



Alterity Therapeutics Parkinson's Disease and Multiple System Atrophy Data Featured at the American Academy of Neurology (AAN) 2024 Annual Meeting

– ATH434 Improved Motor Performance and General Function in a Primate Model of Parkinson's Disease –

– ATH434-201 Phase 2 Baseline Data Confirm Approach to Target Biomarkers for Slowing Disease Progression –

– 12-Month Data from bioMUSE Study Shows Key Biomarker is Associated with Disease Progression in MSA –

MELBOURNE, AUSTRALIA AND SAN FRANCISCO, USA – 17 April 2024: Alterity Therapeutics (ASX: ATH, NASDAQ: ATHE) ("Alterity" or "the Company"), a biotechnology company dedicated to developing disease modifying treatments for neurodegenerative diseases, today announced that three posters were presented at the American Academy of Neurology (AAN) 2024 Annual Meeting taking place April 13-18, 2024, in Denver, Colorado, USA. Featured presentations described the Company's work in Parkinson's disease and Multiple System Atrophy (MSA), including initial biomarker data and baseline characteristics from the ATH434-201 Phase 2 clinical trial.

David Stamler, M.D., Chief Executive Officer of Alterity, commented, "We are excited to present the Parkinson's disease primate study to an international audience because we have shown that ATH434 can reduce Parkinsonism in a higher order animal with symptoms that closely parallel human disease. Importantly, the improvements in motor skills and general functioning that parallel human parkinsonism were associated with reductions in abnormal iron in affected brain regions, validating the approach we are using in our ongoing clinical trials. The data from this study improve our ability to predict clinical outcomes and increases our confidence level in our ongoing Phase 2 clinical trials in Multiple System Atrophy, a parkinsonian disorder with similar underlying pathology to Parkinson's disease."

Dr. Stamler continued, "Through our collaboration with our partners at Vanderbilt University, we have gained a deeper understanding of MSA, and we are now seeing the fruits of this labor in both our bioMUSE natural history study and our Phase 2 clinical trial. At AAN we reported the baseline characteristics from our ATH434-201 Phase 2 trial including fluid biomarkers and neuroimaging data. The data showed increased iron in areas of pathology and elevated plasma Neurofilament Light Chain (NfL) levels at baseline that correlated significantly with disease

severity. These data give us confidence in our approach of using ATH434 to target the labile cellular iron known to promote neurodegeneration, inhibit α -synuclein aggregation, and improve outcomes.”

Dr. Daniel Classen, Professor of Neurology at Vanderbilt University Medical Center and coordinating investigator for the ATH434-201 Phase 2 study, commented, “The specialized neuroimaging and biomarker assessments evaluated and refined in the bioMUSE study were used to select and track patients in the Phase 2 study, making this program unique among current MSA clinical studies. It is vital to select study patients with a high degree of accuracy. The biomarkers being tested in the Alterity program hold promise for assessing the potential disease modifying benefits of ATH434.”

Presentation Summaries:

Title: A Phase 2 Study of ATH434, a Novel Inhibitor of α -Synuclein Aggregation, for the Treatment of Multiple System Atrophy

Lead Author: David Stamler, M.D., Chief Executive Officer of Alterity Therapeutics

Results: The poster describes the baseline characteristics for the 65 evaluable participants from Alterity’s ATH434-201 randomized, double-blind Phase 2 clinical trial, with a focus on baseline fluid biomarkers, neuroimaging and clinical data. The participants met the strict criteria designed to confirm that participants were diagnosed with early-stage MSA and had a mean of two years of motor symptoms. ATH434 is a potential disease modifying therapy based on its ability to redistribute excess labile iron without impairing normal iron storage, inhibit α -synuclein aggregation and reduce oxidative stress. Importantly, the increased iron levels in the trial participants were evident in multiple subcortical brain regions with two distinct patterns of iron accumulations observed. In addition, MSA participants with less than four years of motor symptoms have elevated plasma Neurofilament Light Chain (NfL) levels at baseline which correlate significantly with disease severity.

Title: Neurofilament Light Chain and Clinical Progression in Early Multiple System Atrophy

Lead Author: Daniel O. Claassen, M.D., M.S., Professor of Neurology, Vanderbilt University Medical Center

Results: The poster describes results from the bioMUSE Natural History Study in which changes in clinical severity of 15 patients across a span of 12 months were compared with plasma biomarkers with a goal of establishing meaningful correlations. The advancement of MSA is profoundly aggressive, highlighting the critical need for biomarkers to delineate its progression over time. Emerging interest surrounds the use of the fluid biomarker NfL, found in both cerebrospinal fluid (CSF) and plasma, as an indicator of axonal damage in MSA. This fluid biomarker holds promise for measuring the extent of disease, tracking its progression, and forecasting the onset of clinical manifestations associated with MSA. In this observational study, the plasma NfL and CSF NfL were highly correlated, indicating that the more easily obtained

plasma values have a meaningful relationship with brain pathology. Plasma NfL significantly increased over 12 months, and both plasma and CSF NfL were associated with disease progression in MSA. These data suggest that NfL may be a marker of disease modification in studies of MSA.

Title: Effects of ATH434, a Clinical-Phase Small Molecule with Moderate Affinity for Iron, in Hemiparkinsonian Macaques

Lead Author: Margaret Bradbury, Vice President, Research and Nonclinical Development, Alterity Therapeutics

Results: The presentation demonstrated that ATH434 treatment led to lower iron levels in the affected area of the brain, the substantia nigra, and improved motor performance and general function in monkeys with experimentally induced Parkinson's disease. At week 12, all 6 ATH434-treated macaques had stable or improving scores from Baseline while two of three vehicle-treated macaques did not demonstrate improvement. The improved general behavior was well-correlated with reduced motor impairment. These favorable parkinsonian outcomes observed in each of the ATH434-treated monkeys were also associated with increased levels of striatal synaptophysin, a protein marker that reflects functional connections between neurons, suggesting functional recovery of nerve endings in this critical motor pathway. These results support further investigation of ATH434 for the treatment of Parkinson's disease.

The poster presentations can be found on Alterity's website [here](#).

About ATH434

Alterity's lead candidate, ATH434, is an oral agent designed to inhibit the aggregation of pathological proteins implicated in neurodegeneration. ATH434 has been shown preclinically to reduce α -synuclein pathology and preserve neuronal function by restoring normal iron balance in the brain. As an iron chaperone, it has excellent potential to treat Parkinson's disease as well as various Parkinsonian disorders such as Multiple System Atrophy (MSA). ATH434 successfully completed Phase 1 studies demonstrating the agent is well tolerated and achieved brain levels comparable to efficacious levels in animal models of MSA. ATH434 is currently being studied in two clinical trials: Study ATH434-201 is a randomized, double-blind, placebo-controlled Phase 2 clinical trial in patients with early-stage MSA and Study ATH434-202 is an open-label Phase 2 Biomarker trial in patients with more advanced MSA. ATH434 has been granted Orphan drug designation for the treatment of MSA by the U.S. FDA and the European Commission.

About ATH434-201 Phase 2 Clinical Trial

The ATH434-201 Phase 2 clinical trial is a randomized, double-blind, placebo-controlled investigation of ATH434 in patients with early-stage MSA. The study will evaluate the effect of ATH434 treatment on neuroimaging and protein biomarkers to demonstrate target engagement

and clinical endpoints to demonstrate efficacy, in addition to assessments of safety and pharmacokinetics. Selected biomarkers, such as brain iron and aggregating α -synuclein, are important contributors to MSA pathology and are therefore appropriate targets to demonstrate drug activity. Wearable sensors have also been employed to evaluate motor activities that are important to patients with MSA. The study enrolled 77 adults who were randomly assigned to receive one of two dose levels of ATH434 or placebo. Participants will receive treatment for 12 months which will provide an opportunity to detect changes in efficacy endpoints to optimize design of a definitive Phase 3 study. Additional information on the Phase 2 trial can be found by [ClinicalTrials.gov Identifier: NCT05109091](https://clinicaltrials.gov/ct2/show/study/NCT05109091).

About bioMUSE

Biomarkers of progression in Multiple System Atrophy (bioMUSE) is a natural history study that aims to track the progression of individuals with MSA, a parkinsonian disorder without approved therapy. The study is being conducted in collaboration with Vanderbilt University Medical Center in the U.S. under the direction of Daniel Claassen, M.D., M.S., Professor of Neurology and Principal Investigator. Natural history studies are important for characterizing disease progression in selected patient populations. The study has provided rich data for optimizing the design of Alterity's randomized ATH434-201 Phase 2 clinical trial and enrolled approximately 20 individuals with clinically probable or clinically established MSA. BioMUSE continues to provide vital information on early stage MSA patients, informs the selection of biomarkers suitable to evaluate target engagement and preliminary efficacy, and delivers clinical data to characterize disease progression in a patient population that mirrors those currently enrolling in the Phase 2 clinical trial.

About Multiple System Atrophy

Multiple System Atrophy (MSA) is a rare, neurodegenerative disease characterized by failure of the autonomic nervous system and impaired movement. The symptoms reflect the progressive loss of function and death of different types of nerve cells in the brain and spinal cord. It is a rapidly progressive disease and causes profound disability. MSA is a Parkinsonian disorder characterized by a variable combination of slowed movement and/or rigidity, autonomic instability that affects involuntary functions such as blood pressure maintenance and bladder control, and impaired balance and/or coordination that predisposes to falls. A pathological hallmark of MSA is the accumulation of the protein α -synuclein within glia, the support cells of the central nervous system, and neuron loss in multiple brain regions. MSA affects at least 15,000 individuals in the U.S., and while some of the symptoms of MSA can be treated with medications, currently there are no drugs that are able to slow disease progression and there is no cure.¹

¹[Multiple System Atrophy | National Institute of Neurological Disorders and Stroke \(nih.gov\)](https://www.ninds.nih.gov/health-information/disorders/multiple-system-atrophy)

About Parkinson's Disease

Parkinson's disease (PD) is the second most common neurodegenerative disorder and causes unintended or uncontrollable movements of the body along with neuropsychiatric and other nonmotor features. The precise cause of PD is unknown, but some cases are hereditary while others are thought to occur from a combination of genetics and environmental factors that trigger the disease. In PD, brain cells become damaged or die in the substantia nigra, the part of the brain that produces dopamine--a chemical needed to produce smooth, purposeful movement. The cardinal symptoms of PD are tremors, rigidity, slowing of movements, and later in disease, impaired balance. Other symptoms may include difficulty swallowing, chewing, or speaking; emotional changes; urinary problems or constipation; dementia or other cognitive problems; fatigue; and problems sleeping.³ Nearly one million people in the U.S. and more than 10 million people worldwide are living with PD. Approximately 60,000 Americans are diagnosed with PD each year.⁴

¹Beauchamp et al, "ATH434 Rescues Pre-motor Hyposmia in a Mouse Model of Parkinsonism, *Neurotherapeutics*, DOI:[10.1007/s13311-022-01300-0](https://doi.org/10.1007/s13311-022-01300-0)

²Xiao, et al, "Hyposmia: a possible biomarker of Parkinson's disease" *Neurosci Bull.* 2014 Feb; 30(1): 134–140.

³National Institute of Health: Neurological Disorders and Stroke, Parkinson's Disease Information Page;

⁴Parkinson's Foundation

About Alterity Therapeutics Limited

Alterity Therapeutics is a clinical stage biotechnology company dedicated to creating an alternate future for people living with neurodegenerative diseases. The Company's lead asset, ATH434, has the potential to treat various Parkinsonian disorders and is currently being evaluated in two Phase 2 clinical trials in Multiple System Atrophy. Alterity also has a broad drug discovery platform generating patentable chemical compounds to treat the underlying pathology of neurological diseases. The Company is based in Melbourne, Australia, and San Francisco, California, USA. For further information please visit the Company's web site at www.alteritytherapeutics.com.

Authorisation & Additional information

This announcement was authorized by David Stamler, CEO of Alterity Therapeutics Limited.

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Forward Looking Statements

This press release contains "forward-looking statements" within the meaning of section 27A of the Securities Act of 1933 and section 21E of the Securities Exchange Act of 1934. The Company has tried to identify such forward-looking statements by use of such words as "expects," "intends," "hopes," "anticipates," "believes," "could," "may," "evidences" and "estimates," and other similar expressions, but these words are not the exclusive means of identifying such statements.

Important factors that could cause actual results to differ materially from those indicated by such forward-looking statements are described in the sections titled "Risk Factors" in the Company's filings with the SEC, including its most recent Annual Report on Form 20-F as well as reports on Form 6-K, including, but not limited to the following: statements relating to the Company's drug development program, including, but not limited to the initiation, progress and outcomes of clinical trials of the Company's drug development program, including, but not limited to, ATH434, and any other statements that are not historical facts. Such statements involve risks and uncertainties, including, but not limited to, those risks and uncertainties relating to the difficulties or delays in financing, development, testing, regulatory approval, production and marketing of the Company's drug components, including, but not limited to, ATH434, the ability of the Company to procure additional future sources of financing, unexpected adverse side effects or inadequate therapeutic efficacy of the Company's drug compounds, including, but not limited to, ATH434, that could slow or prevent products coming to market, the uncertainty of obtaining patent protection for the Company's intellectual property or trade secrets, the uncertainty of successfully enforcing the Company's patent rights and the uncertainty of the Company freedom to operate.

Any forward-looking statement made by us in this press release is based only on information currently available to us and speaks only as of the date on which it is made. We undertake no obligation to publicly update any forward-looking statement, whether written or oral, that may be made from time to time, whether as a result of new information, future developments or otherwise.