Alterity Therapeutics Achieves Alignment with U.S. FDA on Pivotal Phase 3 Program for ATH434 in Multiple System Atrophy

– Successful End-of-Phase 2 meeting with FDA agreeing on key elements of the proposed Phase 3 design, including study population, dosing regimen, and treatment duration –

– FDA agrees on UMSARS Part I as primary endpoint after ATH434 demonstrated 48% slowing of disease progression versus placebo in Phase 2 study –

– FDA agrees with 50mg dose level which achieved clinically and statistically significant efficacy in Phase 2 study –

– Pivotal Phase 3 trial activities on track to initiate by year-end 2026 –

MELBOURNE, AUSTRALIA AND SAN FRANCISCO, USA – 9 June 2026: Alterity Therapeutics (ASX: ATH, trading under the ASX code ATHDA until 12 June; NASDAQ: ATHE) ("Alterity" or "the Company"), a biotechnology company dedicated to developing disease modifying treatments for neurodegenerative diseases, today announced the successful outcome of its End-of-Phase 2 (EOP2) meeting with the U.S. Food and Drug Administration (FDA), achieving alignment on the key elements of the Company's registrational Phase 3 program for ATH434 in Multiple System Atrophy (MSA), a rare and rapidly progressive neurodegenerative disease with no approved therapy. The pivotal program is designed to support a potential New Drug Application (NDA) in MSA and represents the final stage of clinical development required to seek regulatory approval in the United States.

Importantly, the FDA agreed with the proposed Phase 3 trial design, including the study population, treatment duration and primary endpoint – the 11-item UMSARS Part I[1] rating scale. The FDA also concurred with Alterity's proposed Phase 3 dose regimen of ATH434 50 mg twice daily, which in Phase 2 achieved clinically and statistically significant efficacy on the 11-item UMSARS I, with 48% slowing of disease progression compared to placebo.

The FDA further indicated that Alterity's planned key secondary endpoints for the Phase 3 study were suitable to support efficacy, including the Swallowing Disturbance Questionnaire, the Orthostatic Hypotension Symptom Assessment, and the Clinical Global Impression of Severity. In addition, the FDA agreed with Alterity's proposed statistical methods for analyzing the primary and key secondary efficacy endpoints and indicated that the size of the anticipated safety database at the conclusion of Phase 3 was reasonable.

ATH434 has previously received Fast Track Designation and Orphan Drug Designation from the FDA for the treatment of MSA, recognizing the significant unmet medical need for patients living with this rare and debilitating neurodegenerative condition. The successful outcome of the EOP2 meeting represents an important de-risking milestone for ATH434 and substantially reduces uncertainty around the design of the pivotal Phase 3 program.

“Achieving alignment with FDA at the End-of-Phase 2 meeting is a critical step for our Phase 3 program in MSA, providing the clarity we need to advance to this next stage,” said David Stamler, M.D., CEO of Alterity Therapeutics. “We are encouraged by the FDA’s agreement with us on the key elements of our Phase 3 program, namely the study population, efficacy endpoints, treatment regimen and anticipated safety database, providing a well-defined registrational pathway built on the strength of our Phase 2 data. The successful outcome of the meeting is an important de-risking milestone and gives us confidence as we finalize the protocol and prepare to initiate trial activities by year-end 2026. The favorable outcome of the meeting is a testimony to the depth of experience our team brings to collaborating with the FDA, especially on neurology development programs. I am confident that ATH434 is well positioned to become a disease-modifying therapy for individuals living with MSA."

About ATH434

Alterity’s lead candidate, ATH434, is an oral agent designed to redistribute excess iron and inhibit abnormal protein aggregation associated with neurodegeneration. ATH434 has been shown 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). Positive results from the randomized, double-blind, placebo-controlled Phase 2 clinical trial in patients with MSA demonstrated robust clinical efficacy, target engagement as indicated by 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 the Phase 3 Clinical Trial

The Phase 3 clinical trial will be a randomized, double-blind, placebo-controlled investigation in participants with clinical and biomarker evidence of MSA. Approximately 200 patients will be randomly assigned, in a 1:1 ratio, to 12 months treatment with ATH434 50 mg bid or matching placebo. The primary endpoint will be the 11-item UMSARS I and the key secondary endpoints will include the Swallowing Disturbance Questionnaire, the Orthostatic Hypotension Symptom Assessment, and the Clinical Global Impression of Severity.

About ATH434-201 Phase 2 Clinical Trial

The ATH434-201 Phase 2 clinical trial was 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 and assessed neuroimaging measures of brain volume and iron-related parameters, together with 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 the Clinical Global Impression of Severity Scale and patient reported outcomes that assessed swallowing impairment (the Swallowing Disturbance Questionnaire) and low blood pressure symptoms with standing (the Orthostatic Hypotension Symptom Assessment). Wearable sensors used to assess outpatient activity levels indicated that patients receiving ATH434 also experienced less decline compared with placebo. Biomarkers were used to evaluate potential drug effect and target engagement relative to placebo. Both dose levels reduced the adverse effect of iron accumulation in MSA affected brain regions and demonstrated 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 at 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 that causes profound disability. MSA is a Parkinsonian disorder characterized by a variable combination of slowed movement and/or rigidity, autonomic dysfunction affecting involuntary functions such as blood pressure maintenance and bladder control, and impaired balance and/or coordination that predispose patients to falls. A pathological hallmark of MSA is the accumulation of abnormal clumping of the protein α-synuclein within oligodendrocytes, the myelin-producing support cells of the central nervous system, along with progressive neuronal 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.[2]

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] 11-item UMSARS Part I (previously described as modified UMSARS I): Unified Multiple System Atrophy Rating Scale, 11-Items include: Orthostatic symptoms, Swallowing, Speech, Handwriting, Cutting food, Dressing, Hygiene, Walking, Falling, Urinary and Bowel function.

[2] Multiple System Atrophy | National Institute of Neurological Disorders and Stroke (nih.gov)

Authorization & Additional information

This announcement was authorized by the Board of Directors 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.