



Phase 2/3 LIFT-AD Interim Analysis Results and Next Steps

October 17, 2022



ADVANCING NEW THERAPIES FOR NEURONAL HEALTH

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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.

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Phase 2/3 LIFT-AD Study Advances

INDEPENDENT UNBLINDED INTERIM ANALYSIS SUPPORTS POTENTIAL CLINICALLY MEANINGFUL ACTIVITY OF FOSGONIMETON WITHOUT BACKGROUND THERAPY AND MITIGATES PROGRAM RISK

- Phase 2 exploratory ACT-AD study results suggested congruent positive effects
 - Cognition (ADAS-Cog11); Function (ADCS-ADL23); Neurodegeneration (neurofilament light chain or NfL)
- Data driven approach was used to determine best path forward to optimize ongoing Phase 2/3 LIFT-AD study in the same patient population as in ACT-AD
- Analysis of ~100 patients supports potential clinically meaningful effects of cognition and function and informs the sample size required to power LIFT-AD
 - Enrollment target of <150 additional patients enables LIFT-AD to be well-powered for the primary endpoint
 - Enrollment completion target by mid 2023 with topline data in early 2024

Hans Moebius, M.D., Ph.D
Chief Medical Officer



Summary of Phase 2 ACT-AD Study Results



EXPLORATORY STUDY TO INFORM LARGER LIFT-AD IN PATIENTS WITHOUT BACKGROUND THERAPY

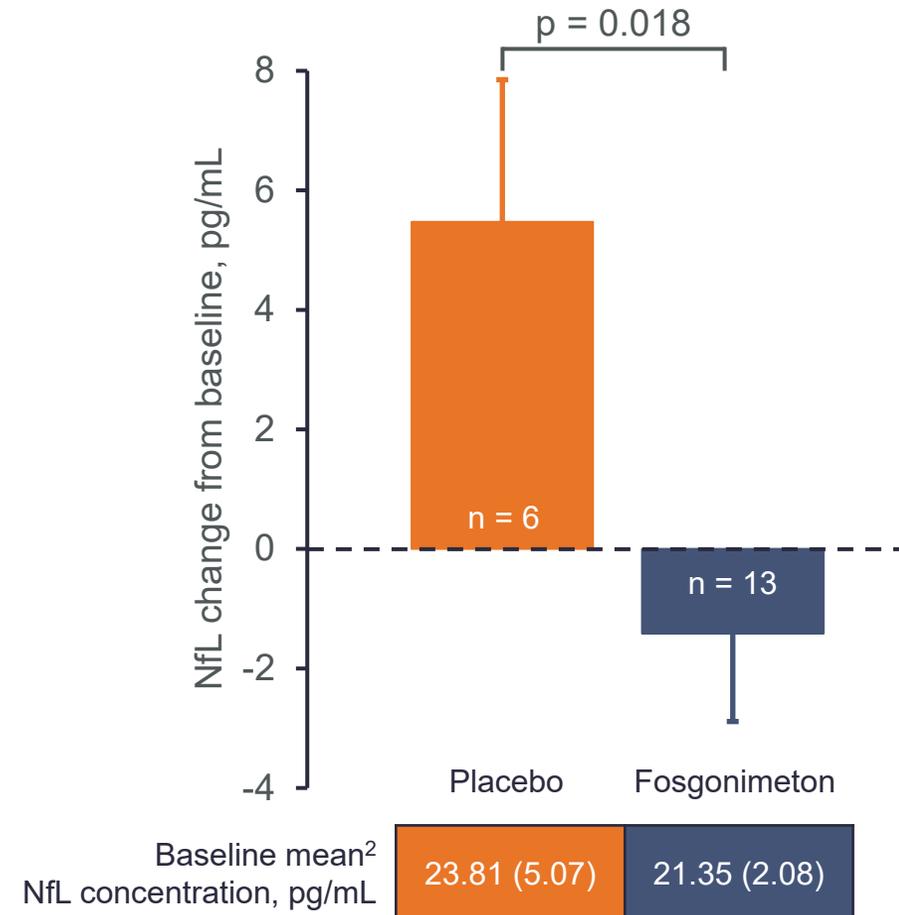
Favorable safety and tolerability profile

Fosgonimeton signals without background therapy compared to placebo (limited subgroup size)

- Reduced ERP P300 latency (n.s.)
- Improved cognition as measured by ADAS-Cog11 (n.s.)
- Improved function as measured by ADCS-ADL23 (n.s.)
- Showed a statistically significant improvement in plasma levels of NfL (p=0.018)

ACT-AD was a similar study design to LIFT-AD to help inform larger LIFT-AD. Both are randomized, double-blind, placebo-controlled, parallel-group studies of fosgonimeton for patients with mild-to-moderate Alzheimer's disease.

NfL at week 26 (fosgonimeton without background therapy)¹



Fosgonimeton Phase 2/3 LIFT-AD Study Design



LEARNINGS FROM ACT-AD INFORM STUDY DESIGN OPTIMIZATION

POPULATION	TREATMENT DURATION	RESULTS
<p>LIFT-AD: Target N=TBD, informed by interim analysis</p> <p>Mild-to-moderate AD subjects</p> <ul style="list-style-type: none"> • 55-85 years • CDR 1 and 2 • MMSE 14-24 • Approximately 40% of patients not on background AChEI <p>Path Forward:</p> <ul style="list-style-type: none"> • Exclusion criterion added for subjects on background AChEIs (Sept 2022) • Independent, unblinded interim analysis to inform sample size for primary endpoint (Oct 2022) 	<p>26-week randomized, double-blind treatment, + optional 18-month OLEX</p> <p>Fosgonimeton (40 mg)</p> <p>Fosgonimeton (70 mg)</p> <p>Placebo</p> <p>Randomization (1:1:1)</p>	<p>PRIMARY ENDPOINT</p> <ul style="list-style-type: none"> • Global Statistical Test (GST) – unbiased composite of data from two key co-secondary endpoints (ADAS-Cog11 and ADCS-ADL23) • Safety <p>SECONDARY ENDPOINTS</p> <ul style="list-style-type: none"> • Cognition: ADAS-Cog11 • Function: ADCS-ADL23 • Global clinical change: ADCS CGIC – Clinician <p>EXPLORATORY ENDPOINTS</p> <ul style="list-style-type: none"> • Fluid biomarkers (e.g., NfL) <p>TIMELINE</p> <ul style="list-style-type: none"> • Enrollment ongoing



AChEI, acetylcholinesterase inhibitor; 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; GST, global statistical test; MMSE, mini-mental state examination; NfL, neurofilament light chain; OLEX, open-label extension.

Systematic and Data-driven Process to Support LIFT-AD

STEPS COMPLETED SINCE ACT-AD READOUT IN JUNE 2022

- Additional analysis of ACT-AD
- DSMB unblinded adjudication of LIFT-AD
- Blinded analysis of LIFT-AD
- Proactively amended Phase 2/3 LIFT-AD in September
- Independent unblinded interim analysis in October

Development plan optimized with mitigated risk

LIFT-AD Sample Size Well Powered for Primary Endpoint

STRINGENT CRITERIA APPLIED TO INCREASE PROBABILITY OF DEMONSTRATING A CLINICALLY MEANINGFUL EFFECT SIZE FOR COGNITION AND FUNCTION

Pre-specified Decision Framework

ADCS-ADL23

	0	+1	+2	+2.5	+3	+4
0	Futility	Futility	Futility	Futility	Futility	Futility
-1	Futility	Futility	Futility	Futility	Futility	Promising Zone*
-2	Futility	Futility	Futility	Futility	Promising Zone*	Promising Zone*
-2.5	Futility	Futility	Futility	Promising Zone*	Promising Zone*	Promising Zone*
-3	Futility	Promising Zone*				
-4	Promising Zone*					

DMC Recommendation: "Continue LIFT-AD Study"

- **Promising Zone* confirmed**
- **<150** patients needed to complete study
- Target enrollment complete by mid 2023 with data in early 2024

Mark Litton, Ph.D
President and Chief Executive Officer



Moving Forward

Target enrollment completion by mid 2023 with data in early 2024

Continued focus on LIFT-AD recruitment and completion to meet timelines

Strong cash and cash equivalents of approximately \$282M* provides support through key data points and beyond

Fosgonimeton – A New Potential Therapy for Alzheimer’s Disease



35 million

Estimated Alzheimer’s cases worldwide¹



Multi-Billion \$ Market

Despite generic entries



Zero

New marketed products since 2003

Over 100 million globally by 2050

~900,000 new patients diagnosed annually in the US alone^{1,2}

6.2 million treatment eligible patients in the US in 2021 based on prevalence data

Growing at 3% per year^{2,3}

Mild to Moderate comprises 81% of all patients with Alzheimer’s disease^{3,4}

Significant opportunity for fosgonimeton

Limited treatment options exist today for those with Alzheimer’s disease; novel approaches to improve cognition, function and neuroprotection are needed

¹ <https://www.who.int/news-room/fact-sheets/detail/dementia>

² <https://www.alz.org/media/documents/alzheimers-facts-and-figures.pdf>

³ GlobalData AD prevalence data access and analysis

⁴ <https://www.nia.nih.gov/news/half-alzheimers-disease-cases-may-be-mild>