



## **Alterity Therapeutics Reports Positive Topline Data from Open-Label Phase 2 Clinical Trial of ATH434 in Multiple System Atrophy**

- ATH434 Demonstrated Clinical Benefit on the Unified MSA Rating Scale and Global Measures of Neurological Symptoms –*
- Neuroimaging Biomarkers Showed Target Engagement and Slowed Brain Atrophy –*
- ATH434 was Well-Tolerated with Favorable Safety Profile –*
- Data are Consistent with Phase 2 Double-Blind Trial and Support Advancement of ATH434 in MSA –*

**MELBOURNE, AUSTRALIA AND SAN FRANCISCO, USA – 28 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 topline data from the ATH434-202 open-label Phase 2 clinical trial in individuals with multiple system atrophy (MSA). The ATH434-202 trial evaluated a patient population with more advanced disease than was studied in Alterity’s double-blind Phase 2 trial ATH434-201. ATH434 has been shown preclinically to reduce  $\alpha$ -synuclein pathology and preserve neuronal function by redistributing iron in the central nervous system.

The topline data showed that ATH434 conferred a clinical benefit on areas of impairment in MSA and stabilized key biomarkers that underpin the pathology of the disease.

The results from the ATH434-202 trial indicate that ATH434 demonstrated a clinical benefit on the Modified Unified MSA Rating Scale Part I (UMSARS I)<sup>1</sup>, as well as stabilization of overall neurological symptoms. Over the 12-month treatment period, disease progression as assessed with UMSARS I was reduced by approximately half as compared to historical controls<sup>2</sup>. In addition, 30% of participants reported stable neurological symptoms over the course of the study. These outcomes are potentially promising as stabilization of MSA symptoms is unexpected in this patient population. On the important symptom of orthostatic hypotension<sup>3</sup>, ATH434 on average stabilized low blood pressure symptoms in study participants. Importantly, the aggregate data indicate that ATH434 has similar clinical efficacy in this advanced MSA population as was observed in the earlier stage patients in Study ATH434-201.

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Biomarker endpoints were used to evaluate potential drug effect and target engagement. Neuroimaging outcomes indicate that ATH434 slowed brain atrophy in MSA affected areas, as measured by the MSA Atrophy Index (MSA-AI)<sup>4</sup>, when compared to placebo-treated participants in Study 201. Moreover, the effects on brain volume were comparable to those observed in participants in the 75 mg dose group in Study 201. In addition, ATH434 led to lower iron accumulation in the putamen and globus pallidus as compared to placebo treated patients in Study 201, providing further evidence of target engagement.

“I am very encouraged by the positive results from the ATH434-202 trial, as they reinforce the robust efficacy we observed in our double-blind study,” said David Stamler, M.D., Chief Executive Officer of Alterity. “The data from our Phase 2 studies are consistent and strongly support advancing our ATH434 program in MSA. With the favorable clinical and biomarker outcomes we have seen, we continue to believe that ATH434 has the potential to slow the progression of this devastating disease. We are committed to bringing this new therapy to patients as soon as possible.”

Daniel Claassen, M.D., M.S., Professor of Neurology at Vanderbilt University Medical Center and principal investigator for the ATH434-202 Phase 2 study, commented, “These results are very helpful in establishing the clinical response to therapy. The consistent changes in UMSARS, along with quantitative measures in imaging, support the findings we noted in Study 201. Currently, there are no disease modifying medications for the treatment of MSA, and these data encourage the continued development of ATH434 to treat this disease. We are indebted to the study participants and their families who contributed to this study.”

### **ATH434-202 Topline Data Summary**

The ATH434-202 Phase 2 clinical trial was an open label study in advanced MSA. Ten (10) participants were enrolled in the trial and were diagnosed with MSA using a multimodal approach (clinical, neuroimaging, fluid biomarkers). Participants were treated with oral ATH434 75 mg twice daily for 12 months. The study assessed the safety and efficacy of ATH434 treatment on clinical and biomarker endpoints. The pre-specified key clinical endpoints included the modified UMSARS I, the clinical global impression of change, and the patient global impression of change. Enrolled participants were more advanced than those in the double blind ATH434-201 Phase 2 trial based on baseline variables including duration of motor symptoms, UMSARS I score, frequency of severe orthostatic hypotension, and plasma NFL levels.

Based on the observed clinical and neuroimaging data, ATH434 improved overall neurological symptoms and slowed disease progression compared to historical data.

### **Clinical Endpoints at 12 months**

#### **Modified Unified MSA Rating Scale Part I (UMSARS I)**

- The mean (SD) UMSARS scores increased from baseline to 12 months by 3.5 (4.7) points. These study data compare favorably to historical data in a similar MSA population, where an increase (worsening) of 6.5 (6.0) points over 12 months was observed.<sup>2</sup>
- 43% (3/7) of participants who completed the study had stable UMSARS scores.

#### **Global Impression of Change**

- 30% (3/10) of participants stabilized or improved on the Clinical Global Impression of Change (CGIC)<sup>5</sup> scale, which asks the investigator to evaluate overall neurological symptoms as compared to immediately before starting therapy.
- 30% (3/10) of participants also stabilized or improved on the Patient Global Impression of Change (PGIC)<sup>6</sup> scale, which asks the patient to evaluate their overall neurological symptoms as compared to immediately before starting therapy.

#### **Orthostatic Hypotension Symptom Assessment (OHSA)**

- The OHSA is a patient reported outcome that evaluates 6 symptoms of low blood pressure associated with moving from a sitting to a standing position.
- On average, symptoms were stable over the 12-month treatment period.

### **Biomarker Endpoints at 12 months**

#### **Brain volume**

The key biomarker endpoint was defined as the change in brain volume from baseline to 12-months, as measured by the MSA Atrophy Index (MSA-AI), which compares brain volume change in MSA affected regions to age matched controls using a composite z-score:

- Brain volume decreased on average, with a mean (SD) z-score of -0.44 (0.138), consistent with that seen in the 75 mg treatment group of Study 201.
- ATH434 slowed atrophy in MSA affected brain regions compared favorably to placebo-treated subjects in Study 201.

#### **Brain iron**

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A secondary biomarker endpoint was change in iron content in MSA affected areas (substantia nigra, putamen, globus pallidus) from baseline to 12-months, as measured by MRI (quantitative susceptibility mapping):

- Reduced iron accumulation in the globus pallidus and putamen, as compared to placebo in Study 201, provide evidence of target engagement and support the clinical efficacy of ATH434.
- The pattern of iron accumulation in the substantia nigra over 12 months was comparable to that observed in the 75 mg dose group in Study 201.

Neurofilament Light Chain (NfL) is a marker of axonal injury in neurons and is elevated in individuals with MSA. On average, plasma and CSF NFL levels were stable over the 12-month treatment period.

### Safety Results

The safety population (n=10) includes all enrolled participants who received at least one dose of study drug.

- No serious adverse events (SAEs) related to ATH434 were reported.
- ATH434 was well-tolerated and most adverse events were mild to moderate in severity.
- There were 3 discontinuations from the study. Two participants discontinued due to progression of MSA and one discontinued for an AE that was not related to treatment.
- There was no evidence of adverse effects on hemoglobin or iron parameters

Additional information on the open label Phase 2 trial can be found at [clinicaltrials.gov NCT05864365](https://clinicaltrials.gov/ct2/show/study/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  $\alpha$ -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 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  $\alpha$ -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.<sup>7</sup>

#### **Definitions and References**

<sup>1</sup> Unified MSA Rating Scale, Part I (historical review) assess activities of daily living. Domains assessed include speech, swallowing, handwriting, cutting food/handling utensils, dressing, hygiene, walking, falling, orthostatic symptoms, urinary function, sexual function and bowel function.

<sup>2</sup> Wenning et al. The natural history of multiple system atrophy: a prospective European cohort study. *Lancet Neurol* 2013; 12: 264–74.

<sup>3</sup> Orthostatic hypotension is a form of low blood pressure that might cause dizziness, lightheadedness or fainting when rising from sitting or lying down. Source: Mayo Clinic.

<sup>4</sup> Trujillo et al. [The MSA Atrophy Index \(MSA-AI\): An Imaging Marker for Diagnosis and Clinical Progression in Multiple System Atrophy](#). *Annals of Clinical and Translational Neurology* 2025.

<sup>5</sup> Clinical Global Impression of Change: a clinician assessment to evaluate overall neurological symptoms as compared to immediately before starting therapy.

<sup>6</sup> Patient Global Impression of Change: a patient assessment to evaluate their overall neurological symptoms as compared to immediately before starting therapy.

<sup>7</sup> [Multiple System Atrophy | National Institute of Neurological Disorders and Stroke \(nih.gov\)](#)

### **About Alteryx Therapeutics Limited**

Alteryx 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. Alteryx 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, Alteryx

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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](http://www.alteritytherapeutics.com).

### **Authorisation & Additional information**

This announcement was authorized by David Stamler, CEO of Alterity Therapeutics Limited.

### **Investor and Media Contacts:**

#### **Australia**

Millie Macdonald  
Head of Investor Relations and Business Development  
[mmacdonald@alteritytherapeutics.com](mailto:mmacdonald@alteritytherapeutics.com)  
+61 468 304 742

Ana Luiza Harrop  
[we-aualteritytherapeutics@we-worldwide.com](mailto:we-aualteritytherapeutics@we-worldwide.com)  
+61 452 510 255

#### **U.S.**

Remy Bernarda  
[remy.bernarda@iradvisory.com](mailto:remy.bernarda@iradvisory.com)  
+1 (415) 203-6386

### **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.*