Lead Up to LIFT-AD Readout:

Understanding the Primary Endpoint and Continued Need for Effective New Treatments in Alzheimer's Disease

June 18, 2024

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 as a potential treatment for Alzheimer's disease, Parkinson's disease, Parkinson's disease dementia, dementia with Lewy bodies, amyotrophic lateral sclerosis, and other neurodegenerative diseases, the anticipated reporting of data, and the potential learnings from preclinical studies and other nonclinical data, the ACT-AD and SHAPE trials and LIFT-AD unblinded interim efficacy and futility analysis and their ability to inform and improve future clinical development plans, potential growth opportunities, competitive position, and industry environment and potential market opportunities.

Forward-looking statements are subject to known and unknown risks, uncertainties, assumptions and other factors. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. These factors, together with those that are described in greater detail in our filings with the Securities and Exchange Commission ("SEC") may cause our actual results, performance or achievements to differ materially and adversely from those anticipated or implied by our forward-looking statements.

In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this presentation, and although we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted a thorough inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and readers are cautioned not to unduly rely upon these statements. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all. We undertake no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

By attending or receiving this presentation you acknowledge that you will be solely responsible for your own assessment of the market and our market position and that you will conduct your own analysis and be solely responsible for forming your own view of the potential future performance of our business. This presentation contains estimates, projections and other information concerning market, industry and other data. We obtained this data from our own internal estimates and research and from academic and industry research, publications, surveys, and studies conducted by third parties, including governmental agencies. These data involve a number of assumptions and limitations, are subject to risks and uncertainties, and are subject to change based on various factors, including those discussed in our filings with the SEC. These and other factors could cause results to differ materially from those expressed in the estimates made by the independent parties and by us. While we believe such information is generally reliable, we have not independently verified any third-party information.

The ACT-AD trial and the related open-label extension for ACT-AD participants 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 press release 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 LinkedIn (https://www.linkedin.com/company/athirapharma), Facebook (https://www.facebook.com/athirapharmainc) and @athirapharma on X (formerly known as Twitter) and Instagram 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.

© Athira Pharma, Inc All Rights Reserved..

Athira™ PHARMA

Our Mission

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

Suzanne Hendrix, Ph.D.

- Founder and President of Pentara, a boutique CRO specializing in statistics and data management in neurodegenerative diseases.
- More than 30 years of clinical trial experience
- Supported the study design, data collection, and analysis of greater than 100 clinical trials
- Primary or co-author on >150 publications
- Developing an intrinsic capacity score to measure the maintenance of health at older ages in collaboration with the World Health Organization
- Ph.D. from Boston University

NOTE: Pentara Corporation, with which Suzanne B. Hendrix is affiliated, is a consultant to Athira Pharma, Inc.

Athira PHARMA

© Athira Pharma, Inc. All Rights Reserved.

Anton P. Porsteinsson, M.D.

- Director of the University of Rochester Alzheimer's Disease Care, Research, and Education Program (AD-CARE)
- Internationally recognized leading expert in Alzheimer's disease and dementia
- Interest in biomarkers, imaging, and novel pharmacologic agents to treat Alzheimer's disease and other dementias
- Leading investigator for prominent national Alzheimer's prevention and treatment trials
- Author and collaborator of hundreds of research publications and PI for research grants from the NIH and other leading funders

Note: Dr. Porsteinsson has received compensation from Athira Pharma, Inc. for consulting services and is an investigator on Athira Pharma, Inc.'s LIFT-AD Phase 2/3 clinical trial of fosgonimeton in mild-to-moderate Alzheimer's disease and Open Label Extension fosgonimeton trial.

Athira PHARMA

© Athira Pharma, Inc. All Rights Reserved.

Today's Agenda

Javier San Martin, M.D.

- Modulating the HGF Neurotrophic System to Treat Neurodegeneration
- Data Supporting Fosgonimeton as a Treatment for Alzheimer's Disease
- Phase 2/3 LIFT-AD Clinical Trial

Suzanne Hendrix, Ph.D.

- The Global Statistical Test and its Relevance in Assessing Treatment Effect

Anton P. Porsteinsson

- Patient Journey and Treatment Landscape

Expert Discussion

Q&A

Athira PHARMA

© Athira Pharma, Inc. All Rights Reserved

Javier San Martin, M.D.

- 25+ years of drug development experience with proven track record leading cross-functional teams to drive global development and commercialization strategies for drugs across large and rare diseases
- Guided therapies PoC through regulatory approval, with special emphasis on aligning late-stage development efforts with viable commercialization paths
- Formerly, CMO of Arrowhead Pharmaceuticals, SVP & Head of Global Clinical Development at Ultragenyx Pharmaceutical & SVP of Clinical Development at Alder Biopharmaceuticals

© Athira Pharma, Inc. All Rights Reserved.

Athira PHARMA

Fosgonimeton Clinical Program Overview

© Athira Pharma, Inc.

Multifactorial Complex Pathologies Lead to Alzheimer's Disease

AD PATHOLOGIES

Aβ and p-Tau pathology and aggregation

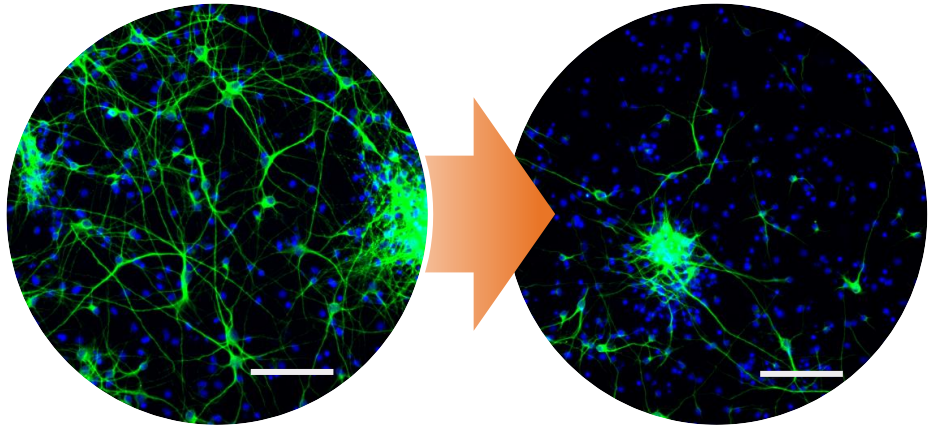
Inflammation

Mitochondrial dysfunction

Oxidative stress

Excitotoxicity

Synaptic dysfunction



HEALTHY **DISEASED**

= Neuron Marker

RESULTING AD NEURODEGENERATION

Neuronal damage

Loss of network connectivity

Brain Atrophy

Loss of memory

Loss of independence

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

© Athira Pharma, Inc. All Rights Reserved.

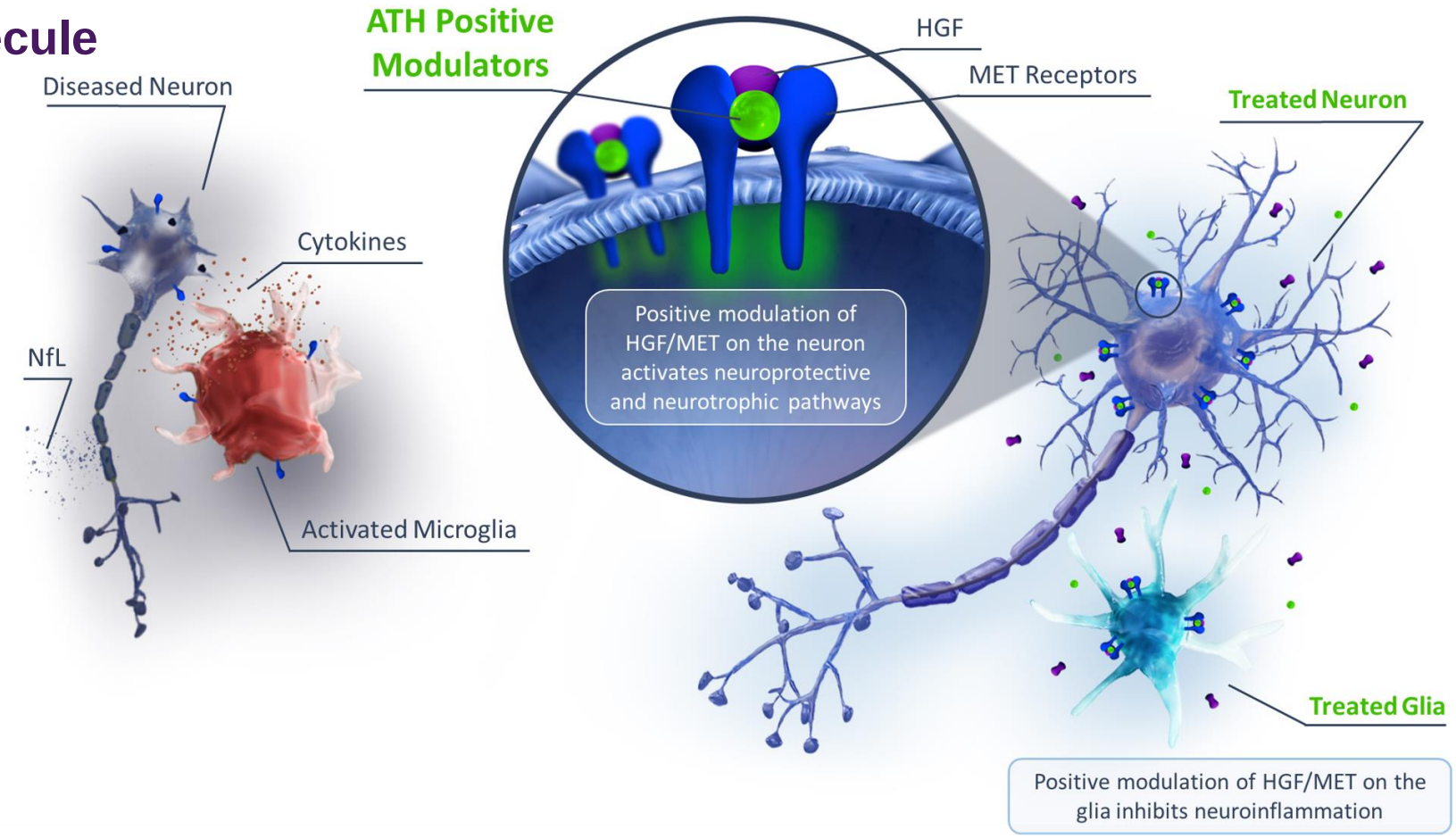
Fosgonimeton Is Designed to Positively Modulate the Neurotrophic HGF Signaling System for the Promotion of Neuronal Health, Repair, and Function

Potential first-in-class small molecule drug candidates

- Able to cross the blood-brain barrier
- Positively modulate HGF/MET

Mechanism of action may

- Reduce inflammation
- Promote regeneration
- Provide neuroprotection
- Modify the course of disease

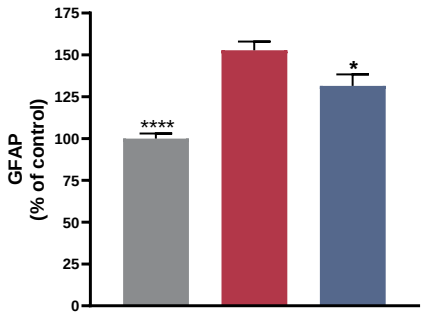


HGF, hepatocyte growth factor.

© Athira Pharma, Inc. All Rights Reserved.

Fosgonimeton Protects and Repairs Neuronal Networks in Preclinical Models of Alzheimer's Disease

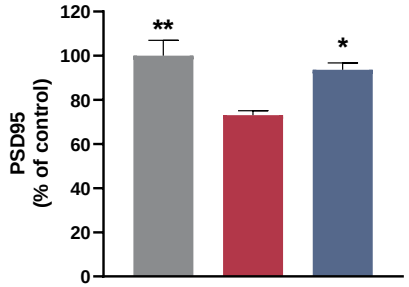
Anti-inflammatory



GFAP in Hippocampus

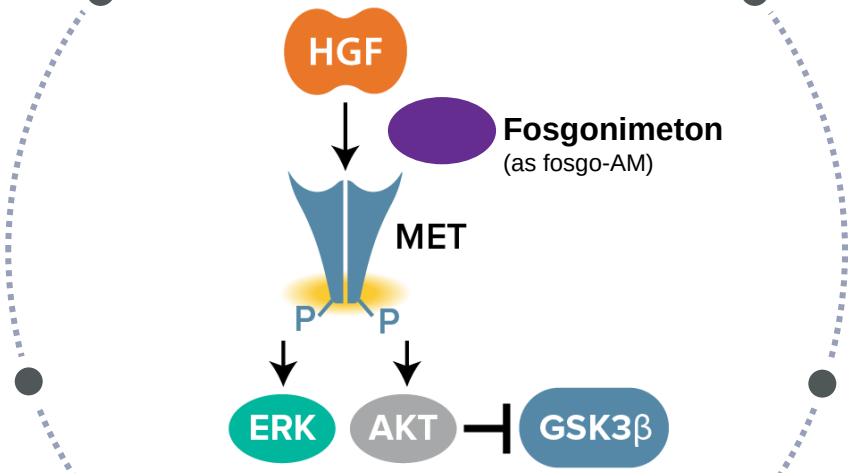
- Sham Control
- Aβ Control
- Aβ + Fosgonimeton

Neurotrophic

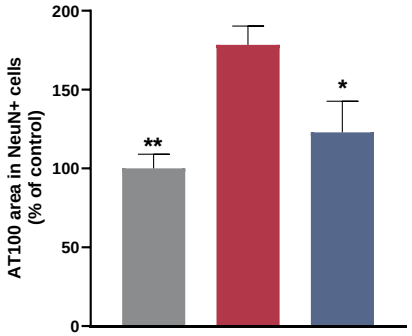


Synapses in Hippocampus

- Sham Control
- Aβ Control
- Aβ + Fosgonimeton



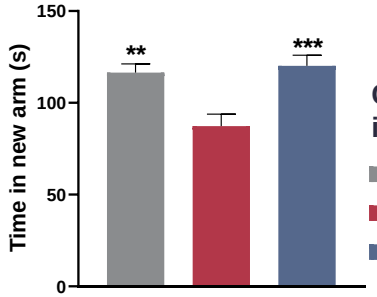
Reduces protein pathology



Phospho-Tau in Hippocampus

- Sham Control
- Aβ Control
- Aβ + Fosgonimeton

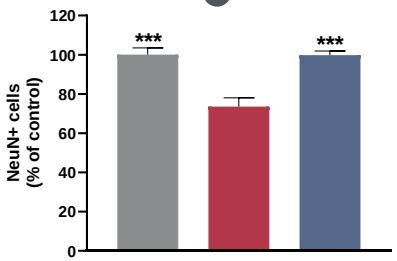
Improves function



Cognitive Function in Y-Maze

- Sham Control
- Aβ Control
- Aβ + Fosgonimeton

Neuroprotective



Hippocampal Neuron Survival

- Sham Control
- Aβ Control
- Aβ + Fosgonimeton

[1]Setti et al., *SfN* 2023.

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;

© Athira Pharma, Inc. All Rights Reserved.

Fosgonimeton Exploratory Phase 2 Trial* in Mild-to-Moderate Alzheimer's Disease

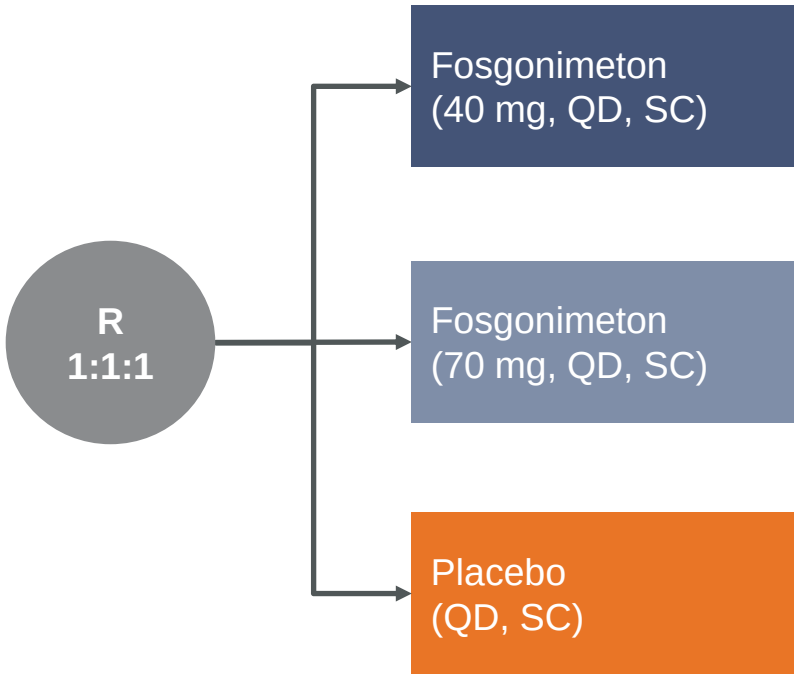
RANDOMIZED PLACEBO-CONTROLLED SIX-MONTH TRIAL (N=77)

Key Inclusion Criteria

- 55–85 years
- MMSE score: 14-24
- CDR global score 1 or 2
- Clinical diagnosis of dementia, probably due to AD[1]
- Could receive prior or concomitant AChEI
- Reliable and capable support person/caregiver

Patient Population
Mean Baseline Characteristics

Age, years:	71.4
MMSE	19.3
Concomitant AChEI, %:	61.0
APOE4 carrier status	
Heterozygous, %:	36.4
Homozygous, %:	19.5
Plasma biomarkers	
Aβ 42/40 ratio:	0.05
p-Tau181, pg/mL:	3.81
NfL, pg/mL:	20.93



Endpoints
Primary: Change in ERP P300 latency, safety and tolerability
Secondary: ADAS-Cog11, ADCS-CGIC, ADCS-ADL23
Exploratory: Plasma biomarkers

Key Learnings from ACT-AD

- Fosgonimeton was well-tolerated with a favorable safety profile
- Unexpected potential pharmacodynamic interaction with AChEIs
- Greater than 85% rollover into OLEX from both ACT-AD and LIFT-AD studies

* Trial did not meet its primary endpoint
[1]McKhann GM et al. Alzheimers Dement. 2011;7:263-269.
Aβ, amyloid beta; AChEI, acetylcholinesterase inhibitor; 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; APOE, apolipoprotein E; CDR, clinical dementia rating; ERP, event-related potential; MMSE, mini-mental state examination; NfL, neurofilament light chain; OLEX, open-label extension; p-Tau181, tau phosphorylated at threonine-181; QD, once daily; R, randomization; SC, subcutaneous; SD, standard deviation.

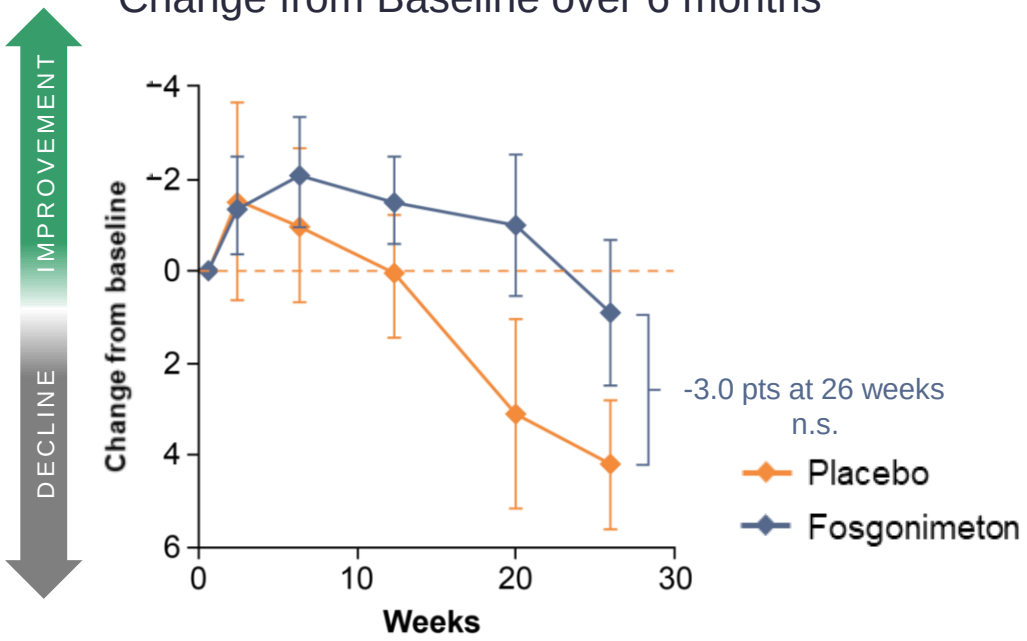
© Athira Pharma, Inc. All Rights Reserved.

Fosgonimeton Was Associated with Improvements in Cognition and Biomarkers of Alzheimer's Disease

Amongst Subjects Not Receiving Concomitant AChEI

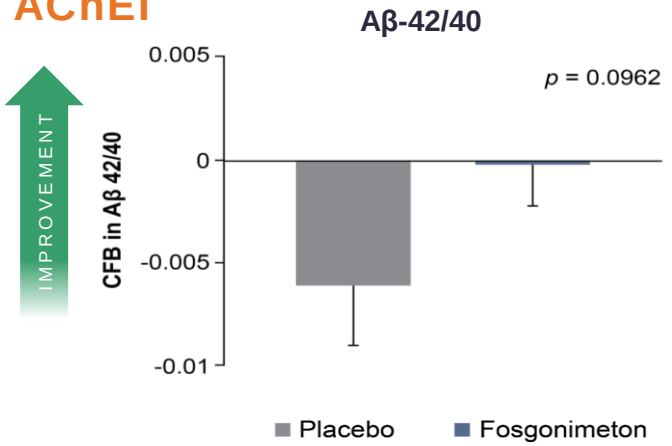
ADAS-COG11 (Procognitive Effect)

Change from Baseline over 6 months

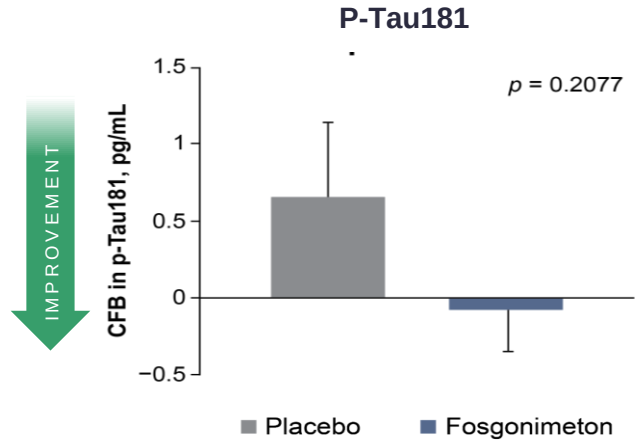


n at each visit	W2	W6	W12	W20	W26
Placebo	8	8	7	7	6
Fosgonimeton	19	19	17	16	17

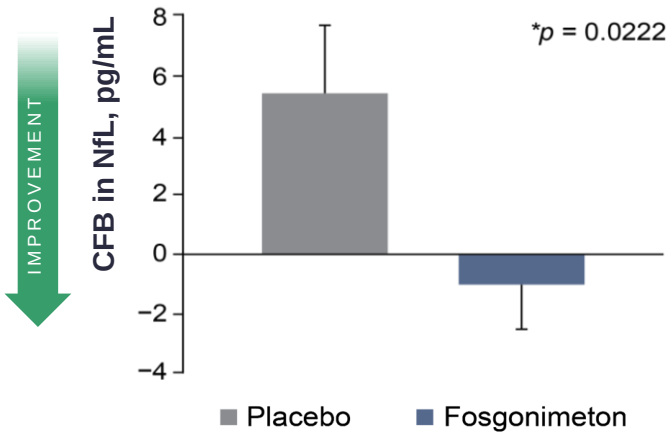
Aβ-42/40



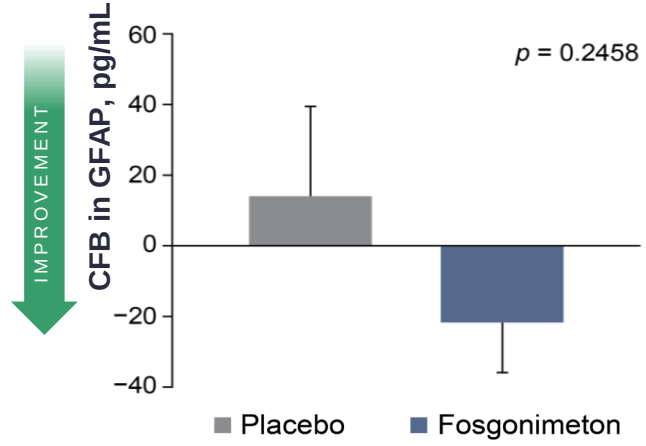
P-Tau181



NfL



GFAP



ADAS-Cog11: Data from mITT population without background therapy and presented as unadjusted mean ± SEM; n.s., not statistically significant.
Biomarkers: Data are least square means from an ANOVA model with change from baselines as the dependent variable with the following in the model: treatment group, AChEI use, baseline biomarker value and the interaction of treatment and AChEI use. Error bars are ± SE. N=5 for placebo treatment; N=12 for fosgonimeton treatment without concomitant AChEI.
Aβ, amyloid beta; AD, Alzheimer's disease; ADAS-Cog11, Alzheimer's Disease Assessment Scale–Cognitive Subscale; CFB, change from baseline; mITT, modified intent-to-treat; p-Tau181, tau phosphorylated at threonine-181; SE, standard error; W, week.
Trial did not meet its primary endpoint

© Athira Pharma, Inc. All Rights Reserved.

LIFT-AD: Phase 2 Trial of Fosgonimeton in Mild-to-Moderate Alzheimer's Disease

Randomized, Placebo-controlled, 6-Month Trial (N=315, Primary Analysis Population)

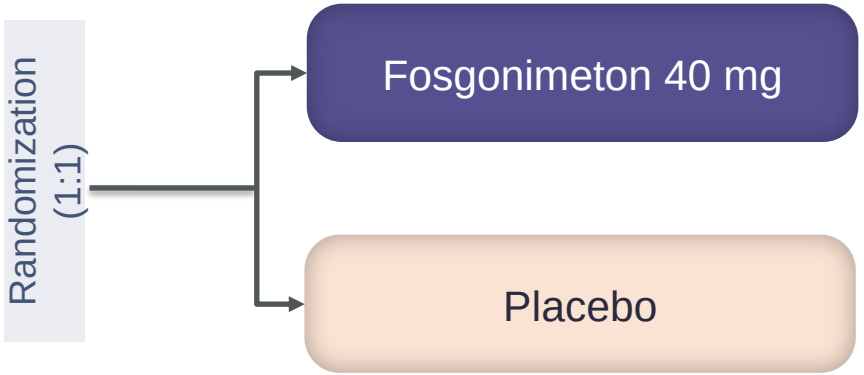
POPULATION

N = ~315 participants without concomitant AChEI

N = 554 safety population

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

26-week randomized, double-blind treatment,
+ optional 48-month Open-Label Extension



ENDPOINTS

PRIMARY

- Global Statistical Test - composite endpoint of cognition (ADAS-Cog11) and function (ADCS-ADL23)
- Safety

SECONDARY

- Cognition: ADAS-Cog11
- Function: ADCS-ADL23
- Neurodegeneration: Plasma NfL biomarker

EXPLORATORY

- AD Protein Pathology: Plasma Aβ-42/40, p-Tau 181 and p-Tau 217
- Inflammation: Plasma GFAP

TIMELINE: **Enrollment Complete; Topline results expected in 2H24**

LIFT-AD Protocol Changes

- ***Initial design:*** *Treatment naïve or on stable AChEI; Randomization 1:1:1 70 mg , 40 mg, Placebo*
- ***Sept 2022 Amendment:*** *– Excluded background AChEI usage and added interim futility and efficacy analysis / samples size re-estimate*
- ***May 2023 Amendment:*** *- Discontinued 70 mg due to tolerability, randomization changed to 1:1 40mg, Placebo*

Aβ, amyloid beta; AchEI, acetylcholinesterase inhibitor; 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; MMSE, Mini Mental State Examination; NfL, neurofilament light chain; p-Tau181, tau phosphorylated at threonine-181

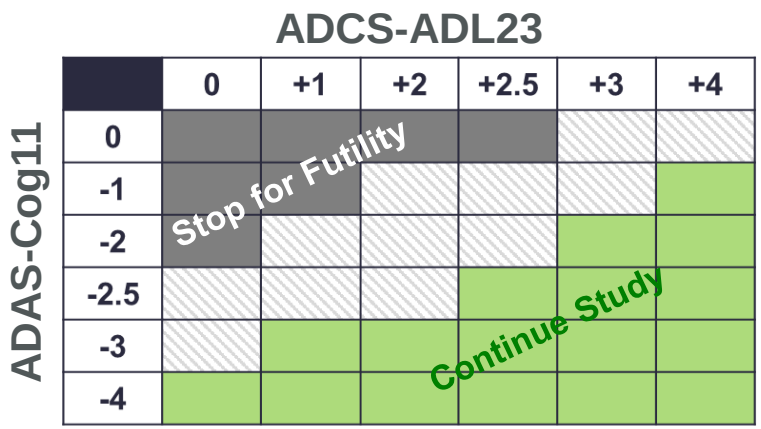
© Athira Pharma, Inc. All Rights Reserved.

Independent Unblinded Analysis by DMC Recommended to Adjust Sample Size of LIFT-AD to Optimize Statistical Power in Global Statistical Test

DEVELOPMENT PLAN OPTIMIZED WITH MITIGATED RISK

Pre-specified Methodology[1]

- Adaptive method enabling sample-size re-estimation based on interim findings that measures a candidate therapy's performance
- Monte Carlo simulations run to inform pre-specified decision framework
- Pre-specified constraints included maximum enrollment limit and minimum target power



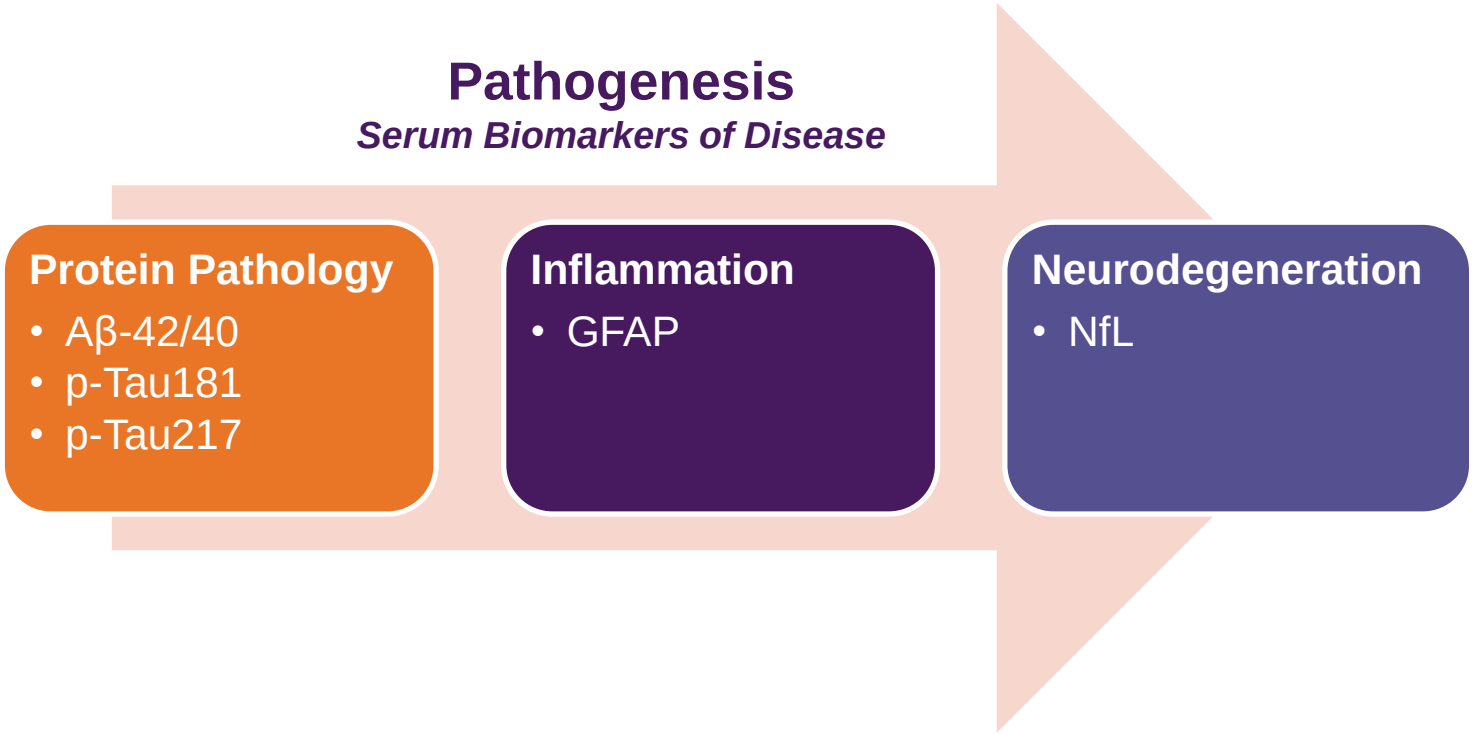
ANALYSIS & OUTCOME

- Efficacy and futility analysis performed on 100 patients without concomitant AChEIs who completed the trial
- DMC Recommendation (Oct 2022): **Continue LIFT-AD Study**
- Supports potential to achieve the primary endpoint, GST, which combines the results from the co-key secondary endpoints of cognition (ADAS-Cog11) and function (ADCS-ADL23)

[1]Conducted by DMC: Chair neurologist (MD) and two biostatisticians (PhD); [2]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; DMC, data monitoring committee.

© Athira Pharma, Inc. All Rights Reserved.

LIFT-AD Was Designed to Evaluate Key Pathophysiologic Features and Clinical Outcomes of Alzheimer's Disease



Clinical Outcomes

Overall Disease Progression

- **Global Statistical Test (GST)**

Cognitive Impairment

- **ADAS-Cognitive Sub-Scale (ADAS-Cog11)**
- Mini-Mental State Exam (MMSE)
- Neuropsychiatric Inventory (NPI)
- Controlled Oral Word Association Test (COWAT)

Functional Impairment

- **Activities of Daily Living (ADCS-ADL23)**
- Clinical Global Impression of Change (ADCS-CGIC)

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; COWAT, controlled oral word association test; GFAP, glial fibrillary acidic protein; MMSE, MMSE, mini-mental state examination; NfL, neurofilament light chain; NPI, neuropsychiatric inventory; p-Tau181, tau phosphorylated at threonine-181; p-Tau217, tau phosphorylated at threonine-217

Athira PHARMA

© Athira Pharma, Inc. All Rights Reserved.

Combining Evidence Across Multiple Endpoints with Global Statistical Tests

Pentara Corporation

Suzanne B Hendrix, PhD, Caleb Dayley MS, Craig H Mallinckrodt, PhD, Samuel P Dickson, PhD

June 18, 2024

Pentara

Both Lecanemab and Donanemab Used a Composite Outcome for Their First Proof of Concept Study

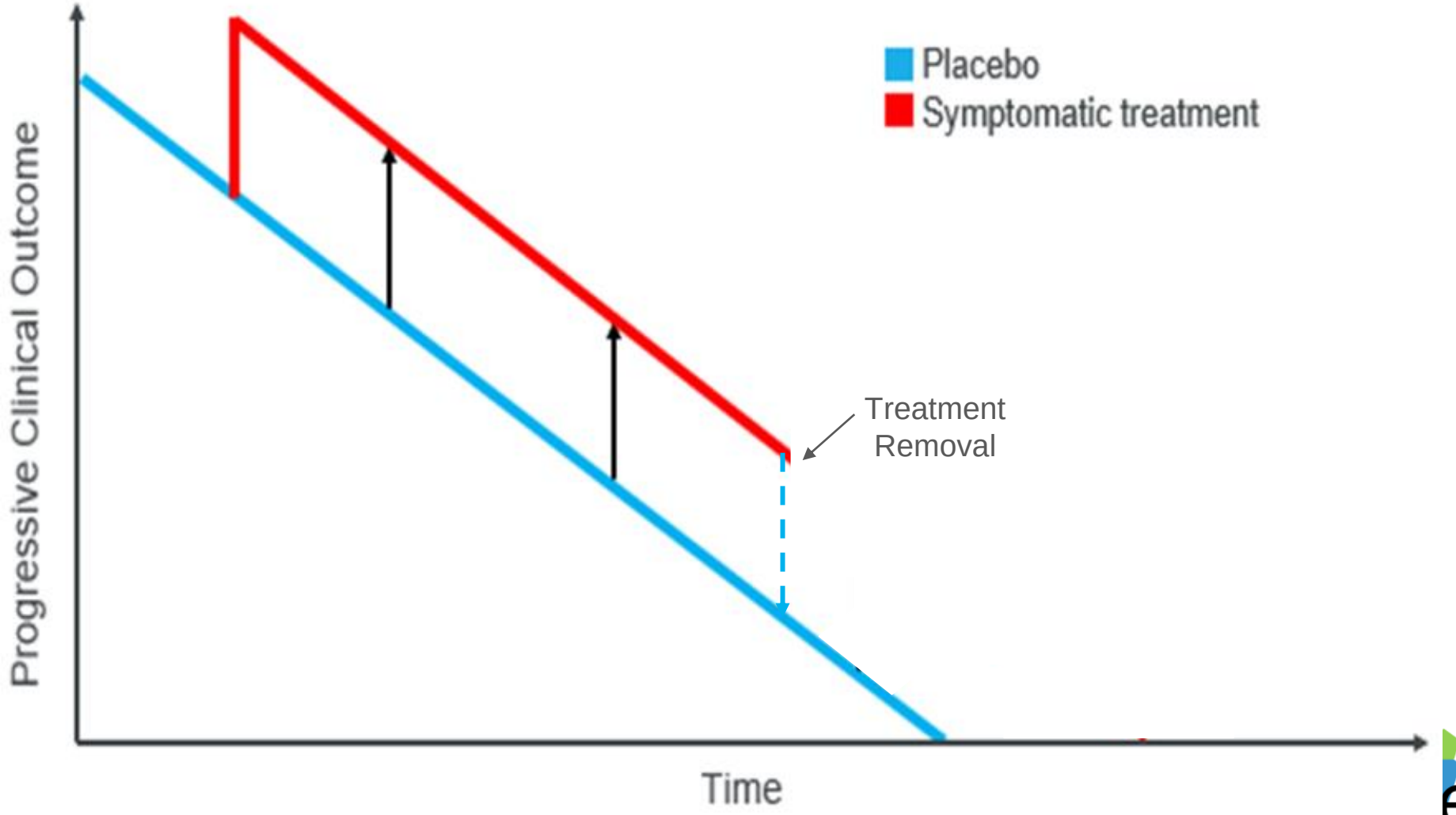
Study	Composite	Composite p-value	CDR-sb p-value
Lecanemab Phase 2	ADCOMS (Cog+global)	0.034	0.125
Lecanemab Phase 3	ADCOMS (Cog+global)	< 0.001	< 0.001
Donanemab Phase 2	iADRS (Cog+ADL)	0.04	0.57
Donanemab Phase 3	iADRS (Cog+ADL)	< 0.001	< 0.001

For Fosgonimeton, the GST combines Cognition + ADLs

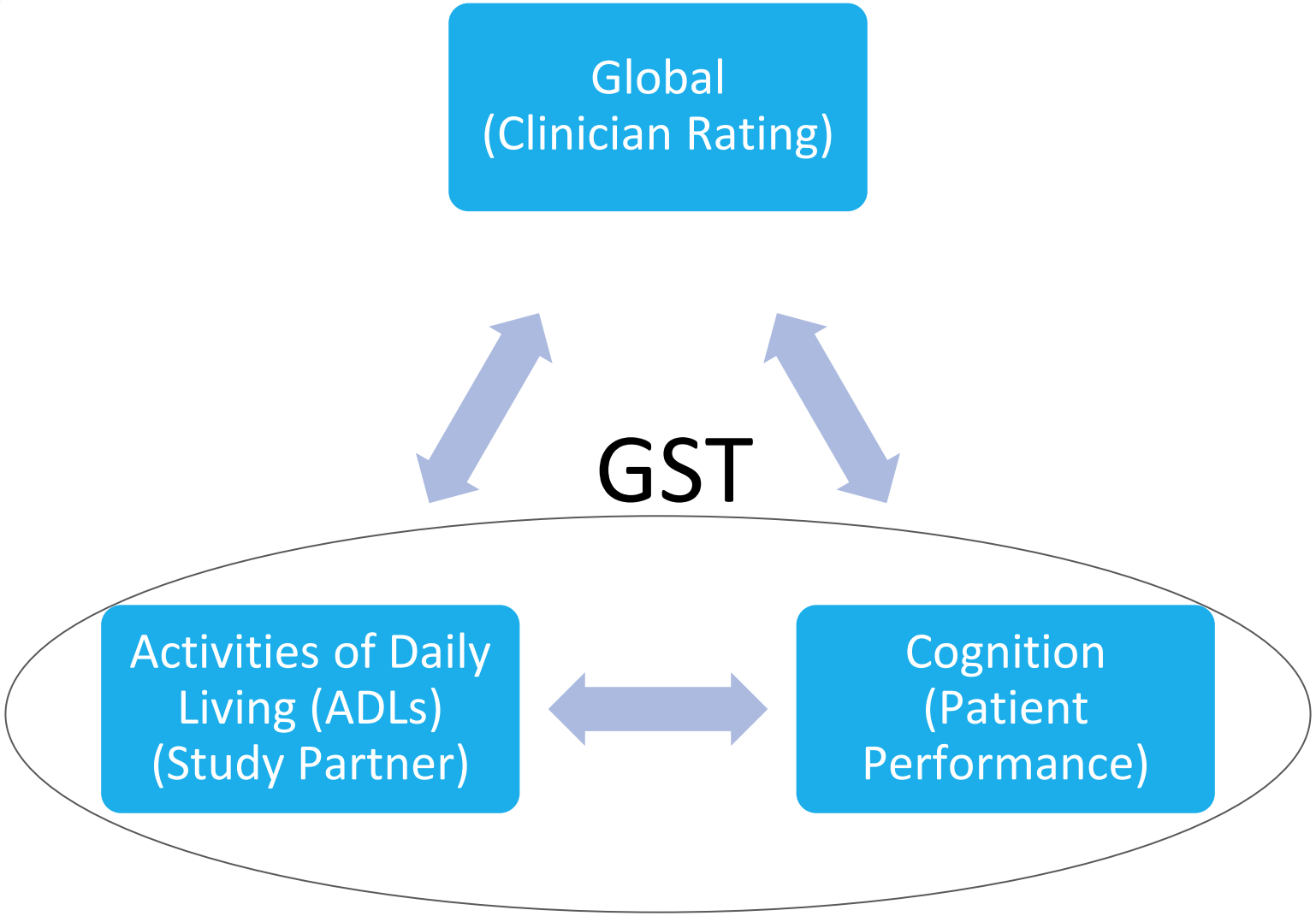
Pentara

Symptomatic Effect - Temporary

Focus on one symptom or domain at a time



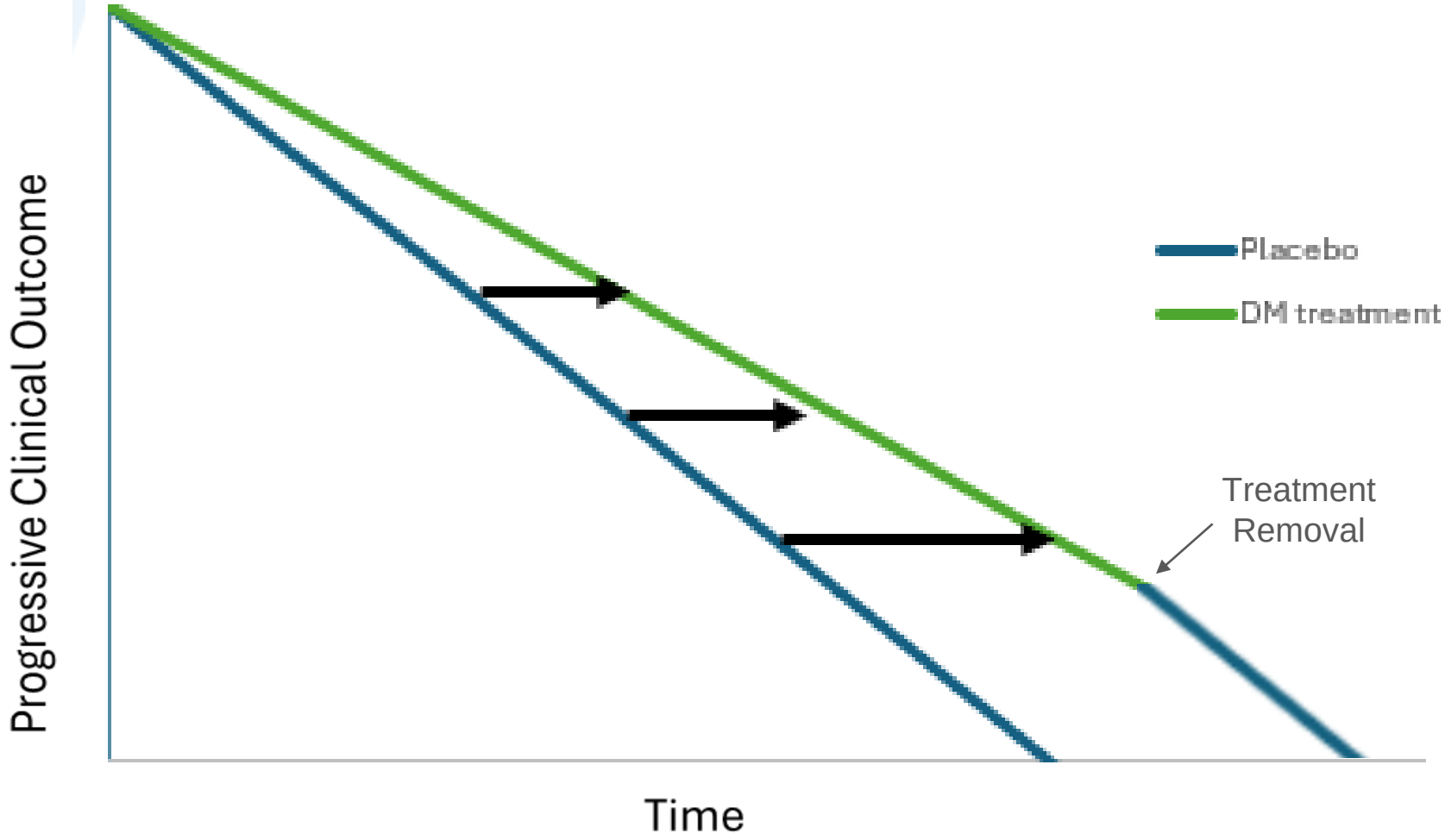
Global Statistical Tests (GSTs) Combines Evidence Across Endpoints



Pentara

Disease Modification - Permanent Effect

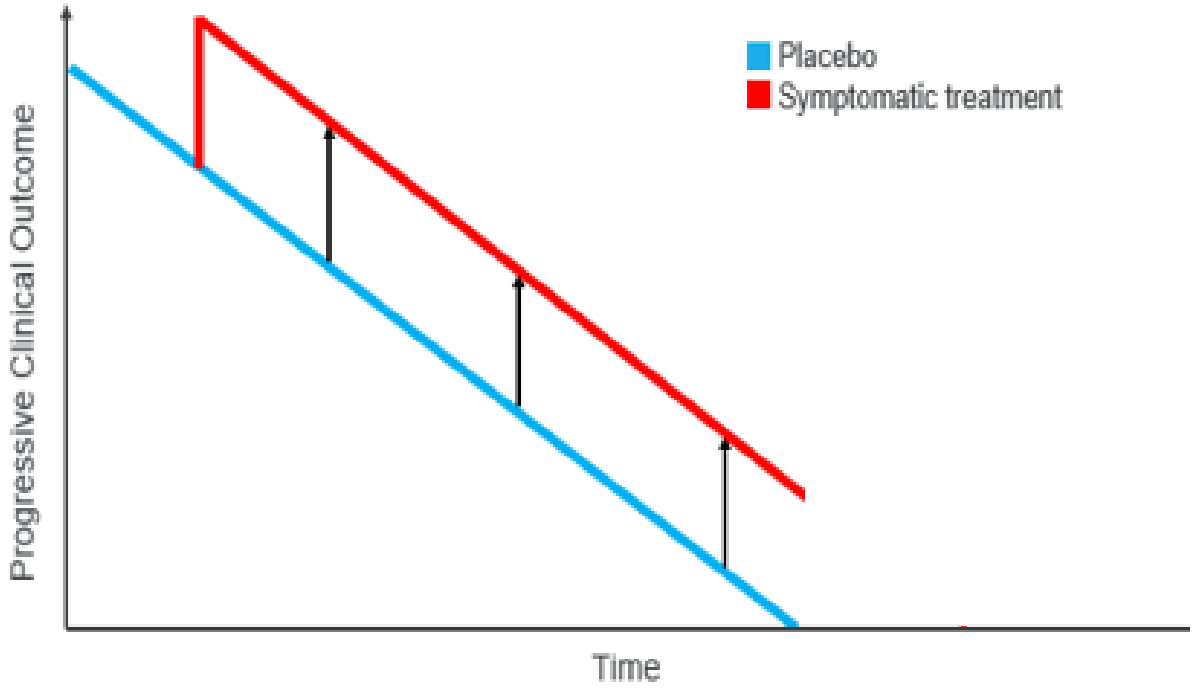
Multiple Domains Affected



Pentara

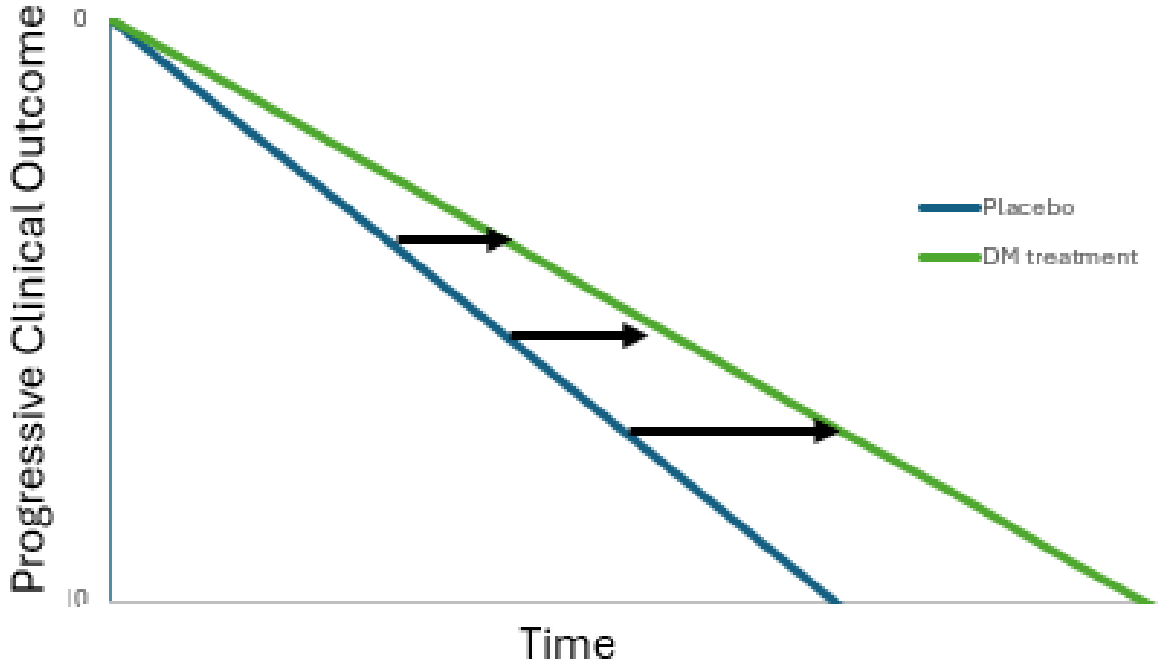
Treatment Effects

Symptomatic Effect- Temporary



Focus on 1 symptom at a time

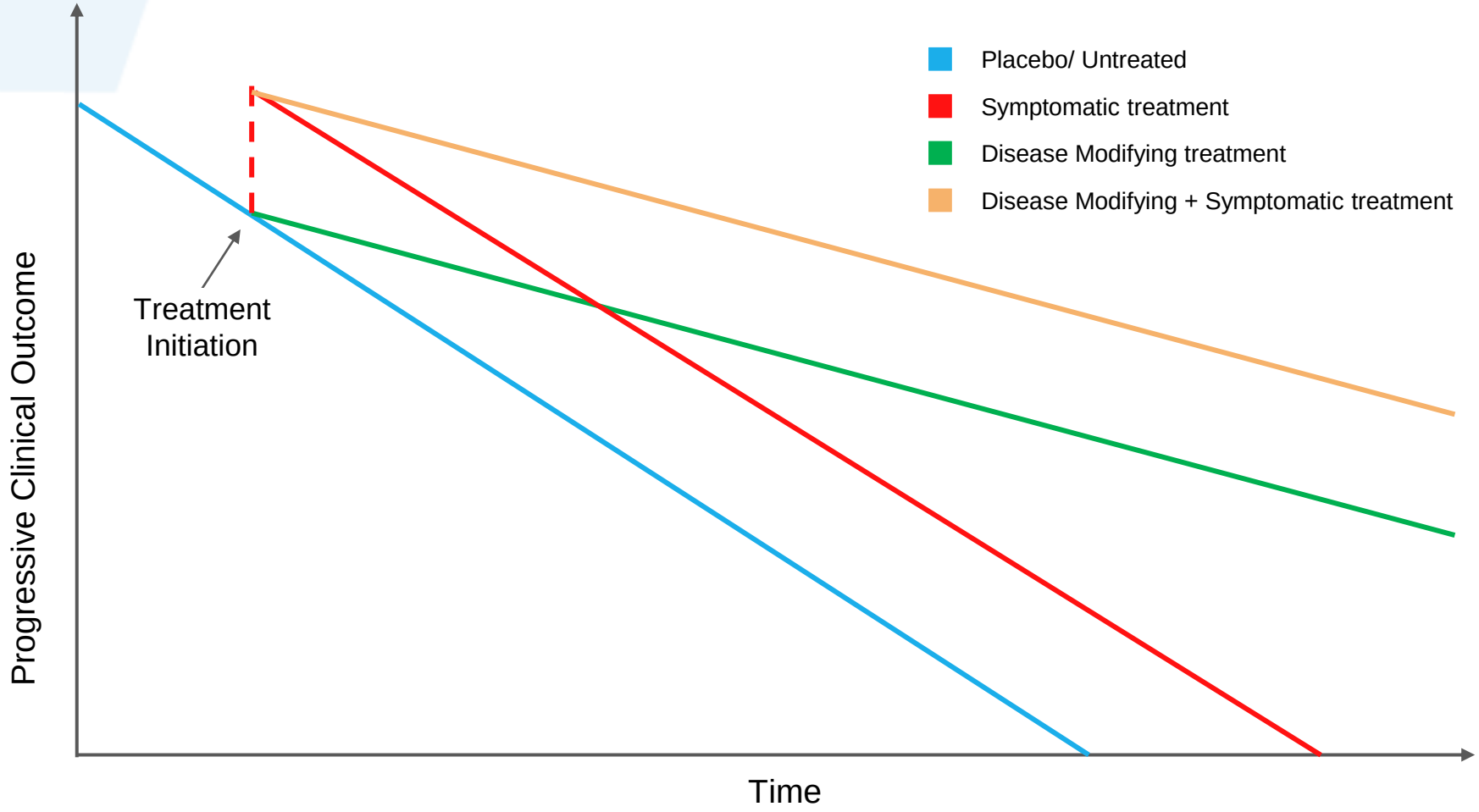
Disease Modification - Permanent



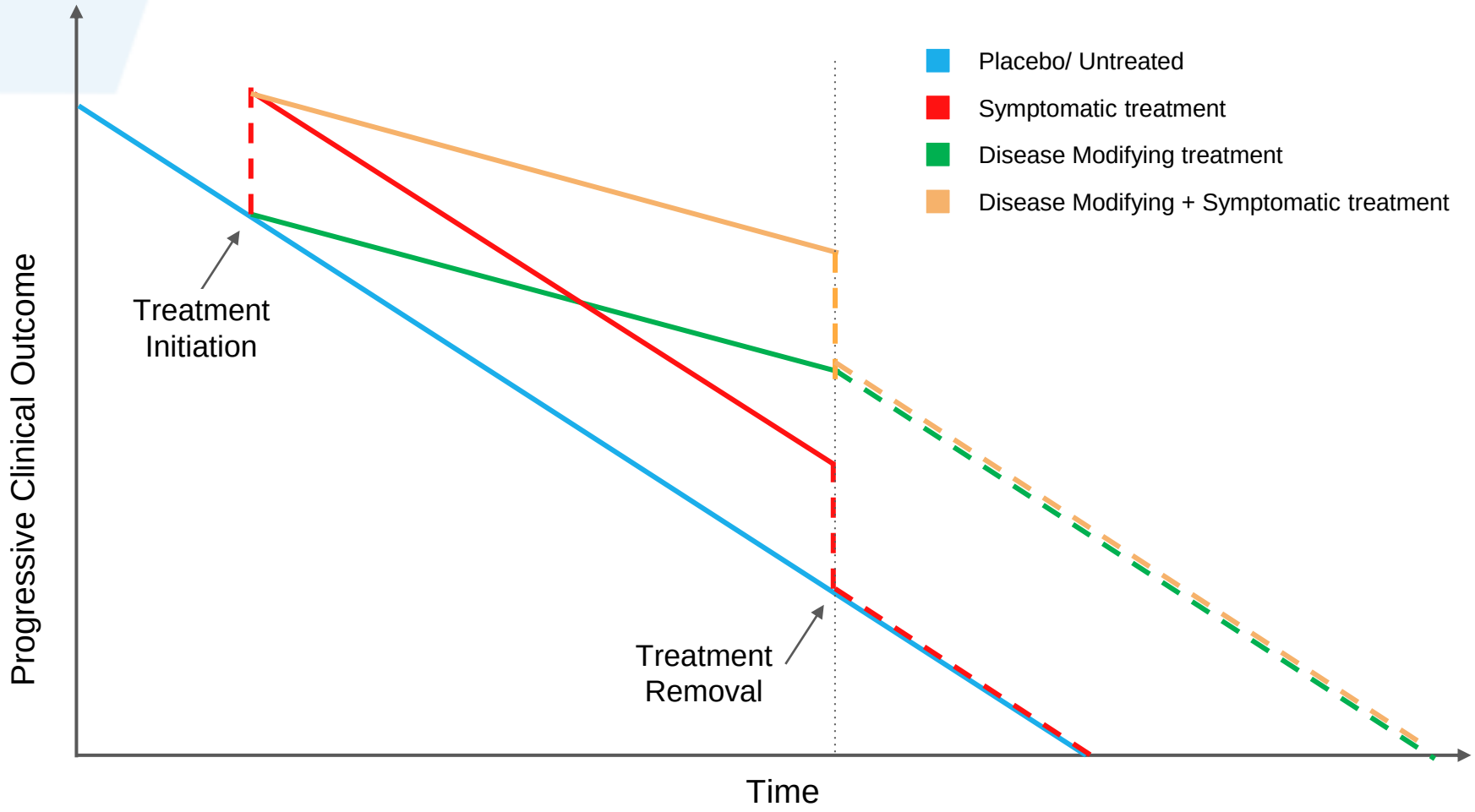
Multiple domains affected

Pentara

Symptomatic And Disease Modifying Effects



Symptomatic And DM Effects After Treatment Removal

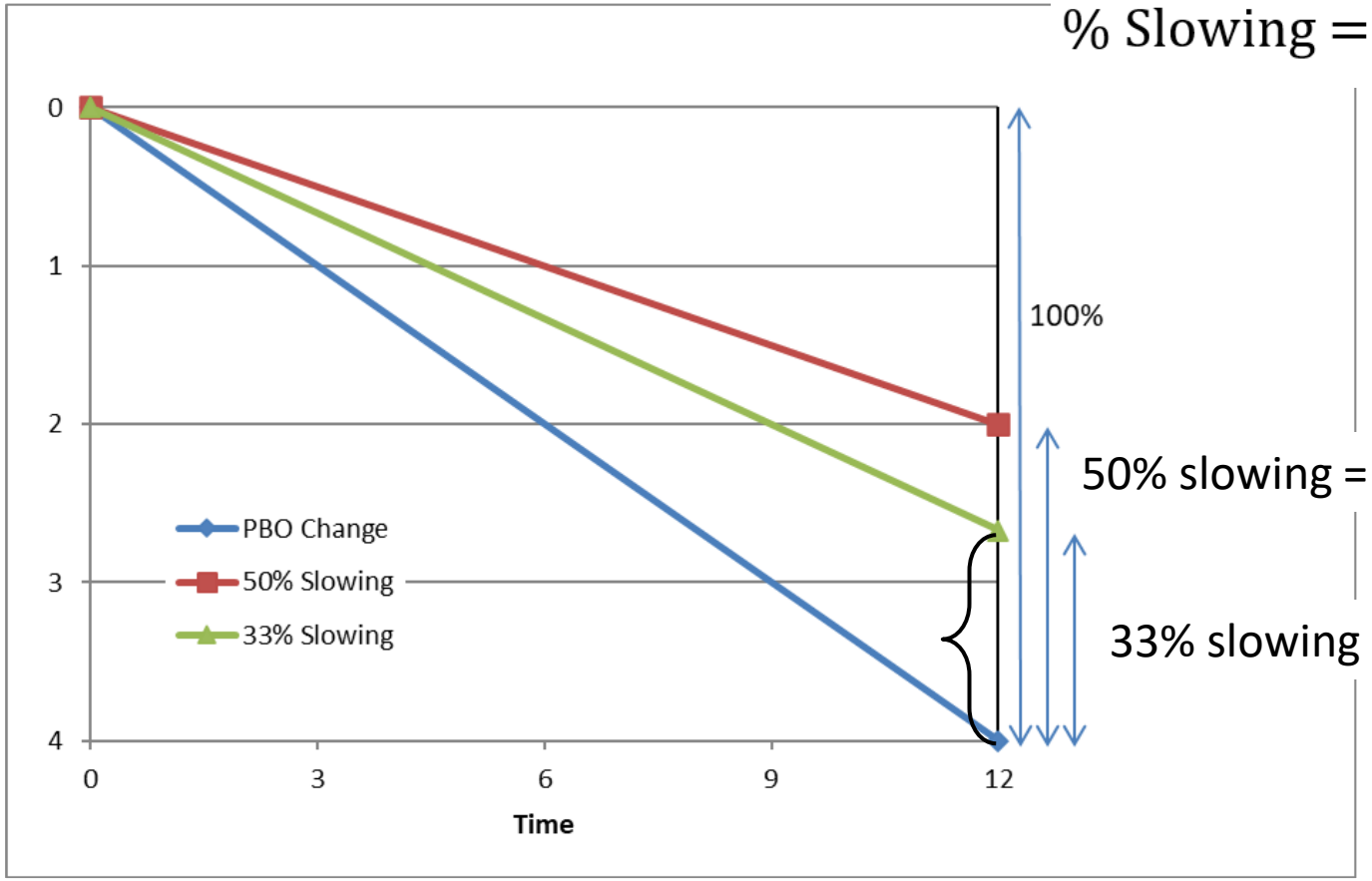


Pentara

Progressive Diseases Decline Over Time
33% and 50% Slowing with Linearity

$$\% \text{ Slowing} = \frac{\text{Placebo} - \text{Active}}{\text{Placebo}}$$

Percent Slowing at the End of the Study

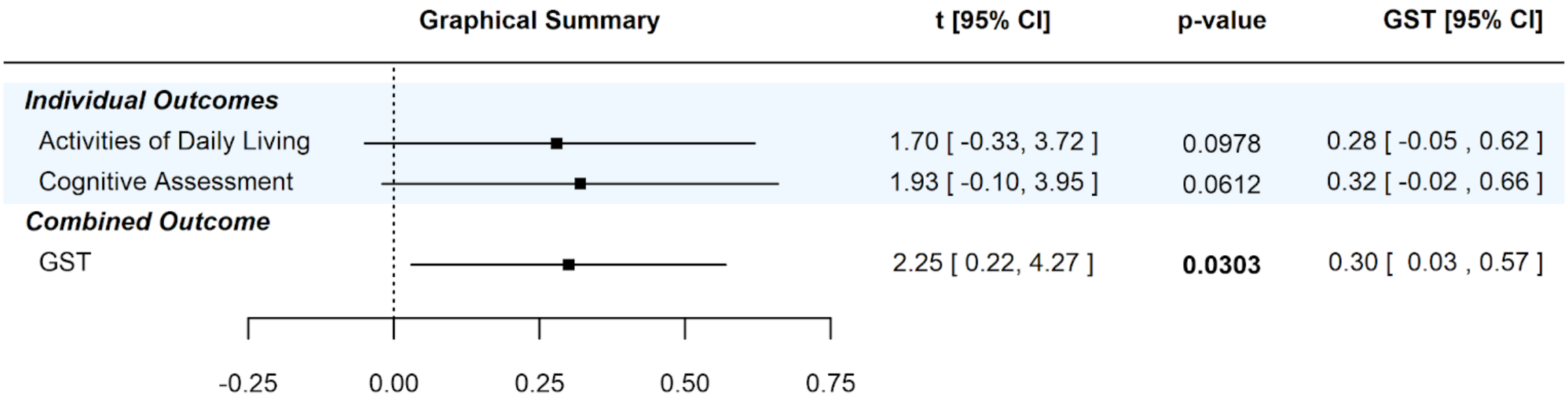


Pentara

Time Savings: True disease progression can be measured against time as a gold standard

GST Example – Simulated Data

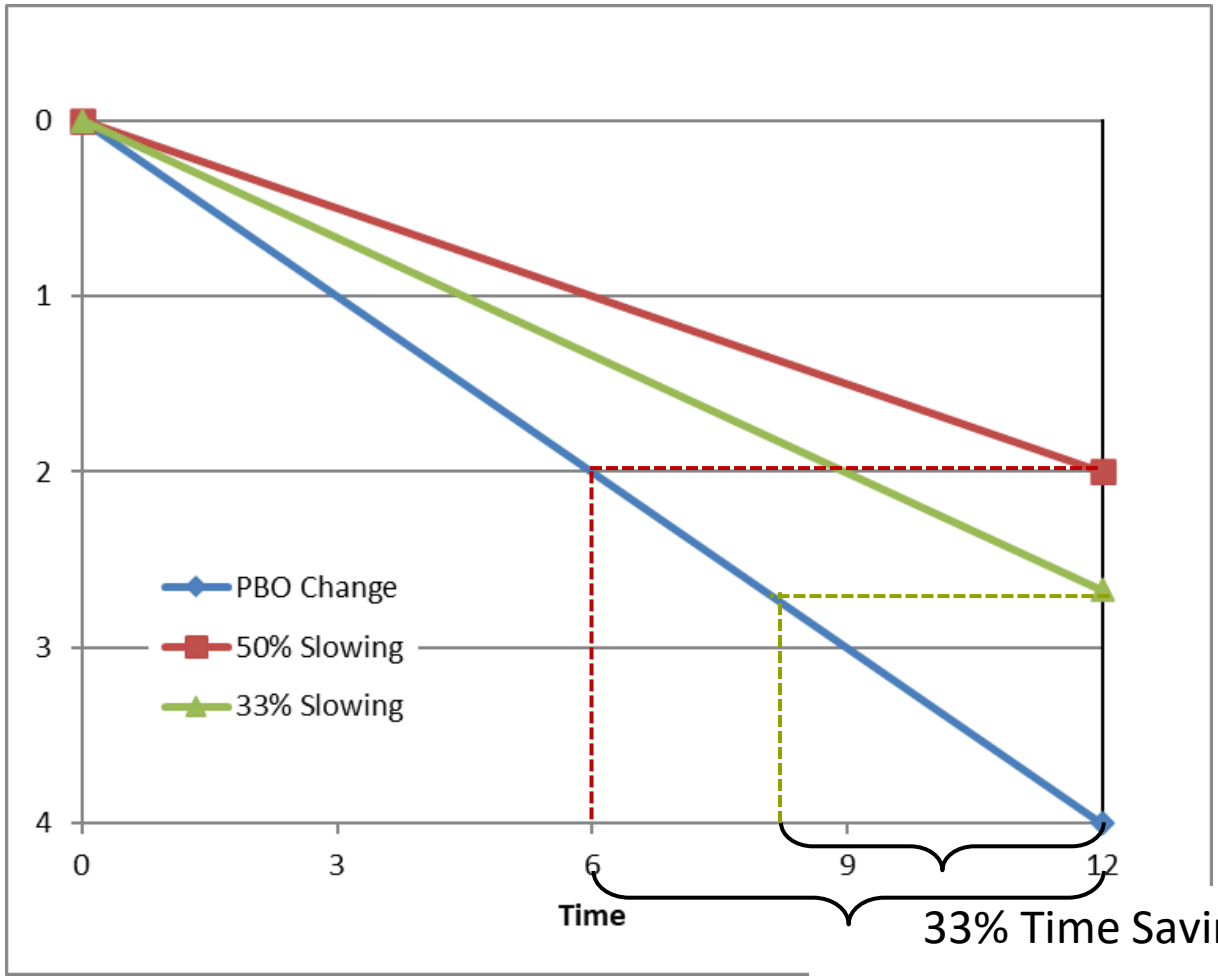
Individual endpoints are not significant, but evidence is consistent
→GST combining the 2 outcomes is significant



Pentara

Progressive Diseases Decline Over Time
33% and 50% Time Savings with Linearity

Time Saved at the End of the Study



33% Time Savings = 4 months out of 1 year

50% Time Savings = 6 months out of 1 year

Pentara

Conclusions about GSTs

- GSTs measure the effect on the whole disease
- GSTs are particularly relevant for disease modifying treatment effects or combination symptomatic and disease modifying effects
- GST effect sizes can be described with percent slowing
  - 100% slowing is halting the disease progression
  - 50% slowing means the treatment group has half the decline of the placebo group
- GSTs can be used to get time savings
  - With linearity, 50% slowing means 3 months of time saved with 6 months of treatment
  - Time savings is interpretable to patients, care partners and clinicians

Pentara

The Medical Need and Current Treatment Landscape in Mild-to-Moderate Alzheimer's Disease

Anton P. Porsteinsson, MD

William B. and Sheila Konar Professor of Psychiatry, Neurology, Neuroscience, and Medicine
Director, Alzheimer's Disease Care, Research and Education Program (AD-CARE)

University of Rochester School of Medicine and Dentistry

Rochester, NY

Prevalence & Impact of AD

- **Worldwide[1]:**
  - 50 million with dementia, rising to 150 million by 2050 (10 million new cases/year), with AD comprising 60%-70% of cases
  - A major cause of disability among older people
  - Physical, psychological, social, and economic impact, not only on those with dementia, but on their careers, families, and society at large
- **USA[2]:**
  - There are 6.9 million individuals with AD, projected to rise to 14 million by 2050
  - Sixth leading cause of death; kills more than breast cancer and prostate cancer combined
  - $305 billion cost to nation in 2020, rising to $1.1 trillion by 2050
  - 16 million provided unpaid care, at an estimated 18.6 billion hours, valued at $244 billion

1. World Health Organization (WHO). [Published] September 21, 2020. Accessed January 4, 2021. https://www.who.int/news-room/fact-sheets/detail/dementia
2. Alzheimer's Association. Updated June 30, 2023. Accessed January 4, 2024. https://www.alz.org/media/Documents/annual-report-2020.pdf

AD: Beyond the Numbers

- A disease of personal frustration and despair
- Stigma, loneliness, loss of self over a prolonged time
- Insufficient attention by most physicians
- Limited treatment options
- Fragmented care and support services
- Frequent family discord and family breakdown outlasting the life of the individual with the disease

AD: The Clinical Continuum

- AD is a much longer disease than previously recognized
- Transitions between stages are seamless, with dementia being the end stage
- **Pre-symptomatic or preclinical phase**
  - Begins up to 20 years before symptoms
  - Brain changes are evolving, and brain cells are dying
  - Towards the latter part, subtle symptoms may arise (Subjective Cognitive Decline or SCD)
- **MCI stage of AD**
  - Cognitive complaints; abnormal cognitive testing; independence in IADL/BADL preserved
- **Dementia stages (mild, moderate, severe)**
  - Continued decline in cognition and functional independence; behavioral symptoms common

MCI = mild cognitive impairment.

Sperling RA, et al. *Alzheimers Dement*. 2011;7(3):280-292.

AD: The Pathophysiologal Continuum

- Cerebral amyloidosis
  - The earliest detectable change, present in preclinical AD
  - Identifiable in life through elevated PET Aβ or low CSF Aβ
- Hyperphosphorylated tau
  - Detectable closer to time of symptom onset
  - Identifiable in life through elevated PET tau or CSF p-tau
- Loss of synapses, brain cells, and neurotransmitters follow
  - Multiple markers of neuro-degeneration, neuroinflammation, and metabolic disruption
- Cognitive and functional decline result from the above processes

Jack Jr CR, et al. *Lancet Neurol.* 2010;9(1):119-128.
Alzheimers Dement. 2020;16(3):391-460.

Current Medications for Mild-to-Moderate Alzheimer's Disease

- Approved therapies for mild-to-moderate Alzheimer's disease (AD) are:
  - Cholinesterase inhibitors (donepezil, galantamine, rivastigmine)
  - NMDA antagonists (memantine)
- Approved therapies have a modest effect on cognitive symptoms
- These symptomatic treatments do not impact brain pathology
- New therapies (hMabs) are approved for earlier stages of disease (ie, Early Symptomatic AD)

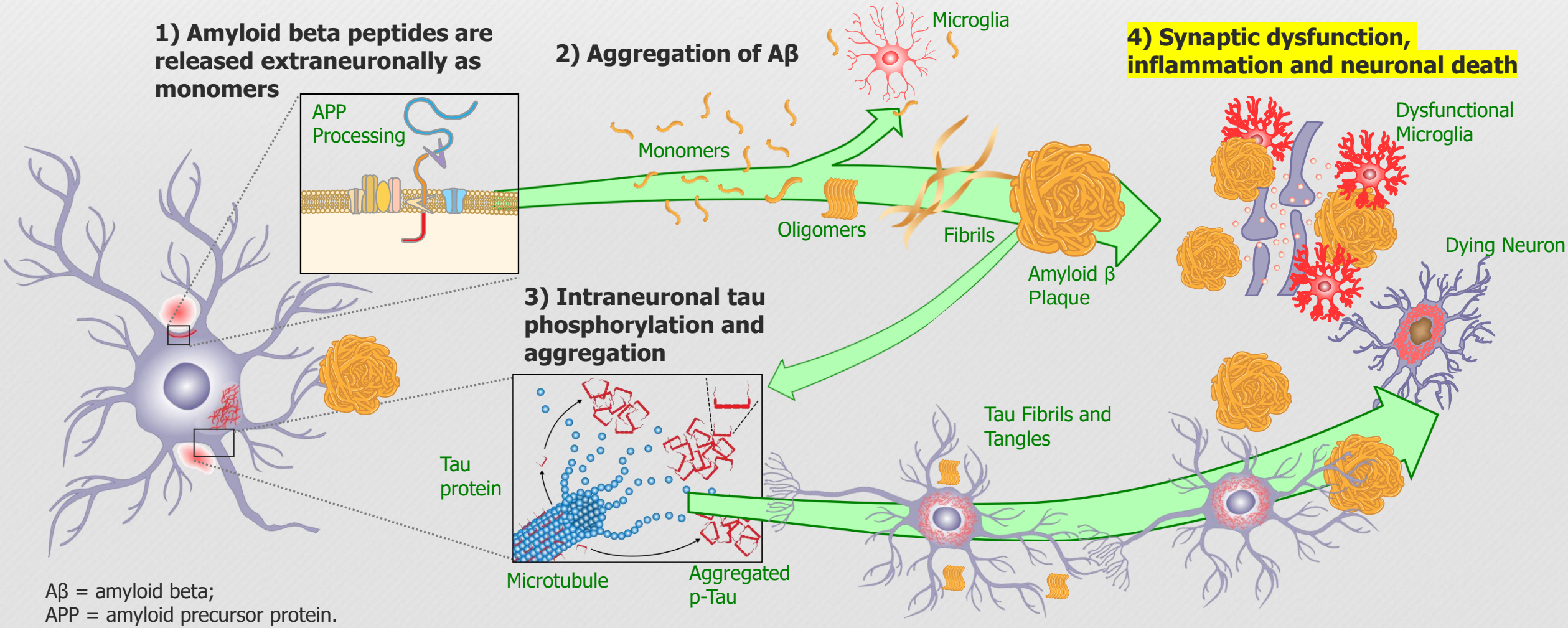
MCI = mild cognitive impairment; NMDA = N-methyl-D-aspartate.

Common Side Effects Associated With Available Therapies for Mild-to-Moderate AD

Cholinesterase Inhibitors	Memantine
Nausea/vomiting	Confusion
Diarrhea	Sedation
Loss of appetite	Dizziness
Dizziness	Constipation
Syncope	
Leg cramps	
Ulcers	
Cardiac arrhythmias	

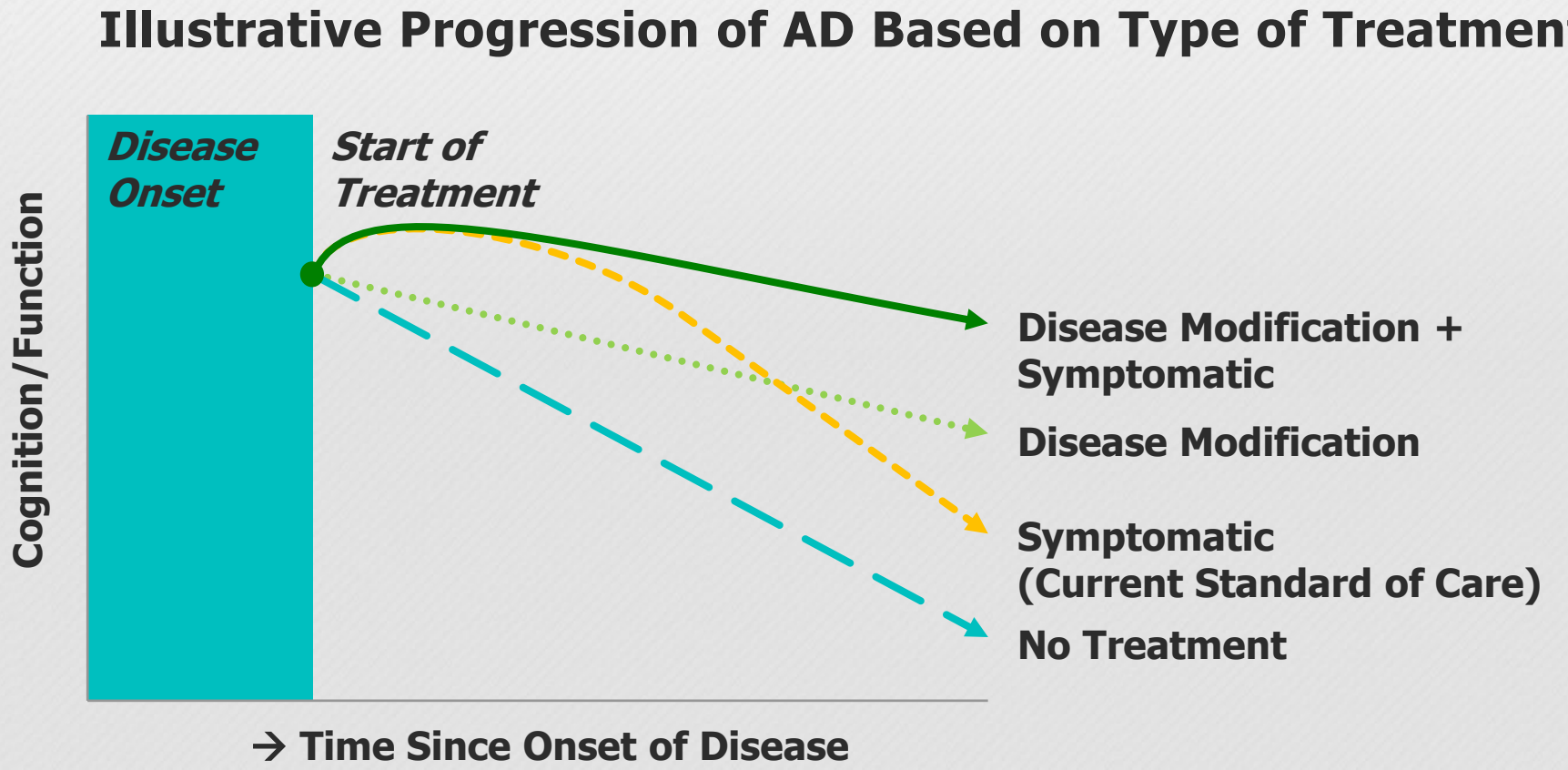
Birks J. *Cochrane Database Syst Rev.* 2006;1:CD005593.
Emre M, et al. *J Alzheimers Dis.* 2008;14(2):193-199.
Homma A, et al. *Dement Geriatr Cogn Disord.* 2008;25(5):399-407.

The 2 Pathological Hallmarks of AD in the Brain Are Aβ Plaques and Neurofibrillary Tangles



Aβ = amyloid beta;
APP = amyloid precursor protein.
Based on Pospich S, Raunser S. *Science.* 2017;358(6359):45-46.

No Approved Disease-modifying Therapies for Mild-to-Mod AD



Adapted from: Kennedy GJ. *Prim Psychiatry.* 2007;14(11):30-34.

Why Do We Need Disease-modifying Drugs for Mild-to-Moderate AD?

- Disabling and ultimately fatal dementing disease
- Increasing incidence due to an aging population
- Enormous economic and societal burden
- Delaying the onset and progression of AD by 2 years may result in a 22.5% reduction in the global burden by the year 2050[1]

1. Brookmeyer R, et al. *Am J Public Health.* 1998;88(9):1337-1342.

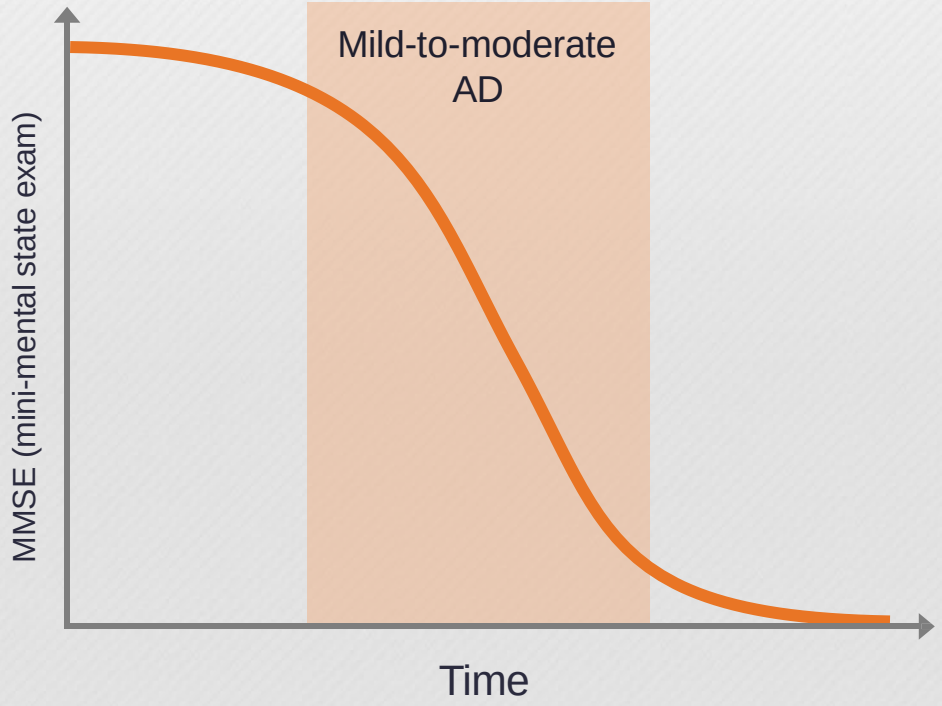
New Treatment Options Needed for Mild-to-Moderate Alzheimer's Disease

Medical need:

The point of most accelerated disease progression[1,2]

Few treatment options with only modest effects[3]

Higher financial burden than pre-dementia[4]



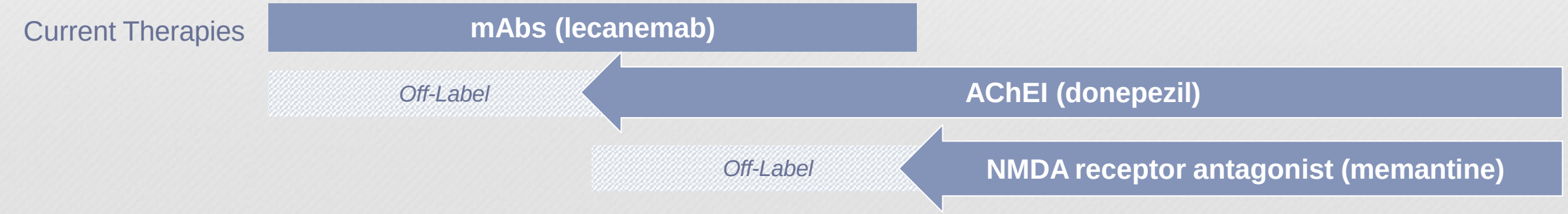
Reduced development risk:

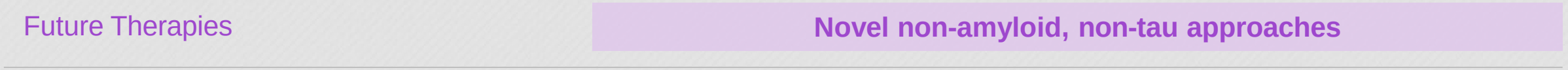
Clinical, syndromal diagnosis is possible[5]

Increased likelihood of tangible placebo decline

1. Ower et al, *Eur J Epidemiol* 2018
2. Caroli et al, *Neurobiol Aging* 2010
3. Fink et al, *Ann Intern Med* 2020
4. Cerejeira et al, *Front Neurol* 2012
5. de Aquino et al, *Front Neurol* 2021

Significant opportunity in Alzheimer's disease





81% of all patients diagnosed with Alzheimer's disease are mild-to-moderate

2.1 million mild-to-moderate Alzheimer's patients diagnosed in 2021 in the US

Few available options

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

Data sources: Decision Resources Group, accessed 2H2022; National Institute on Aging; Yuan et al., *Journal of Alzheimer's Disease* 2021.

AChEI, acetylcholinesterase inhibitor; AD, Alzheimer's disease; mAbs, monoclonal antibodies; MCI, mild cognitive impairment; NANT, non-amyloid, non-tau; NMDA, N-methyl-aspartate.

Strong rationale to advance fosgonimeton

SIGNIFICANT OPPORTUNITY TO TRANSFORM THE TREATMENT PARADIGM FOR NEURODEGENERATIVE DISEASES

Disease modifying

Improves cognition

Improves function

Reduces inflammation

Prevents nerve cell death

Favorable safety and tolerability profile

Risk mitigated Ph 2/3 LIFT-AD following interim analysis

Differentiated and Risk Mitigated

+

High unmet need

Enormous potential market

Favorable external landscape

Conclusions: Why Do We Need a Drug Like fosgonimeton for Alzheimer's Disease?

- Disabling and ultimately fatal dementing disease
- Increasing incidence due to an aging population
- Enormous economic and societal burden
- Delaying the onset and progression of Alzheimer's disease by 2 years may result in a 22.5% reduction in the global burden by the year 2050[a]
- Fosgonimeton has the potential to slow clinical decline, extending the time people can live with conserved cognitive abilities, preserving autonomy in activities of daily living, and lessening behavioral symptoms

[a] Brookmeyer R, et al. *Am J Public Health.* 1998;88(9):1337-1342.

DC Source: Brookmeyer et al. Am J Public Health; 1998; 88:1337

Q&A

© Athira Pharma, Inc. All Rights Reserved.

Thank You

Athira PHARMA

© Athira Pharma, Inc. All Rights Reserved.