AI-116 for Dementia: Positive Pre-clinical Neuronal Cell Viability Results

Highlights:

- *Pre-clinical data demonstrates neuroprotective effect of AI-116, exceeding that for the existing FDA registered drug for dementia, Donepezil (originally marketed as Aricept).*
- *Cell viability increased by 20.1% for AI-116 versus 2.1% for Donepezil, in pre-clinical studies.*
- *Results demonstrate synergistic method of action within AI-116.*
- *RNA sequencing analysis to commence to further assess AI-116, including for neuroinflammation which plays a multifaceted role in the pathogenesis of dementia.*

Melbourne, Australia, 08 April 2024: Algorae Pharmaceuticals Limited (**Algorae** or the **Company**) (ASX code: 1AI) is pleased to announce positive results from *in vitro* pre-clinical studies undertaken to assess AI-116 for the treatment of neurodegenerative disorders, including those characterised by dementia.

AI-116 is Algorae's combination drug candidate comprising Donepezil Hydrochloride (**Donepezil**), an acetylcholinesterase inhibitor (**AChE inhibitor**), and cannabidiol (**CBD**). AChE inhibitors are FDA registered first line treatments for Alzheimer's Disease, which are also prescribed off-label for other neurodegenerative disorders, including Parkinson's Disease and vascular dementia.

In vitro assays were conducted to further assess the therapeutic potential of AI-116 by comparing the viability of neuronal cells in the presence of Amyloid β with varying exploratory doses of AI-116 against the two drugs alone. The *in vitro* assays measured cell viability and drug synergy, which occurs when the effect of the two drugs in combination is superior to the sum of their individual effects.

In these assays, neuroblastoma cells were concurrently treated with varying doses of CBD and Donepezil in the presence of Amyloid β. Cell viability was measured using the MTT assay. Improvement in cell viability was determined as a percentage increase in cell survival over cells treated with Amyloid β alone.

In the data reported below, the control arm of the *in vitro* study demonstrated high levels of toxicity when neuronal cells are exposed to Amyloid β, the improvements in cell viability observed with the AChE inhibitor and CBD alone was substantially improved with the optimal fixed dose combination of AI-116 (Figure 1).

Algorae Pharmaceuticals Limited [ABN: 14 104 028 042]
Level 23, Rialto South Tower, 525 Collins St, Melbourne VIC 3000
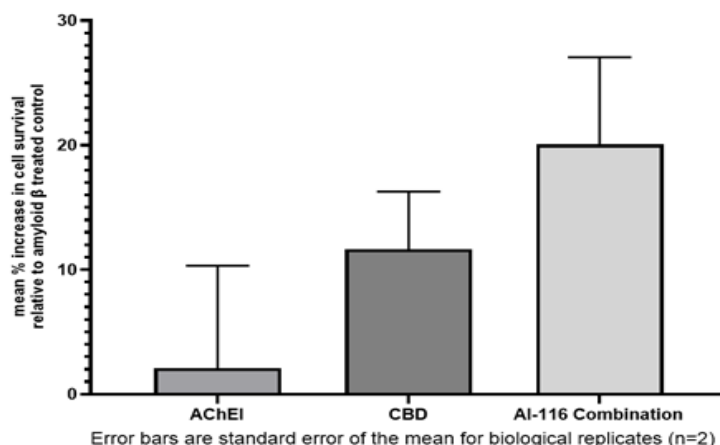P: +61 422 180 317

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Figure 1. Average percentage increase in cell survival relative to amyloid β treated control cells. Zero is the benchmark for AB effected cells with no treatments, whereby cell viability was 65.5%. Cell viability increased by 2.1% to 67.6% for Donepezil, by 11.6% to 77.1% for CBD and by 20.1% to 85.6% for AI-116.

These results demonstrate that the combination of CBD and Donepezil synergise to increase the neuroprotective effect in neuronal cells that are exposed to toxic Amyloid β, with the observed combined effect of the two drugs on cell viability is 33% greater than what would be expected if we added together the effects of each drug used alone.

Principal Investigator, **Professor Garrie Arumugam**, said, *"These preliminary in vitro results are very promising, showing a clear pattern of neuronal cell protection and synergistic method of action. I am eager to further investigate the implications of these findings and how they could pave the way for new insights and potentially advancements in drug development."*

Additional analyses, including RNA sequencing analysis will now commence to assess the therapeutic mechanism associated with the use of AI-116, including assessments for neuroinflammation, which plays a multifaceted role in the pathogenesis of neurodegenerative disorders and dementia.

Algorae has developed an intellectual property (IP) strategy to support its commercial objectives, which includes the continuous monitoring of the results of its research and development program with a view to identifying and protecting new IP that aligns with those commercial objectives. Accordingly, these pre-clinical data have been incorporated into provisional patent applications that pursue aspects of AI-116 and its associated therapeutic uses.

About Donepezil

Donepezil (i.e., Aricept) was registered by the US Food and Drug Administration (FDA) in 1996 for the symptomatic treatment of Alzheimer's disease, helping to improve cognitive function and quality of life for individuals with the condition. It has been prescribed off-label in the treatment of other neurodegenerative disorders, such as Parkinson's disease, vascular dementia and dementia with Lewy bodies. It belongs to a class of drugs known as AChE inhibitors, which work by increasing the levels of acetylcholine, a neurotransmitter involved in memory and learning, in the brain. The market size for AChE inhibitors in 2024 is estimated to be US$21B and is driven by the rising prevalence of Alzheimer's disease[1].

This announcement has been approved by the Board of Directors of Algorae Pharmaceuticals Limited.

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For more information, please visit www.algoraepharma.com

Corporate and Media Enquiries
Mr Brad Dilkes - Director
P: +61 422 180 317
E: brad@algoraepharma.com

About Algorae Pharmaceuticals

Algorae is a pharmaceutical development company focussed on addressing unmet medical needs through the discovery and development of novel treatments. The Company has assembled a proficient R&D team and established collaborations with reputable academic institutions to advance its promising drug candidates, which include AI-116 for the treatment of neurodegenerative disorders and/or dementia, AI-168 for cardiovascular disease and NTCELL for Parkinson's disease. Algorae intends to expand its therapeutic pipeline using a proprietary artificial intelligence (AI) drug discovery and

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P: +61 422 180 317

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development platform. Known as Algorae Operating System (AlgoraeOS), the AI platform leverages extensive medical and scientific databases from various disciplines within an advanced system at the intersection of AI and pharmaceutical research. By employing machine learning, deep learning, and neural networks, the aim of AlgoraeOS is to uncover synergistic drug combinations that lead to the development of novel and effective treatments for any medical condition, aligning with Algorae's commitment to address unmet medical needs. Algorae is listed and publicly traded on the Australian Stock Exchange (ASX: 1AI), providing investors an opportunity to participate in the Company's growth.

References:

[1]Cholinesterase Inhibitors Market Analysis by Application (Alzheimer's Disease, Other Neurological Disorders), by Type of Drug (Donepezil, Rivastigmine, Galantamine), by Distribution Channel (Hospital Pharmacies, Retail Pharmacies and Drug Stores, Online Pharmacies) and by Region: Global Forecast, 2024 - 2033.

Forward-looking Statements

This document may contain certain forward-looking statements, relating to Algorae's business, which can be identified by the use of forward-looking terminology such as "promising," "probable", "plans," "anticipated," "will," "project," "believe," "forecast," "expected," "estimated," "targeting," "aiming," "set to," "potential," "seeking to," "goal," "could provide," "intends," "is being developed," "could be," "on track," or similar expressions, or by express or implied discussions regarding potential filings or marketing approvals, or potential future sales of product candidates. Such forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause actual results to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no assurance that any existing or future regulatory filings will satisfy the FDA's and other health authorities' requirements regarding any one or more product candidates, nor can there be any assurance that such product candidates will be approved by any health authorities for sale in any market or that they will reach any particular level of sales. In particular, management's expectations regarding the approval and commercialisation of the product candidates could be affected by, among other things, unexpected clinical trial results, including additional analysis of existing clinical data, and new clinical data; unexpected regulatory actions or delays, or government regulation generally; our ability to obtain or maintain patent or other proprietary intellectual property protection; competition in general; government, industry, and general public pricing pressures; and additional factors that involve significant risks and uncertainties about our products, product candidates, financial results and business prospects. Should one or more of these risks or uncertainties materialise, or should underlying assumptions prove incorrect, actual results may vary materially from those described herein as anticipated, believed, estimated, or expected. Algorae is providing this information and does not assume any obligation to update any forward-looking statements contained in this document as a result of new information, future events or developments or otherwise.

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