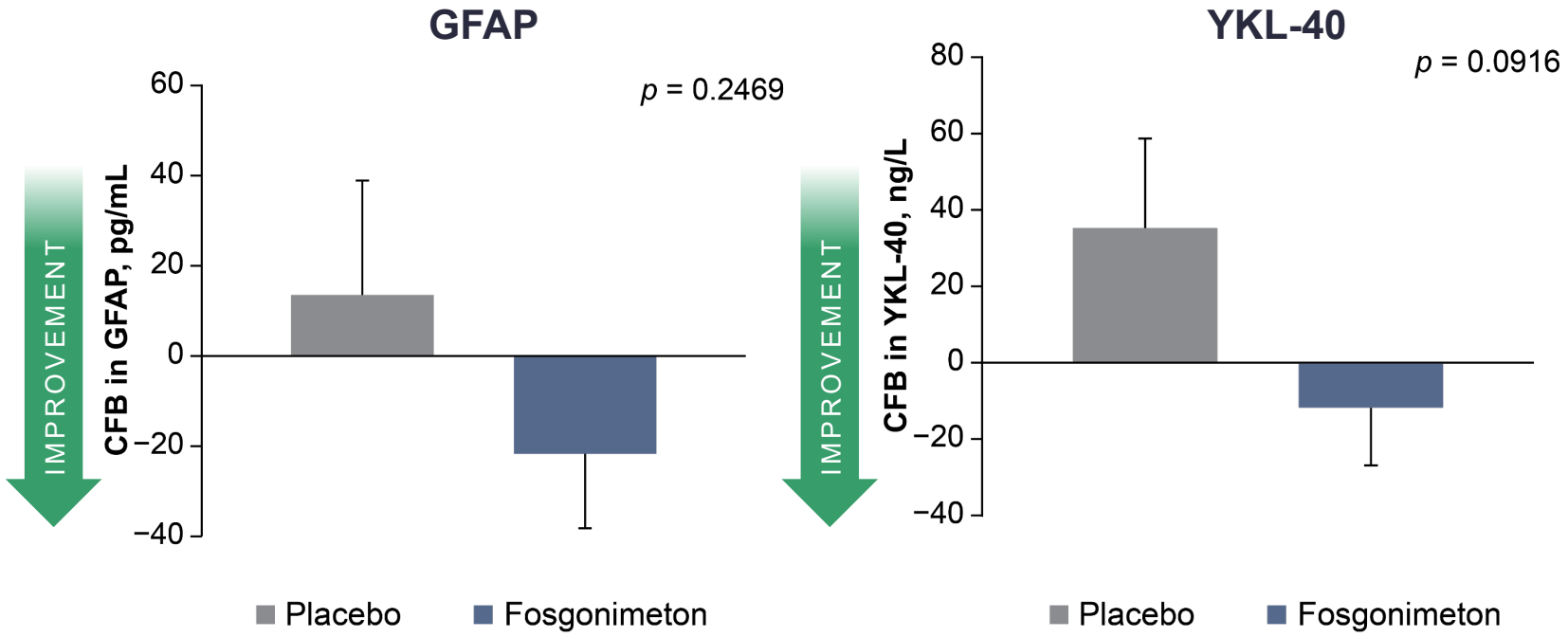
SUPPORTS THE THERAPEUTIC POTENTIAL OF FOSGONIMETON IN ALZHEIMER'S DISEASE



Aβ, amyloid beta; ADAS-Cog11, Alzheimer's Disease Assessment Scale–Cognitive Subscale; ADCS-ADL23, Alzheimer's Disease Cooperative Study–Activities of Daily Living, 23-item version; AKT, protein kinase B; ERK, extracellular-signal regulated kinase; ERP, event-related potential; GFAP, glial fibrillary acidic protein; GSK3β, glycogen synthase kinase-3 beta; HGF, hepatocyte growth factor; NfL, neurofilament light chain; p-Tau181, tau phosphorylated at threonine-181; YKL-40, chitinase-3–like protein 1.

Anti-inflammatory: Fosgonimeton appears to improve neuroinflammation in mild-to-moderate Alzheimer's patients

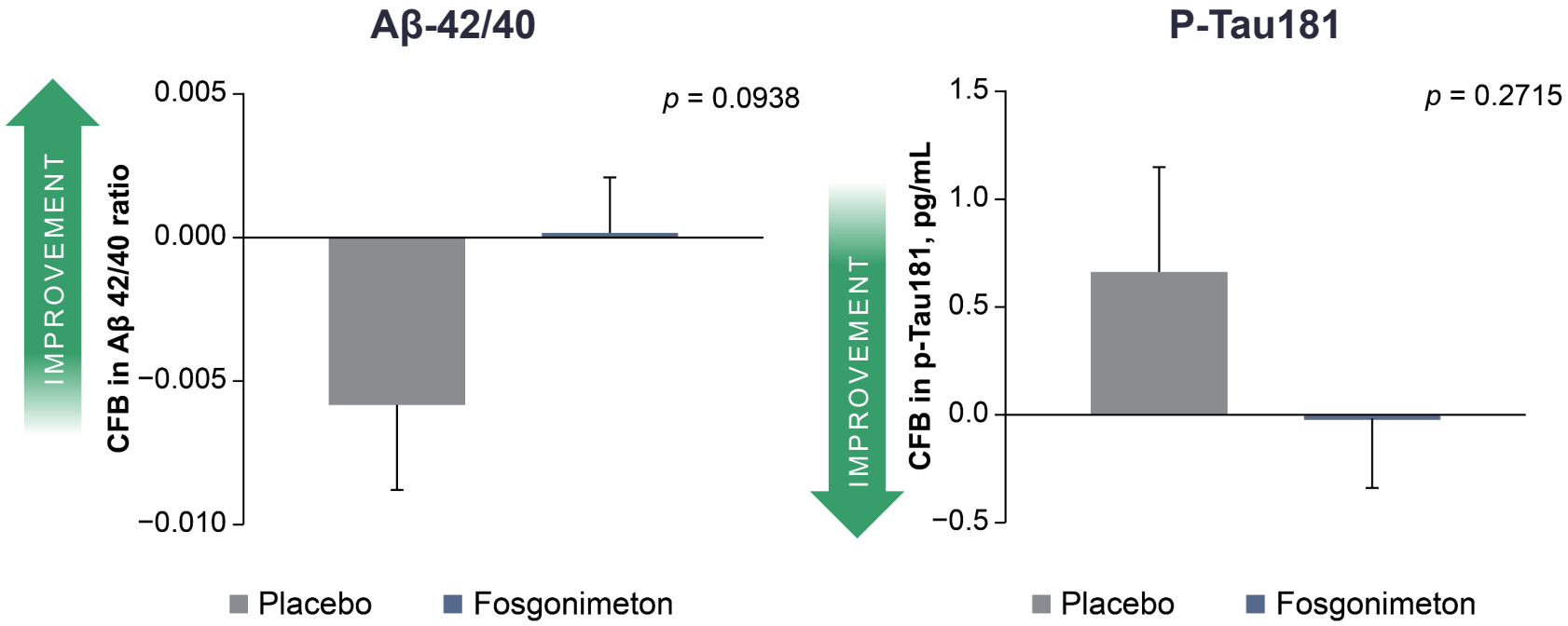
- GFAP and YKL-40 are markers of neuroinflammation
- Magnitude of decrease below baseline levels encouraging in this continuously progressive condition
- Supports potential anti-inflammatory mechanism of action of fosgonimeton



N=5 for placebo treatment; N=11 or 12 for fosgonimeton treatment.
GFAP, glial fibrillary acidic protein; YKL-40, chitinase-3–like protein 1.

Protein Pathology: Fosgonimeton induces directional improvements in hallmarks of Alzheimer's disease

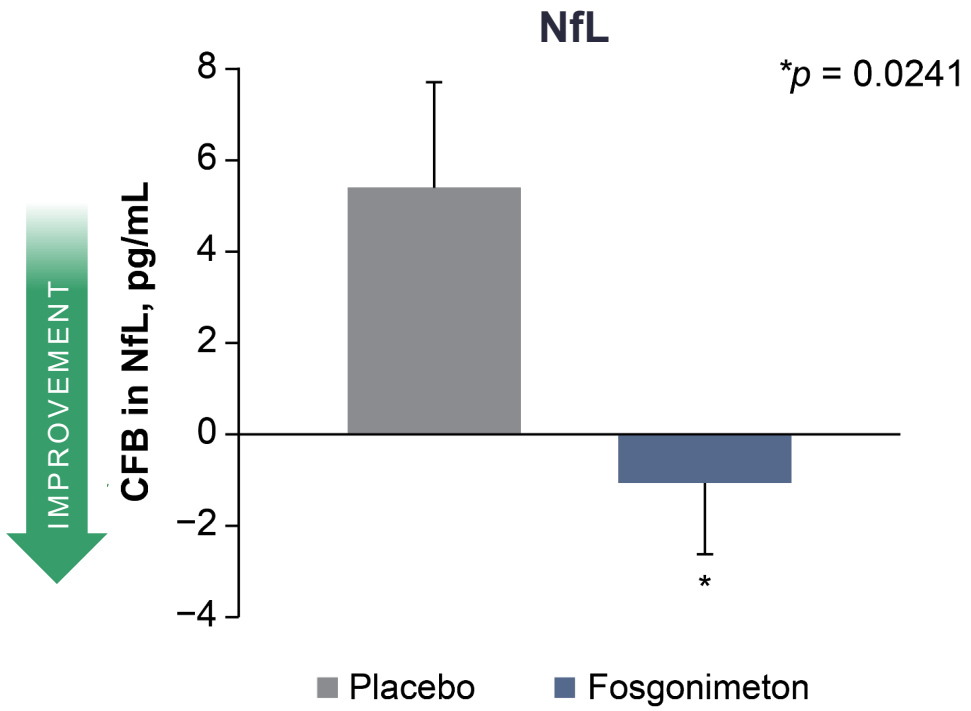
- Decreased Aβ 42/40 ratio and increased absolute p-tau values are hallmarks of Alzheimer's disease
- Changes support relevance of the HGF/MET pathway also to Alzheimer's-specific protein pathology
- Supports disease modifying potential of fosgonimeton



N=5 for placebo treatment; N=11 for fosgonimeton treatment.
Aβ, amyloid beta; p-Tau181, tau phosphorylated at threonine-181.

Neuroprotective: Fosgonimeton shows potential neuroprotection in mild-to-moderate Alzheimer's patients

- Neurofilament light (NfL) is an established, objective biomarker of neurodegeneration
- Fosgonimeton showed a statistically significant decrease in plasma levels of NfL (-6.49 pg/mL, p=0.024)
- Decrease of NfL to below baseline levels suggestive of repair in this continuously progressive disease
- Supports potential neuroprotective mechanism of action of fosgonimeton



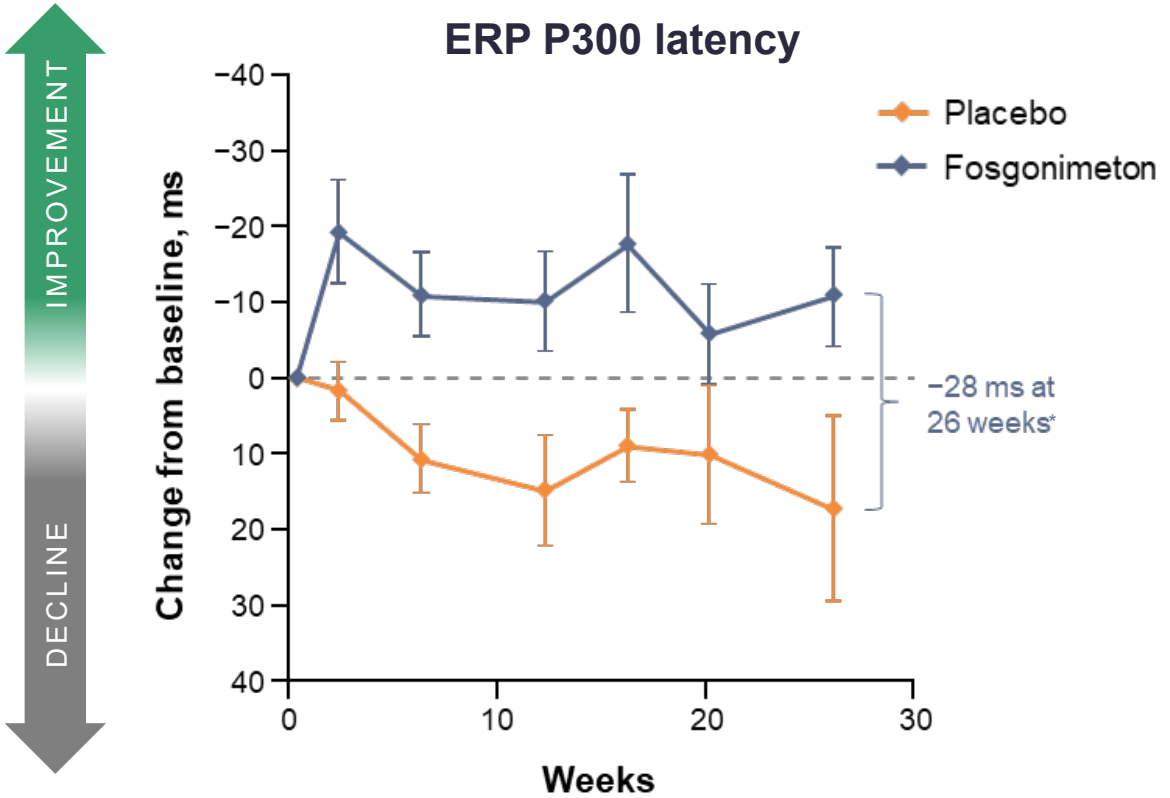
N=5 for placebo treatment; N=12 for fosgonimeton treatment.
NfL, neurofilament light chain.

Neurotrophic: Fosgonimeton results in directional improvements in ERP P300 latency

ERP P300 latency

- Functional measurement for working memory access and executive function
- Biomarker for neuroplasticity

ERP P300 latency results from ACT-AD consistent with Phase 1b results in patients without background therapy



n at each visit	W2	W6	W12	W16	W20	W26
Placebo	8	8	6	6	7	6
Fosgonimeton	20	19	18	15	16	17

*Primary endpoint, ERP P300 latency, was not met; observed effect against placebo was not statistically significant.
mITT population without background therapy. Data presented as unadjusted mean ± SEM.
AD, Alzheimer's disease; ERP, Event Related Potential; mITT, modified intent-to-treat; W, week.

Functional Improvements: Potential benefits in cognition and function from fosgonimeton treatment

SUPPORTS POTENTIAL TO BE A SAFE AND DIFFERENTIATED FUTURE THERAPY

79% | **-3.3** points n.s.

IMPROVED COGNITION

Improvement over placebo over 6 months as measured by ADAS-Cog11 in patients without background therapy

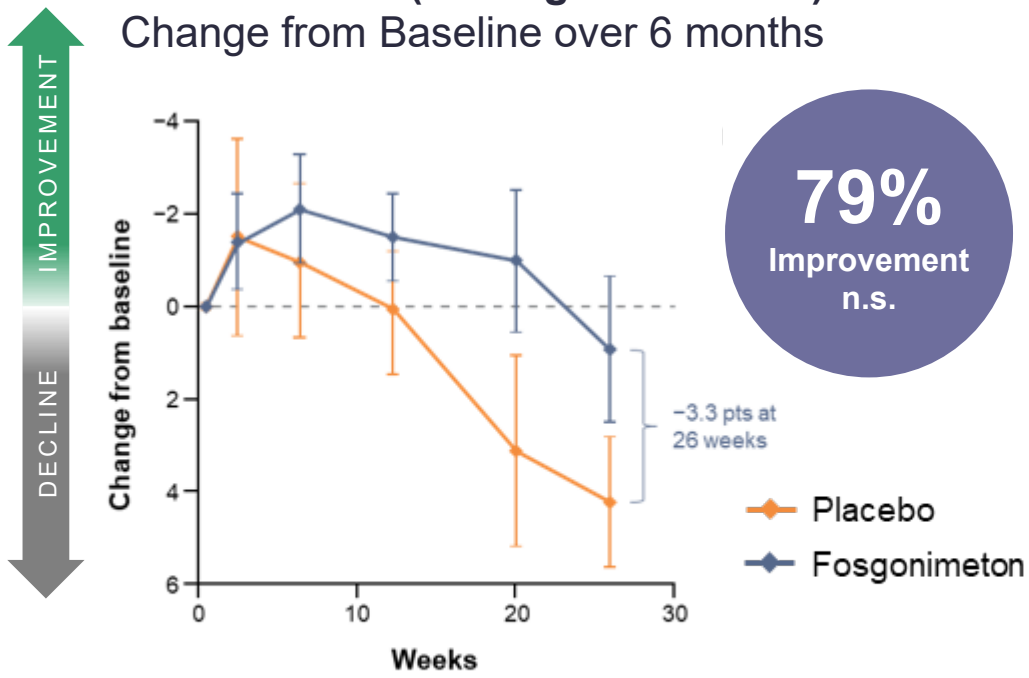
51% | **+2.1** points n.s.

IMPROVED FUNCTION

Improvement over placebo over 6 months as measured by ADCS-ADL23 in full study population

Favorable safety and tolerability profile, injection site reactions are most frequent AE

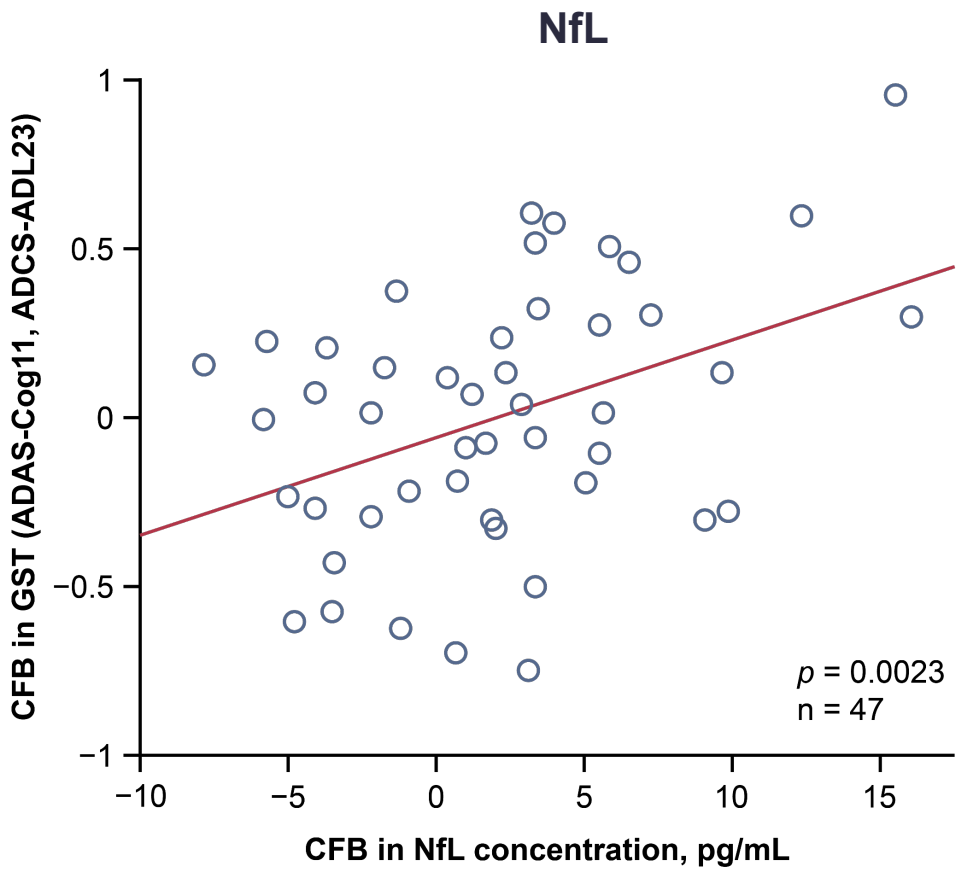
ADAS-COG11 (Procognitive Effect)
Change from Baseline over 6 months

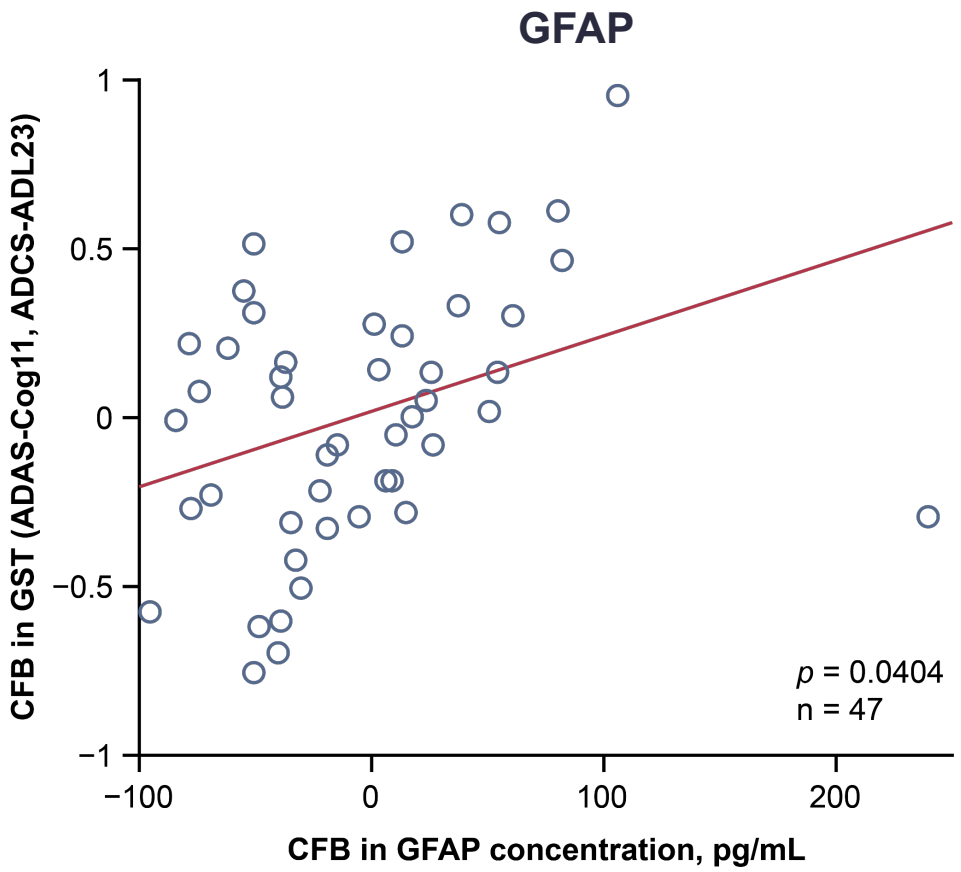


n at each visit	W2	W6	W12	W20	W26
Placebo	8	8	7	7	6
Fosgonimeton	20	20	18	17	18

mITT population without background therapy. Data presented as unadjusted mean ± SEM; n.s., not statistically significant.
AD, Alzheimer's disease; ADAS-Cog11, Alzheimer's Disease Assessment Scale–Cognitive Subscale; ADCS-ADL23, Alzheimer's Disease Cooperative Study–Activities of Daily Living, 23-item version; AE, adverse event; mITT, modified intent-to-treat; W, week.

Decreases in disease state biomarkers significantly correlate with improvements in cognitive and functional measures

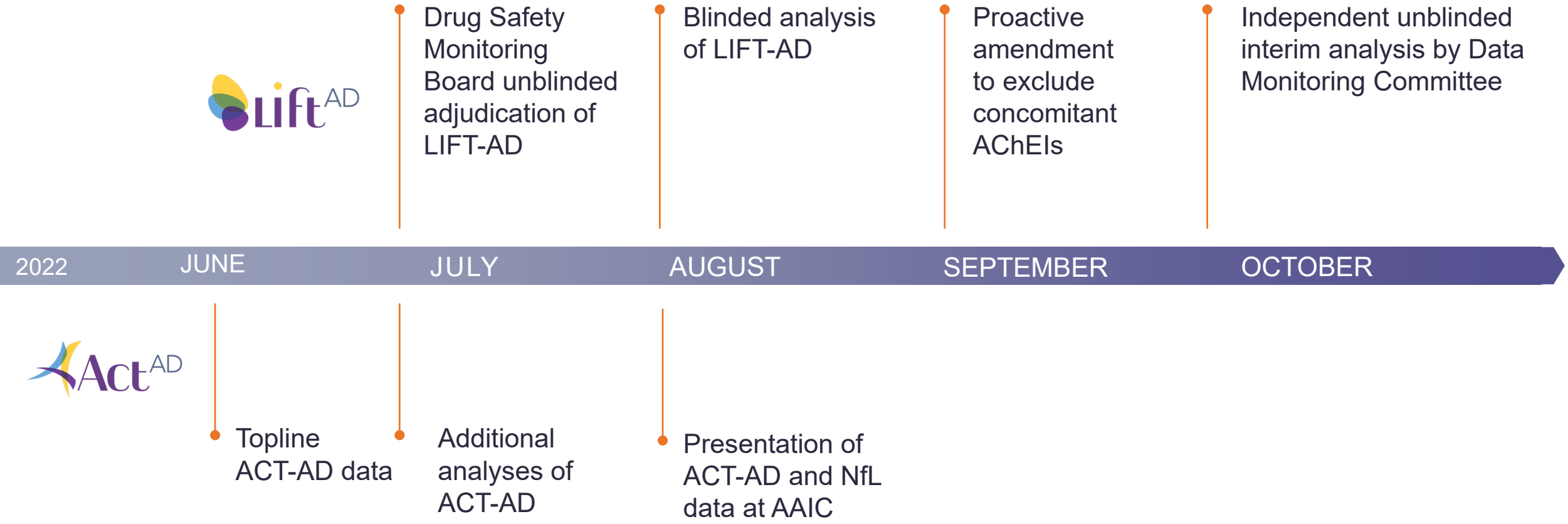




ADAS-Cog11, Alzheimer's Disease Assessment Scale–Cognitive Subscale; ADCS-ADL23, Alzheimer's Disease Cooperative Study–Activities of Daily Living, 23-item version; CFB, change from baseline; GFAP, glial fibrillary acidic protein; GST, global statistical test; NfL, neurofilament light chain.

Applied Learnings from Exploratory ACT-AD to Amend LIFT-AD

SYSTEMATIC AND DATA-DRIVEN PROCESS



AChEI, acetylcholinesterase inhibitor; AD, Alzheimer's disease; NfL, neurofilament light chain.

Interim analysis criteria set to increase the probability of demonstrating a meaningful effect size

Interim Analysis Methodology[1]

- Conducted by an independent data monitoring committee: Chair neurologist (MD) and two biostatisticians (PhD)
- Adaptive method, that enables a sample-size re-estimation to occur based on findings of an interim look that measures a candidate therapy's performance
- Monte Carlo simulations run to inform pre-specified sample size range and resulting effect sizes

INPUTS

Unblinded data

- Effect size of GST score at 26-weeks
  - Change from baseline of ADAS-Cog11
  - Change from baseline of ADCS- ADL23
- Variance

Pre-specified constraints

- Sample size range with maximum enrollment limit
- Minimum target power for well-powered GST score (primary endpoint)

FORMAL EFFICACY ANALYSES

- **Patient population:** Patients without background AChEI
- **N = Approximate 100 completers** (mITT) of 26-week double-blind treatment period
- **Calculation:** The primary analysis used a mixed model for repeated measures (MMRM) to compare the change from baseline in the Global Statistical Test score (GST; O'Brien, 1984) between the pooled fosgonimeton treatment arms and placebo

POTENTIAL OUTCOMES

1. **Stop study for futility**
   a. If the results do not achieve the pre-specified lower boundary for conditional power OR
   b. If the sample size required to reach desired conditional power exceeds pre-specified maximum
2. **Continue enrollment within a pre-specified range to achieve target power of primary endpoint**

[1]Mehta and Pocock (2000). Adaptive Increase in Sample Size when Interim Results are Promising: A Practical Guide with Examples. *Statist. Med.* 00:1–6.

AChEI, acetylcholinesterase inhibitor; ADAS-Cog11, Alzheimer's Disease Assessment Scale–Cognitive Subscale; ADCS-ADL23, Alzheimer's Disease Cooperative Study–Activities of Daily Living, 23-item version; GST, global statistical test, a composite score of cognition and function; mITT, modified intent-to-treat; MMRM, mixed-model repeated measures.

DMC confirmed activity and indicated new sample size estimation

DEVELOPMENT PLAN OPTIMIZED WITH MITIGATED RISK

Pre-specified Decision Framework

Fosgonimeton treatment effect vs placebo on composite score[1] of cognition and function

Independent Unblinded Analysis Outcome

- DMC Recommendation (Oct 2022): **Continue LIFT-AD Study**
- New sample size estimation based on **actual effect size and variability observed in first 100 completers to achieve adequate target power**
- **<150** more patients needed to complete study with well-powered primary endpoint; total sample size <300
- Target enrollment complete **by mid 2023 with data in early 2024**

[1]Primary endpoint is the global statistical test, an unweighted composite of ADAS-Cog11 and ADCS-ADL23.
AD, Alzheimer's disease; ADAS-Cog11, Alzheimer's Disease Assessment Scale–Cognitive Subscale; ADCS-ADL23, Alzheimer's Disease Cooperative Study–Activities of Daily Living, 23-item version; DMC, data monitoring committee.

Fosgonimeton Phase 2/3 LIFT-AD Trial after Amendment

LEARNINGS FROM ACT-AD INFORM TRIAL DESIGN OPTIMIZATION

POPULATION

N= ~300 subjects without background therapy

Mild-to-moderate AD
(MMSE 14-24; CDR 1-2)

26-week randomized, double-blind treatment,
+ optional 18-month OLEX

- Fosgonimeton (40 mg)
- Fosgonimeton (70 mg)
- Placebo

TIMELINE:

- Complete enrollment **mid-2023**
- Topline data **early 1H24**

ENDPOINTS

PRIMARY

- Composite GST score of two key secondary endpoints of cognition and function (ADAS-Cog11 and ADCS-ADL23)
- Safety

SECONDARY

- Cognition: ADAS-Cog11
- Function: ADCS-ADL23
- Global clinical change: ADCS CGIC – Clinician
- Plasma NfL biomarker

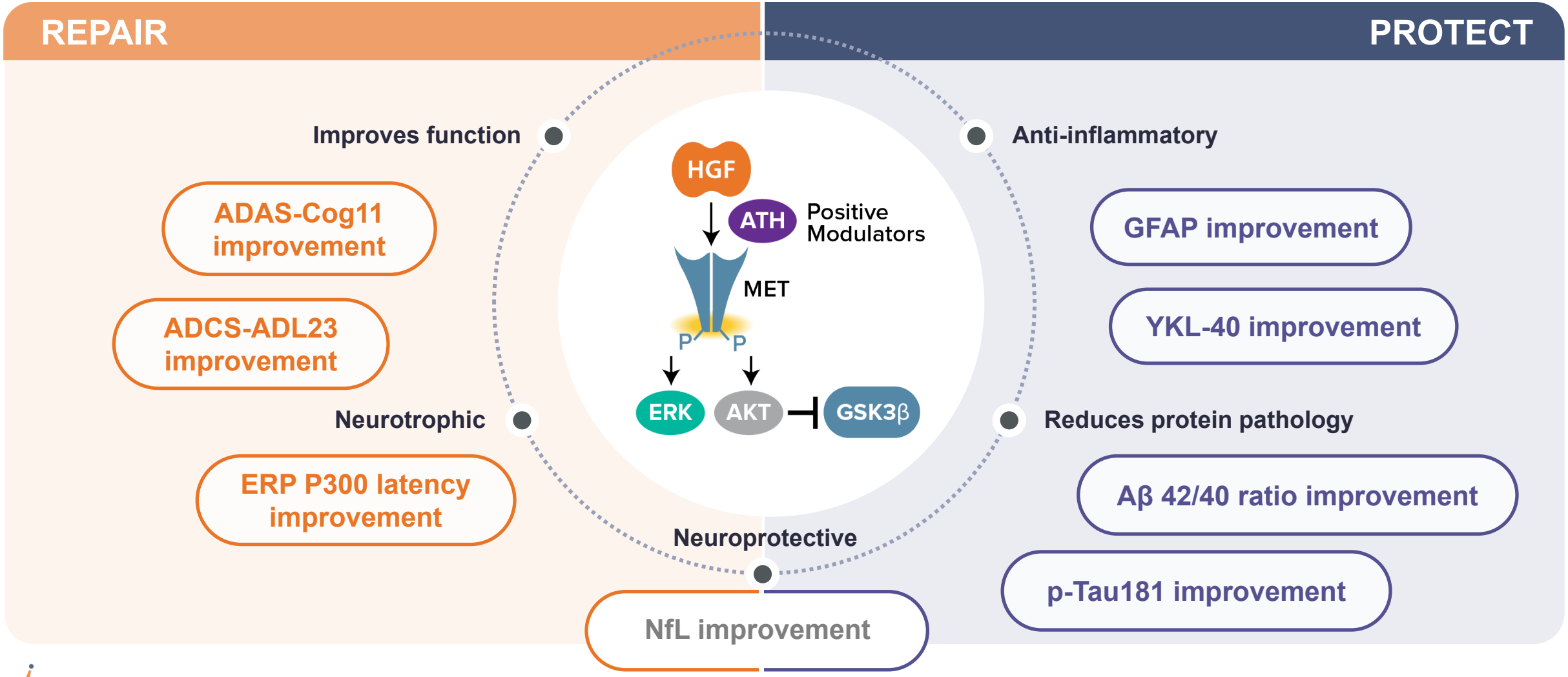
EXPLORATORY

- Additional plasma biomarkers (GFAP, YKL-40, Aβ 42/40 ratio, p-Tau181, p-Tau217)

Aβ, amyloid beta; AD, Alzheimer's disease; ADAS-Cog11, Alzheimer's Disease Assessment Scale–Cognitive Subscale; ADCS-ADL23, Alzheimer's Disease Cooperative Study–Activities of Daily Living; ADCS-CGIC, Alzheimer's Disease Cooperative Study–Clinical Global Impression of Change; CDR, clinical dementia rating; GFAP, glial fibrillary acidic protein; GST, global statistical test; NfL, neurofilament light chain; OLEX, open-label extension; p-Tau181, tau phosphorylated at threonine 181; p-Tau217, YKL-40, tau phosphorylated at threonine 217; YKL-40, chitinase-3–like protein 1.

Evidence Suggests Translation of Preclinical Findings to Clinical Effects

FINDINGS SUPPORT THERAPEUTIC POTENTIAL OF FOSGONIMETON



Aβ, amyloid beta; ADAS-Cog11, Alzheimer's Disease Assessment Scale–Cognitive Subscale; ADCS-ADL23, Alzheimer's Disease Cooperative Study–Activities of Daily Living, 23-item version; AKT, protein kinase B; ERK, extracellular-signal regulated kinase; ERP, event-related potential; GFAP, glial fibrillary acidic protein; GSK3β, glycogen synthase kinase-3 beta; HGF, hepatocyte growth factor; NfL, neurofilament light chain; p-Tau181, tau phosphorylated at threonine-181; YKL-40, chitinase-3–like protein 1.

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Alzheimer's Disease Landscape

Rachel Lenington
Chief Operating Officer

Biomarkers gaining traction to support FDA accelerated approvals in neurodegenerative diseases

FAVORABLE EXTERNAL ENVIRONMENT MAY SUPPORT ACCELERATED DEVELOPMENT OF NOVEL THERAPIES

Biogen's aducanumab accelerated approval in June 2021 set regulatory precedent with the first biomarker-based approval in Alzheimer's disease

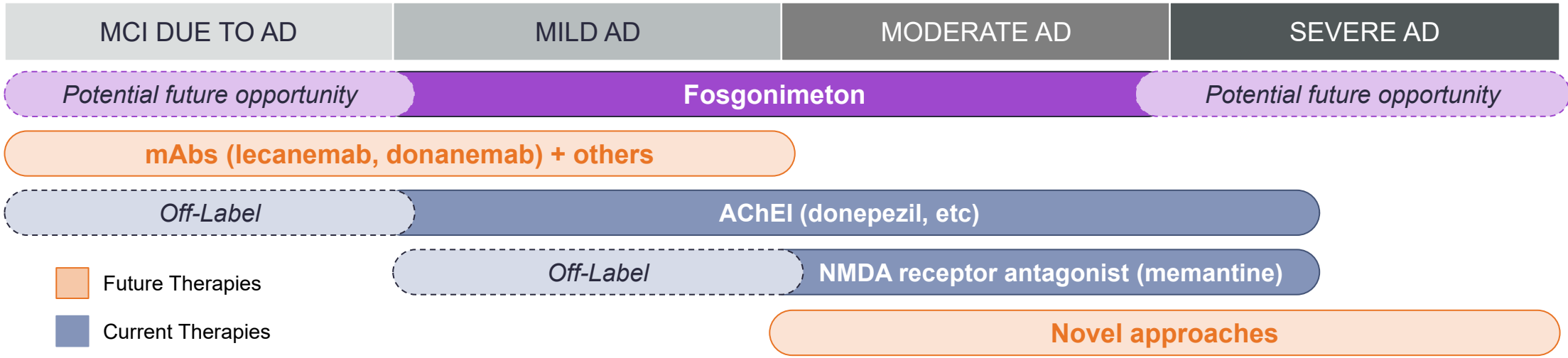
Eisai/Biogen and Lilly anticipate accelerated approvals in early 2023 based on effects on biomarkers (Aβ) and supportive composite clinical endpoints (ADCOMS and iADRS)

In SOD-1 ALS, Biogen filed for accelerated approval for toferson based on effects on NfL

Aβ, amyloid beta; ALS, amyotrophic lateral sclerosis; ADCOMS, Alzheimer's disease composite score; iADRS, integrated Alzheimer's disease rating scale; NfL, neurofilament light chain; SOD-1, superoxide dismutase type-1.

Significant opportunity in mild-to-moderate Alzheimer's disease

COMPETITIVE ENVIRONMENT



- **Most new therapies under development target pre-dementia**
- **2.1 million mild-to-moderate Alzheimer's patients diagnosed in 2021**
  Comprises 81% of all patients diagnosed with Alzheimer's disease
- **Currently available drugs in mild-to-moderate space have limited effects**
  1.1 million patients are treated with AChEIs or memantine currently

  75% of patients move to a second-line treatment in less than a year

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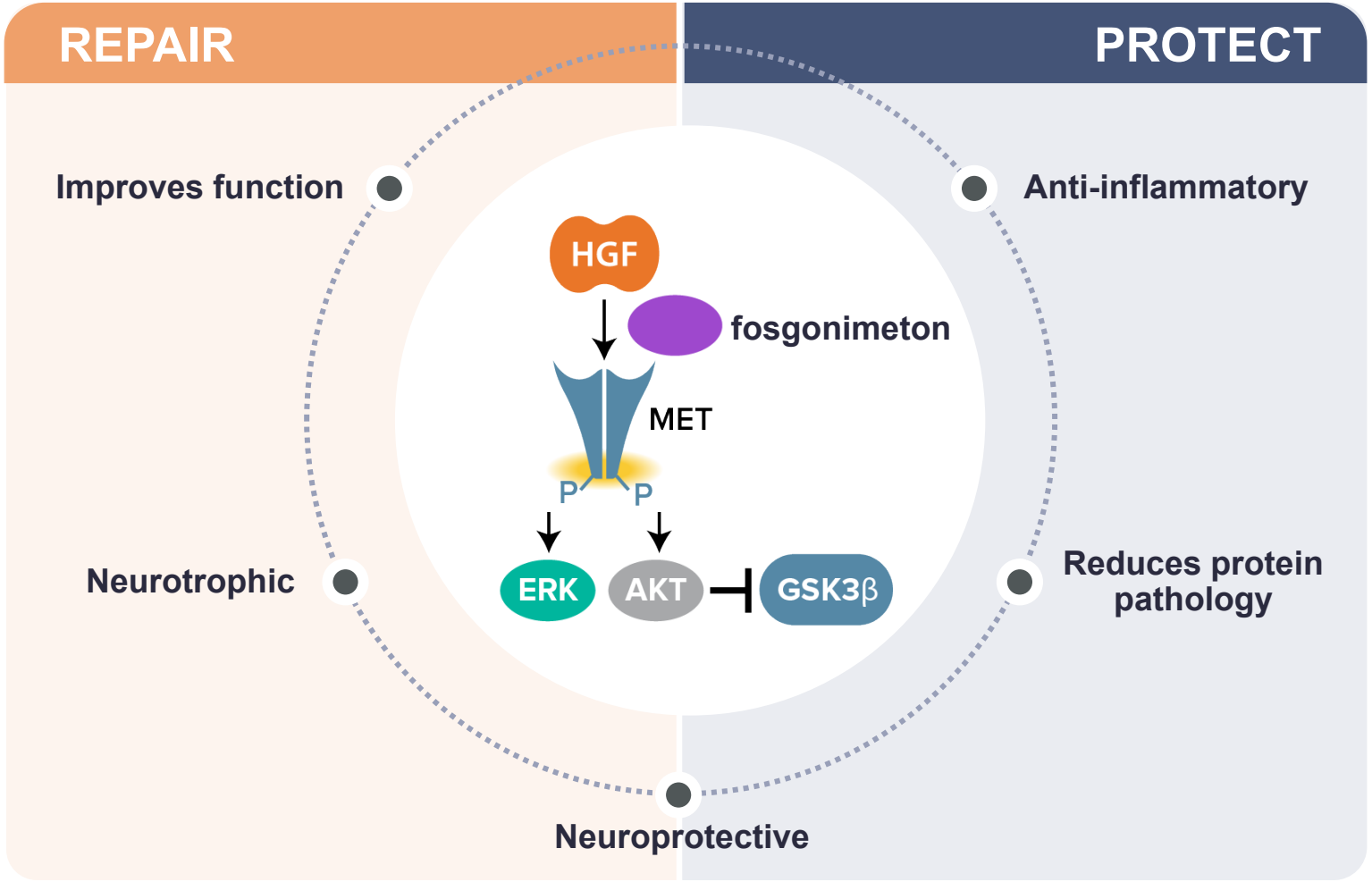
Data from Decision Resources Group.
AChEI, acetylcholinesterase inhibitor; AD, Alzheimer's disease; mAbs, monoclonal antibodies; MCI, mild cognitive impairment; NMDA, N-methyl-aspartate.

Enhancing HGF/MET with fosgonimeton may represent a differentiated new class of therapy for Alzheimer's patients

DESIGNED TO PROTECT AND REPAIR NEURAL NETWORKS



AKT, protein kinase B; ERK, extracellular-signal regulated kinase; GSK3β, glycogen synthase kinase-3 beta; HGF, hepatocyte growth factor.

Strong rationale to advance fosgonimeton

SIGNIFICANT OPPORTUNITY TO TRANSFORM THE TREATMENT PARADIGM FOR NEURODEGENERATIVE DISEASES

- Anti-Inflammatory
- Neuroprotective
- Improves Cognition
- Improves Function
- Potentially Disease Modifying
- Favorable Safety and Tolerability Profile
- Risk Mitigated Ph 2/3 LIFT-AD following Interim Analysis

Differentiated and Risk Mitigated

+

- Evolving Regulatory Environment
- Low Competitive Intensity

Favorable external landscape

AD, Alzheimer's disease.

Athira PHARMA

Preclinical Results of ATH-1105 in ALS

Kevin Church, PhD

Executive Vice President, Research

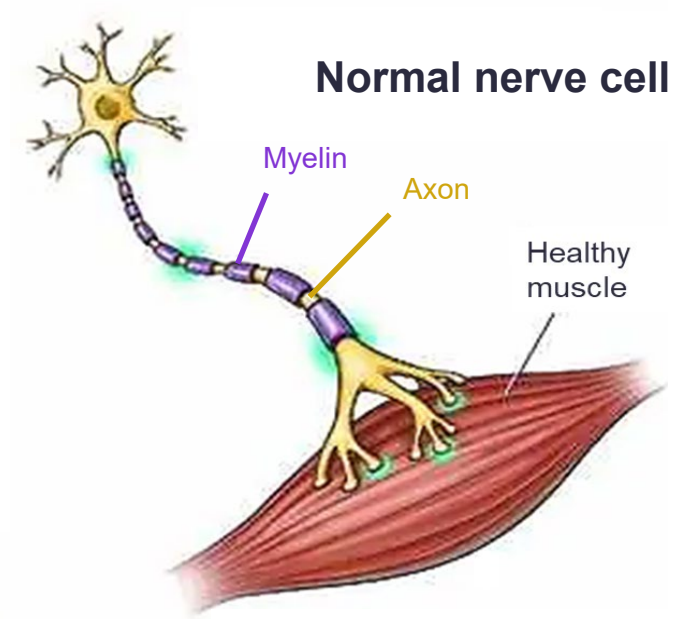
Positive modulation of HGF/MET as a potential treatment for ALS

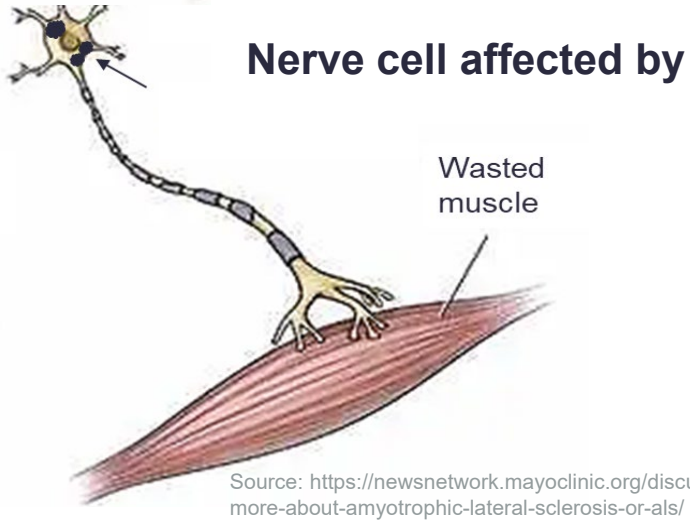
Reported beneficial effects of targeting HGF/MET in preclinical models of ALS:

- Transgenic overexpression or intrathecal delivery of HGF delays disease progression in ALS animal models[1,2]
- Delivery of a recombinant HGF reduces muscle impairment and motor neuron loss in an ALS mouse model[3]

Modeling ALS

- Approximately 97% of ALS patients have TDP-43 pathology[4]
  - TDP-43 is a nuclear protein under normal conditions but in ALS forms toxic aggregates in the cytoplasm of motor neurons
  - TDP-43 mouse models have been developed that exhibit TDP-43 pathology and ALS-like symptoms



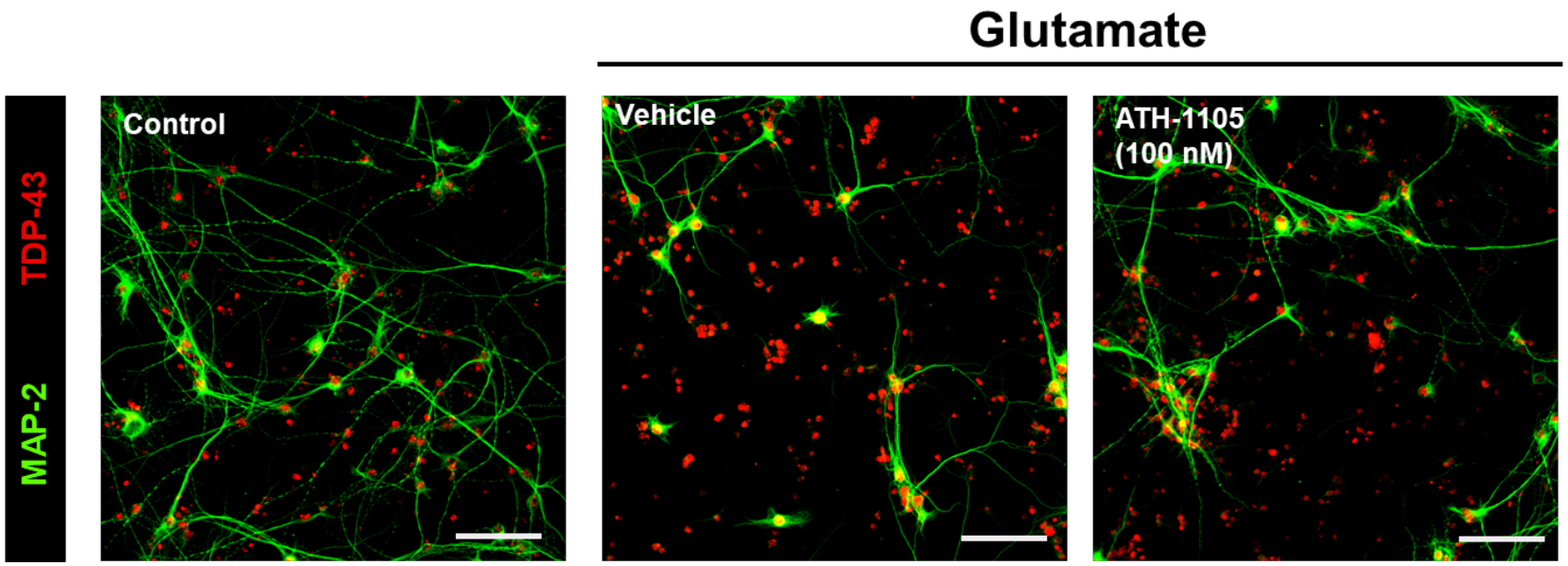


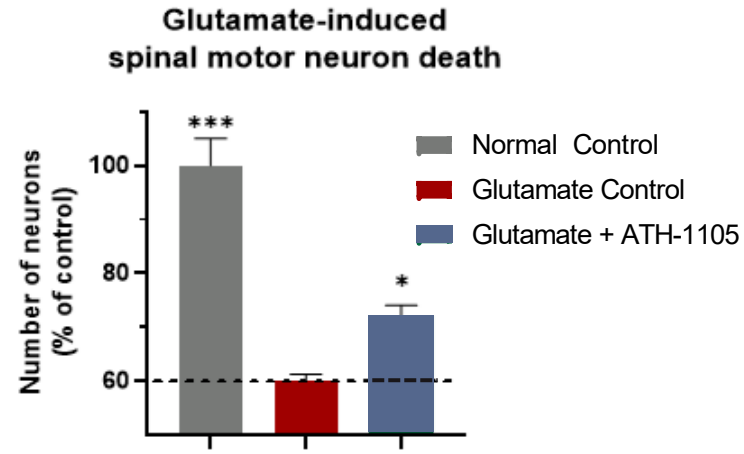
Source: https://newsnetwork.mayoclinic.org/discussion/learning-more-about-amyotrophic-lateral-sclerosis-or-als/

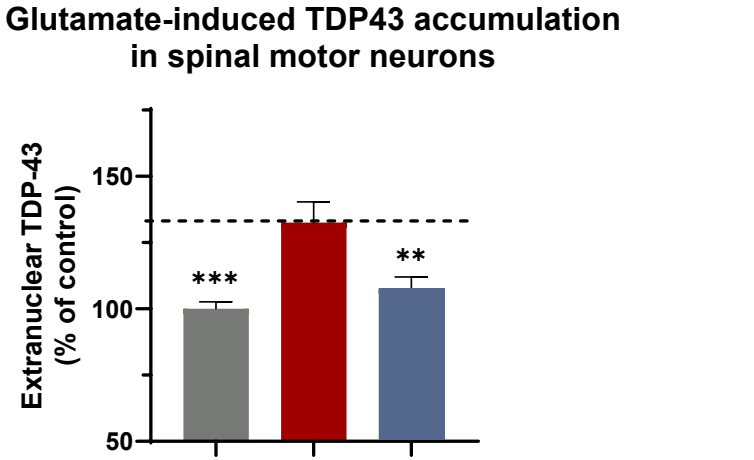
[1]Ishigaki et al., J Neuropathol Exp Neurol, 2007. [2]Lee et al., Acta Neuropathol Commun, 2019. [3]Vallarola et al., Int j Mol Sci, 2020. [4]Scotter et al., Neurotherapeutics, 2015.

Neuroprotection and Protein Pathology: ATH-1105 reduces extranuclear TDP-43 accumulation and enhances neuron survival

GLUTAMATE CHALLENGE MODEL IN MOTOR NEURON CULTURES







Primary rat spinal motor neurons. Cultures treated with vehicle control or 5 µM glutamate.
Data presented as mean ± SEM. Statistics applied: 1-way ANOVA with Fisher least significant difference test. *P<0.05, ** P < 0.01, ***P < 0.001 versus Glutamate Control; n = 6.
Scale bar: 100 µm.
MAP-2, microtubule-associated protein-2; TDP-43, TAR DNA-binding protein 43.

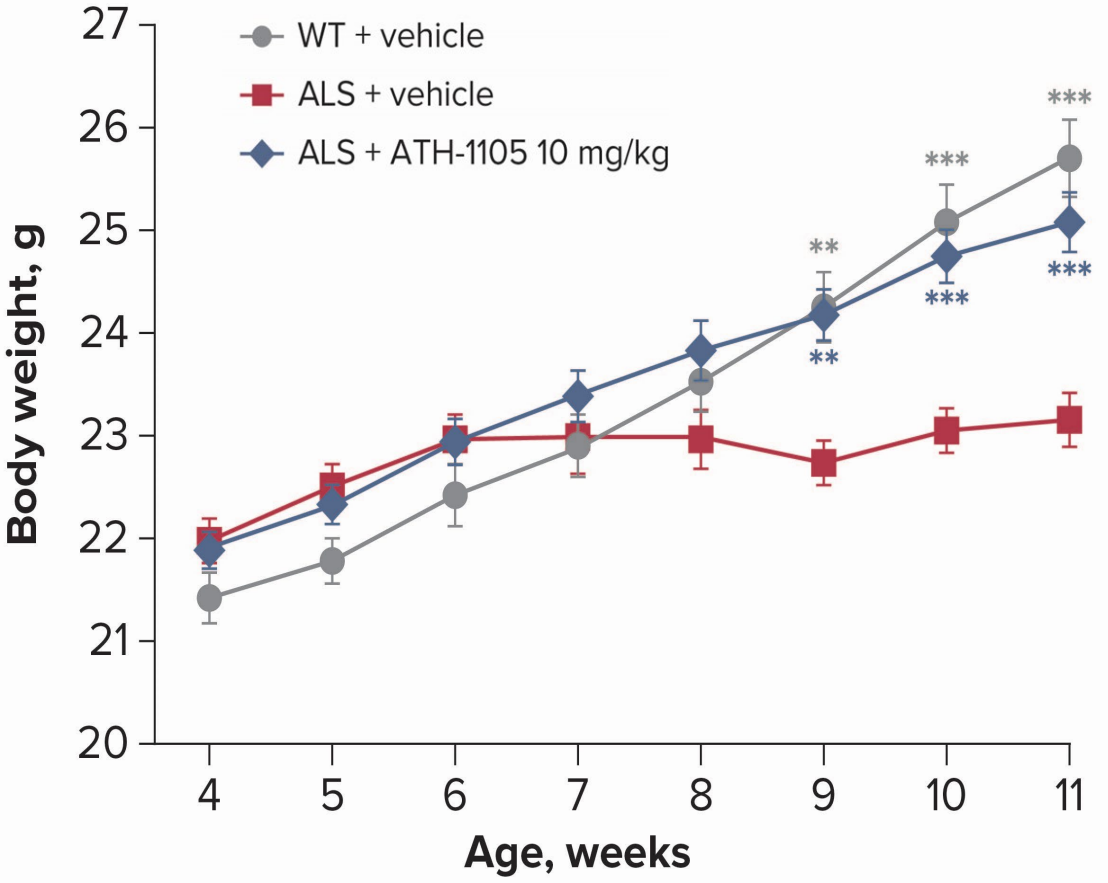
ATH-1105 significantly protects against loss of body weight

TDP-43 MOUSE MODEL OF ALS

STUDY DESIGN

Mice were divided into 3 groups (n=10 each) and received once daily treatment for 2 months

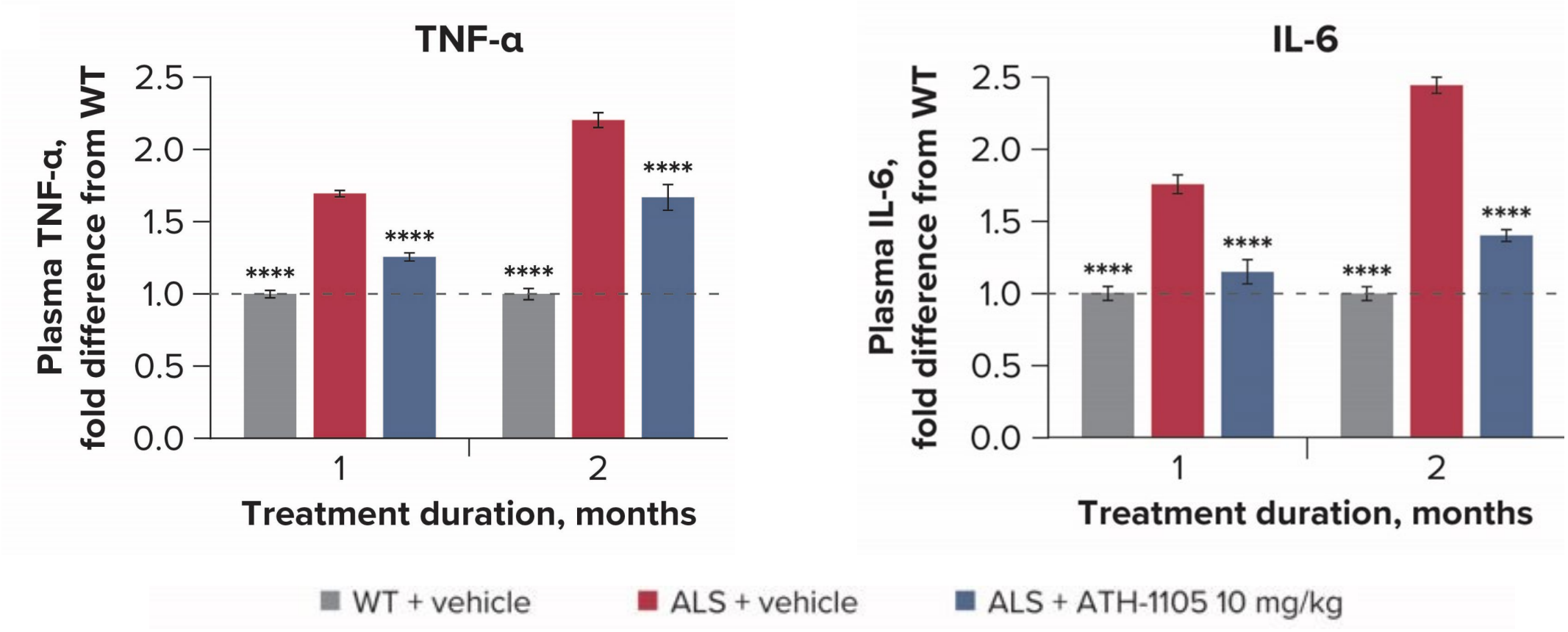
- **Group 1 (healthy control)**
  included WT mice treated with oral vehicle
- **Group 2 (disease control)**
  included TDP-43^{A315T} mice treated with oral vehicle
- **Group 3 (ALS + ATH-1105)**
  included TDP-43^{A315T} mice treated with oral ATH-1105



Data presented as mean ± SEM. Statistical significance was determined by 2-way ANOVA with the Dunnett test versus ALS + vehicle. **P < 0.01; ***P < 0.001.
ALS, amyotrophic lateral sclerosis; TDP-43, TAR DNA-binding protein 43; WT, wild-type.

Anti-inflammatory: ATH-1105 reduced markers of inflammation

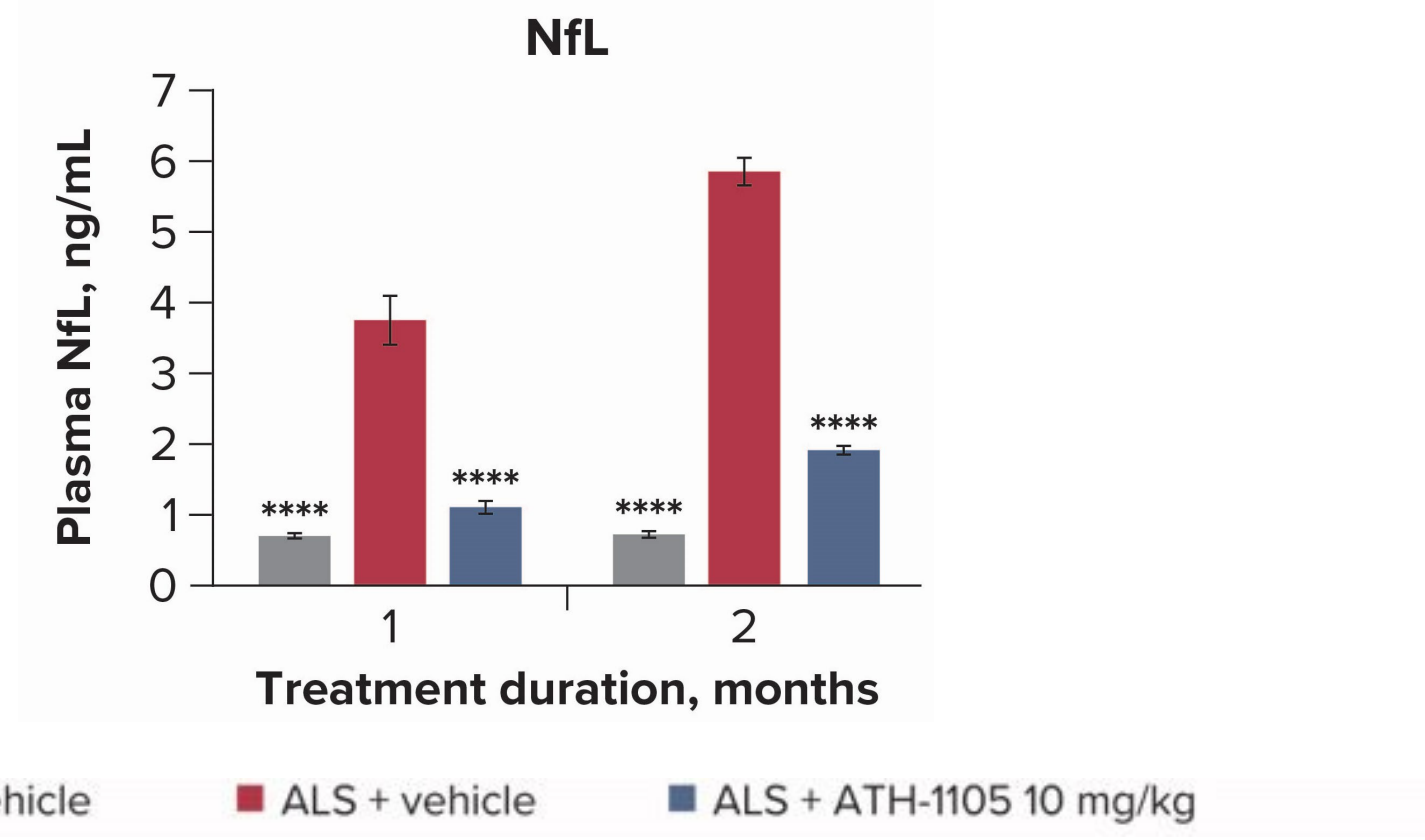
TDP-43 MOUSE MODEL OF ALS



Data presented as mean ± SEM.
Statistical significance was determined by 2-way ANOVA with the Dunnett test versus ALS + vehicle. ****P < 0.0001.
ALS, amyotrophic lateral sclerosis; IL-6, interleukin 6; TDP-43, TAR DNA-binding protein 43; TNF-α, tumor necrosis factor alpha; WT, wild-type.

Neuroprotective: ATH-1105 reduced marker of neurodegeneration

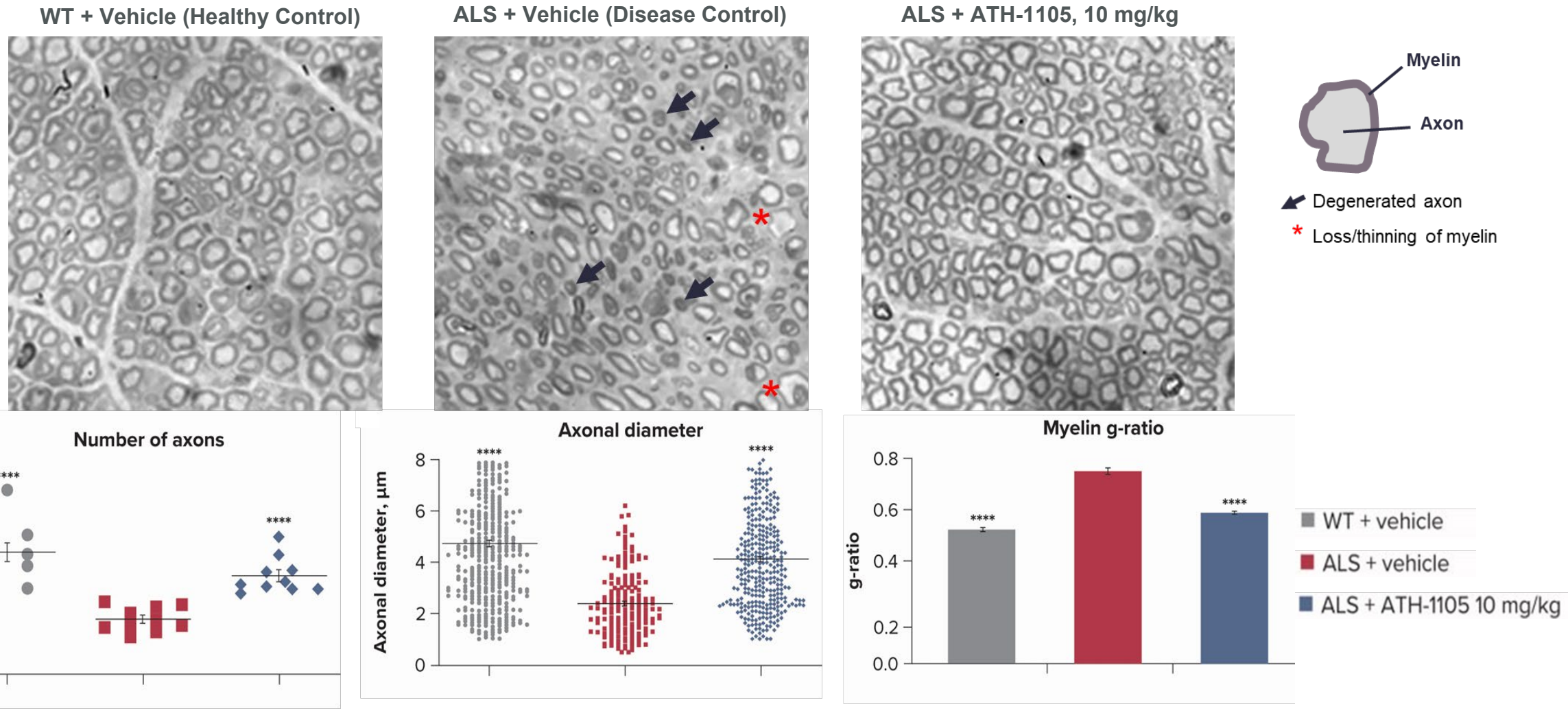
TDP-43 MOUSE MODEL OF ALS



Data presented as mean ± SEM.
Statistical significance was determined by 2-way ANOVA with the Dunnett test versus ALS + vehicle. ****P < 0.0001.
ALS, amyotrophic lateral sclerosis; NfL, neurofilament light chain; TDP-43, TAR DNA-binding protein 43; WT, wild-type.

Neuroprotective: ATH-1105 protected against axon degeneration and demyelination

TDP-43 MOUSE MODEL OF ALS

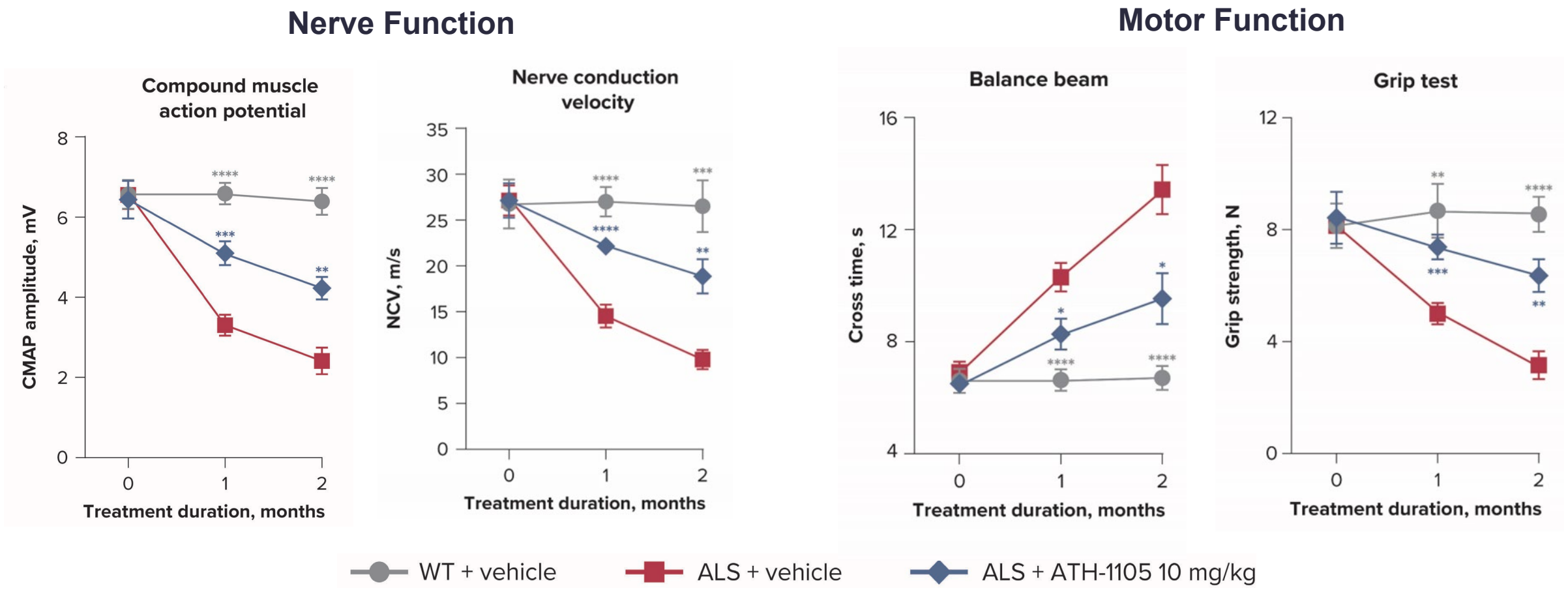


Graphical representation of the number of axons (per 100 µm2), axonal diameter (in micrometers), and mean of myelin g-ratio, defined as the ratio of the inner axonal diameter to the total axonal diameter, following 2 months of treatment. Data presented as mean ± SEM. Statistical significance was determined by 1-way ANOVA with the Dunnett test versus ALS + vehicle. ****P < 0.0001.

ALS, amyotrophic lateral sclerosis; TDP-43, TAR DNA-binding protein 43; WT, wild-type.

Function: ATH-1105 improved nerve and motor function

TDP-43 MOUSE MODEL OF ALS



Data presented as mean ± SEM.

Statistical significance was determined by 2-way ANOVA with the Dunnett test versus ALS + vehicle. *p < 0.05 ,**p < 0.01; ***p < 0.001; ****p < 0.0001. n = 10 mice per group.

ALS, amyotrophic lateral sclerosis; CMAP, compound muscle action potential; NCV, nerve conduction velocity; TDP-43, TAR DNA-binding protein 43; WT, wild-type.

ATH-1105 Preclinical Data Summary

In the TDP-43 mouse model of ALS, daily oral treatment of ATH-1105 resulted in:

- Preservation of normal body weight
- Reduced levels of plasma biomarkers of inflammation and neurodegeneration
- Protection of nerve structure and function
- Improved balance, coordination, and muscle strength

These results highlight the therapeutic potential of ATH-1105 in ALS and support further development

ALS, amyotrophic lateral sclerosis; TDP-43, TAR DNA-binding protein 43.

Athira PHARMA

Closing and Q&A

Mark Litton, PhD
Chief Executive Officer

Strong rationale to advance fosgonimeton

SIGNIFICANT OPPORTUNITY TO TRANSFORM THE TREATMENT PARADIGM FOR NEURODEGENERATIVE DISEASES

- Anti-Inflammatory
- Neuroprotective
- Improves Cognition
- Improves Function
- Potentially Disease Modifying
- Favorable Safety and Tolerability Profile
- Risk Mitigated Ph 2/3 LIFT-AD following Interim Analysis

Differentiated and Risk Mitigated

+

- Evolving Regulatory Environment
- Low Competitive Intensity

Favorable external landscape

AD, Alzheimer's disease.

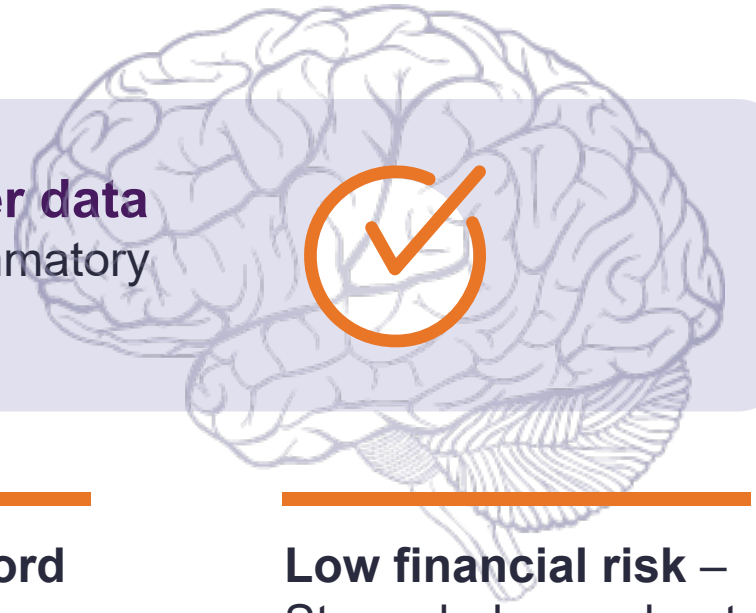
Moving Forward

✓ Independent, unblinded interim analysis of Phase 2/3 LIFT-AD	• Complete enrollment Phase 2/3 LIFT-AD study in mid-2023 • Topline data from Phase 2/3 LIFT-AD study in early 2024
✓ Enrolled 28 patients in Phase 2 SHAPE POC study in PD and Lewy Body Dementia	• Complete SHAPE with 28 patients and evaluate next steps
✓ Completed single ascending dose escalation portion of Phase 1 study of ATH-1020 with no safety findings.	• Evaluate plans for next steps
✓ Demonstrated consistent improvements in motor function, nerve function, biomarkers and nerve morphology in transgenic mouse model of ALS	• Advance ATH-1105 in ALS with IND filing in 2023

AD, Alzheimer's disease; ALS, amyotrophic lateral sclerosis; IND, investigational new drug; PD, Parkinson's disease; POC, proof-of-concept.

Well Positioned to Lead with Innovative Approach to Battling Neurodegenerative Diseases

Consistent and correlative preclinical, clinical and biomarker data showing the potential of fosgonimeton to be neuroprotective, anti-inflammatory and disease modifying in a number of neurodegenerative diseases



Mitigated development risk through independent, unblinded interim analysis of Phase 2/3 LIFT-AD study

Evolving regulatory environment and favorable competitive landscape

Strong track record of execution and leadership team with significant CNS product development and approval experience

Low financial risk – Strong balance sheet to support programs through to key inflection points

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