Alterity Therapeutics Prominently Featured at the International MSA Congress

– ATH434 Phase 2 data demonstrated clinically meaningful efficacy on multiple clinical endpoints –

– MSA Atrophy Index (MSAai) enhances MSA diagnosis and monitoring –

– bioMUSE Study shows higher α- synuclein concentration is associated with greater burden of orthostatic symptoms –

MELBOURNE, AUSTRALIA AND SAN FRANCISCO, USA – 12 May 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 several oral and poster presentations related to Alterity's clinical programs in Multiple System Atrophy (MSA) were featured at the 2025 International MSA Congress. The Congress was presented by Mission MSA, a non-profit organization dedicated to improving the quality of life and building hope for people affected by MSA through support services, educational resources, research funding, and community engagement.

"The MSA Congress gave us an opportunity to share the results of our Phase 2 double-blind trial of ATH434 with prominent MSA clinicians and scientists as well as community members affected by MSA," said David Stamler, M.D., Chief Executive Officer of Alterity. "The robust efficacy of ATH434, as indicated by reduced disease severity on the MSA activities of daily living scale along with improvement in key symptoms of MSA and preserved activity in the outpatient setting, continue to generate enthusiasm. Our clinical progress is generating significant excitement, and we are focused on bringing this therapy to patients as quickly as possible."

"In addition, our colleagues at Vanderbilt University Medical Center presented data from our bioMUSE Natural History Study that highlights the understanding of MSA we have brought to our development program. Because of the variability in MSA presentation and progression and its similarity to Parkinson's disease, it is critical to improve diagnostic and monitoring tools. Through development of a novel imaging biomarker known as the MSA Atrophy Index (MSAai), we have a new tool to measure and track brain volume in individuals with MSA. In a separate presentation, the bioMUSE study demonstrated that α-synuclein levels in the skin increased over the 12-month follow-up period, and that a higher concentration of α-synuclein in skin is associated with greater burden of orthostatic symptoms, a valuable finding that confers insight into disease progression."

Presentation Highlights:

ATH434 Slowed Disease Progression in a Phase 2 Study in Multiple System Atrophy
Presenter: David Stamler, M.D., Chief Executive Officer of Alterity

The oral and poster presentation highlighted data from Alterity's ATH434-201 Phase 2 clinical trial. The clinical analysis included 71 patients who had at least one post-baseline assessment of the key clinical endpoint, the modified UMSARS[1] I activities of daily living scale. On this endpoint, ATH434 demonstrated a clinically significant reduction in disease severity versus placebo, with a 48% relative treatment effect at the 50 mg dose (p=0.02)^ and a 30% relative treatment effect at the 75 mg dose (p=0.16) at 52 weeks. Additional efficacy assessments showed improvement consistent with the UMSARS I findings: the Clinical Global Impression of Severity Scale[2] demonstrated improvement compared to placebo at both dose levels, with difference at 50 mg achieving nominal statistical significance (p=0.0088). On the Orthostatic Hypotension Symptom Assessment (a patient reported outcome), on average placebo patients worsened by approximately 6 points over 52 weeks whereas both ATH434 treatment groups improved over the same period (p=0.08 at 50 mg, p=0.14 at 75 mg). Baseline differences in disease severity likely explain different response in 50 mg and 75 mg treatment groups.

Increased activity in the outpatient setting was observed at both dose levels as compared to placebo with wearable sensors, with clinically meaningful improvements in step count, bouts of walking, total walking time, and total standing time. ATH434 was well tolerated with similar adverse event rates compared to placebo and no serious adverse events attributed to ATH434. Regarding neuroimaging in 61 participants, ATH434 demonstrated target engagement by stabilizing or reducing iron accumulation at both dose levels compared to placebo in MSA affected brain regions. In addition, ATH434 demonstrated trends in reducing brain atrophy at both dose levels compared to placebo. Overall, the study results support continued advancement of ATH434 for the treatment of MSA.

MSA Atrophy Index (MSAai): A Quantitative Imaging Marker for Diagnosis and Monitoring of Multiple System Atrophy
Presenter: Amy Brown, M.D., M.S., Assistant Professor, Movement Disorders Division, Department of Neurology, Vanderbilt University Medical Center

This oral presentation described the MSA Atrophy Index (MSAai) as a promising imaging biomarker that distinguishes MSA from related disorders, correlates with clinical presentation, and tracks disease progression. Its implementation has the potential to enhance MSA diagnosis and monitoring in both clinical trials and clinical practice. The MSAai imaging tool was developed by the team at Vanderbilt University Medical Center as part of the bioMUSE Natural History Study. The study evaluated the utility of volumetric measures and the MSAai in distinguishing early MSA from other movement-related disorders, correlating with clinical presentation, and

tracking longitudinal changes in brain structure. The study results showed that fluid biomarkers classified bioMUSE participants into MSA (n=10), Lewy body disorders (n=5; PD or DLB), and α-synuclein-negative (n=2) groups. At baseline, MSA patients had significantly lower LN, brainstem, cerebellum, and MSAai values compared to HC, PD, DLB, and PAF (all p<0.001). The MSAai demonstrated strong group discrimination, correlated with UMSARS scores (ρ=-0.46, p=0.038), and predicted clinical progression (ρ=0.58, p=0.022). Longitudinally, reductions in LN, brainstem, and MSAai volumes were strongly associated with UMSARS progression.

Cutaneous Phosphorylated Alpha-Synuclein Deposition Informs Autonomic Function in Individuals with Early-Stage Multiple System Atrophy
Presenter: Leah Mann, PhD, Postdoctoral Research Fellow, Vanderbilt University Medical Center

This poster presentation evaluated 17 participants from the bioMUSE Natural History Study who met criteria for clinically probable MSA. The study compared α-synuclein deposition in skin at baseline and 12 months later and examined associations between clinical measures and α-synuclein quantitation over the year. The analysis described the relationship between α-synuclein and autonomic function and revealed that cutaneous α-synuclein detection may serve as an effective diagnostic biomarker that can additionally track progression of MSA. Importantly, deposition of α-synuclein may confer insight into symptomatology, as higher α- synuclein concentration is associated with greater burden of orthostatic symptoms. In the analysis, 100% (17/17) of patients exhibited detection of phosphorylated α-synuclein by skin biopsy. Cutaneous α-synuclein deposition significantly increased (p = 0.042) from baseline (mean = 6.59 ± 4.37) to 12-month follow-up (mean = 7.71 ± 4.22). Deposition at 12-month follow-up was positively correlated with Orthostatic Hypotension Questionnaire (OHQ) and Composite Autonomic Symptom Score-31 (COMPASS-31) (OHQ: coefficient = 0.579, p = 0.015; COMPASS-31: coefficient = 0.560, p = 0.024).

Presentations will be available on the Alterity Therapeutics 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 in preclinical models. 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). Phase 1 studies have demonstrated the agent is well tolerated and achieved brain levels comparable to efficacious levels in animal models of MSA. Positive results from the randomized, double-blind, placebo-controlled Phase 2 clinical trial in patients with MSA demonstrated robust clinical efficacy, target engagement on key biomarkers, and a favorable safety profile. A second

Phase 2 open-label biomarker trial in patients with more advanced MSA is ongoing. ATH434 has been granted Fast Track Designation by the U.S. FDA, and Orphan Drug Designation by the U.S. FDA and the European Commission for the treatment of MSA.

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 data showed that, compared to placebo, ATH434 produced clinically and statistically significant improvement on the modified Unified Multiple System Atrophy Rating Scale (UMSARS) Part I, a functional rating scale that assesses disability on activities of daily living affected in MSA. Additional efficacy assessments demonstrated improvement consistent with the positive UMSARS Part I findings including trends in improved motor performance on the Parkinson's Plus rating scale, the Clinical Global Impression of Severity Scale, and the Orthostatic Hypotension Symptom Assessment (a patient reported outcome). Wearable sensor data indicated that ATH434 also led to increased activity in an outpatient setting. Biomarkers were used to evaluate potential drug effect and target engagement relative to placebo. Both dose levels reduced iron accumulation in MSA affected brain regions with trends in preservation of brain volume. ATH434 was well tolerated with similar adverse event rates compared to placebo and no serious adverse events attributed to ATH434. 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]

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

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.

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.