AI-ENABLED ANALYSIS REVEALS SIGNIFICANT EFFICACY OF ARG-007 IN SEVERE STROKE PATIENTS

Key Findings

- ***ARG-007 delivered statistically significant improvement in follow up infarct volume and functional outcomes in more severe stroke patients*** *when stroke severity scoring was standardised using an FDA approved AI tool.*

- *Functional outcomes measured by the NIH Stroke Scale (NIHSS) at 24hours and the modified Rankin Scale at 90 days were* ***significantly improved*** *compared to placebo (p=0.011 and p=0.005 respectively). This demonstrates ARG-007's potential to meaningfully improve independence in patients with substantial early brain injury.*

- *ARG-007 treatment also resulted in* ***significantly smaller final infarct volumes*** *in patients with larger infarct cores at baseline (p=0.025). This is a defining hallmark of neuroprotection and a key validation of ARG-007's mechanism of action.*

- *These findings* ***build on previously reported findings***[1] *showing a trend in efficacy in patients with slow collateral blood flow (that have more severe strokes), and a broader trend to functional outcome improvements following ARG-007 treatment, and provide greater accuracy in determining outcomes based on stroke severity.*

- *Analysis confirms* ***ARG-007's strongest benefit in more severe stroke patients who have the greatest need for neuroprotection, unlocking a significant commercial opportunity****, and identifying the target population for ARG-007 treatment.*

- *Given the strength of this data, combined with previously reported efficacy trends, Argenica is utilising these finding to* ***enable a precision medicine approach for a Phase 2b trial design****, optimising inclusion criteria around stroke severity utilising AI tools for diagnostics to enrich for patients most likely to benefit and to maximise the probability of success.*

Perth, Australia; 11 December, 2025 - 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 transformational new results from an

[1] ASX Announcements dated 3 September and 15 October 2025.

advanced AI-driven reanalysis of its Phase 2 trial, confirming statistically significant and clinically meaningful efficacy of ARG-007 in severe acute ischaemic stroke patients — a population with the highest unmet need as they tend to have poorer outcomes post thrombectomy.

ARG-007 SIGNIFICANTLY IMPROVED DISABILITY IN SEVERE STROKE PATIENTS

The Brainomix 360 Stroke NCCT module was utilised to standardise the grading of stroke severity at baseline (when the patient first presents to the emergency department, and prior to treatment) in patients enrolled in Argenica's recently completed Phase 2 clinical trial of ARG-007.

Accurately determining the severity of the stroke at baseline is extremely important in a neuroprotection drug trial, because any inaccuracies can mask the real effect of the drug due to an imbalance between groups.

In the Phase 2 trial, stoke severity was graded by the principal neurologist reviewing the brain imaging and assigning an ASPECTS (Alberta Stroke Program Early CT Score). Assigning a manual ASPECTS on imaging is notoriously variable, even between experts; inter-rater agreement is usually only fair–moderate. To account for the potential variability in the Phase 2 trial, Argenica engaged Brainomix to undertake this post hoc analysis to provide a more accurate analysis of stroke severity utilising their regulatory approved AI tool. Utilising this approach in the next clinical trial will ensure a significant reduction in variability in patient selection and outcomes.

The analysis showed participants with more extensive infarct cores at baseline had significantly greater chances of early neurological improvement at 24 hours (lower NIHSS) (OR -0.37, CI: -0.66- -0.09, p=0.011) and significantly greater chances of being less disabled at 90 days (shift towards lower mRS, figure 1) post-stroke (OR 0.91, CI: 0.85 – 0.97 p=0.005) if treated with ARG-007 compared to placebo.

In subgroup analyses, in general ARG-007 treatment improved functional outcomes (mRS 0-3, the preferred clinical endpoint for large core stroke) compared to placebo in more severe stroke patients (i.e those with poor collaterals, or larger infarct cores, or more severe brain frailty) which reached statistical significance for patients with an e-ASPECTS $\leq$6 (figure 1; p=0.0400) compared to the placebo patient with the same baseline e-ASPECTS. This severe stroke population comprised 38% of trial participants. A similar trend was seen when this was expanded to e-ASPECTS $\leq$ 7 (p=0.0669), with around 51% of trial participants making up this group.

In contrast, patients with smaller baseline cores (higher ASPECTS/smaller acute ischaemic volume) did not appear to benefit from being treated with ARG-007. These patients typically suffer minimal secondary injury if successfully recanalized and so the opportunity to improve outcomes with neuroprotection is limited.

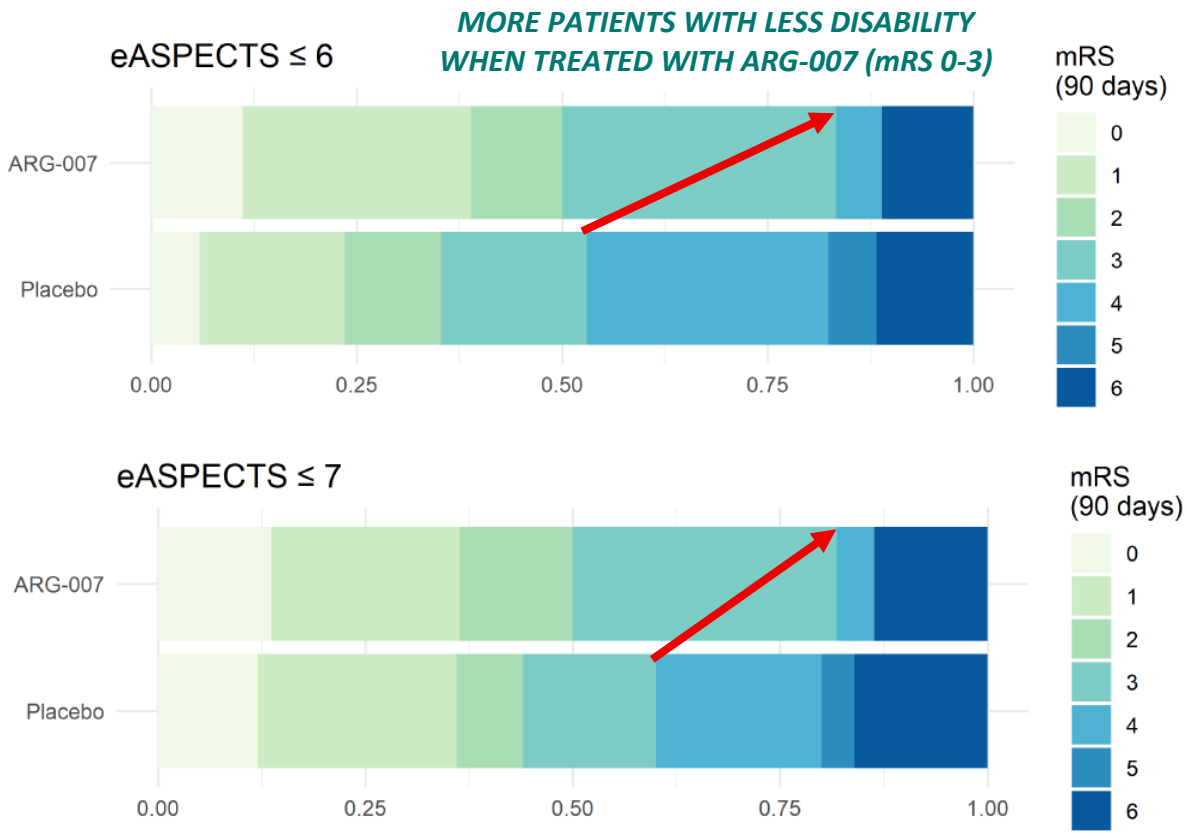

***Figure 1**: Distribution of the mRS at 90 days across treatment arms using e-ASPECTS or AIV to exclude patients with small infarct cores alongside patients with very large cores. Significantly more patients with e-ASPECTS 6 or lower achieved an mRS 0-3 when treated with ARG-007 compared with placebo (p=0.0400). A similar trend was observed in patients with e-ASPECTS of 7 or lower (p=0.0669).*

ARG-007 SIGNIFICANTLY REDUCED INFARCT VOLUME IN SEVERE STROKE PATIENTS

The greatest effect of ARG-007 was a significant reduction in follow-up infarct volume (FIV) in patients with larger baseline infarct cores (higher acute infarct volume (AIV)/lower e-ASPECTS).

There was a significant interaction effect between ARG-007 treatment and baseline AIV, suggesting that the infarct core size may modulate the effect of ARG-007 on follow-up infarct volume, ischemic volume and corrected ischemic volume.

Compared to placebo, FIV estimates were significantly smaller for larger baseline infarct volumes in the ARG-007 group (AIV: 30ml, p-value=0.025). When assessing the corrected ischaemic lesion volume (cISC), which is correcting for haemorrhagic transformation and vasogenic oedema, patients with larger infarct cores at baseline (AIV) treated with ARG-007

had significantly smaller ischaemic lesion volumes at follow-up (figure 2; p=0.034), whilst no significant difference was observed for smaller volumes (AIV 0ml, p-value: 0.132).

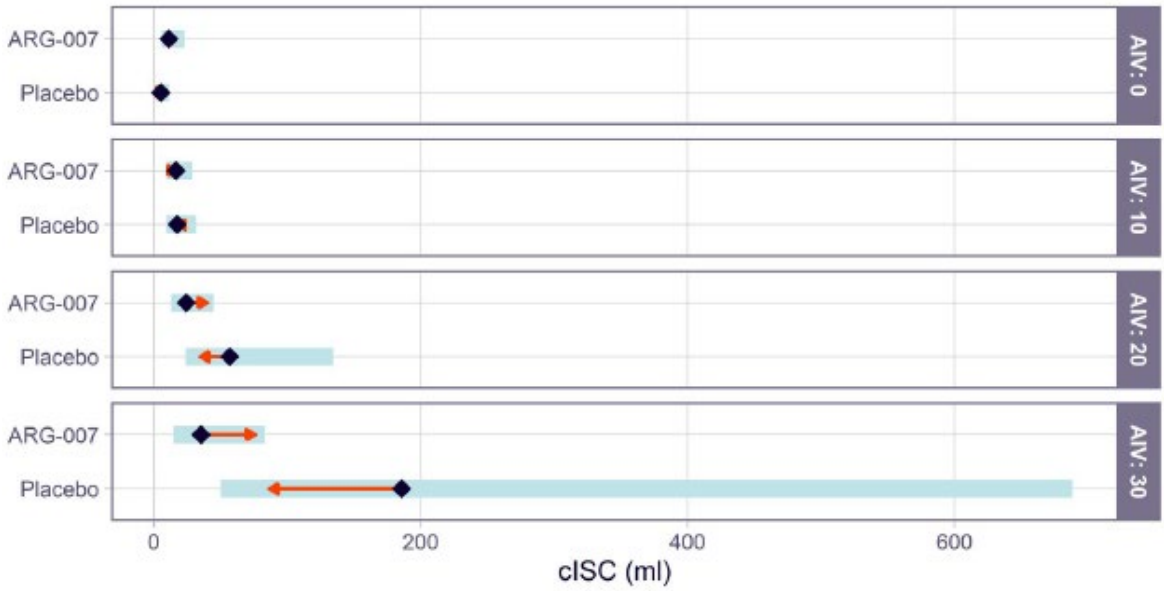

Figure 2: *Total corrected ischaemic lesion volumes (cISC) in ml as predicted from the corresponding multivariate model across different baseline AIV values (0ml, 10ml, 20ml; 30 ml). The estimate corresponds to the estimated marginal means, and represents the predicted difference between groups, after adjusting for the other covariates. Compared to placebo cISC were significantly smaller for larger volume (AIV 30ml, p-value 0.034), whilst no significant difference was observed for smaller volumes (AIV 0ml, p-value: 0.132)*

The Brainomix data analysis also confirmed the random imbalance in baseline stroke severity in this study, with the ARG-007 group enrolling a more severe stroke population at higher risk for worse outcomes. Based on the findings from this Brainomix analysis, it is clear this randomisation skew impacted the topline data outcomes.

A detailed explanation of the study aims and methods is provided in Appendix 1.

Argenica's Managing Director, Dr Liz Dallimore said: "*We are extremely excited by the outcomes of this analysis from Brainomix, a Company at the forefront of data and imaging analysis in stroke clinical trials. ARG-007 demonstrates a treatment effect in severe large-core LVO patients undergoing thrombectomy, highlighting its potential to become the first adjunctive neuroprotective therapy to improve outcomes in the highest-need and highest-value segment of the stroke market. This analysis accurately classifies trial participants based on stroke severity at baseline to provide a clear treatment effect. We are excited to progress to the next stage of development having the confidence to design a more targeted Phase 2b trial.*"

MARKET OPPORTUNITY IN SEVERE ACUTE ISCHAEMIC STROKE

Severe acute ischaemic stroke (AIS) represents a major global unmet medical need, with approximately 87% of all strokes classified as ischaemic according to the U.S. Centers for Disease Control and Prevention (CDC)[2]. Among these patients, a meaningful proportion present with moderate-to-large infarct cores, reflected by ASPECTS scores of 7 or below and typically with slow collateral blood flow —a subgroup consistently associated with poorer outcomes and limited treatment options despite advances in reperfusion therapy[3]. With large vessel occlusion (LVO) strokes accounting for ~38% of all ischaemic strokes[4], and Argenica's Phase 2 trial demonstrating that 51% of LVO patients present with ASPECTS 7 or lower, approximately 20% of all AIS patients fall into this high-severity category and could potentially benefit from ARG-007 treatment. This represents a multi–hundred-thousand–patient annual market globally. Importantly, this population experiences the highest levels of long-term disability and healthcare expenditure, making a clinically proven neuroprotective therapy such as ARG-007 highly compelling to clinicians, payers, and health systems. Showing functional benefit in these more severe strokes therefore represents a significant commercial opportunity for Argenica, supported by strong health-economic rationale and a clearly differentiated therapeutic value proposition.

NEXT STEPS

The combination of this new AI-driven imaging analysis and the previously announced functional outcome data[5] provides Argenica with strong conviction in the efficacy of ARG-007, particularly in patients with severe acute ischaemic stroke who have limited treatment options. Furthermore, these results greatly inform on key elements of study design for future clinical studies to enrich for stroke patients that demonstrate greatest likelihood of benefit from treatment with ARG-007. These consistent and reinforcing signals give the Company the confidence to progress planning for a later stage clinical trial of ARG-007. As part of this next phase, Argenica is undertaking a detailed review of the specialised clinical, operational, regulatory and commercial capabilities required to ensure the successful execution of this next larger clinical study in this high-value patient population, with further updates to be provided as preparations advance.

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

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

[2] U.S. Centers for Disease Control and Prevention (CDC), Stroke Facts, 2023.
[3] Barber et al., *The ASPECT Score to Assess Early Ischaemic Changes on CT in Acute Stroke*, The Lancet, 2000
[4] Malhotra K, Gornbein J, Saver JL. "Ischemic Strokes Due to Large-Vessel Occlusions Contribute Disproportionately to Stroke-Related Dependence and Death." *Frontiers in Neurology.* 2017;8:651
[5] ASX Announcement dated 15 October, 2025 "Promising Improvements in Functional Outcomes in ARG-007 Treated Stroke Patients in Phase 2 Trial".

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. Our lead neuroprotective peptide candidate, ARG-007, has been successfully demonstrated to improve outcomes in pre-clinical stroke models, traumatic brain injury (TBI) and hypoxic ischaemic encephalopathy (HIE). 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 has recently completed a Phase 2 clinical trial in ischaemic stroke patients, as well as continuing to generate preclinical data in other neurological conditions.

APPENDIX 1 – OVERVIEW OF ANALYSIS

BRAINOMIX 360 Stroke

Brainomix 360 Stroke provides a suite of FDA cleared and CE marked AI derived automated imaging biomarkers to support interpretation of CT imaging in acute stroke. This includes automated and standardized assessment of the ASPECT Score (e-ASPECTS), which is an extensively validated and widely used clinical tool for assessing the extent ischemic damage in acute stroke. The automated scores are then reviewed by an expert neuroradiologist, and adjusted as needed, to generate the final AI-assisted biomarker result. Brainomix 360 stroke also provides automated volumetric quantification of ischemic tissue, as defined by reduced tissue attenuation, also termed hypodensity. Widely adopted across hospitals globally, Brainomix 360 Stroke improves speed, accuracy, and standardisation of stroke assessment, making it particularly valuable in clinical trials—such as those for neuroprotective drugs—where consistent identification of stroke severity and infarct burden is essential for patient selection and outcome analysis.

AIMS

The imaging analysis aims were:

- To describe baseline population imaging characteristics and to identify any imbalances in imaging characteristics between study arms,
- To quantify the treatment effect of ARG-007 using Brainomix imaging biomarkers as efficacy and safety endpoints,
- To explore the observed mechanism of action of ARG-007 using mechanistic biomarkers (such as infarct growth, penumbral salvage, edema and hemorrhagic trans-formation), and
- Interrogate whether Brainomix imaging biomarkers can improve the stratification of treatment effect in the study population, through the analysis of subgroup responses.

STUDY DESIGN AND OVERSIGHT

This retrospective analysis of the SEANCON clinical trial was commissioned by Argenica Therapeutics and delivered by the Brainomix AI Imaging Core Lab.

SEANCON was a randomised placebo-controlled trial of ARG-007, a novel neuroprotective peptide agent. (1) As part of the trial, 93 patients were randomized to either a single-dose of 0.3 mg/kg of ARG-007 or Placebo. Subjects received either ARG-007 or placebo within 24 hours of “last known normal”, as soon as possible after randomization, and prior to endovascular revascularization therapy.

In the SEANCON trial brain imaging was acquired at baseline, at 24h (Day 2 non-contrast CT, NCCT) and at 48h (Day 3 MRI). Whenever MRI was not available at the study site or contraindicated, a Day 3 NCCT was acquired instead. Baseline imaging was as part of standard of care for suspected stroke and included NCCT, CT angiography (CTA), and CT perfusion (CTP) when acquired.

Given the superior contrast-to-noise of MRI for defining infarction compared to NCCT, imaging collected at Day 3 (48h ± 24h) was prioritised whenever possible for generating Brainomix follow-up imaging endpoints.

PATIENTS

Patients 18 years of age or older with a diagnosis of acute ischemic stroke were recruited following written informed consent. Last known well time was less than 24 hours. The dose of ARG-007 was administered as soon as possible after randomization, and before endovascular revascularization therapy. For study inclusion pre-stroke modified Rankin Scale (mRS) of patients was required to be ≤3, and NIHSS score at the time of randomization to be ≥5. CTA imaging was used to confirm patient inclusion based upon on evidence of symptomatic intracranial occlusion, at either the intracranial internal carotid or M1 segment of the middle cerebral artery. Patients were excluded if the standard of care imaging showed a mass lesion or acute intracranial hemorrhage.

BASELINE IMAGING BIOMARKERS

In this analysis of ARG-007, the following imaging biomarkers were generated from SOC baseline imaging:

- Biomarkers of Ischemic Core Extent
- e-ASPECTS
- Acute Infarct Volume
- Biomarkers of Acute Ischemic Insult Severity (Acute Cerebral Edema)
- Biomarkers Assessing Cerebral Collateral Circulation
- Biomarkers of Hypoperfusion
- Biomarkers of Brain Frailty

Follow-up Imaging Biomarkers

The following biomarkers were generated to explore their use as potential imaging endpoints for safety and efficacy:

- Biomarkers of Follow-up Infarct/Lesion Volume
- Biomarkers of Hemorrhagic Transformation
- Biomarkers of Follow-up Infarct Volume Corrected for Edema
- Biomarkers of Infarct Progression
- Penumbral Salvage

STATISTICAL ANALYSIS

The analysis used the following approaches:

1. **Descriptive Analysis of Imaging Variables:** Distribution of baseline and follow-up biomarkers were summarized using descriptive statistics (n, mean, median, standard deviation, interquartile range) and visualized with boxplots.

2. **Differences between treatment arms** were calculated using different statistical univariate models based on imaging biomarker distribution (e.g. Log-transform, Gaussian, Binomial, Tweedie for HT). When appropriate, analyses were repeated adjusting for key covariates such as age, thrombolytic status, stroke to reperfusion

time, baseline (Day 1) infarct volumes, and collateral status, including interaction terms as needed.

3. **Subgroup analyses:** the effect size for pre-specified subgroups were estimated for both imaging and clinical endpoints using appropriate models based on the dependant variable distribution In light of the sample sizes, subgroup analyses were not adjusted for covariates.

Imaging analysis was conducted blinded to treatment arm. A significance level of $\alpha=0.05$ was used for all inferential statistical tests, adjusted for multiple comparisons where necessary.