Alterity Therapeutics Presents Encouraging New Data from its ATH434 Phase 2 Trial in Multiple System Atrophy at the American Academy of Neurology Annual Meeting

– Clinically Meaningful Efficacy Observed on Multiple Assessments –

– Confirmed Target Engagement with Reduced Iron Signal in MSA Affected Brain Regions –

MELBOURNE, AUSTRALIA AND SAN FRANCISCO, USA – 10 April 2025: 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 new presentations related to its Multiple System Atrophy (MSA) program were delivered at the American Academy of Neurology (AAN) 2025 Annual Meeting, one of the premier global neurology meetings. Notably, new data from the ATH434-201 trial was prominently featured via an oral presentation during a Scientific Platform Session on Movement Disorders.

"We are excited to present these new data from our double-blind Phase 2 trial, reinforcing the potential of ATH434 to significantly modify disease progression in MSA. The clinical results from this study are important given the lack of available treatments to address the underlying pathology in MSA," said, David Stamler, M.D., Chief Executive Officer of Alterity. "Importantly, we saw clinically meaningful efficacy on multiple measures including the UMSARS[1] I activities of daily living scale, the clinical global impression of severity, the orthostatic hypotension symptom assessment, and activity levels from wearable sensors. In addition, new analyses of neuroimaging data show target engagement of ATH434 on iron levels in MSA affected regions of the brain. We look forward to engaging with the U.S. Food and Drug Administration and other regulatory authorities as we seek to advance the development of this potentially disease modifying therapy for individuals living with MSA."

"In addition, results from the bioMUSE natural history study were presented by our collaborators at Vanderbilt University Medical Center on the use of wearable sensors to assess outpatient activity. These data support the utility of digital outcomes in MSA trials and reinforce the relevance of the findings in our double-blind trial," concluded Dr. Stamler.

Type: **Oral Presentation**

Title: **Topline Data from a Randomized, Double Blind, Placebo Controlled Phase 2 Study of ATH434 in Multiple System Atrophy**

Presenter: Daniel Claassen, M.D., M.S., Professor of Neurology at Vanderbilt University Medical Center

Summary: The oral presentation produced additional data on Alterity's ATH434-201 Phase 2 clinical trial. Overall, the study results support continued advancement of ATH434 for the treatment of MSA. The imaging outcomes in n=61 participants indicate a heterogeneous localization of pathology and evidence that ATH434 reduces the iron signal in MSA affected brain regions. The clinical analysis included 71 patients who had at least one-post baseline UMSARS I assessment. The data showed that on the modified UMSARS I rating scale, ATH434 demonstrated a clinically significant treatment effect versus placebo with a 48% decrease in clinical progression at the 50 mg dose ($p=0.02$)^ and a 30% decrease in clinical progression at the 75 mg dose at 52 weeks. Additional assessments showed improvement: the Clinical Global Impression of Severity Scale[2] (7-point scale, higher score worse), including a nominally significant difference at the 50 mg dose ($p=0.0088$) at 52 weeks. The Orthostatic Hypotension Symptom Assessment (patient reported outcome) showed trends favoring benefit in both groups ($p=0.08$ at 50 mg dose, $p=0.14$ at 75 mg dose). Increased activity in the outpatient setting was seen on wearable sensors at both dose levels as compared to placebo, with observed improvements in step count, bouts of walking, total walking time, and total standing time. The benefit on step count at 50 mg was nominally significant ($p<0.05$).

Type: **Poster Presentation**

Title: **Association Between Wearable Sensor Data and Clinical Scores in Individuals with Early-stage Multiple System Atrophy**

Presenter: Ashkan Vaziri, PhD, BioSensics LLC

Summary: The poster described the n=18 patients with clinically probable MSA who wore sensors for continuous monitoring of physical activity during our bioMUSE natural history study. The study determined the association between gold-standard clinical measures and sensor-derived parameters of locomotion, posture, and postural transitions at baseline. From this, machine learning models were developed to investigate whether sensor-derived measures could predict scores and performance on clinical evaluations. The study found that sensor-derived metrics, specifically those measuring walking and postural transitions, may increase the understanding of impairments associated with MSA. Across several tests, the participants who had increased walking time, walking episodes, and higher step counts had better scores on the tandem walk and Timed Up and Go (TUG). Additionally, positive relationships were identified between the average sit-to-stand and stand-to-sit durations with motor rating scales such as the MSA Rating Scale (UMSARS-II), the motor section of the Parkinson's Plus Rating Scale (NNIPPS-PPS[3]), and the TUG. Importantly, regression models established successful prediction of clinical scores, with TUG demonstrating the highest explained variance.

The poster presentations will be available on the Alterity 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 recently announced positive results from the randomized, double-blind, placebo-controlled Phase 2 clinical trial in patients with early-stage MSA. A second Phase 2 open-label 2 Biomarker trial in patients with more advanced MSA is ongoing. 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 12 months treatment with ATH434 in patients with MSA. The study evaluated the efficacy, safety and pharmacokinetics of ATH434 as well as the effect of ATH434 on neuroimaging and protein biomarkers. Wearable sensors were employed to evaluate motor activities outside of the clinic. The study enrolled 77 adults who were randomly assigned to receive ATH434 50 mg or 75 mg twice daily or matching placebo. The topline data showed that ATH434 produced clinically and statistically significant improvement on the modified UMSARS Part I, a functional rating scale that assesses disability on activities of daily living affected in MSA. In addition to the robust efficacy demonstrated on the UMSARS Part I, trends in improved motor performance were observed on the Parkinson's Plus rating scale and overall benefit was shown on the Clinical Global Impression of Severity at the 50 mg dose. Wearable sensor data indicated that both dose levels of ATH434 led to increased activity in an outpatient setting as compared to placebo. Biomarkers were used to evaluate potential drug effect and target engagement. Both dose levels reduced iron accumulation in MSA affected brain regions and trends in preservation of brain volume were observed relative to placebo. 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.[4]

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 is initially focused on developing disease modifying therapies in Parkinson's disease and related disorders. Alterity recently reported positive data for its lead asset, ATH434, in a Phase 2 clinical trial in participants with Multiple System Atrophy (MSA), a rare and rapidly progressive Parkinsonian disorder. ATH434 is also being evaluated in a Phase 2 clinical trial in advanced MSA. In addition, Alterity 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 website at www.alteritytherapeutics.com.

References:

[1] UMSARS: Unified Multiple System Atrophy Rating Scale

^ All p-values are uncorrected

[2] Clinical Global Impression of Severity: a clinician assessment of the total picture of the subject including the impact of the illness on function and level of distress

[3] NNIPPS-PPS: Natural History and Neuroprotection in Parkinson Plus Syndromes - Parkinson Plus Scale

[4] Multiple System Atrophy | National Institute of Neurological Disorders and Stroke (nih.gov)

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.