Athira Pharma Provides Update on Plans for Ongoing LIFT-AD Clinical Study of Fosgonimeton in Mild-to-Moderate Alzheimer's Patients

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Adapting study to focus on the evaluation of fosgonimeton monotherapy

Conducting an independent, unblinded interim analysis to confirm sample size for primary endpoint of Global Statistical Test (GST)

BOTHELL, Wash., Sept. 06, 2022 (GLOBE NEWSWIRE) -- Athira Pharma, Inc. (NASDAQ: ATHA), a late clinical-stage biopharmaceutical company focused on developing small molecules to restore neuronal health and slow neurodegeneration, today announced an update to its plans for the ongoing LIFT-AD clinical trial of fosgonimeton (ATH-1017), a small-molecule positive modulator of the HGF/MET neurotrophic factor system, in patients with mild-to-moderate Alzheimer's disease (AD).

The completed, exploratory ACT-AD study was designed to better understand fosgonimeton's effect on biomarkers, psychometric measures and safety over six months as well as to inform the larger ongoing LIFT-AD study in the same mild-to-moderate AD population. Study results from ACT-AD suggested positive effects on measures of cognition, function and neurodegeneration in patients taking fosgonimeton alone without background acetylcholinesterase inhibitors (AChEIs) during the study period. Leveraging these results, the company will amend the LIFT-AD trial to investigate the effects of fosgonimeton compared with placebo, without background AChEIs. The overall design of LIFT-AD remains unchanged, including the Global Statistical Test as the primary endpoint. An independent, unblinded interim analysis will be conducted to inform the required sample size needed to appropriately power the primary endpoint in the target patient population.

"We look forward to advancing the clinical evaluation of fosgonimeton in a way that will best determine its potential for Alzheimer's disease patients while preserving the integrity of the LIFT-AD study and optimizing its chances for success," said Hans Moebius, M.D., Ph.D., Chief Medical Officer of Athira. "Our decision to focus LIFT-AD on fosgonimeton treatment without background cholinergics was guided by results from the ACT-AD trial and a blinded analysis of the ongoing LIFT-AD study. Importantly, fosgonimeton remains well tolerated, with a favorable safety profile in the full study population."

"We believe that fosgonimeton has the potential to be a novel therapeutic option for the millions of patients with mild-to-moderate Alzheimer's disease, and the ACT-AD results support our enthusiasm for its continued development," said Mark Litton, Ph.D., President and Chief Executive Officer of Athira. "We are encouraged by the biologic activity and safety profile shown in ACT-AD and look forward to having the additional insights provided by this interim analysis in the fall of 2022."

ACT-AD Study Design and Results
ACT-AD was an exploratory, randomized, double-blind, placebo-controlled, parallel-group 26-week trial evaluating fosgonimeton compared to placebo in patients with mild-to-moderate Alzheimer's disease. The study enrolled 77 patients in the United States and Australia (age 55 to 85 years, Mini-Mental State Exam (MMSE) score of 14-24 and Clinical Dementia Rating (CDR) scale global score of 1 or 2). Patients were allowed to continue receiving AChEIs; 60 percent remained on stable doses of AChEIs and 40 percent were not receiving AChEIs during the study. Patients were randomized 1:1:1 to receive placebo or fosgonimeton at either 40 mg/day or 70 mg/day. The primary endpoint for ACT-AD was Event-Related-Potential (ERP) P300 Latency, a functional measure of working memory processing speed. Secondary endpoints included ADAS-Cog11, a measure of cognition; ADCS-CGIC, a measure of global clinical change; and ADCS-ADL23, a measure of functional change. Safety data were evaluated throughout.

As previously reported, the ACT-AD study did not meet the primary endpoint of a statistically significant change in ERP P300 latency. However, the data showed a numerical improvement in the functional measure of ADCS-ADL23, which evaluates patients' activities of daily living as assessed by their caregivers, compared to placebo at 26 weeks (+2.12 points, n.s.). Additional analyses of the data from patients treated with fosgonimeton alone suggested a potentially beneficial change in ERP P300 latency (-28 milliseconds, n.s.), as well as cognitive improvement, as measured by ADAS-Cog11 (-3.3 points, n.s.), compared with placebo at 26 weeks. Among patients treated with fosgonimeton alone, there was a statistically significant improvement of plasma Neurofilament light Chain (NfL), a validated fluid biomarker of neurodegeneration, (6.89 pg/ml, p=0.018).

These encouraging findings further support the decision to focus the ongoing clinical evaluation on fosgonimeton alone without background AChEIs.

Athira reports that, to date, more than 90 percent of patients completing the ACT-AD and LIFT-AD studies have elected to participate in the ongoing open label extension study.

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 press release and at AAIC is solely the responsibility of Athira and does not necessarily represent the official views of the National Institutes of Health.

About the LIFT-AD Clinical Study
LIFT-AD is a randomized, double-blind, placebo-controlled, parallel-group study of fosgonimeton for patients with mild-to-moderate Alzheimer's disease. The study has enrolled more than 300 patients in the United States, with enrollment ongoing. Patients are randomized across two dose groups and one placebo group on a 1:1:1 basis to receive a subcutaneous injection of fosgonimeton or placebo once daily over a treatment course of 26 weeks. The primary endpoint for LIFT-AD will be measured by the Global Statistical Test, which is a mathematical algorithm combining the scores from cognition (Alzheimer's Disease Assessment Scale-Cognitive Subscale [ADAS-Cog11]), and function (Alzheimer's Disease Cooperative Study-Activities of Daily Living [ADCS-ADL23]). Additional information on the study can be found at: NCT04488419.

About Fosgonimeton
Fosgonimeton is a small molecule designed to enhance the activity of hepatocyte growth factor (HGF) and its receptor, MET, to impact neurodegeneration and regenerate brain tissue. The function of the HGF/MET receptor system may be impaired in the brain under conditions of neurodegeneration. In addition to Alzheimer's disease, fosgonimeton has the potential to address the broader dementia population, including Parkinson's disease dementia and Dementia with Lewy bodies, as the mode of action focuses on network recovery and synaptic signal transmission in the brain.

About Athira Pharma, Inc.
Athira Pharma, Inc., headquartered in the Seattle, Washington area, is a late clinical-stage biopharmaceutical company focused on developing small molecules to restore neuronal health and slow neurodegeneration. Athira aims to provide rapid cognitive improvement and alter the course of neurological diseases with its novel mechanism of action. Athira is currently advancing its pipeline therapeutic candidates targeting the HGF/MET neurotrophic system for Alzheimer's and Parkinson's disease dementia, Dementia with Lewy bodies and neuropsychiatric indications. For more information, visit www.athira.com. You can also follow Athira on Facebook, LinkedIn and @athirapharma on Twitter and Instagram.

Forward-Looking Statements
This communication contains "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933, Section 21E of the Securities Exchange Act of 1934 and the Private Securities Litigation Reform Act of 1995. These forward-looking statements are not based on historical fact and include statements regarding fosgonimeton as a potential treatment for Alzheimer's disease, Parkinson's disease dementia, Dementia with Lewy bodies, and other dementias, and neuropsychiatric indications; Athira's platform technology and potential therapies; future development plans; clinical and regulatory objectives and the timing thereof; expectations regarding the potential efficacy and commercial potential of Athira's product candidates; the anticipated reporting of data; the potential learnings from the ACT-AD trial and their ability to inform and improve future clinical development plans; and Athira's ability to advance its product candidates into later stages of development. Forward-looking statements generally include statements that are predictive in nature and depend upon or refer to future events or conditions, and include words such as "may," "will," "should," "on track," "would," "expect," "plan," "believe," "intend," "pursue," "continue," and other similar expressions, among others. Any forward-looking statements are based on management's current expectations of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. These risks and uncertainties include, but are not limited to, the data for our product candidates from or preclinical and clinical trials will not support the safety, efficacy and tolerability of our product candidates; cessation or delay of any of the ongoing clinical trials and/or Athira's development of fosgonimeton and other product candidates may occur; future potential regulatory milestones of fosgonimeton and other product candidates, including those related to current and planned clinical studies may be insufficient to support regulatory submissions or approval; the impact of the COVID-19 pandemic on Athira's business, research and clinical development plans and timelines, and the regulatory process for Athira product candidates; Athira may not be able to recruit sufficient patients for its clinical trials; the outcome of legal proceedings that have been or may in the future be instituted against us and certain of our directors and officers; clinical trials may not demonstrate safety and efficacy of any of Athira's product candidates; possible negative interactions of Athira's product candidates with other treatments; Athira's assumptions regarding the sufficiency of its cash, cash equivalents and investments to fund its planned operations may be incorrect; adverse conditions in the general domestic and global economic markets; the impact of competition; regulatory agencies may be delayed in reviewing, commenting on or approving any of Athira's clinical development plans as a result of the COVID-19 pandemic, which could further delay development timelines; the impact of expanded product development and clinical activities on operating expenses; the impact of new or changing laws and regulations; as well as the other risks detailed in Athira's filings with the Securities and Exchange Commission. These forward-looking statements speak only as of the date hereof and Athira undertakes no obligation to update forward-looking statements. Athira may not actually achieve the plans, intentions, or expectations disclosed in its forward-looking statements, and you should not place undue reliance on the forward-looking statements.

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