Alterity Therapeutics Reports Positive Interim Data from ATH434-202 Phase 2 Clinical Trial in Multiple System Atrophy

– 43% of Participants Showed Improvement on the UMSARS Activities of Daily Living Scale –

– 29% of Participants had Stable or Improved Neurological Symptoms –

– Objective Biomarkers Demonstrated Improvement Consistent with Clinical Findings –

– ATH434 was Well-Tolerated with No Safety Signals Detected –

MELBOURNE, AUSTRALIA AND SAN FRANCISCO, USA – 17 July 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 positive interim data from the ATH434-202 open-label Phase 2 clinical trial in patients with multiple system atrophy (MSA). ATH434 has been shown preclinically to reduce α-synuclein pathology and preserve neuronal function by restoring normal iron balance in the brain.

The interim analysis included clinical and biomarker data on 7 participants treated with ATH434 for 6 months and neuroimaging data on 3 participants who were treated for 12 months. After 6 months of treatment, 43% of participants showed improvement on the UMSARS[1], indicating reduced disability on activities of daily living. Over the same period, 29% of participants had stable or improved neurological symptoms (clinical responders) as assessed by both the treating physician and the patient. Importantly, the clinical responders on average had reduced accumulation of iron on MRI in the substantia nigra, putamen and globus pallidus and stable levels of NFL, a marker of axonal injury, when compared to participants who declined.

"I am very encouraged by these positive interim data in advanced MSA patients," said David Stamler, M.D., Chief Executive Officer of Alterity. "As MSA is a rapidly progressive and unremitting disease, we expected to see decline in all participants. Instead, we saw favorable clinical and biomarker outcomes in some patients suggesting that ATH434 has the potential to modify the course of this devastating condition. We were also very pleased to see that the clinical responders had biomarker evidence of stable disease as this provides an objective indication of potential efficacy."

Dr. Stamler, continued, "In the ATH434-202 trial, the participants who stabilized or improved with ATH434 treatment had less advanced disease than those who progressed. This is noteworthy as we have enrolled earlier stage MSA patients in our randomized, double-blind clinical trial ATH434-201. Although the number of patients studied thus far is small, the new data reinforces that we have taken the right approach in our randomized trial and increases my overall confidence in the ATH434 development program."

Daniel Classen, M.D., M.S., Professor of Neurology at Vanderbilt University Medical Center and principal investigator for the ATH434-202 Phase 2 study, commented "I am gratified to see that the work we have done over the last several years is bearing fruit as we enhance our understanding of MSA. This has led to improved patient selection and optimized biomarker endpoints in the Alterity Phase 2 trials. The clinical observations in the ATH434-202 study are supported by the objective biomarkers of brain volume, brain iron, and NfL. These early data increase our confidence that we have chosen the right biomarker and clinical endpoints to evaluate the potential effect of ATH434 in individuals with MSA. I am grateful to the study participants and their family members for their contributions to the study."

ATH434-202 Interim Results

A total of 10 participants have been enrolled in the trial. The interim data reported today is from the 7 patients who have completed six months of treatment with ATH434, 3 of whom have also completed 12 months of treatment. Only neuroimaging data are available from month 12. The participants in the trial were diagnosed with MSA using a multimodal approach (clinical, neuroimaging, fluid biomarkers) and treated with oral ATH434 75 mg twice daily.

Clinical, biomarker and safety assessments were conducted during the study. While the data are preliminary, the Company sees a positive trend with the current participant patient outcomes.

Clinical Assessments at Month 6

Unified MSA Rating Scale Part I, historical review (UMSARS)

- 43% (3/7) of participants had lower scores (improvement) on the UMSARS that assesses activities of daily living affected in MSA, such as speech, swallowing, walking and urinary/bowel function.
- In the trial, mean (SD) UMSARS scores (N=7) increased from baseline to 6 months by 1.7 (5.1) points. These study data compare favorably to historical data in a similar MSA population that demonstrated an increase of 3.9 (4.6) points over 6 months.[2]

Global Impression of Change

- 29% (2/7) of participants stabilized or improved on the Clinical Global Impression of

Change (CGIC) scale, which asks the investigator to evaluate overall neurological symptoms as compared to immediately before starting therapy.

- 29% (2/7) of participants also stabilized or improved on the Patient Global Impression of Change (PGIC) scale which asks the patient to evaluate their overall neurological symptoms as compared to immediately before starting therapy.

Safety

- In general, ATH434 was well tolerated by study participants and most adverse events were mild to moderate in severity.
- No serious adverse events related to study drug were reported.

Biomarker Assessments at Month 6 and Month 12

MRI Biomarkers (n=7):

- Brain Volume:
  - At Month 6, there were similar declines in brain volume, as assessed by the MSA-atrophy index (MSA-AI)[3] in all participants consistent with the nature of MSA.
  - However, in the clinical responders, brain volume assessed by the MSA-AI was stable between Month 6 and Month 12.
- Iron content in the substantia nigra was stable over 12 months in the clinical responders.
- Myoinositol is an exploratory biomarker of glial cell pathology in MSA. Treatment with ATH434 led to smaller increases in myoinositol in clinical responders compared to participants who worsened.

Fluid Biomarkers (n=5):

- Neurofilament Light Chain (NfL) is a marker of axonal injury in neurons and has been shown to correlate with disease severity in many neurological diseases. In the trial, clinical responders had stable spinal fluid NfL levels on average whereas those who declined clinically had increased spinal fluid NfL levels.

Definitions and References

[1] Unified MSA Rating Scale, Part I (historical review). Areas assessed include: Speech, swallowing, handwriting, cutting food/handling utensils, dressing, hygiene, walking, falling, orthostatic symptoms, urinary function, sexual function and bowel function.

[2] Wenning et al. The natural history of multiple system atrophy: a prospective European cohort study. Lancet Neurol 2013; 12: 264–74.

[3] MSA Atrophy Index: This index measures the degree of atrophy relative to a normal population, with more negative values indicating greater atrophy

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 NCT05864365.

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 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'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.

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.