ARG-007 EFFICACIOUS DOSE VALIDATED IN NEW PRECLINICAL STROKE STUDY

Highlights:

- *Argenica engaged clinical research organisation MD Biosciences to independently validate the efficacy of ARG-007 in a rat model of ischemic stroke that mimics human large vessel occlusion strokes to provide further conviction on the efficacy and dosing of ARG-007.*

- *Consistent with previous studies conducted by Argenica's Chief Scientific Officer at the Perron Institute, a dose of 325 nmol/kg ARG-007 showed a* ***statistically significant reduction in infarct volume of 47.3%.*** *Further, statistically significant but smaller reductions of 28.4% and 27.9% were seen in the 650 nmol/kg and 1100 nmol/kg ARG-007 dose groups, respectively, indicating an inverted "U" shaped therapeutic window.*

- *This MCAo study data taken together with the clinical pharmacokinetic (PK) data from both the Phase 1 and Phase 2 clinical trials provides a more* ***complete picture of ARG-007's dose–exposure relationships****. These integrated datasets will enable a more informed dose strategy as the Company continues to integrate emerging pharmacology and PK/PD insights in clinical trial design moving forward.*

- *This is the first time ARG-007 efficacy has been* ***independently validated*** *in a transient rat model of acute ischaemic stroke in a validated middle cerebral arterial occlusion (MCAo) model.*

- *This new efficacy data, together with the recent efficacy data from the Phase 2 clinical trial in acute ischemic stroke patients, will assist Argenica in determining the future clinical development of ARG-007 in acute ischaemic stroke (AIS).*

Perth, Australia; 25 November 2025 - Argenica Therapeutics Limited (ASX: AGN) ("Argenica" or the "Company"), a biotechnology company developing novel therapeutics to reduce brain tissue death after stroke and other neurological conditions, is pleased to announce new data from an independent study conducted by leading preclinical and translational clinical research organisation MD Biosciences using the gold-standard middle cerebral artery occlusion (MCAo) rat model of ischemic stroke, which has been extensively validated by MD Biosciences.

In this blinded study, ARG-007 significantly reduced infarct volume compared with saline controls, with the 325 nmol/kg dose showing a 47.3% reduction. This dose represents the **optimal exposure window** identified in previous preclinical work and continues to demonstrate the compound's potent neuroprotective activity *in vivo*. Higher doses of ARG-007 at 650 nmol/kg and 1100 nmol/kg also showed smaller statistically significant reductions in infarct volume of 28.4% and 27.9% respectively (n=10 in each group), indicating ARG-007's therapeutic window is an inverted "U" shaped curve with doses that are too high losing their therapeutic effect.

The transient MCAo rat model is a reliable model that emulates a large vessel occlusion ischaemic stroke with reperfusion in humans. Occlusion of the MCA leads to injury of the sensorimotor cortex. The level of this injury is then assessed by histology evaluation of the infarct size. Details of the study are outlined in Appendix 1.

These findings **independently** validate for the first time ARG-007's potent neuroprotective activity and complement Argenica's existing preclinical data portfolio, confirming the nature of the therapeutic window of the drug. The new MCAO results provide important insights into ARG-007's therapeutic window, suggesting that neuroprotection is strongest within a defined exposure range. These findings, together with the Phase 1 and Phase 2 pharmacokinetic (PK) data, now guide a more targeted dose strategy for the next clinical study.

The refined MCAo model developed by MD Biosciences incorporated updated methodologies and more contemporary standards of preclinical stroke research, improving reproducibility and translational relevance. The results replicate and strengthen earlier findings demonstrating the exposures required to **deliver the greatest neuroprotective benefit**, providing important insight into ARG-007's pharmacology.

Although the company's Phase 2 trial in acute ischemic stroke showed no overall infarct-volume difference between ARG-007 and placebo, the clinical study provided important safety, pharmacokinetic, and subgroup insights, in what was a small sample size, to guide further decision making on the future development of ARG-007 in AIS.

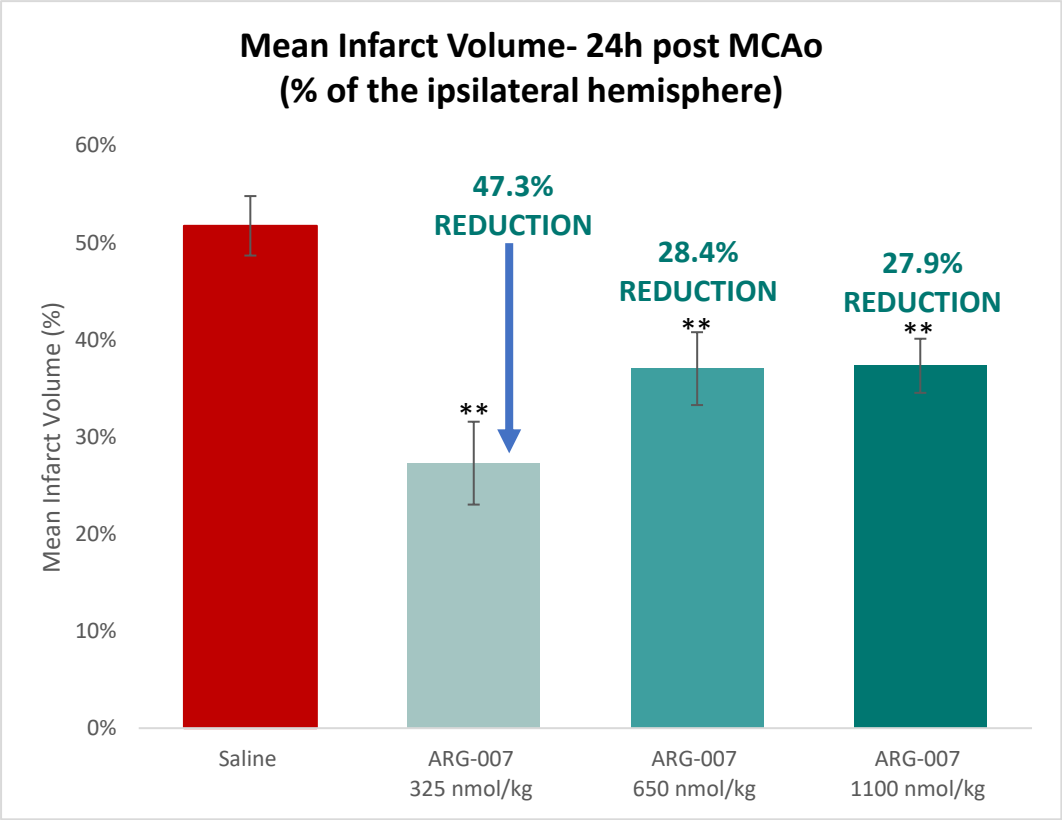

Figure 1. Mean Infarct volume (% of Ipsilateral hemisphere) of the saline control and three different doses of ARG-007, administered 30 minutes before reperfusion. ** p<0.01 using Student's T-test in comparison to the Saline group

Argenica's Managing Director, Dr Liz Dallimore said: "These new data reinforce the biological activity of ARG-007 and provide additional data to support the Company's decision making on the future clinical development of ARG-007, which may include refining patient selection, dosing, and optimising treatment timing. These data provide a clear confirmation of ARG-007's neuroprotective effects in an established and clinically relevant stroke model and shows the importance of reducing patient variability to heighten the efficacy signal in clinical development. Importantly, the new study reinforces the presence of a defined therapeutic window and deepens our understanding of the compound's dose–response characteristics."

Argenica will use these data, along with data from the recently completed Phase 2 study and further analysis from AI stroke imaging company Brainomix to guide its ongoing evaluation of ARG-007's mechanism of action and to inform future development planning including dose selection. While the recent Phase 2 clinical study in acute ischaemic stroke did not demonstrate a difference between ARG-007 and placebo on overall infarct volume, the trial

did show trends in functional outcome improvements[1]. Therefore, the company continues to analyse imaging and subgroup data to identify additional insights that may relate to patient selection, exposure ranges, or disease biology.

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. 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.

[1] ASX Announcement dated 15 October, 2025 "Promising Improvements in Functional Outcomes in ARG-007 treated stroke patients in Phase 2 Trial".

APPENDIX 1 – STUDY OVERVIEW

OBJECTIVE:

The objective of the present study was to examine the beneficial efficacy and PK of ARG-007 (R18D) in the transient Middle Cerebral Artery occlusion (MCAo) model for stroke in rats.

SUMMARY:

Rat model of stroke was induced by transient occlusion of the middle cerebral artery for 90 minutes. Animals were treated with ARG-007 or Saline intravenous (IV), as a 10 min infusion starting 30 min before reperfusion (n=10 in each group). ARG-007 was administered at three doses: 325, 650 and 1100 nmol/kg.

Body weight measurements were performed before MCAo and after 24 hrs.

Animals treated with ARG-007 were bled for PK 10 min, 15 min, 30 min, 1h, 2h, 4h and 8h after the start of infusion. Three animals were bled at each time point per group.

Infarct volume was measured using TTC staining one day post-surgery.

Body weight

All animals showed a decrease in their body weight compared to the baseline level one day after surgery. A reduction of ~10% of the baseline level was demonstrated in all groups. This reduction is typical for this model.
No statistical differences were found between the groups.

Infarct volume (Table 2, Figure 2):

Infarct volume was measured using TTC staining at one day post-surgery. Upon termination, the animals' brains were harvested, sliced into ~2mm thick slices using a dedicated matrix, and stained using TTC 1% solution to evaluate the infarct size. The infarct percentage from the right hemisphere (infarct volume/ hemisphere volume) was calculated for a total of 5 slices cut from each brain. The infarct volume was also presented in mm3.
Animals treated with ARG-007 at doses of 325, 650 and 1100 nmol/kg showed statistically significant reduction in the mean infarct volume (% of ipsilateral hemisphere) in comparison to the Saline group (27.30±4.27% or 37.03±3.75% or 37.32±2.79% vs. 51.74±3.06%, for groups; $p<0.01$). The smallest infarct volume was found in the lowest dose of ARG-007.

CONCLUSIONS:

Under the conditions of this study, animals treated IV by ARG-007 at a dose of 325, 650 and 1100 nmol/kg showed statistically significant reduction in the mean infarct volume (% of ipsilateral hemisphere) in comparison to the Saline group in a transient MCAo model in rats. No statistically significant differences in the mean infarct volume were found between the study groups treated with lower doses of ARG-007.