STUDY ADDITIONAL INFORMATION

Perth, Australia; 13 JULY 2021 - Argenica Therapeutics Limited (ASX: AGN) ("Argenica" or the "Company"), a biotechnology company developing novel therapeutics to reduce brain tissue death after stroke, would like to provide the following additional information with regards to its announcement titled "Study Shows ARG-007 Does Not Degrade", released on the ASX on 12 July 2021.

The announcement referred to results from studies with other potential competitive neuroprotective peptides which have suggested that the active peptide can get degraded following administration of tPA. These studies refer to data published in a recent publication of a Phase 3 clinical trial of Nerinetide, an arginine rich peptide with some similarities to ARG-007. The reference for this publication is Hill MD, Goyal M, Menon BK, et al. **Efficacy and safety of nerinetide for the treatment of acute ischaemic stroke (ESCAPE-NA1): a multicentre, double-blind, randomised controlled trial.** *Lancet*. 2020;395(10227):878-887.

This publication reports the Phase 3 clinical trial for Nerinetide where investigators observed evidence of "treatment effect modification resulting in inhibition of treatment effect in patients receiving alteplase". Argenica has conducted the in vitro studies reported in the announcement to assist in determining whether ARG-007 would have similar effect modifications after tPA treatment. Argenica is also closely reviewing how the Nerinetide Phase 3 clinical trial is being conducted in order to inform our own clinical trial program for ARG-007.

The announcement referred to a previous study which confirmed the neuroprotective stability of ARG-007 when incubated with plasmin, an enzyme activated by tPA that dissolves the clot causing the stroke. These results suggest that ARG-007 could potentially continue to provide neuroprotective benefits after clot dissolving drugs are administered to stroke patients. This study, conducted by Argenica's Chief Scientific Officer, Prof Bruno Meloni, was an *in vitro* anti-excitotoxic neuroprotective efficacy study of ARG-007 (R18D) which also demonstrated ARG-007 to be unaffected when preincubated for 1-3 h or overnight, in a cell lysate prepared from dying neurons or with the proteolytic enzyme, plasmin. The reference for this study is Milani, D., Clark, V. W., Feindel, K. W., Blacker, D. J., Bynevelt, M., Edwards, A. B., Anderton, R. S., Knuckey, N. W., & Meloni, B. P. (2021). **Comparative Assessment of the Proteolytic Stability and Impact of Poly-Arginine Peptides R18 and R18D on Infarct Growth and Penumbral Tissue Preservation Following Middle Cerebral Artery Occlusion in the Sprague Dawley Rat**. *Neurochemical research*, *46*(5), 1166–1176.

The announcement stated that in previous animal studies, ARG-007 has already shown a reduction in brain tissue death up to 28 days after a stroke. The previous animal studies mentioned were conducted by Prof Meloni and showed administration of ARG-007 resulted

in a reduction in brain tissue death up to 28 days after a stroke. These studies were conducted in a non-human primate (NHP) stroke model and examined whether ARG-007 (R18) treatment could reduce ischemic brain injury and improve functional outcome. The reference for this study is Meloni, B. P., Chen, Y., Harrison, K. A., Nashed, J. Y., Blacker, D. J., South, S. M., Anderton, R. S., Mastaglia, F. L., Winterborn, A., Knuckey, N. W., & Cook, D. J. (2020). **Poly-Arginine Peptide-18 (R18) Reduces Brain Injury and Improves Functional Outcomes in a Nonhuman Primate Stroke Model**. *Neurotherapeutics: the journal of the American Society for Experimental NeuroTherapeutics*, *17*(2), 627–634. This previous research, combined with the additional promising preliminary data indicating that ARG-007 efficacy does not degrade following administration of tPA, continues to suggest ARG-007's potential to offer neuroprotection both prior to formal diagnosis (imaging) and after treatment with tPA. This could lead to improved outcomes and faster recovery for all stroke patients, regardless of tPA treatment.

'Figure 1' in the announcement is a graph showing how ARG-007 does not reduce its neuroprotective effect following incubation with tPA. This figure is the data from the *in vitro* study with which the announcement relates. The graph provides the data on how viable the brain cells (neurons) are following toxicity from glutamate, which mimics the toxicity to neurons following oxygen depravation due to stroke. The overall cell viability when exposed to glutamate is approximately 5%. However, when these cells are exposed to glutamate and ARG-007 followed by incubation with tPA, the viability of the cells increases and this neuroprotective effect remains relatively stable up to 20 hours after tPA administration.

The announcement stated that the Company is currently undertaking additional further pre-clinical trials to confirm the results of the *in vitro* study in an animal model of stroke. These subsequent trials, to be undertaken by Prof Meloni, will examine the in vivo neuroprotective efficacy of ARG-007 when administered with tPA following stroke in animals. These further pre-clinical trials are anticipated to be available in October 2021 and finalised for publication by December 2021. **This study will be conducted to examine the dose response neuroprotective efficacy of ARG-007 when administered with the thrombolytic agent alteplase (tPA) following transient middle cerebral arterial occlusion (MCAO) stroke in rodents.** ARG-007 will be administered intravenously 60 minutes after MCAO (600 µl infusion over 10 min) and treatment with tPA will commence 20 minutes (1h infusion) after MCAO. The controls will consist of vehicle (saline) and the NA-1 peptide (1000 nmol/kg). These studies will measure the areas of infarcted tissue (TTC staining) and functional assessment (neurologic deficit score, adhesive tape test, Rota-rod).

This announcement has been approved for release by the Chairman and CEO of Argenica

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ABOUT ARGENICA

Argenica (ASX: AGN) is developing novel therapeutics to reduce brain tissue death after stroke and improve patient outcomes. Our lead neuroprotective peptide candidate, ARG-007 has been successfully demonstrated to improve outcomes in pre-clinical stroke models and is in the process of being verified for its safety and toxicity before commencing Phase 1 clinical trials in humans. The aim is for our therapeutic to be administered by first responders to protect brain tissue against damage during a stroke with further potential to enhance recovery once a stroke has taken place.