Alterity Therapeutics Announces New Publications Providing Further Evidence of the Potential of ATH434 to Treat Neurodegenerative Diseases

Colorectal impairment reversed in a preclinical model of Parkinson's Disease

ATH434 presents a novel mechanism of action for the treatment of neurodegenerative diseases

MELBOURNE, AUSTRALIA AND SAN FRANCISCO, USA – 4 November 2021: Alterity Therapeutics (ASX: ATH, NASDAQ: ATHE) ("Alterity" or "the Company"), a biotechnology company dedicated to developing disease modifying treatments for neurodegenerative conditions, today announced the publication of two preclinical studies demonstrating the potential of ATH434 to treat Parkinsonian disorders.

Non-motor symptoms (NMS) are common in patients with Parkinsonian disorders, such as Parkinson's disease (PD) and Multiple System Atrophy. Parkinson's disease patients experience gastrointestinal (GI) complications, cognitive deficits, autonomic dysfunction, and mood disturbance and these non-motor manifestations are an important source of morbidity and reduced quality of life. As published in the *Journal of Parkinson's Disease*, "ATH434 Reverses Colorectal Dysfunction in the A53T Mouse Model of Parkinson's Disease" presents results from a preclinical study investigating the effect of ATH434 on GI complications of PD.

"This published study provides further evidence of the potential for ATH434 to modify the course of Parkinson's disease. The reversal of colonic dysfunction in this preclinical model of PD may translate to clinical benefit in alleviating non-motor symptoms for individuals living with the disease," said David Stamler, M.D., Chief Executive Officer, Alterity. "Practicing clinicians are well aware of the substantial impact that these symptoms have on the quality of life of individuals with Parkinson's disease. We are currently conducting additional preclinical studies to evaluate the potential of ATH434 for the treatment of PD and look forward to advancing it into a future proof-of-concept study."

Common gastrointestinal complications associated with PD include swallowing difficulty, delayed stomach emptying, slower nutrient absorption from the gut, and chronic constipation. These complications are thought to be caused by damage to the neurons in the enteric nervous system due to the accumulation of alpha-synuclein. ATH434 has been shown preclinically to reduce the aggregation of alpha-synuclein by binding and redistributing excess iron in areas of pathology.

In the PD animal study, ATH434 treatment was started after GI dysfunction was established and resulted in a reversal of slowed colonic propulsion and gut transit deficits. Importantly, the study concluded that ATH434 can reverse some of the GI deficits and damage to the enteric nervous system, and thus may have potential clinical benefit in alleviating the GI complications associated with PD.

The publication can be accessed here.

Alterity also announced the publication of an in vitro study concluding that the novel mechanism of action of ATH434, previously known as PBT434, provides a compelling case for its continued development as a therapeutic agent in neurodegenerative diseases associated with iron accumulation. As published in *Plos One*, the publication, entitled, "The iron chelator, PBT434, modulates transcellular iron trafficking in brain microvascular endothelial cells," demonstrated that ATH434 is able to bind and redistribute iron, thus limiting the downstream oxidative stress involved in cytotoxic protein aggregation. Additionally, the investigation showed that while ATH434 has moderate effects on the regulation of iron-dependent protein expression, it does not interfere with normal cell physiology, unlike high affinity iron chelators.

Dr. Stamler, concluded, "This study explains how ATH434 promotes removal of excess iron from cells, thus reducing aggregation of proteins such as α-synuclein that are implicated in the pathology of Parkinsonian disorders. The findings are consistent with previous research on our lead clinical asset and support our strategy of targeting the excess iron implicated in these important neurodegenerative diseases."

The publication can be accessed here.

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 Parkinson's Disease

Parkinson's disease (PD) belongs to a group of conditions called motor system disorders, which cause unintended or uncontrollable movements of the body. The precise cause of PD is unknown, but some cases are hereditary while others are thought to occur from a combination of genetics and environmental factors that trigger the disease. In PD, brain cells become damaged or die in the part of the brain that produces dopamine--a chemical needed to produce smooth, purposeful movement. The four primary symptoms of PD are tremors, rigidity, slowing of spontaneous and automatic movement, and impaired balance. Other symptoms may include difficulty swallowing, chewing, or speaking; emotional changes; urinary problems or constipation; dementia or other cognitive problems; fatigue; and problems sleeping.[1] Nearly one million people in the U.S. are living with PD, and more than 10 million people worldwide are living with PD. Approximately 60,000 Americans are diagnosed with PD each year.[2]

[1]National Institute of Health: Neurological Disorders and Stroke, Parkinson's Disease Information Page; [2]Parkinson's Foundation

About Multiple System Atrophy

Multiple System Atrophy (MSA) is a rare, neurodegenerative disease characterized by a combination of symptoms that affect both the autonomic nervous system and 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 motor impairment, 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 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 Systems 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 forms of Parkinsonian disorders. Alterity also has a broad drug discovery platform generating patentable chemical 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.

Contact: Investor Relations

Australia
Rebecca Wilson
E: WE-AUAlterity@we-worldwide.com
Tp: +61 417 382 391

US
Remy Bernarda
remy.bernarda@iradvisory.com
Tp: +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, 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.