



Alterity Therapeutics Presents New Analyses of ATH434 Phase 2 Data in Multiple System Atrophy at the 2026 International Congress of Parkinson's Disease and Movement Disorders

ATH434 50 mg significantly slowed functional decline in MSA by approximately 52% versus placebo on the 11-item UMSARS at Week 52 with CSF NfL as a covariate

Baseline CSF NfL predicted the rate of functional decline, supporting its use as a severity covariate in Phase 3

MELBOURNE, AUSTRALIA AND SAN FRANCISCO, USA – 5 October 2026: [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 additional analyses from its randomized, double-blind, placebo-controlled ATH434-201 Phase 2 trial in Multiple System Atrophy (MSA) were presented at the 2026 International Congress of Parkinson's Disease and Movement Disorders (MDS Congress) in Seoul, Korea. The poster brings together clinical, biomarker, and imaging results from the trial after adjusting for baseline disease severity, measured by cerebrospinal fluid neurofilament light chain (CSF NfL).

“These additional analyses strengthen our confidence in ATH434 as a potential disease-modifying therapy for MSA. When we account for differences in baseline disease severity using CSF NfL, ATH434 50 mg significantly slowed functional decline by more than 50% compared with placebo over one year, a treatment effect well above the threshold considered clinically meaningful,” said David Stamler, M.D., CEO.

“I continue to be impressed by the strength of the efficacy signal in our Phase 2 study in the context of other treatments that are in development for MSA. By incorporating the learnings regarding NfL into our Phase 3 confirmatory trial, we continue to build on our de-risking strategy that has been so successful in Phase 2,” concluded Dr. Stamler.

The poster, entitled, “ATH434 in Multiple System Atrophy: Results from a Randomized, Double-Blind, Placebo-Controlled Phase 2 Study with CSF Neurofilament Light Chain as a Disease Severity

Covariate,” analyzed baseline CSF NfL, an established prognostic biomarker of clinical decline in MSA, as a covariate to account for variability in baseline disease severity.

The analysis demonstrated that CSF NfL, a prespecified covariate in the Phase 2 trial, predicts functional decline in individuals with MSA. Higher baseline CSF NfL predicted greater decline at Week 52: each 1,000 pg/mL increase was associated with approximately 0.9 additional points of worsening on UMSARS I¹, an effect that was significant ($p=0.033$). This supports using CSF NfL as a covariate in future MSA trials since adjusting for a known predictor of decline can produce a more precise measurement of treatment effect.

ATH434 50 mg significantly slowed functional decline on the 11-item UMSARS Part I

The analysis utilized a mixed model for repeated measures (MMRM)² applied to align with the imaging analyses conducted on the Modified Intent-to-treat (mITT) population ($N=61$)³. After adjustment for baseline CSF NFL, ATH434 50 mg significantly slowed functional decline on the 11-item UMSARS Part I⁴ at Week 52 with a -4.64 -point difference versus placebo in change from baseline ($p=0.032$), roughly 3-fold more improvement compared to the 1.5-point minimal clinically important difference (MCID). This represents an approximate 52% slowing of functional decline in the 50 mg dose group relative to placebo. The 75 mg dose also slowed functional decline with a -2.81 -point difference versus placebo in change from baseline at Week 26 ($p=0.072$) and Week 52 ($p=0.179$). These results are consistent with the previously reported analysis of the 11-item UMSARS Part I in the Phase 2 clinical analysis population, in which ATH434 50 mg slowed decline by 46% versus placebo ($p=0.037$). The difference between the two figures reflects the distinct analysis populations and statistical models.

Advanced brain iron MRI imaging is consistent with the ATH434 mechanism of action as an iron-chaperone

The poster also reported brain iron measured by quantitative susceptibility mapping (QSM) MRI analyzed with the same CSF NfL-adjusted model. ATH434 is designed as an iron chaperone and is intended to redistribute reactive (labile) iron that is driving MSA pathology. MRI can detect iron leaving cells but cannot measure iron that has been stored or buffered within cells. Although the trial’s primary endpoint of change in substantia nigra iron at Week 52 was not met, change from baseline in iron was numerically lower in the putamen and globus pallidus with ATH434 vs placebo. In the dentate nucleus, iron signal increased relative to placebo at Week 52 (50 mg: $+0.016$ ppm, $p=0.021$), which is hypothesized to reflect redistribution of mobilized iron through the brain’s glymphatic system. The poster noted that regional differences may reflect region-

specific iron handling because an MRI captures iron efflux but not the potential storage or buffering effects of ATH434.

The presentation is available on the Alterity Therapeutics website [here](#).

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 50 mg produced clinically and statistically significant slowing of decline on the 11-item 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 Clinical Global Impression of Severity Scale, the Swallowing Disturbance Questionnaire and the Orthostatic Hypotension Symptom Assessment. 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](https://clinicaltrials.gov/ct2/show/study/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 focused on developing disease modifying therapies in Multiple System Atrophy (MSA) and related Parkinsonian disorders. Alterity is preparing to initiate a Phase 3 pivotal trial in MSA, a rare and rapidly progressive disease. ATH434, the Company's lead asset, has demonstrated clinically meaningful efficacy in a randomized, double-blind, placebo-controlled Phase 2 clinical trial in participants with MSA. Alterity has further reported positive data in its open label Phase 2 clinical trial in participants with 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 <https://alteritytx.com>.

References:

¹ UMSARS: 11-item Unified Multiple System Atrophy Rating Scale Part I (excludes sexual function)

² Mixed Models for Repeated Measures (MMRM) analysis using all visits without imputation (treatment, visit, treatment-by-visit interaction, sex; covariates age, baseline score, baseline CSF NfL), added post hoc to align with the imaging analyses; the prespecified analysis was a Week 52 Analysis of Covariance (ANCOVA).

³ Modified Intent-to-treat (mITT) population (N=61): randomized and dosed, CSF α -synuclein seed amplification assay positive, with ≥ 1 postbaseline QSM assessment.

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.

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