Alterity Therapeutics Presents Positive Data from ATH434 Phase 2 Trial at the 2025 International Congress of Parkinson's Disease and Movement Disorders

– Data demonstrate ATH434 slows disease progression and stabilizes orthostatic hypotension –

– New analysis increases overall confidence in the Phase 2 trial results –

– State-of-the-art neuroimaging and biomarker analysis advance understanding of MSA diagnosis –

MELBOURNE, AUSTRALIA AND SAN FRANCISCO, USA – 9 October 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 data from the ATH434-201 randomized, double-blind Phase 2 clinical trial in Multiple System Atrophy (MSA) was featured at the 2025 International Congress of Parkinson's Disease and Movement Disorders (MDS) that took place in Honolulu, HI, USA.

"The aggregate data from our double-blind trial continue to demonstrate the potential of ATH434 as a disease modifying therapy for MSA," said David Stamler, M.D., Chief Executive Officer of Alterity. "The positive data from our ATH434-201 trial have demonstrated a slowing of disease progression and stabilization of orthostatic hypotension, one of the most challenging MSA symptoms to manage. The MDS conference gave us the opportunity to present new analyses from our double-blind Phase 2 trial that increase our overall confidence in ATH434. When we accounted for baseline differences in an important predictor of disease progression, the efficacy signal at the 75 mg dose strengthened meaningfully on the key clinical endpoint of UMSARS I[1] at 52 weeks. This new analysis continues to support our belief that ATH434 has great potential to treat this devastating disease."

"In addition, we presented data assessing the state-of-the-art neuroimaging and biomarkers employed in our trial to refine the diagnosis of MSA and track the evolution of the disease across the two main clinical phenotypes, MSA-P and MSA-C. We remain committed to advancing ATH434 to the next stage of development while striving to become the market leader dedicated to improving the overall treatment paradigm for MSA," concluded Dr. Stamler.

Presentation Highlights:

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

Dr. Stamler's oral platform presentation provided results from the ATH434-201 trial with new analyses related to orthostatic hypotension (OH), one of the most debilitating MSA symptoms. Clinical endpoints were analyzed in the clinical analysis population (n=71) that included patients randomized to treatment who had at least one post-baseline assessment of the key clinical endpoint, the UMSARS I. There were three arms in the trial comparing two dose levels of ATH434 50 mg (n=25) and 75 mg (n=24) to placebo (n=22), all of which were administered twice daily. Treatment with ATH434 resulted in a clinically significant reduction in disease severity relative to placebo on the modified UMSARS I activities of daily living scale at both dose levels, with a 48% relative treatment effect at the 50 mg dose ($p=0.02$)[2] and a 30% relative treatment effect at the 75 mg dose at 52 weeks. UMSARS I is the key outcome measure of interest to regulatory authorities such as the FDA.

The presentation described additional analysis regarding OH, which is a form of low blood pressure that occurs when a person stands up from a sitting or lying position, resulting in symptoms like dizziness, lightheadedness, or fainting. It is defined as a sustained decrease in systolic blood pressure of at least 20 mm Hg or diastolic blood pressure of at least 10 mm Hg within three minutes of standing.

Because baseline data revealed that severe OH was substantially higher in the 75 mg group (29.2% vs 4% in 50 mg and 4.5% in placebo) at enrollment, a new analysis of the USMARS I was conducted that included the baseline OH systolic blood pressure change as a covariate. When this variable was included in the analysis of the UMSARS I at 52 weeks, the efficacy signal in 75 mg dose group strengthened to -2.8 points for a relative treatment effect of 35%. This baseline difference in severe OH largely explains the different responses in 50 mg and 75 mg treatment groups. Notably, ATH434 demonstrated a beneficial effect on OH symptoms as assessed with the OH Symptom Assessment, a patient reported outcome. On this scale, placebo patients worsened on average by approximately 6 points over 52 weeks whereas the 50 mg and 75 mg groups were stable over the same period of time.

Additional efficacy assessments showed improvement consistent with the UMSARS I findings. The Clinical Global Impression of Severity Scale[3] demonstrated improvement compared to placebo at both dose levels, with difference at 50 mg achieving statistical significance ($p=0.009$). Increased activity in the outpatient setting, as measured by wearable movement sensors, was observed at both dose levels as compared to placebo, with clinically meaningful improvements in step count, total walking time, bouts of walking, and total standing time. Regarding neuroimaging data in 61 participants, ATH434 demonstrated target engagement by reducing iron accumulation at both dose levels compared to placebo in the globus pallidus, and in the putamen and substantia nigra at the 50 mg dose level. In addition, ATH434 demonstrated trends in reducing brain atrophy at both dose levels compared to placebo. ATH434 was well tolerated with

similar adverse event rates compared to placebo and no serious or severe adverse events attributed to ATH434.

Relationship Between Alpha-Synuclein Aggregation Profiles, Imaging Biomarkers, and Disease Severity in a Phase 2 Study of ATH434 in MSA

Presenter: Margaret Bradbury, Ph.D., Vice President, Research and Nonclinical Development, Alterity

As a Parkinsonian disorder, MSA shares several symptoms with Parkinson's disease that can hamper accurate diagnoses and differentiation between the two diseases. Alterity's ATH434-201 trial provides an opportunity to compare α-synuclein aggregation profiles, imaging biomarkers, and disease severity at baseline to inform future patient selection. In Dr. Bradbury's presentation the imaging biomarkers utilized in the ATH434-201 trial presented supportive features of MSA in 96.1% of the 77 enrolled subjects as compared to 78.9% for α-synuclein aggregation profiles in cerebrospinal fluid (CSF) alone (60 of 76). Of the 11 participants with an α-synuclein aggregation profile consistent with Parkinson's disease and/or dementia with Lewy bodies, 80% demonstrated supportive imaging features of MSA. Two of the 5 participants without evidence of α-synuclein aggregation had imaging consistent with MSA. Therefore, the presentation concludes that a multimodal approach combining α-synuclein aggregation profiles with clinical and imaging data may enhance diagnostic accuracy in MSA.

Differences Between Clinical and Imaging Phenotypes in Phase 2 Study of ATH434 in Multiple System Atrophy

Author: Paula Trujillo, Ph.D., Research Assistant Professor, Department of Neurology, Vanderbilt University Medical Center

Dr. Trujillo's presentation assessed the two main clinical phenotypes of MSA in Alterity's ATH434-201 trial: the parkinsonian (MSA-P, n=47) and cerebellar (MSA-C, n=25). The clinical subtypes were assigned by the site investigators and were compared with multiple neuroimaging assessments including MRI, quantitative susceptibility mapping (QSM) to measure brain iron, and automated segmentation to measure brain atrophy. The results show that quantitative MRI largely complements clinical classification (90% concordance), reinforcing its role as an objective biomarker. The observed discordance (10%) suggests MRI may capture underlying pathology not evident clinically, highlighting its value in refining diagnosis and tracking disease evolution.

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. Positive data from a second Phase 2 open-label biomarker trial in patients with more advanced MSA reinforced these results. ATH434 has been granted Fast Track Designation by the U.S. Food and Drug Administration (FDA), and Orphan Drug Designation by the 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 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 up to 50,000 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 has demonstrated clinically meaningful efficacy for its lead asset, ATH434, in a randomized, double-blind, placebo-controlled Phase 2 clinical trial in participants with Multiple System Atrophy (MSA), a rare and rapidly progressive Parkinsonian disorder. ATH434 recently reported positive data in its open label 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.

[1] UMSARS I: Unified Multiple System Atrophy Rating Scale Part I

[2] All p-values are uncorrected

[3] 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

[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.

Contacts:

Investors
Remy Bernarda
Investor Relations Advisory Solutions
ir@alteritytx.com
+1 (415) 203-6386

Media
Casey McDonald
Tiberend Strategic Advisors, Inc.
cmcdonald@tiberend.com
+1 (646) 577-8520

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.