Athira Pharma Presents Data from ACT-AD Phase 2 Proof-of-Concept Clinical Study of Fosgonimeton in Mild-to-Moderate Alzheimer's Patients at the Alzheimer's Association International Conference 2022

August 3, 2022

Additional data showed numerical improvement in activities of daily living (ADCS-ADL23), a protocoled secondary endpoint and a functional measure of independence

Plasma biomarker data in a pre-specified subgroup analysis showed a statistically significant reduction in neurofilament light chain (NfL), a validated biomarker of neurodegeneration, in subjects treated with fosgonimeton monotherapy compared to placebo, and showed a numerical reduction in NfL across all fosgonimeton treated patients

BOTHELL, Wash., Aug. 03, 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, announced that Hans Moebius, M.D., Ph.D., Athira's Chief Medical Officer, is leading an oral presentation titled, "ACT-AD: Fosgonimeton in Mild-to-Moderate Alzheimer's Disease – First Results of a Randomized, Placebo-Controlled, 26-Week Phase 2 Proof-of-Concept Trial" today at the Alzheimer's Association International Conference (AAIC) 2022.

Athira's lead candidate, fosgonimeton (ATH-1017), is a small-molecule positive modulator of the HGF/MET neurotrophic factor system.

"The primary objective of the proof-of-concept ACT-AD study was to evaluate the effects of fosgonimeton treatment on event related potential (ERP) P300 latency, to assess its safety profile and to inform the ongoing LIFT-AD study," said Dr. Moebius. "While the primary outcome analysis (mITT, MMRM) did not reach statistical significance, these data have given us meaningful insights into fosgonimeton's potential effects. Importantly, they showed fosgonimeton's potential activity, including a reduction in plasma levels of the fluid biomarker, neurofilament light chain (NfL), a validated biomarker of neurodegeneration, in this mild-to-moderate Alzheimer's disease patient population and demonstrated its favorable tolerability and safety profile over six months.

"We were particularly pleased to detect numerical improvements in ADCS-ADL23, a functional measure of activities of daily living and a secondary endpoint in ACT-AD. Independence and function are critically important to patients and caregivers, impacting quality of life, caregiver burden and healthcare costs. Current treatment options have limited effect on this measure, and we believe that, if borne out in further clinical trials, fosgonimeton may potentially lead to functional improvement in patients suffering with Alzheimer's disease.

"In addition, we detected a statistically significant (p=0.018) improvement in NfL plasma concentration in a pre-specified subgroup analysis of subjects treated with fosgonimeton monotherapy compared with placebo, and a numerical improvement was shown in all fosgonimeton treated patients. Overall, these findings are congruent with the previously reported numerical improvements in ERP P300 latency and ADAS-Cog11 in subjects treated with fosgonimeton monotherapy and suggest that fosgonimeton may have potential benefit for Alzheimer's patients," added Dr. Moebius.

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 standard-of-care therapy (AChEIs), with 60 percent remaining on stable doses of AChEIs and 40 percent not receiving AChEIs during the study. Patients were randomized 1:1:1 to receive placebo or fosgonimeton at either 40 mg/d or 70 mg/d. 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 for the modified intent to treat (mITT) population by a mixed model repeated measures (MMRM) analysis when compared with placebo at 26 weeks in a pooled analysis of the 40 mg and 70 mg dose groups. Secondary endpoints, including ADAS-Cog11, ADCS-CGIC, and ADCS-ADL23, were not statistically significant in treated subjects compared with placebo at 26 weeks as the study was only powered to show statistical significance for change in ERP P300 latency.

While not statistically significant, the data showed a numerical improvement in the functional measure of ADCS-ADL23, which evaluates improvements in patients' activities of daily living as assessed by their caregivers compared to placebo at 26 weeks (+2.12 points). A post hoc analysis, based on the mITT population on fosgonimeton monotherapy, showed a potentially beneficial change in ERP P300 latency compared to placebo at 26 weeks (-28 milliseconds) as well as cognitive improvement as measured by ADAS-Cog11 (-3.3 points) compared with placebo at 26 weeks.

In addition, among subjects treated with fosgonimeton monotherapy, a prespecified subgroup analysis of the plasma levels of NfL, a validated fluid biomarker of neurodegeneration, demonstrated a statistically significant improvement compared with placebo, Least Squared (LS) means difference of 6.89 pg/ml (p=0.018), and showed a numerical improvement in all fosgonimeton treated patients compared with placebo, LS means difference 1.67 pg/ml (n.s.), regardless of background therapy.

Athira reports that 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.

“Along with feedback from our Scientific Advisory Board, the Data Safety Monitoring Board, and other experts, we continue to evaluate the best next steps for LIFT-AD,” said Mark Litton, Ph.D., President and Chief Executive Officer of Athira. “We remain very encouraged by the biologic activity and safety demonstrated in ACT-AD and are fortunate to have this larger, ongoing LIFT-AD study underway, which should provide even greater insight into fosgonimeton’s effect in mild-to moderate Alzheimer’s disease patients.”

“Athira is advancing a novel, non-amyloid target to treat Alzheimer’s disease that we believe could potentially impact function and cognition, which are important for patients and caregivers. The new plasma biomarker data support our hypothesis that fosgonimeton is neuroprotective and correlates with the cognitive improvement we saw in fosgonimeton monotherapy in the ACT-AD study. We are taking a thoughtful approach to the development of fosgonimeton, mindful that we want to bring this drug to patients as expeditiously as possible given the urgent and growing patient need. Importantly, we have a strong balance sheet to support continued clinical development of our novel approach,” added Dr. Litton.

Slides from the oral AAIC presentation are available on the Scientific Publications and Presentations section of Athira’s website.

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 that combines the scores from cognition (Alzheimer's Disease Assessment Scale-Cognitive Subscale [ADAS-Cog11]), and either global impression of change (Alzheimer's Disease Cooperative Study-Clinical Global Impression of Change [ADCS-CGIC]), or function (Alzheimer’s Disease Cooperative Study-Activities of Daily Living [ADCS-ADL23]). Additional information on the study can be found at: NCT04488419.

About Fosgonimeton (ATH-1017)
Fosgonimeton (ATH-1017) 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.

Investor & Media Contact:

Julie Rathbun
Athira Pharma
Julie.rathbun@athira.com
206-769-9219