TOPLINE PHASE 2 TRIAL RESULTS OF ARG-007 IN ACUTE ISCHEMIC STROKE PATIENTS

Key Points:

- *Primary endpoint was met with ARG-007 found to be **safe and well tolerated** in acute ischemic stroke (AIS) patients with no statistically significant difference in treatment emergent adverse events between ARG-007 and placebo groups.*
- ***No evidence of drug-to-drug interactions** seen with the thrombolytic clot dissolving drugs, meaning ARG-007 can be delivered regardless of whether a patient receives these drugs or not.*
- *The secondary endpoint, being efficacy and reduced infarct volumes across all AIS patients at Day 3 post drug/placebo administration, did not show an overall ARG-007 treatment effect compared to placebo. An analysis of the data showed large variations in infarct volumes which made it difficult to see an overall treatment* effect.
    - *Argenica had anticipated efficacy data could be difficult to clearly ascertain across a heterogeneous patient population so had set predefined subgroups of patients to look for signals in efficacy.*
- *Efficacy signal seen with the analysis of a prespecified subgroup who represent highly at-risk patients (specifically those with slow collateral blood flow, or "rapid progressors", comprising 30% of trial participants), showed a **15% mean infarct volume reduction** (5mL total reduction on model adjusted mean[1]).*
    - *This outcome aligns with the Company's pre-existing hypothesis that these patients, due to their slow collateral blood flow would benefit most from ARG-007's neuroprotective potential, as there is more vulnerable penumbra to protect). These patients typically have the worst outcomes under current standards of care because there is more at-risk brain tissue that is not supported by sufficient collateral blood flow.*

[1] The model adjusted mean was computed using a linear regression model with treatment as the main effect and the stratification and minimization variables as covariates. LS Mean Ratio reflects ration of ARG-007 to Placebo. Lower volumes indicate less damage, therefore ratios less than 1 indicate treatment benefit with ARG-007. This statistical method ensures the data gives greater confidence to data being related to treatment effect (95% CI ratio 0.230, 3.14)

- *Given the clear success on safety and a signal of efficacy in a significant at-risk patient sub-group, future trials can be designed to focus on this patient population, estimated to be approximately 33% of LVO AIS patients[2], and powered more accurately to provide the best chance of showing a definitive treatment effect.*
- *This first Phase 2 study in 92 AIS patients has yielded important and instructive information on patient selection, dosing and imaging time frames, to optimize any future AIS trial design. Taken together with the robust, validated preclinical animal data which has consistently demonstrated significant treatment outcomes, the company maintains high confidence in ARG-007's therapeutic potential for further development and commercial attractiveness. The company remains well funded to pursue further development activities with a current cash balance of $7M and an expected R&D Tax Rebate of $3.5-4M.*

Perth, Australia; 3 September 2025 - Argenica Therapeutics Limited (ASX: AGN) ("Argenica" or the "Company"), a biotechnology company developing novel therapeutics to reduce brain tissue death after stroke, received unblinded data from its Clinical Research Organisation, ProPharma, for its Phase 2 trial evaluating ARG-007 in patients with acute ischaemic stroke (AIS) undergoing endovascular revascularisation (thrombectomy) on Saturday 30 August 2025, and is pleased to announce top-line results.

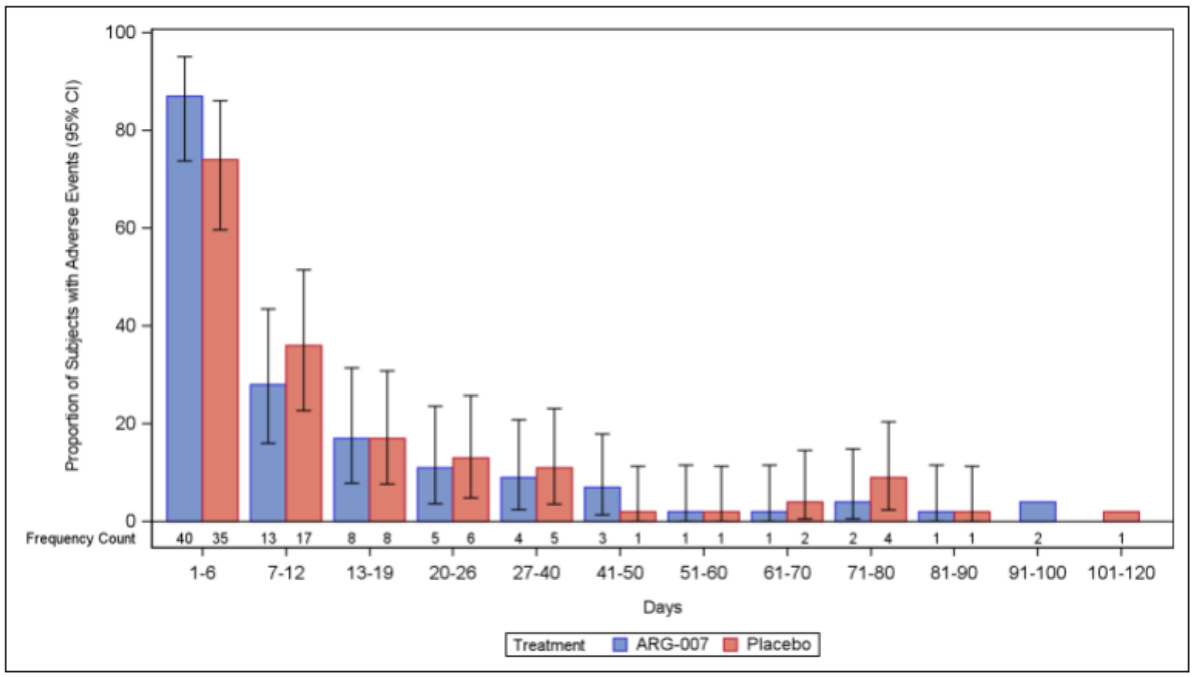
The Phase 2 SEANCON trial was a multicentre, double-blind, randomised, placebo-controlled, single-dose clinical study assessing the safety, preliminary efficacy and pharmacokinetics of ARG-007 in participants with AIS undergoing thrombectomy.

PRIMARY ENDPOINT - SAFETY

The primary endpoint in the trial aimed to evaluate the safety of a single dose of ARG-007 in participants with AIS. **ARG-007 was generally well tolerated with no statistically significant difference in treatment emergent adverse events** between ARG-007 treated patients and the placebo patient group.

[2] Jansen IG, et al; MR CLEAN Registry investigators. Impact of single-phase CT angiography collateral status on functional outcome over time: results from the MR CLEAN Registry. J Neurointerv Surg. 2019 Sep;11(9):866-873.

Figure 1: Temporal profile of Treatment-Emergent Adverse Events



Before any efficacy signal can be translated into patient benefit, a therapy must be shown to be safe. Successful demonstration of safety is a requirement for moving into larger, later stage trials. This positive safety data is a significant milestone for the clinical development of ARG-007 in neurology.

The trial also confirmed there was no drug-to-drug interaction with thrombolytic clot dissolving drugs (Alteplase or Tenecteplase), a significant advantage for trials moving forward as it means ARG-007 can be delivered to a patient whether they receive these clot dissolving drugs or not.

SECONDARY ENDPOINT

Analysis of the overall infarct volume at Day 3 (48 hours ±1 day) showed no treatment effect across all patients receiving ARG-007 compared with placebo. An analysis of the data showed large variations in infarct volumes which made it difficult to see an overall treatment effect.

As part of the upfront trial design, broad enrolment of different patient categories of large vessel occlusion (LVO) AIS patients was essential to provide safety data across all patient groups. Given the nature of infarct volume progression across different LVO patient groups, Argenica had anticipated efficacy data could be difficult to clearly ascertain. The Company accordingly set predefined subgroups of patients to look for signals in efficacy to ensure future trials can target the most prospective AIS patient subgroups to increase the chances of future trial success.

INFARCT VOLUME REDUCTION IN PREDEFINED SUBGROUP OF MOST AT-RISK PATIENTS

One specific subgroup Argenica hypothesised may see a greater effect was in patients with more at-risk penumbra (i.e. vulnerable, but not dead, brain tissue which is still "salvageable") due to slow collateral circulation – these patients are typically known as rapid progressors. This is because a lack of blood supply to these parts of the brain which have been affected and are still vulnerable to death means the neurons (brain cells) are hypoxic but not dead. This is the state in which excitotoxicity and mitochondrial dysfunction are active – the process ARG-007 interrupts[3].

Analysis of the prespecified secondary endpoint of infarct volume at Day 3 (48 hours ±1 day) in patients with slow collateral circulation showed a trend in efficacy with a **15% infarct volume reduction** (5mL total reduction on model adjusted mean, 95% CI ratio 0.230, 3.14) in patients receiving ARG-007 (n=10) compared with placebo (n=18).

Patients with slow collateral circulation are the most at-risk of poor outcomes post stroke. When someone has a large vessel stroke (a blockage in one of the brain's main arteries), the brain relies on "backup" blood vessels called collaterals. These collaterals act like side roads that help blood flow around the clot to various parts of the brain.

In some stroke patients, these backup vessels are strong and plentiful, so blood gets through to vulnerable parts of the brain post stroke, meaning the brain tissue is not as vulnerable to death and reperfusion injury post thrombectomy.

However, around 30% of acute ischaemic stroke patients with large vessel occlusion have poor or slow collateral blood supply. Not enough blood gets through to the affected parts of the brain, so the brain tissue dies faster, and patients typically do worse, even if the clot is later removed.

From previous studies[4], Argenica hypothesised that good collaterals would support better tissue outcomes even without additional neuroprotection, while slow (incomplete) collaterals may leave more penumbra at risk, but still able to be salvaged, enhancing ARG-007's neuroprotective drug potential. Pleasingly, the analysis of the prespecified secondary endpoint of infarct volume at Day 3 (48 hours ±1 day) in patients with slow collateral circulation showed a trend in efficacy with a 15% infarct volume reduction on the model adjusted mean (95% CI ratio 0.230, 3.14) and lends itself to supporting this hypothesis.

This supporting efficacy signal now defines a clear patient population to target in later stage trials. Further, in these patients, earlier intervention can take advantage of more salvageable

[3] MacDougall G, Anderton RS, Trimble A, Mastaglia FL, Knuckey NW, Meloni BP. Poly-arginine-18 (R18) Confers Neuroprotection through Glutamate Receptor Modulation, Intracellular Calcium Reduction, and Preservation of Mitochondrial Function. Molecules. 2020 Jun 29;25(13):2977

[4] Seymour T, Kobeissi H, Ghozy S, Gupta R, Kadirvel R, Kallmes DF. Under (back) pressure: Better collateral flow may facilitate clot removal in ischemic stroke: A systematic review and meta-analysis. Interv Neuroradiol. 2023 Mar 29.

tissue and limit irreversible damage[5], which will also be factored into future trial design, to potentially show an even greater efficacy signal in this and other patient subgroups.

Argenica CEO and Managing Director, Dr Liz Dallimore, said: "*These topline data represent a significant milestone for Argenica. ARG-007 has now been evaluated in a successfully executed Phase 2 trial involving patients with acute ischaemic stroke, and importantly the results show the drug is safe and well tolerated in AIS patients, without any drug-to-drug interaction with clot dissolving drugs.*

Passing safety was of the utmost importance in this trial, as it allows the Company to continue advancing ARG-007 in any future AIS trials, but also provide confidence of ARG-007's safety when being explored for other indications outside of stroke (such as TBI and HIE).

As is the objective for Phase 2 trials in large therapeutic indications in heterogenous populations, we have investigated the underlying signals of efficacy to determine in which patient group our drug worked best. We are delighted to have seen an efficacy signal in the most at-risk patients with slow collateral circulation, which are the patients that need a neuroprotection drug the most.

This information will allow us to target prespecified patient subgroups in later stage clinical trials and together with all our pre-clinical data, provides a compelling opportunity to explore the therapeutic potential of ARG-007.

We are now one step closer to ARG-007's potential to address a significant unmet need in stroke treatment".

NEXT STEPS

A full analysis of the trial data, including patient subpopulations, will be completed over coming months to determine next steps, and this will be supplemented with further preclinical data to gather more information on efficacious doses and timing of delivery. Further, Argenica has engaged Brainomix, an AI stroke diagnostic company, to provide greater data insights into the imaging generated during the trial, in particular in the slow collateral patient subgroup. These analyses will assist in developing a targeted later stage trial design. It is expected this analysis will be completed by the end of calendar year 2025 and the Company will keep shareholders informed as further material information becomes known.

Further, the Company awaits the release of important data on the drug's pharmacokinetic profile in ischaemic stroke patients. This will be a critical piece of data to determine whether the drug behaves in the same way in stroke patients as it does in healthy patients, and therefore whether dosing can also be optimised. Again, the Company will inform shareholders once further information is known.

[5] Maguida G, Shuaib A. Collateral Circulation in Ischemic Stroke: An Updated Review. J Stroke. 2023 May;25(2):179-198

Argenica will continue discussions with regulatory agencies and is looking forward to updating potential partners regarding the results of the subgroup in its Phase II trial, and the potential design of the next phase of clinical development.

The Company remains well funded to progress its programs until further data points become known with current cash of $7 million and an expected R&D refund of between $3.5-$4 million.

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 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 is now conducting a Phase 2 clinical trial in ischaemic stroke patients, as well as continuing to generate preclinical data in other neurological conditions.

PHASE 2 STROKE CLINICAL TRIAL OVERVIEW

The Phase 2 trial was a Multicentre, 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 (SEANCON).

The trial was designed to test how safe ARG-007 is in AIS patients, with safety being a significant regulatory hurdle in neurology drug development. Proving ARG-007 is safe in AIS patients paves the way for Argenica to progress to later stage pivotal trials and further engage with global pharmaceutical companies.

Furthermore, the trial was designed to generate preliminary data on the ability of ARG-007 to reduce brain tissue death following stroke and mechanical removal of brain clot (thrombectomy) across a number of patient subgroups. Proving the neuroprotective ability of ARG-007 in at least one prespecified patient subgroup is a significant de-risking milestone for the Company and opportunity to place Argenica at the forefront of neuroprotective clinical validation.

The trial enrolled only patients with a diagnosed large vessel occlusion (LVO) stroke that were eligible for endovascular thrombectomy (mechanical removal of a clot in the brain). The trial also embedded predefined subgroups based on collateral blood flow as part of the analysis.

LVO strokes account for close to 40% of all acute ischaemic strokes, and LVO strokes are responsible for 60% of post-stroke dependency and 90% of mortalities after stroke and therefore are considered the most devastating type of stroke[6].

The trial was conducted in 8 hospitals across Australia that have dedicated stroke care units capable of performing endovascular thrombectomy. As patients enter the emergency department with a suspected AIS, they were assessed for eligibility to participate in the trial by the principal investigator (PI) neurologist at each trial site.

Following treatment, patients were assessed for key safety outcomes as well as infarct volumes as measured on imaging.

[6] Malhotra K, Gornbein J, Saver JL. Ischemic Strokes Due to Large-Vessel Occlusions Contribute Disproportionately to Stroke-Related Dependence and Death: A Review. Front Neurol. 2017 Nov 30;8:651.