ARGENICA RECEIVES ETHICS APPROVAL FOR ITS PIVOTAL PHASE 2 TRIAL IN STROKE PATIENTS

Highlights:

- *Argenica receives ethics approval allowing the Company to undertake its pivotal Phase 2 clinical trial of ARG-007 in acute ischaemic stroke patients (AIS).*
- *Trial sites will now be established in up to ten hospitals across Australia over the coming months, with nine sites expected to be established by Q4 CY 2023.*
- *Up to 92 patients will be dosed in this Phase 2 trial. Patients will be randomly assigned to receive either ARG-007 or a saline placebo (ratio 1:1 respectively) administered as a single intravenous (IV) dose.*
- *Patient recruitment and dosing is expected to commence in Q1 CY 2024.*

Perth, Australia; 12 September 2023 - Argenica Therapeutics Limited (ASX: AGN) ("Argenica" or the "Company"), a biotechnology company developing novel therapeutics to reduce brain tissue death after stroke and other brain injuries, is pleased to announce the Company's ethics application to St Vincent's Hospital Melbourne's Human Research Ethics Committee (HREC) **has been approved**, allowing the Company to undertake a Phase 2 *proof of concept* clinical trial of ARG-007 in acute ischaemic stroke (AIS) patients.

This approval allows Argenica to commence establishing trial sites in up to ten hospitals across Australia. To date, hospitals that have confirmed their participation in the trial include Sir Charles Gardiner Hospital and Fiona Stanley Hospital in Western Australia; Royal Melbourne Hospital, Monash Medical Centre and Sunshine Hospital in Victoria; Royal Adelaide Hospital in South Australia, John Hunter Hospital and Liverpool Hospital in New South Wales, and Princess Alexandra Hospital in Queensland. Once site governance is completed at each hospital, which is expected in late Q4 CY 2023, patients presenting to the emergency department at these hospitals with a confirmed AIS caused by an occlusion in a large vessel in the brain and to be treated with endovascular thrombectomy will be considered for eligibility to participate in the trial. Eligible patients will then immediately receive either a dose of ARG-007 or placebo prior to undergoing a thrombectomy procedure. **Patient recruitment and dosing is expected to commence in Q1 CY 2024.**

Argenica CEO and Managing Director, Dr Liz Dallimore said: "We are delighted to receive ethics approval for this pivotal proof of concept clinical trial of ARG-007 in stroke patients. Proving safety and preliminary efficacy in a human patient population is a pivotal moment for Argenica and the culmination of over a decade of research work to get to this point. We look forward to working with all the hospitals and principal investigators on this groundbreaking trial and will provide regular updates as we progress the dosing of patients. We are confident we have designed a robust trial that is well structured and considered. Should the trial meet some or all of its endpoints, Argenica and ARG-007 are likely to garner significant commercial interest from large pharmaceutical companies."

Clinical Trial Design

Up to 92 patients will be dosed in the Phase 2 trial to be conducted in hospitals across Australia. Patients will be randomly assigned to receive either ARG-007 or a saline placebo (ratio 1:1 respectively) administered as a single intravenous (IV) dose soon after presentation to the emergency department, and confirmation of eligibility and receipt of consent to participate in the trial. Both the site staff treating patients and the patients themselves will be blinded to the treatments being administered.

The Primary Objective of the trial is to evaluate the safety of a single dose of ARG-007 in participants with AIS. The Secondary Objective is to characterize the effect of ARG-007 on reducing infarct volume (volume of brain cell death) in participants with AIS.

A number of functional assessments will also be investigated as Exploratory Objectives, including the effect of ARG-007 on improving neurological outcomes in participants with AIS, the effect of ARG-007 on improving degree of disability in participants with AIS, and the effect of ARG-007 on improving quality of life in participants with AIS. However, the clinical trial recruitment numbers are not sufficient enough to see a statistically significant difference in these exploratory endpoints, and therefore the outcomes of these exploratory endpoints will be used as information only, rather than forming part of the final trial outcome.

Specific details of the Clinical Trial Design can be found in Appendix 1.

This announcement has been approved for release by the Board of Argenica.

For more information please contact: info@argenica.com.au

ABOUT ARGENICA

Argenica (ASX: AGN) is developing novel therapeutics to reduce brain tissue death after stroke and other types of brain injury and neurodegenerative diseases to improve patient outcomes. The Company has recently completed a Phase 1 clinical trial in healthy human volunteers to assess the safety and tolerability of a single dose of ARG-007. Argenica is now progressing

towards a Phase 2 clinical trial in ischaemic stroke patients, as well as continuing to generate preclinical data in other neurological conditions, including in TBI, HIE and Alzheimer's Disease.

APPENDIX 1 – PHASE 2 CLINICAL TRIAL DETAILS

Title:	A Phase II, Multicenter, Double Blinded, Randomized, Placebo Controlled, Parallel-Group, Single-Dose Study to Determine the Safety, Preliminary Efficacy, and Pharmacokinetics of ARG-007 in Acute Ischemic Stroke Patients
Investigational Product Name:	ARG-007 (GMP)
National Coordinating Principle Investigator:	Prof Graeme Hankey
Study Centre:	Multiple Emergency Departments across Australia including include Sir Charles Gardiner Hospital and Fiona Stanley Hospital in Western Australia; Royal Melbourne Hospital, Monash Medical Centre and Sunshine Hospital in Victoria; Royal Adelaide Hospital in South Australia, John Hunter Hospital and Liverpool Hospital in New South Wales, and Princess Alexandra Hospital in Queensland.
Development Phase:	Phase II
Study Type:	Double-blind, randomized, placebo-controlled
Objectives and Endpoints:	**Primary Objective**: To evaluate the safety of a single dose of ARG-007 in participants with acute ischemic stroke (AIS). **Secondary Objective**: To characterize the effect of ARG-007 on reducing infarct volume in participants with AIS. **Exploratory Objective**: • To characterize the effect of ARG-007 on change in infarct volume growth in participants with AIS. • To characterize the effect of ARG-007 on improving neurological outcomes in participants with AIS. • To characterize the effect of ARG-007 on improving degree of disability in participants with AIS. • To characterize the effect of ARG-007 on improving quality of life in participants with AIS. • To assess the pharmacokinetic (PK) profile of ARG-007 in participants with AIS.

Investigational Product Administration:	Intravenous infusion over a 10 minute period
Inclusion Criteria:	1) Diagnosis of AIS deemed suitable for endovascular revascularization (mechanical thrombectomy with or without a thrombolytic agent). 2) Aged ≥ 18 years. 3) Stroke onset (last known well) time ≤ 24 hours before randomization. 4) NIHSS ≥ 5 points at time of randomization. 5) Pre-stroke mRS ≤ 3. Participant must have been living in their own home, apartment, or a senior's lodge where no nursing care is required. 6) Confirmed symptomatic intracranial occlusion, based on computed tomographic angiography (CTA), at one or more of the following locations: intracranial internal carotid artery (T/L morphology) or M1 middle cerebral artery. 7) For participants transferring to stroke centre from another hospital, CTA for study eligibility is to be performed or repeated at stroke centre with endovascular suite onsite if there is a long delay (> 6 hours) from time of first CTA to time of repeat CTA. 8) Signed informed consent from participant or their legally authorized representative, or if required to enable inclusion by applicable national laws and regulations and the applicable Institutional Review Board/Ethics Committee requirements for obtaining consent from the investigator after consultation with an independent physician who is not otherwise participating in the study. 9) Willing (participant and/or caretaker) to commit to follow-up assessments.
Exclusion Criteria:	1) Evidence of a large core of established infarction defined as ASPECTS of 0 to 5. 2) Evidence of intracranial haemorrhage or mass lesion on the qualifying imaging. 3) Endovascular revascularization procedure has already been completed at the time of Screening/randomization or has been completed before administration of study drug. 4) Planned use of an endovascular device that is not approved or does not have clearance by the relevant regulatory authority.

	5) Rapid spontaneous improvement of neurological signs during Screening, as defined by a reduction of ≥ 8 on the NIHSS between onset of symptoms and randomization. 6) History of stroke (ischemic or haemorrhagic) or penetrating head injury within 90 days before enrolment. 7) Uncontrolled blood pressure (BP) ≥ 180/110 mmHg before endovascular revascularization procedure is initiated. 8) No femoral pulses, very difficult endovascular access, or extreme tortuosity of the great vessels that is predicted to result in an inability to timely deliver endovascular therapy. Direct common carotid or radial/brachial/axillary access is permissible. 9) Estimated or known body weight < 45 kg or > 130 kg. 10) Pregnancy: If a woman is of childbearing potential and has a positive point-of-care urine beta-human chorionic gonadotropin (β-HCG) test or is breastfeeding. 11) Severe known renal impairment defined as requiring dialysis (hemo- or peritoneal) or a creatinine clearance < 29 mL/min. 12) Severe or fatal comorbid illness that will prevent improvement or follow-up. 13) Cannot complete follow-up visits because participant is a visitor to the area, or any other known reason that would prevent attendance at follow-up visits. 14) Received treatment with an investigational drug or device within 30 days before enrolment. 15) Any other condition that, in the opinion of the investigator, may adversely affect the safety of the participant, the participant's ability to complete the study, or the outcome of the study.
Number of Participants Planned:	92 (n = 46 ARG-007; n = 46 placebo) A sample size of approximately 92 participants was calculated based on the evaluation of the secondary efficacy outcome of difference in infarct volume at 48 hours (Day 3 ± 1 day) post-treatment.
Study Design:	This is a Phase II, multicenter, double-blind, randomized, placebo-controlled, parallel-group, single-dose clinical study to assess the safety, preliminary efficacy, and PK of ARG-007 in participants with AIS undergoing endovascular revascularization. Based on local institutional clinical practices, participants who have a large-vessel occlusion with a small established infarct core who

	undergo endovascular revascularization (with or without thrombolytic agent use) will be eligible. *Consent* Consent should be obtained per individual state regulations. Due to the time-sensitive nature of treatment, and given that all screening procedures are standard of care (SOC) for stroke, participants will be screened for study eligibility at the time of presentation at the study center hospital for stroke, in parallel to obtaining informed consent. Participants unable to provide consent before randomization will have informed consent obtained from a legally authorized representative. If informed consent was originally provided by a legally authorized representative, and, in the opinion of the study site Principal Investigator, the participant's mental status improves sufficiently to enable them to provide informed consent, the participant must be re-consented in person at the current or next study visit. *Randomization* As soon as eligibility is confirmed, the participant will be randomized in a 1:1 ratio to ARG-007 or placebo in a blinded fashion and randomization stratified based on thrombolytic agent use. Minimization will be employed to reduce imbalance between treatment groups for the following factors: age, intracranial arterial occlusion location, time since onset of occlusion to randomization, Baseline (Day 1) National Institutes of Health Stroke Score (NIHSS), and Baseline (Day 1) Alberta Stroke Program Early Computed Tomography Score (ASPECTS). *Intervention* As soon as possible after randomization, and before the completion of the endovascular revascularization procedure (including thrombolytic agent use), participants will be administered a single, 0.3 mg/kg intravenous (IV) dose of ARG-007 or placebo infused over a 10-minute period using an infusion pump. All participants will be planned for endovascular revascularization and considered for adjunctive thrombolytic therapy. The chosen method of endovascular revascularization (eg, by means of a stent retriever or clot aspiration device) will be at the discretion of the interventionalist, according to clinical judgment, preference, and

	best clinical practice recommendations, in accordance with current local medical jurisdictional guidelines. *Follow-up* Participants will then be followed up on Day 2, Day 3, Day 6 (or Discharge), Day 30, and Day 90 (End of Study [EoS]). Safety measures include vital signs, electrocardiogram (ECG), complete blood count (CBC), clinical chemistry, renal function, and coagulation parameters as well as recording of any adverse events (AEs) and concomitant medications as per the Schedule of Assessments. Efficacy measures include brain infarct volume between treatment groups as measured by magnetic resonance imaging (MRI) or non-contrast computed tomography (NCCT, if MRI is not available) performed on Day 3 (± 1 day only), change in brain infarct volume (by NCCT) from Screening to Day 2 (± 12 hours), neurological impairment (NIHSS), global disability (Modified Rankin Score [mRS] and Barthel Index [BI]), quality of life (QoL; abridged Stroke Impact Scale-16 [SIS-16]; EuroQol 5 Dimension 5 Level [EQ-5D-5L]), and cognitive impairment (Telephone-Montreal Cognitive Assessment [T-MoCA]) assessments. These assessments will be completed as per the Schedule of Assessments.
Recruitment Period	1-2 years. The Company expects to provide updates to the market as it reaches relevant recruitment milestones throughout the clinical trial.