Public Announcement
ASX Code: 1AI

Algorae's Preclinical Assessment of Drug Candidate AI-168 Demonstrates Statistically Significant Cardioprotective Qualities

Highlights:

- Algorae's cardiovascular drug candidate AI-168 demonstrated strong cardioprotective qualities, outperforming existing first line FDA-approved beta blockers in three cardiovascular cell lines.
- The results of these pre-clinical studies have further refined the composition of AI-168, culminating in the filing of an international Patent Cooperation Treaty ('PCT') application, which will enable Algorae to pursue patent protection for AI-168 in commercially important jurisdictions.
- Therapeutic application of AI-168 to be compared to cardio selective beta blockers (with a global market valued at US$6.2B[1] per annum) in animal studies of cardiovascular disease being evaluated with the Monash University Biomedicine Discovery Institute.

Melbourne, Australia – 29 November 2024: Algorae Pharmaceuticals ('Algorae' or the 'Company') (ASX: 1AI), an artificial intelligence ('AI') enabled drug discovery and development company today announces positive results from preclinical studies, which evaluated the cardioprotective qualities of drug candidate AI-168.

Algorae has undertaken preclinical assessments at the Monash University Victorian Heart Institute Research Laboratories to further assess the formulation of AI-168 and compare the performance of AI-168 with beta blockers using well-established *in vitro* models of cardiovascular disease.

Three cardiovascular cell lines were used to assess the dysregulation of cell growth caused by cardiac stressors. In the first model, human umbilical vein endothelial cells ('HUVECs') were treated with Angiotensin II ('AngII'). Angiotensin II is known to play a significant role in the pathophysiology of cardiovascular diseases. When HUVECs are grown the presence of AngII, there is a significant reduction in cell proliferation (Figure 1). While the addition of beta blocker alone did resolve some loss of cell proliferation, the AI-168 combination was able to effectively restore normal cell proliferation, with a relative improvement of approximately 94% from vehicle to control (healthy cells with no stressors or pharmaceutical intervention) (Figure 1).

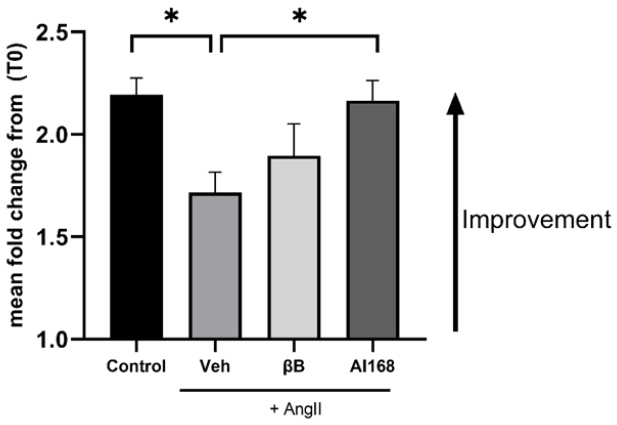

Figure 1. Proliferation of Human Umbilical Vein Endothelial Cells ('HUVECs') treated with Angiotensin II ('AngII') for 48 hours. The y-axis reports the mean fold change in cell proliferation from time zero (T0) after 48 hours relative to the vehicle control. Treatments were **Control** (no AngII), **Veh** (Vehicle with AngII only), **βB** (β blocker with AngII) and **AI-168** (β blocker & CBD, with Ang II). Error bars report Standard Error of the Mean. Significant differences were determined by ANOVA (*-P ≤ 0.05, **-P ≤ 0.01).

In the second model, human pulmonary artery smooth muscle cells ('hPASMCs') were treated with platelet derived growth factor ('PDGF'). The aberrant activation of the PDGF signalling pathway has been demonstrated to drive progression of cardiopulmonary diseases. When hPASMCs are grown the presence of PDGF, there is a significant increase in uncontrolled cell proliferation (Figure 2). In this model, the addition of the beta blocker alone had a minimal effect on PDGF-mediated cell proliferation, whereas AI-168 was able to restore cell proliferation to near normal levels, with a relative improvement (normalisation) of cell proliferation by approximately 80% from vehicle to control (Figure 2).

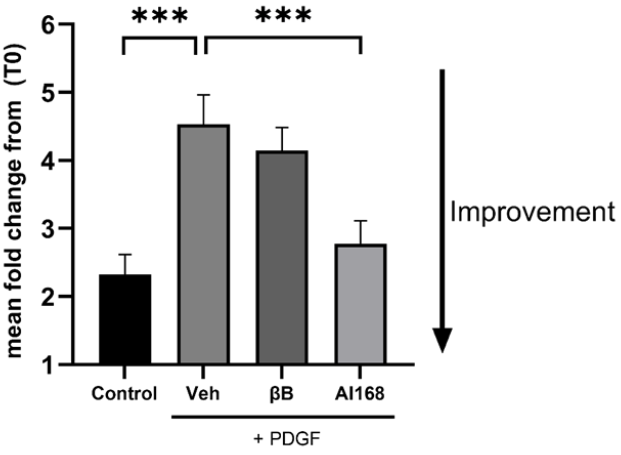

Figure 2. Proliferation of Human Pulmonary Artery Smooth Muscle Cells ('hPASMCs') treated with Platelet derived growth factor ('PDGF') for 48 hours. The y-axis reports the mean fold change in cell proliferation from time zero (T0) after 48 hours. Treatments were, **Control** (no PDGF), **Veh** (Vehicle with PDGF only), **βB** (β blocker with PDGF) and **AI-168** (β blocker & CBD, with PDGF). Error bars report Standard Error of the Mean. Significant differences were determined by ANOVA (*-P ≤ 0.05, **-P ≤ 0.01).

In the third model, rat cardiomyoblasts were treated with doxorubicin. Doxorubicin is an anthracycline, which is an important class of chemotherapeutic drugs used for the treatment of several types of cancer. A known adverse effect of anthracycline treatment is chemotherapy-induced cardiotoxicity, which can occur during or after the completion of treatment. In this model, doxorubicin was shown to be toxic to the cardiomyoblasts, causing cell death and/or significantly reducing cell proliferation (Figure 3). By contrast, AI-168 restored approximately 68% of the cardiomyoblast growth lost to doxorubicin toxicity.

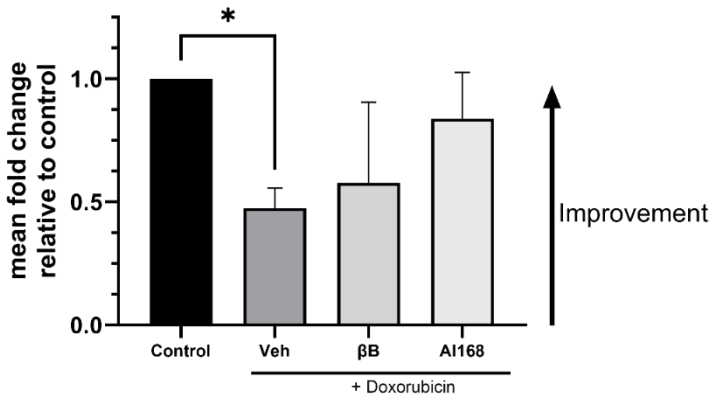

Figure 3. Proliferation of Rat Cardiomyoblast cells (H9C2) treated with doxorubicin (Dox) for 24 hours. The y-axis reports the mean fold change in cell proliferation relative to the control after 24 hours. Treatments were, **Control** (no Dox), **Veh** (Vehicle with Dox only), **βB** (β blocker with Dox) and **AI-168** (β blocker & CBD, with Dox). Error bars report Standard Error of the Mean. Significant differences were determined by ANOVA (*-P ≤ 0.05, **-P ≤ 0.01).

The results observed from these *in vitro* assays will be used to identify the most appropriate *in vivo* models of cardiovascular disease, which Algorae is evaluating in conjunction with the Monash University researchers.

About AI-168

AI-168 is a fixed dose combination drug candidate that combines a cardio selective beta blocker with cannabidiol. Combining a cardio selective beta blocker (such as bisoprolol or metoprolol) with cannabidiol ('CBD') enhances the therapeutic effects of traditional beta blocker treatments. AI-168 will continue to be assessed for use in medical indications in which beta blockers are commonly prescribed.

Intellectual Property Strategy

The filing of an international PCT patent application represents an important step in pursuing patent protection for AI-168, and its use for the treatment or prevention of cardiovascular diseases or disorders. The PCT application incorporates additional preclinical data generated after the submission of the provisional patent application announced on 23 November 2023. This is consistent with Algorae's approach to identify new opportunities to develop intellectual property assets that align with the Company's commercial strategy.

Algorae's global IP strategy includes pursuing patent protection in key markets such as the United States, Europe, Japan and the UK. The Company continues to work closely with its patent attorneys to identify and protect any new IP that is generated from its Research and Development ('R&D') programs.

The international PCT patent application is not a granted patent. The processing of an international PCT patent application will result in the issuance of an International Search Report ('ISR') and an International Search Opinion ('ISO'). These non-binding reports will provide the Company with some indication of the patentability of the subject matter claimed in the international PCT patent application.

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

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Reference: [1]https://www.transparencymarketresearch.com/cardio-selective-beta-blockers-market.html

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 is expanding its therapeutic pipeline using a proprietary artificial intelligence drug discovery and 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.

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.