ARGENICA ACHIEVES MANUFACTURING MILESTONES ALLOWING ADVANCEMENT TOWARDS CLINICAL TRIAL

Highlights:

- *Scaled up batches of Argenica's lead stroke therapeutic ARG-007, have been successfully produced to Good Manufacturing Practice (GMP) requirements by Australian based manufacturing partner.*

- *Scaled up GMP grade ARG-007 achieved a purity profile of 99.9%, well above the required level for clinical trials.*

- *Meeting these requirements was essential for Argenica to progress towards the Phase 1 clinical trial in healthy volunteers.*

- *Manufacturing production risks have been mitigated with the engagement of an additional peptide manufacturer in the U.S, who can produce the required quantities of GMP grade ARG-007 for the Phase 1 clinical trial.*

Perth, Australia; 14 SEPTEMBER 2021 - Argenica Therapeutics Limited (ASX: AGN) ("Argenica" or the "Company"), a biotechnology company developing novel therapeutics to reduce brain tissue death after stroke, is pleased to announce successful scale up manufacture of ARG-007 to Good Manufacturing Practice (GMP) guidelines through our manufacturing partner in Australia.

GMP is a globally-recognised standard for ensuring rigorous and continually monitored processes in drug manufacturing to minimise risks and ensure drugs are safe and effective when administered to patients. These strict regulatory guidelines also meet the standards required for clinical trials in Australia, the U.S. and Europe.

Argenica's Australian based peptide manufacturer, AusPep, has tested all aspects of ARG-007 production and have confirmed the successful process development and scale up of GMP grade ARG-007. Achieving GMP manufacturing of ARG-007 was essential for Argenica to undertake safety and toxicology studies in pre-clinical experiments before commencing its in-human Phase 1 clinical trials.

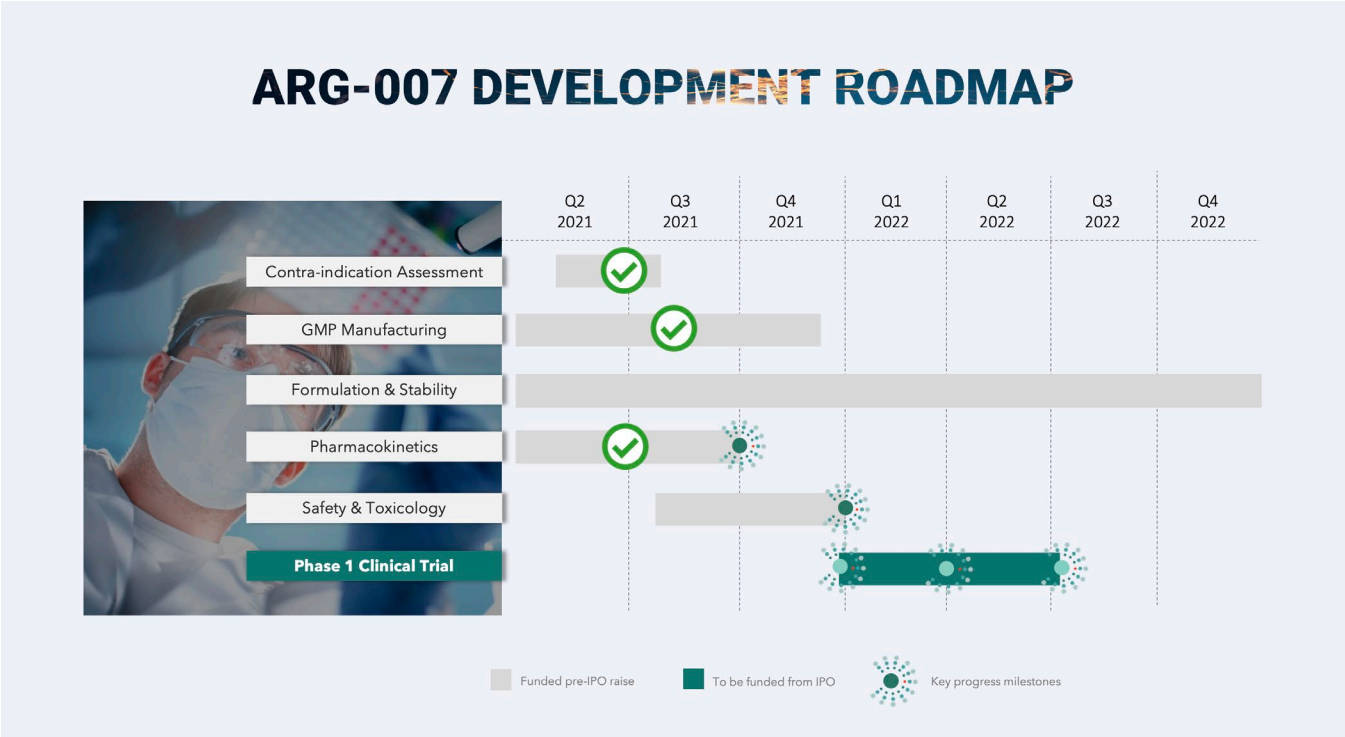
The scaled-up manufacturing process by AusPep resulted in a final product with a purity of 99.9%. This is an important milestone, as peptide purity can have a fundamental impact on the drug's safety, as the quality of a peptide drug will be impacted by its impurity profile. Impurities in a peptide drug may change the desired efficacy of that drug, or induce unwanted

toxicity[i]. For a drug to be used in clinical trials, a peptide drug must achieve a purity level of greater than 98%.

To mitigate manufacturing production risks associated with a single manufacturing partner, the Company separately engaged a US based GMP peptide manufacturer, AmbioPharm, who also achieved process development optimisation of the manufacturing of ARG-007 at a purity of 99.3%. Reaching these purity levels indicates AmbioPharm should be able to produce GMP ARG-007.

Both these milestones allow the Company to progress towards clinical trials with increased confidence surrounding manufacturing and safety. The GMP grade material is now with the company's Clinical Research Organisation partner for use in pre-clinical studies required before conducing its Phase 1 clinical trials, including the standard genotoxicology, final pharmacokinetics, safety, and toxicology studies.

Argenica's Chief Executive Officer, Dr Liz Dallimore said: "Passing the GMP scale up manufacturing milestone and process optimisation is incredibly exciting for Argenica, especially at the very high peptide purities generated. We have de-risked our reliance on a sole manufacturing partner and achieved high purity product from both manufacturers. We now have a high purity GMP grade product that we will use in both our pre-clinical studies and Phase 1 clinical trial."



This announcement has been approved for release by the Board 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.

ABOUT ARG-007

Argenica's lead drug candidate, ARG-007, is a cationic arginine-rich peptide which has been in preclinical development by the company's Chief Scientific Officer Prof Bruno Meloni for over 6 years. ARG-007 has shown preclinical evidence of induced neuroprotection in animal models of stroke. Most recently data published in May 2021[ii] utilising a rodent model of a middle cerebral artery occlusion (MCAO) type stroke showed ARG-007 administration at a dose of 300 nmol/kg resulted in slowing of the infarct core growth and preservation of penumbral tissue. Data gathered in non-human primate animal models of MCAO[iii] showed ARG-007 treatment reduced infarct lesion volume by up to 65.2% and 69.7% at 24 hours and 28 days poststroke, respectively. In this study animals receiving ARG-007 also displayed reduced functional deficits.

ARG-007 has also been shown to be resistant to proteolytic degradation by tissue plasminogen activator (tPA) *in vitro* as described in the company's announcement of 12 July 2021. Argenica believes ARG-007 may have applications beyond stroke with preclinical evidence of efficacy in animal models of traumatic brain injury[iv] and perinatal hypoxic-ischaemic encephalopathy (HIE)[v], the latter being a leading cause of mortality and morbidity in newborn infants.

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[i] Dorpe, Sylvia & Verbeken, Mathieu & Wynendaele, Evelien & De Spiegeleer, Bart. (2012). **Purity profiling of Peptide Drugs.** *Journal of Bioanalysis & Biomedicine*. S6. 10.4172/1948-593X.S6-003.

[ii] 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.

[iii] 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.

[iv] Chiu, L. S., Anderton, R. S., Clark, V. W., Cross, J. L., Knuckey, N. W., & Meloni, B. P. (2020). **Effect of Polyarginine Peptide R18D Following a Traumatic Brain Injury in Sprague-Dawley Rats.** *Current therapeutic research, clinical and experimental*, *92*, 100584

[v] Edwards, A. B., Anderton, R. S., Knuckey, N. W., & Meloni, B. P. (2018). **Assessment of therapeutic window for poly-arginine-18D (R18D) in a P7 rat model of perinatal hypoxic-ischaemic encephalopathy.** *Journal of neuroscience research*, *96*(11), 1816–1826.