Alterity Therapeutics Announces Publication Demonstrating that ATH434 is Neuroprotective in Animal Model of Parkinsonian Disorder in the Journal of Parkinson's Disease

Study demonstrates reduction of α-synuclein aggregation and preservation of neurons

MELBOURNE, AUSTRALIA AND SAN FRANCISCO, USA – 28 January 2022: 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 data in an animal model of Multiple System Atrophy (MSA) were published in the *Journal of Parkinson's Disease.* MSA is a devastating neurodegenerative disorder without approved therapy.

The publication, entitled, "The Compound ATH434 Prevents Alpha-Synuclein Toxicity in a Murine Model of Multiple System Atrophy" describes a study evaluating the efficacy of ATH434 in genetically altered mice that develop manifestations of MSA. The investigation demonstrated that in the studied brain region, ATH434 treatment reduced both the toxic oligomeric and aggregated forms of α-synuclein, a central nervous system protein important for normal function of nerve cells. At the same time, ATH434 treatment reduced the cardinal pathology of MSA (glial cell inclusions), reduced brain iron, preserved neurons and improved motor performance. The publication concluded that ATH434 is a promising small molecule drug candidate that has potential for treating MSA. The study was led by David I. Finkelstein, Ph.D., Head of Parkinson's Disease Laboratory at the Florey Institute of Neuroscience and Mental Health and the University of Melbourne. The full publication can be accessed here.

"These preclinical data are extremely valuable as they demonstrate our thesis that by binding and redistributing excess iron in the brain of patients with Parkinsonian disorders, we can reduce α-synuclein aggregation and oxidative stress and rescue neurons in multiple brain regions to address the underlying pathology of disease," said David Stamler, M.D., Chief Executive Officer, Alterity. "We believe that these preclinical studies may translate to clinical benefit in patients with MSA, and we look forward to further patient evaluation in our upcoming Phase 2 clinical trial."

Elevation in regional brain iron together with accumulation of aggregated α-synuclein are important contributors to the pathology of MSA. Previous studies with ATH434 in preclinical models of Parkinson's disease have shown that it is brain-penetrant, reduces iron accumulation and iron-mediated redox activity, provides neuroprotection, inhibits α-synuclein aggregation and improves motor function. The compound was also well-tolerated in a first-in-human oral dosing study in healthy and older adult volunteers with a favorable, dose-dependent pharmacokinetic profile.

In this study, genetically altered, or transgenic, mice overexpress α-synuclein, develop glial cell inclusions, and manifest motor and non-motor aspects of MSA. Animals received ATH434 in food or a control diet for 4 months starting at 12 months of age. Western blot analysis was used to assess oligomeric and aggregated forms of α-synuclein levels in brain and stereology was used to quantitate the number of neurons and glial cell inclusions in the substantia nigra pars compacta.

About ATH434

Alterity's lead candidate, ATH434, is the first of a new generation of small molecules designed to inhibit the aggregation of pathological proteins implicated in neurodegeneration. ATH434 has been shown preclinically to reduce α-synuclein pathology and preserve nerve cells by restoring normal iron balance in the brain. In this way, it has excellent potential to treat Parkinson's disease as well as various forms of atypical Parkinsonism such as Multiple System Atrophy (MSA). ATH434 has successfully completed a Phase 1 clinical trial demonstrating the agent is well tolerated, orally bioavailable, and achieved brain levels comparable to efficacious levels in animal models of MSA, with the objective of restoring function in patients with MSA and other Parkinsonian disorders.

ATH434 has been granted Orphan 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 approximately 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]National Institute of Health: Neurological Disorders and Stroke, Multiple System Atrophy Fact Sheet

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. Alterity also has a broad drug discovery platform generating patentable chemical compounds to intercede in disease processes. 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, uncertainties relating to the impact of the novel coronavirus (COVID-19) pandemic on the company's business, operations and employees, 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.