Athira Pharma Presents New Clinical and Preclinical Data at the American Academy of Neurology (AAN) 2023 Annual Meeting

April 25, 2023

Fosgonimeton improves MMSE (mini-mental state evaluation) after six months in a post hoc analysis from the Phase 2 ACT-AD trial in mild-to-moderate Alzheimer's disease

Preclinical findings with fosgonimeton further elucidate its multimodal effects and continue to support therapeutic potential for Alzheimer's and Parkinson's

ATH-1105 significantly prolongs survival and improves motor function in a mouse model of ALS; strongly supports its potential for ALS

BOTHELL, Wash., April 25, 2023 (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 the presentation of new data from its small molecule programs enhancing the HGF/MET neurotrophic system. The data were presented in oral and poster presentations at the American Academy of Neurology (AAN) 2023 Annual Meeting taking place from April 22-27, 2023, in person in Boston, Mass. and virtually.

"We are pleased to report that a post hoc analysis showed statistically significant improvements in Mini-Mental State Exam (MMSE) scores in patients treated with fosgonimeton without concomitant acetylcholinesterase inhibitors (AChEIs) in the exploratory six month Phase 2 ACT-AD trial," said Hans J. Moebius, M.D., Ph.D., Chief Medical Officer, Athira Pharma. "These and other data presented at this year's AAN Annual Meeting further support other previously reported post hoc findings from ACT-AD that showed improvements in plasma biomarkers and measures of cognition. Additionally, we reported new data that further elucidate the interaction between fosgonimeton and AChEIs. Preclinical data indicate that the neuroprotective effects of fosgonimeton are reduced in combination with donepezil, and suggest this is due, in part, to interference in AKT signaling, one of the multimodal neuroprotective mechanisms enhanced by targeting the HGF/MET system."

Kevin Church, Ph.D., Chief Scientific Officer, Athira Pharma, stated, "We are encouraged by the compelling preclinical evidence with ATH-1105, which demonstrates statistically significant improvements on survival and nerve and motor function in an ALS animal model. We are advancing IND-enabling studies with ATH-1105 and plan to begin clinical evaluation next year."

"The data presented at AAN 2023 add to our growing body of evidence and we believe strongly support the therapeutic potential of enhancing the HGF/MET system with our novel small molecule product candidates, which are designed to protect and repair neuronal networks in neurodegenerative diseases," added Dr. Church.

Oral presentation (Abstract: 4214, Program: S26.008): "*Fosgonimeton provides congruent improvements on neurodegeneration biomarkers, significantly correlating with composite clinical score of cognition and function* in Alzheimer's disease"

Dr. Moebius presented data from the completed, exploratory six month Phase 2 ACT-AD trial of fosgonimeton (ATH-1017) in mild-to-moderate Alzheimer's disease. Highlights from the oral presentation showed fosgonimeton treatment without AChEIs:

- Led to a significant improvement in MMSE scores from baseline (+1.6 pts, p=0.0350);
- dDemonstrated a statistically significant decrease in plasma NfL levels compared with placebo (-6.48 pg/mL, p=0.0222); an
- Showed consistent and descriptive improvements compared with placebo across biomarkers of neuroinflammation (GFAP and YKL-40) and AD-specific protein pathology (Aβ 42/40 ratio and p-Tau181).

In the full study population, statistically significant associations were observed between change from baseline (CFB) of a composite measure of cognition and function and CFB in neurofilament light chain (NfL, an established biomarker of neurodegeneration, p=0.0023), and GFAP (a biomarker of neuroinflammation, p=0.0402).

Oral presentation (Abstract 3944, Program: S14.008)**: "***Therapeutic Potential of Fosgonimeton, a Small-Molecule Positive Modulator of the Neurotrophic HGF/MET Pathway, in Neurodegenerative Conditions"*

Dr. Church reviewed compelling preclinical data that continue to elucidate fosgonimeton's multimodal mechanism of action and therapeutic potential in neurodegenerative diseases, including:

- Neurotrophic effects demonstrated by an increase in synaptogenesis and neurite length in hippocampal and cortical neurons, respectively;
- Neuroprotective effects on cortical neurons subjected to various neurotoxic insults, including oxidative stress, neuroinflammation, excitotoxicity, and mitochondrial dysfunction;
- Reduced protein pathology including Aβ-induced p-tau accumulation in cortical neurons and 6-OHDA–induced α-synuclein aggregation in dopaminergic neurons; and
- Improved function in several animal models including an LPS-induced neuroinflammation model of cognitive impairment and a model of 6-OHDA–induced motor deficits.

Poster presentation (Abstract 3277, Program P08.007)**: "***Small Molecule Positive Modulator of Hepatocyte Growth Factor (HGF)/MET, ATH-1105,*

Improves Function and Reduces Disease Biomarkers in a TDP-43 Mouse Model of Amyotrophic Lateral Sclerosis"

Preclinical findings with ATH-1105 demonstrated statistically significant improvements on nerve and motor function, biomarkers of inflammation and neurodegeneration, and survival in an animal model of amyotrophic lateral sclerosis (ALS), including:

- Prolonged survival and delayed time to first mortality ($p=0.0035$);
- Improvement in balance, coordination, and muscle strength in motor function tests ($p<0.0001$);
- Protection against body weight reduction ($p<0.01$);
- Preservation of nerve function and structure ($p<0.001$); and
- Reduction of plasma biomarkers of systemic inflammation and neurodegeneration ($p<0.0001$).

All presentations will be available on the Scientific Publications & Presentations page of the company's website at www.athira.com.

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

About Fosgonimeton
Fosgonimeton is a small molecule designed to enhance the activity of hepatocyte growth factor (HGF) and its receptor, MET, an endogenous repair mechanism for a healthy nervous system. The function of the HGF/MET neurotrophic system may be impaired in conditions of neurodegeneration. Targeting the protection and repair of neuronal networks, fosgonimeton has disease-modifying potential to address a broad range of neurodegenerative diseases, including Alzheimer's disease, Parkinson's disease and Dementia with Lewy bodies.

About ATH-1105
ATH-1105 is an orally available small molecule positive modulator of the HGF/MET system. In preclinical models of amyotrophic lateral sclerosis (ALS), ATH-1105 was shown to significantly improve survival while delayed time to first death, motor and nerve function, preservation of motor neuron demyelination and axon degeneration, as well as biomarkers of neurodegeneration and inflammation.

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 of therapeutic candidates targeting the HGF/MET neurotrophic system for Alzheimer's and Parkinson's disease, Dementia with Lewy bodies and amyotrophic lateral sclerosis (ALS). 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: product candidates as a potential treatment for Alzheimer's disease, Parkinson's disease, Dementia with Lewy bodies, and other neurodegenerative diseases, such as amyotrophic lateral sclerosis; Athira's platform technology and potential therapies; future development plans; expectations regarding the potential efficacy and commercial potential of Athira's product candidates; 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," "suggest," "potential," 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 our preclinical and clinical trials not supporting the safety, efficacy and tolerability of our product candidates; cessation or delay of Athira's development of product candidates may occur; regulatory authorities could object to protocols, amendments and other submissions; future potential regulatory milestones for 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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