Alterity Therapeutics Announces Publication on Novel MRI Endpoint from the bioMUSE Natural History Study

– Peer-reviewed publication in Annals of Clinical and Translational Neurology highlights the use of the MSA Atrophy Index developed to diagnose and track disease progression in Multiple System Atrophy –

MELBOURNE, AUSTRALIA AND SAN FRANCISCO, USA – 24 July 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 an innovative neuroimaging measure developed in Alterity's Biomarkers of Progression in Multiple System Atrophy (bioMUSE) Natural History Study was featured in the peer-reviewed journal *Annals of Clinical and Translational Neurology*.

The publication, entitled "The MSA Atrophy Index (MSA-AI): An Imaging Marker for Diagnosis and Clinical Progression in Multiple System Atrophy," describes how deep learning methods, a form of artificial intelligence, were used to precisely define the neuroanatomy of key regions in the brain and the development of a novel brain atrophy measure for tracking disease progression in MSA patients over one year. The results were then correlated with clinical measures of disease severity over the same timeframe.

"This research used state-of-the-art technology employed in the bioMUSE study that goes above and beyond traditional MRI methods for assessing brain volume in patients with MSA," said David Stamler, M.D., Chief Executive Officer of Alterity. "Based on the creativity and technical skill of our colleagues at Vanderbilt University Medical Center, we now have superior tools for diagnosing MSA and tracking brain atrophy over time. Importantly, we observed that statistically significant reductions in brain volume over 12 months correlated with clinical worsening of the disease. The results underscore the importance of utilizing advanced neuroimaging methods and analytical tools in evaluating MSA, which we implemented in our Phase 2 clinical program."

"While previous MRI studies have reported brain volume reductions in MSA affected brain regions, tracking these changes reliably has been challenging. Development of the MSA Atrophy Index can enhance the understanding of MSA progression and provide support for using brain atrophy markers for the evaluation of disease-modifying therapies. These tools offer potential applications in diagnosis, staging, and monitoring of disease severity, contributing to more personalized care in MSA. We look forward to leveraging this invaluable technology for patient selection and disease progression in our Phase 3 clinical trial," concluded Dr. Stamler.

The MSA-AI offers an objective, quantifiable measure of brain atrophy in regions commonly affected by MSA, streamlining the evaluation of disease progression and treatment response. This is especially valuable in MSA, where early diagnosis is often hindered by overlapping features with Parkinson's disease (PD) and Dementia with Lewy Bodies (DLB). The MSA-AI provides a phenotype-independent assessment, making it applicable to both MSA-P and MSA-C, despite differing atrophy patterns. By offering a standardized metric of structural change, the MSA-AI has potential to support earlier, more accurate diagnosis and improve clinical trial participant selection.

By leveraging a longitudinal cohort from bioMUSE and a cross-sectional cohort including individuals with more advanced MSA, the study captured a broad spectrum of clinical severity and atrophy patterns. This complementary design allowed the authors to assess both early and established disease, strengthening the generalizability of the findings. MSA patients exhibited significantly lower MSA-AI scores (i.e., reduced brain volumes) compared to all other diagnostic groups ($p < 0.001$). The MSA-AI effectively distinguished MSA from related synucleinopathies (PD and DLB, both $p<0.001$), correlated with baseline clinical severity ($\rho=-0.57$, $p<0.001$), and predicted disease progression ($\rho=-0.55$, $p=0.035$). Longitudinal reductions in MSA-AI were associated with worsening clinical scores over 12 months ($\rho=-0.65$, $p=0.01$).

The full publication can be accessed on Alterity's website here.

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 an 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.