PHASE 1 CLINICAL TRIAL PROGRESSES AS SENTINEL SUBJECTS DOSED IN THIRD COHORT OF ARG-007 PHASE 1 TRIAL

Perth, Australia; 25 November 2022 - 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 that the first subjects in the third cohort of its Phase 1 clinical trial of ARG-007 have been dosed. The subjects in the third cohort will receive a higher dose of ARG-007 than the second cohort.

Importantly, the dosed subjects in the sentinel group showed **no serious safety issues** 24 hours after dosing and therefore dosing of the remaining participants in cohort three will now be completed over the next few days. Following the dosing of these participants, all follow up data will be presented to the Safety Review Committee who will then confirm the progress of the trial to the fourth and final cohort.

CLINICAL TRIAL UPDATE FROM FIRST TWO COHORTS

The Company is pleased to advise that data analysed from the first two cohorts of participants in the Phase 1 clinical trial **showed no clinically relevant changes** across all assessments performed in both Cohorts 1 and 2. Of the possibly related AEs previously announced (see ASX announcement dated 2 November 2022 and 18 November 2022) the safety review committee determined that they **were not clinically significant** and therefore the doses of ARG-007 appeared to be safe and well tolerated, and dose escalation could proceed**.**

A summary of the trial data analysed and results from the Safety Review Committee is presented in Appendix 1.

Argenica CEO and Managing Director, Dr Liz Dallimore said: "This is good news, and the trial is progressing extremely well, all participants dosed to date have shown good safety and tolerability profiles. The data from these first two cohorts, as well as the 24-hour sentinel data from the third cohort, gives us the confidence to look forward to our Phase 2 trial in stroke patients. This is a really exciting stage for the Company, and we look forward to continuing to progress the clinical development of ARG-007."

The Phase 1 clinical trial, conducted at Linear Clinical Research facility in Perth, Western Australia, is designed to assess the safety and tolerability of ARG-007 across four cohorts of healthy adult volunteers, with each cohort receiving an ascending dose of ARG-007. The first volunteer dosed in each cohort is a sentinel subject, meaning this single volunteer receives

the investigational drug at least 24 hours prior to the remaining subjects in the dose cohort. A second volunteer receives a placebo injection of saline at the same time as the sentinel subject. The intention of the sentinel is to identify any unpredicted serious safety issues related to drug dosing in a single subject prior to exposing a larger group of subjects.

For further information on the Phase 1 trial design, please refer to the Phase 1 Trial Summary announced on 8 September, 2022.

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.

APPENDIX 1

Safety and tolerability assessment data collected from Phase 1 trial participants is outlined below:

Vital Signs

The participants' vital signs were assessed during the trial to determine the incidence of changes from baseline in oral or tympanic temperature, pulse rate, respiratory rate, and blood pressure. Blood pressure and pulse measurements were assessed after the subject has rested comfortably in the supine position for at least 5 minutes with a completely automated device.

In both cohort 1 and 2, the safety review committee determined that there were **no clinically relevant vital sign changes**.

Electrocardiogram (ECG) Parameters

A 12-lead ECG was performed using an ECG machine that automatically calculates the heart rate and measures different parts of the cardiac cycle, known as the PR, QRS, QT, and QTc intervals. The ECGs were performed after the subject has rested comfortably in the supine position for at least 5 minutes.

In both cohort 1 and 2, the safety review committee determined that there were **no clinically relevant ECG parameter changes**.

Clinical Laboratory Safety Assessments

A number of clinical laboratory assessments were performed on blood and urine samples taken from participants.

Blood samples (between 17 to 18 mL at screening and between 12 to 13 mL at all other time points) were collected for the following tests:

- Clinical Chemistry (fasted): alanine transaminase, albumin, alkaline phosphatase, aspartate transaminase, bicarbonate, blood glucose, calcium, chloride, creatinine, creatine kinase, gamma glutamyl transferase, lactate dehydrogenase, potassium, sodium, total protein, urea, total bilirubin, triglyceride, total cholesterol, and uric acid.
- Hematology: Hemoglobin, hematocrit, red blood cell count, white blood cell (WBC), platelet count, WBC subset count (neutrophils, eosinophils, basophils, lymphocytes, and monocytes absolute values), mean corpuscular volume, mean corpuscular hemoglobin, mean cell hemoglobin concentration.
- Coagulation: to include determination of activated partial thromboplastin time, prothrombin time and international normalized ratio.
- Viral Serology: HBsAg, HCV antibodies and HIV.

Urine samples were collected for the following tests:

- Urinalysis: Urine specific gravity, pH, protein, glucose, ketones, urobilinogen, bilirubin, leukocytes and blood. Urine microscopy, if required, was performed at the investigator's discretion.

In both cohort 1 and 2, the safety review committee determined that there were **no clinically relevant laboratory assessment changes**.

Physical Examination

Full physical examinations were performed by a study delegated registered physician. The physical examination included examination of the following: general appearance, head, ears, eyes, nose, throat, neck (including thyroid), skin, cardiovascular system, respiratory system, gastrointestinal system, musculoskeletal system, lymph nodes and nervous system. As a minimum, the study protocol required assessments of the skin, lungs, cardiovascular system, and abdomen (liver and spleen).

Neurological examinations were also performed and included examination of: cranial nerves, muscle tone, muscle power, reflexes, light touch sensation, balance, gait, co-ordination, cerebellar system.

Additional symptom-directed physical examinations were performed as required at any time through the study as clinically indicated.

In both cohort 1 and 2, the safety review committee determined that there were **no clinically relevant physical changes**.

Adverse Events (AEs)

An AE is defined as any untoward medical occurrence in a clinical study subject who has been administered a medicinal product which does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not it is related to the medicinal (investigational) product. It is the responsibility of the investigator to document all AEs that occur during the study, regardless of whether they are likely caused by the investigational product, or not.

Participants experienced a number of AEs, all of which were mild or moderate in severity, and many of which were not related to the drug product.

The causal relationship of the AE to the administration of ARG-007 or the study procedure used in this Phase 1 trial was assessed by the medically qualified investigator using the following classifications:

Not Related	Concomitant illness, accident, or event with no reasonable association with treatment.
Unlikely	The reaction has little or no temporal sequence from administration of the investigational product, and/or a more likely alternative etiology exists.
Possibly Related	The reaction follows a reasonably temporal sequence from administration of the investigational product but could have been caused by the study subject's clinical state or other modes of therapy administered to the subject.
Likely Related	The reaction follows a reasonably temporal sequence from administration of the investigational product; is confirmed by discontinuation of the investigational product, and cannot be reasonably explained by the known characteristics of the subject's clinical state

Of the possibly related AEs previously announced (see ASX announcement dated 2 November 2022 and 18 November 2022) the safety review committee determined that they were **not clinically significant** and therefore the doses of ARG-007 appeared to be safe and well tolerated**.**