Alterity Therapeutics Raises Profile with Multiple Data Presentations at the International Congress of Parkinson's Disease and Movement Disorders®

- ATH434 shows promise as a disease-modifying therapy for MSA -

- ATH434-202 Phase 2 interim data demonstrate stabilization of clinical symptoms and biomarkers in clinical responders -

MELBOURNE, AUSTRALIA AND SAN FRANCISCO, USA – 2 October 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 multiple oral and poster presentations were presented at the International Congress of Parkinson's Disease and Movement Disorders® (MDS).

"We significantly raised the profile of Alterity and ATH434 at the MDS Congress with several data presentations, including a late breaking oral presentation on data from our ATH434-202 Phase 2 open-label clinical trial in Multiple System Atrophy (MSA)," said, David Stamler, M.D., Chief Executive Officer of Alterity Therapeutics. "At the Congress, we presented data from both of our Phase 2 clinical trials with ATH434, preclinical data on ATH434 in Parkinson's disease, and findings from our bioMUSE natural history study that continues to advance our understanding of MSA. Taken together, the data demonstrate the potential for ATH434 to modify disease progression and reduce disability in individuals living with MSA."

Dr. Stamler, continued, "In the open-label Phase 2 study, 30% of participants showed stable or improved clinical outcomes (clinical responders). In addition, the clinical responders demonstrated stability in objective biomarkers such as brain iron and a protein marker of nerve damage, when compared to non-responders. Taken together, these data suggest that ATH434 has potential as a disease modifying treatment."

"At the conference, we also presented baseline clinical and biomarker data from our ATH434-201 randomized, double-blind clinical trial. Based on the learnings from our bioMUSE natural history study, we employed strict selection criteria to confirm that participants were diagnosed with early-stage (clinically probable) MSA, giving us the best chance of success from the trial. Looking ahead, we expect to present the topline data from ATH434-201 in January 2025 and the 12-month data from ATH434-202 later in the year. We are grateful to the study participants and their families as well as the clinical sites for their dedication to make the Phase 2 trials successful," concluded Dr. Stamler.

Presentation Summaries

Late-Breaking Oral Presentation and Poster on ATH434-202 Interim Data

Title: **Preliminary Efficacy and Safety of ATH434 in Multiple System Atrophy**

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

Format: Late Breaking Oral Platform Presentation and Poster Session

Results: The interim data suggest that ATH434 may have a disease-modifying effect in MSA, with 30% of participants showing stable or improved clinical outcomes (clinical responders). The average change in Unified MSA Rating Scale Part I (UMSARS I) scores over 6 months is smaller than typically observed in untreated MSA patients. At 6 months all participants exhibited brain volume declines consistent with MSA progression; however, the clinical responders maintained stable brain volumes at 12 months. Importantly, ATH434 was well tolerated with no drug-related serious adverse events, and most adverse events were mild to moderate, showing a favorable safety profile. Together, these early outcomes suggest that ATH434 could have a potential to modify disease progression.

Neurofilament light chain (NfL) levels are a measure of neuronal injury and are often correlated with disease severity. In the Phase 2 trial, the clinical responders had stable or reduced NfL levels: at 6 months, the average increases in NfL were 2.7% in CSF and 4.5% in plasma, compared to 17.9% and 19.3% in Alterity's bioMUSE natural history participants, respectively. In addition, clinical responders also showed stability in iron levels in the substantia nigra, putamen, and globus pallidus compared to non-responders with increased iron. The stabilization of iron content in these subcortical brain regions, combined with NfL biomarker data, indicates that ATH434 may slow neurodegeneration by modulating brain iron levels and reducing oxidative injury.

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

Format: Oral Platform Presentation and Poster Session

Results: The oral presentation and poster describe the baseline characteristics for the 77 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 strict selection criteria designed to confirm that participants had early-stage (clinically probable) MSA. The accuracy of diagnosing clinically probable MSA may be increased using a multimodal approach that includes neuroimaging biomarkers (increased iron content, reduced subcortical volumes) and fluid biomarkers such as NfL. 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 injury. Importantly, increased iron levels were

evident in multiple subcortical brain regions, with increased levels being observed in the substantia nigra in nearly all subjects.

Title: **Association Between Clinical Progression in Multiple System Atrophy and Brain Volume Changes Evaluated via Deep Learning Segmentation**

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

Format: Poster Session

Results: The poster describes results from the "Biomarkers of progression in Multiple System Atrophy" (bioMUSE) natural history study designed to track the progression of individuals with MSA. For participants enrolled in bioMUSE, fluid and imaging biomarkers, along with clinical manifestations, were used to classify patients as MSA (n=10: 6 MSA-P, 4 MSA-C) or Parkinson's Disease/Dementia with Lewy Bodies (n=5). Patients who tested negative for alpha-synuclein (n=2) were excluded from the analyses. In the trial, novel MRI imaging techniques and deep learning segmentation were used to assess brain volume across brain Regions of Interest (ROI) relevant to MSA. Structural MRI plays a critical role in both diagnosing MSA and monitoring disease progression. Subcortical brain volume shows potential as a biomarker for evaluating disease-modifying therapies. Over the course of one year, MRI with deep-learning segmentation revealed significant brain volume reduction in MSA ROIs whereas the PD patients showed no significant brain volume changes. In contrast, the MSA patients exhibited significant volume reductions in the cerebellum, globus pallidus, and brainstem. In addition, the MSA-P patients showed significant volume loss in the putamen. The results illustrate the correlation between the brain volume reduction and worsening clinical scores, as measured by the UMSARS, providing a visual representation of disease progression.

Title: **Effects of ATH434, a Clinical-Phase Small Molecule with Moderate Affinity for Iron, in a Parkinson's Disease Model in Macaques**

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

Presentation: Poster Session

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 5 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 ATH434-202 Phase 2 Clinical Trial

The ATH434-202 Phase 2 clinical trial is an open label study, entitled "A Biomarker Study of ATH434 in Participants with MSA." The Biomarker trial enrolled 10 individuals with advanced MSA. ATH434-202 study participants will receive treatment with ATH434 for 12-months. The study will assess the effect of ATH434 treatment on neuroimaging and protein biomarkers to evaluate target engagement, in addition to clinical measures, safety, and pharmacokinetics. The selected biomarkers, including brain volume, iron and aggregating α-synuclein, are important contributors to MSA pathology and are appropriate targets to demonstrate drug activity. The primary objective of this study is to evaluate the impact of 12 months treatment with ATH434 on brain volume in a more advanced patient population than is being studied in Alterity's randomized Phase 2 trial. Final, 12-month data from the ATH434-202 trial are expected in the first half of 2025. Additional information on the open label Phase 2 trial can be found at clinicaltrials.gov identifier: NCT05864365.

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.

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]

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.[2] 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.[3]

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.

Sources:
[1]Multiple System Atrophy | National Institute of Neurological Disorders and Stroke (nih.gov)
[2]National Institute of Health: Neurological Disorders and Stroke, Parkinson's Disease Information Page; [3]Parkinson's Foundation

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.