# PHASE 2 TRIAL RESULTS

## ASX: AGN

SEPTEMBER 2025

MANAGING DIRECTOR PRESENTATION

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# LEADING RESEARCH & CLINICAL TEAM

## Prof. Bruno Meloni
## CSO & Research Lead

Head of Stroke Laboratory Research at UWA and the Perron Institute. Professor Meloni has over 25 years experience as a research scientist, the last 20 in the field of stroke/cerebral ischaemia. Research in the stroke/cerebral ischaemia field has focused on understanding the mechanisms associated with ischaemic brain injury, the identification of potential neuroprotective targets and the development of new therapies. A/Prof Meloni has experience with designing preclinical stroke trials, and the use of peptides as neuroprotective agents.

## Dr David Blacker
## Chairman – CAC & Co-National PI

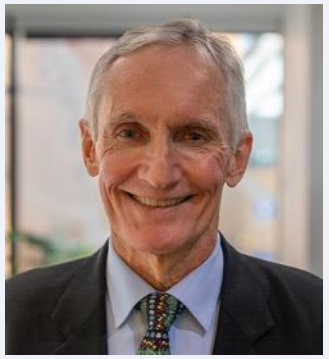
Acute stroke clinician/neurologist who has previous experience initiating neuroprotection clinical stroke trials in Western Australia and being the local Principal Investigator of a number of national and international acute and secondary prevention stroke studies. Prof Blacker is the Perron Institute Medical Director and consultant neurologist and stroke physician.

## Jane Taylor
## Phase 2 Project Lead

Project Lead for Argenica ARG-007 Phase 2 stroke study. Experienced Clinical Trial Project Lead with proven international experience in successful end-to-end trial management. Special interest in Neurology and imaging studies. Over 20 years' experience running clinical trials in both large global clinical research organisations including ICON Clinical Research and Syneos Health, as well as in Australian based companies.

## Dr Meghan Thomas
## VP Clinical & Regulatory Development

15 years experience in basic research, clinical trial design and oversight, regulatory pathways, and product development. Previous role as VP Clinical Programs and Operations at Zelira Therapeutics (ASX: ZLD). Experience running centralised research ethics and governance system across a state-wide public health service



## Prof. Graeme Hankey
## Co-National Coordinating Principal Investigator

As a neurologist-scientist, Professor Hankey has made an outstanding lifetime contribution to stroke research, with a special interest in epidemiological studies and clinical trials of interventions for the treatment and prevention of stroke. He is internationally recognised for his achievements and has led several pivotal studies in collaboration with leading researchers worldwide. He chairs 4 DSMBs for stroke trials and is a member of a further 6 DSMBs.

## Ana Lucia Meyborg
## Senior Clinical Project Manager, ProPharma

Ana has 25 years Clinical Research experience commencing as a Research Nurse and progressing through Study Coordinator, CRA, SCRA and Clinical Trial Manager / Clinical Project Manager / Senior Clinical Project Management positions.

# PATIENT & CONSUMER ENGAGEMENT – ADVISORY COMMITTEE

## Prof Geoffrey Donnan
## Member - CAC

Professor of Neurology at The University of Melbourne and former Director of The Florey Institute of Neuroscience and Mental Health. Co-founder of the Australian Stroke Trials Network (ASTN) within which there have been conducted numerous investigator driven and other stroke trials. Past President of the World Stroke Organization. Current Co-Chair of the Australian Stroke Alliance which have a focus on patient outcomes in rural and remote communities

## Dr Jeffery Saver
## Member - CAC

Dr Saver is Professor and Senior Associate Vice-Chari of Neurology at UCLA, and Director of the UCLA Comprehensive Stroke Centre. He has served as the principle investigator on a number of key stroke trials, including the Global PI for the SWIFT PRIME trial.

## Dr Paul Bailey
## Member - CAC

Dr Bailey is a medical doctor withextensive experience in emergency medicine and critical care. Dr Bailey was the Medical Director for St John's Ambulance Service for 7 years and brings detailed knowledge of patient care requirements in an ambulance setting.

## Dr Tim Phillips
## Member - CAC

Interventional Neuroradiologist with 15 years' experience, currently working at NIIS W). He undertook post-specialist fellowship training at the Royal Melbourne Hospital, The Royal London Hospital, Queens Hospital Romford, The National Hospital for Neurology and Neurosurgery, and Great Ormond Street Hospital in London.

## Mr Tony Rolfe
## Member - CAC

Mr Rolfe is a stroke survivor and provides critical input into our clinical and consumer advisory committee. Mr Rolfe assist Argenica to determine the potential impact of our trial protocol on how a patient would want to consent, how the follow up checks would impact recovery, and a person with a lived experience of stroke's view on ARG-007.

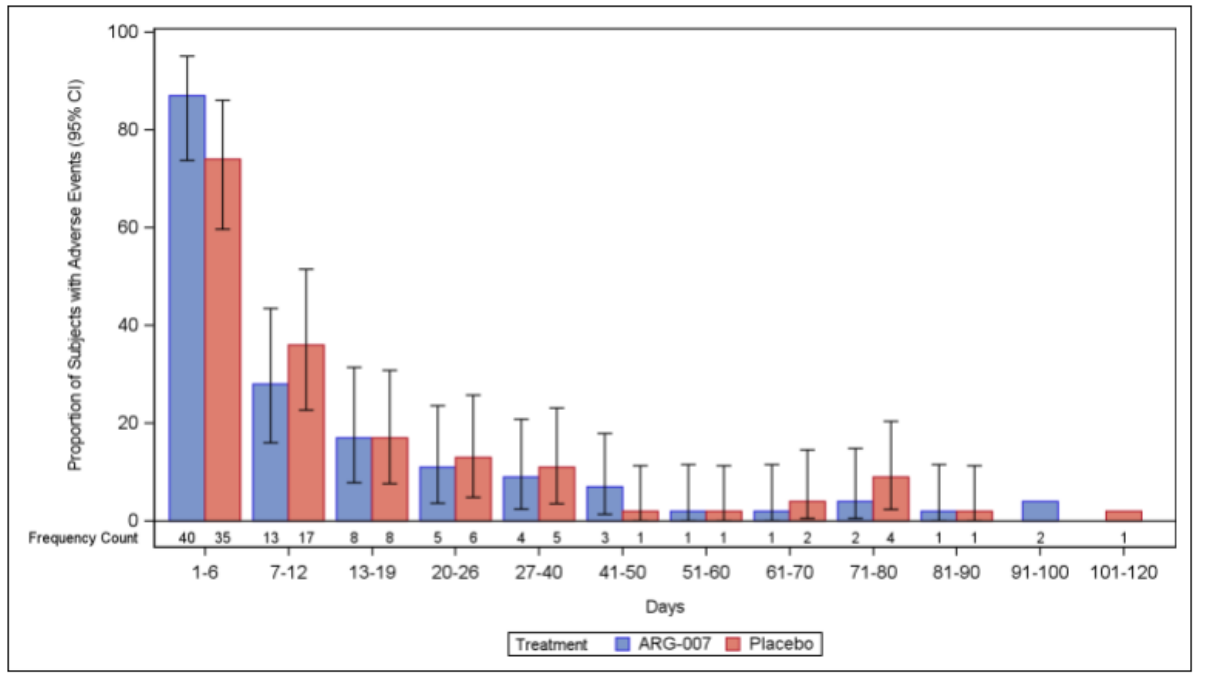
# OVERVIEW OF PHASE 2 TRIAL RESULTS

***Argenica's Phase 2 trial for ARG-007 in AIS has met its primary endpoint, missed on its overall secondary endpoint, but showed encouraging signal of efficacy in the "slow collateral" patients.***

**KEY SUMMARY**

- Phase 2 double blinded, placebo-controlled trial
- 92 patients recruited and dosed
- Primary endpoint (safety): safe and well tolerated
- No drug-to-drug interactions seen with clot dissolving drugs
- Secondary endpoint (infarct volume reduction): no overall difference
- Secondary endpoint subgroup analysis (infarct volume reduction): efficacy signal in slow collateral patients*

**Temporal profile of Treatment-Emergent Adverse Events**




**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. This statistical method ensures the data gives greater confidence to data being due to treatment effect. 95% CI ratio 0,230, 3.14)*

# PHASE 2 CLINICAL TRIAL
# SECONDARY ENDPOINT DATA

# PHASE 2 TRIAL DESIGN

**PATIENT HAS A STROKE**

**PATIENT IN AMBULANCE**

**ARRIVES AT HOSPITAL**

**DIAGNOSE STROKE TYPE**

**THROMBECTOMY**

**REHAB BEGINS**

- Initial screening of patients to meet inclusion criteria
- Consent for thrombectomy & ARG-007 trial

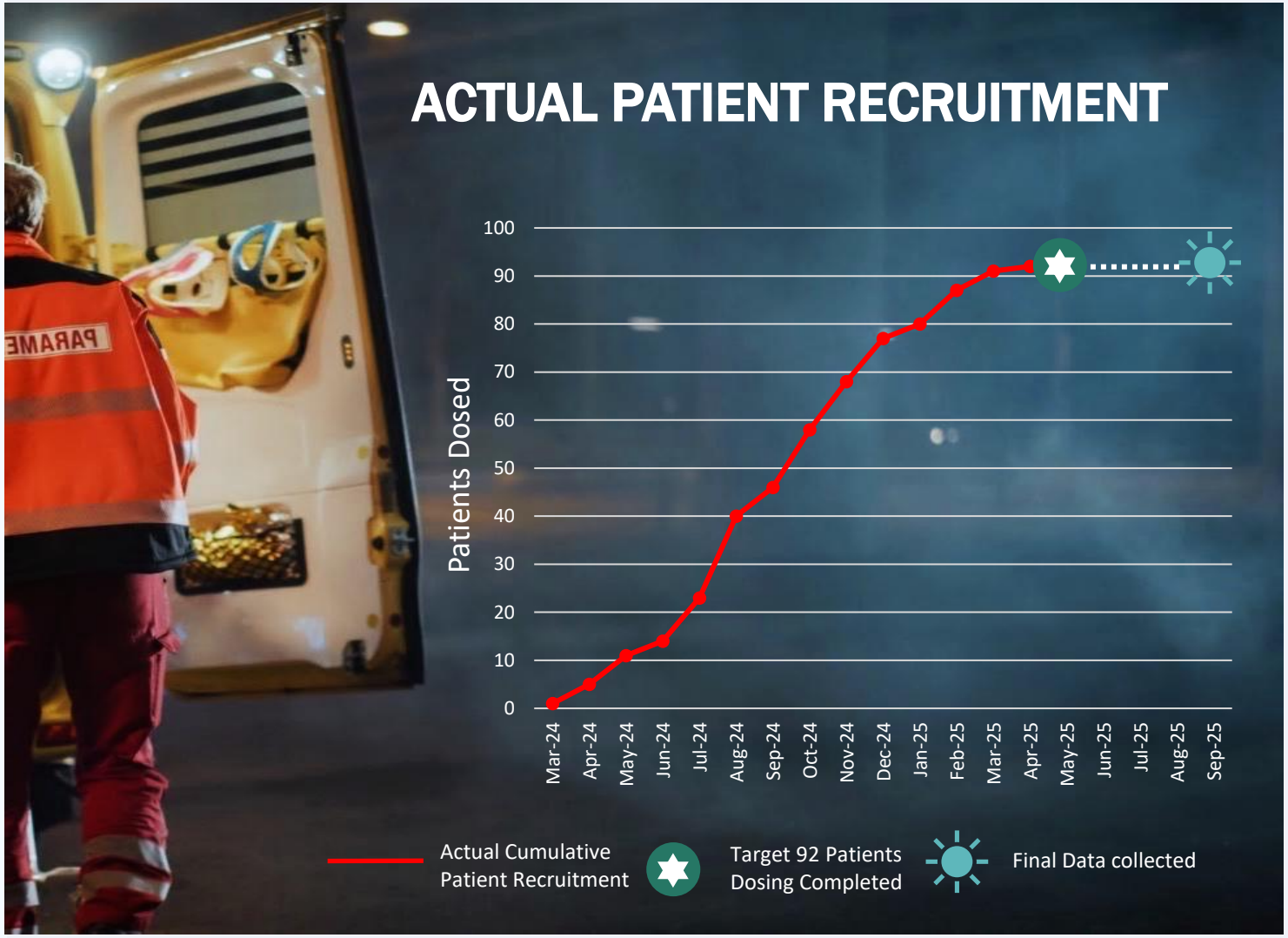
- Administration of **0.3mg/kg** ARG-007 or saline placebo
- All patients receive thrombectomy

**Endpoints**

- Mortality rate and frequency of **Adverse and Serious Adverse Events**; timepoints of Day 1, Day 2, Day 3, Day 6 or Discharge, Day 30 and Day 90
- **Infarct volume reduction** between ARG-007 and placebo at 48 hours (Day 3 ± 1 day)

*Potential benefits only. ARG-007 is under development and subject to clinical validation.*

# PHASE 2 CLINICAL TRIAL IN STROKE




- 92 patients dosed at 8 Australian hospitals

KEY OBJECTIVES:

1. Safety/Tolerability – significantly derisks the drug, critical in neurology drug development
2. Pharmacokinetics – is the drug behaving the same as it does in healthy people?
3. Preliminary Efficacy – Is there a treatment benefit with ARG-007? Is the benefit the same in all treated patients?

# SECONDARY ENDPOINT

- **Infarct volume reduction** between ARG-007 and placebo at 48 hours (Day 3 ± 1 day) across all patients

  ➢ ***No overall effect seen***

- **Infarct volume reduction** between ARG-007 and placebo at 48 hours (Day 3 ± 1 day) **in slow collateral subgroup**

  ➢ ***15% (5mL) infarct volume reduction on model adjusted mean****

**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. This statistical method ensures the data gives greater confidence to data being due to treatment effect. 95% CI ratio 0,230, 3.14)*

# RELEVANCE OF COLLATERAL BLOOD FLOW IN AIS PATIENTS[1]

## Good Collaterals

- Robust collateral blood flow maintains penumbra until EVT
- High reperfusion success better → functional outcomes
- Neuroprotection targeting acute injury may not show benefit (tissue already protected)

## Slow Collaterals

- Partial perfusion: penumbra survives but is stressed
- Active excitotoxicity, oxidative stress, mitochondrial dysfunction
- EVT alone → moderate outcomes

**Best target for ARG-007**

- Drug delivery possible (enough flow)
- Tissue vulnerable but salvageable
- Neuroprotection may extend survival window until reperfusion

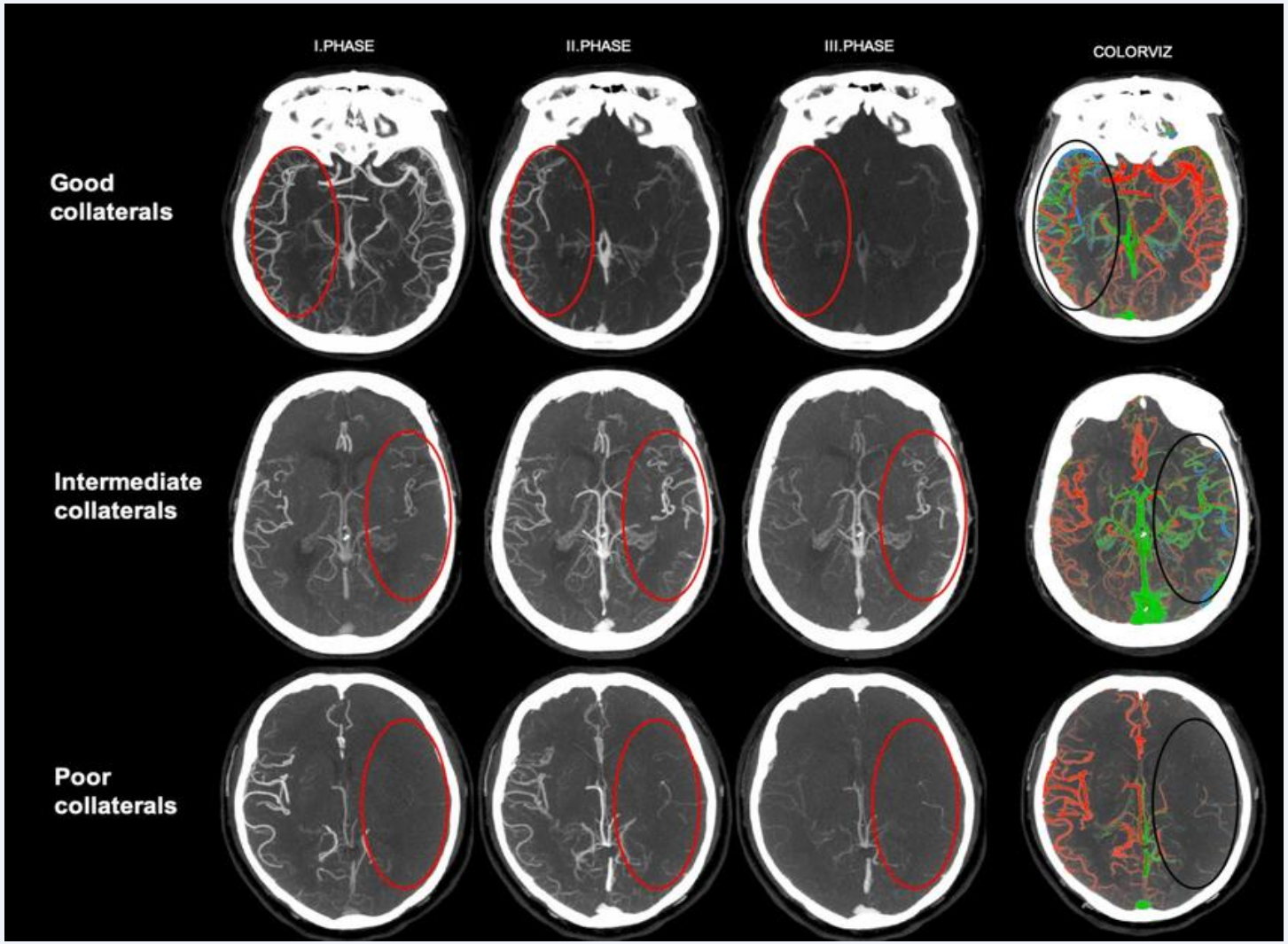
## Incomplete Collaterals

- Minimal or no collateral flow → rapid infarct expansion
- Large ischaemic core, poor EVT outcomes
- Drug exposure in brain is limited so little opportunity to benefit from ARG-007

*1. Referencing provided at Appendix 1*

# SLOW COLLATERAL PATIENTS – 30% OF PARTICIPANTS[1]

## THE MOST AT-RISK PATIENTS OF VULNERABLE BRAIN TISSUE (PENUMBRA) TURNING TO INFARCT

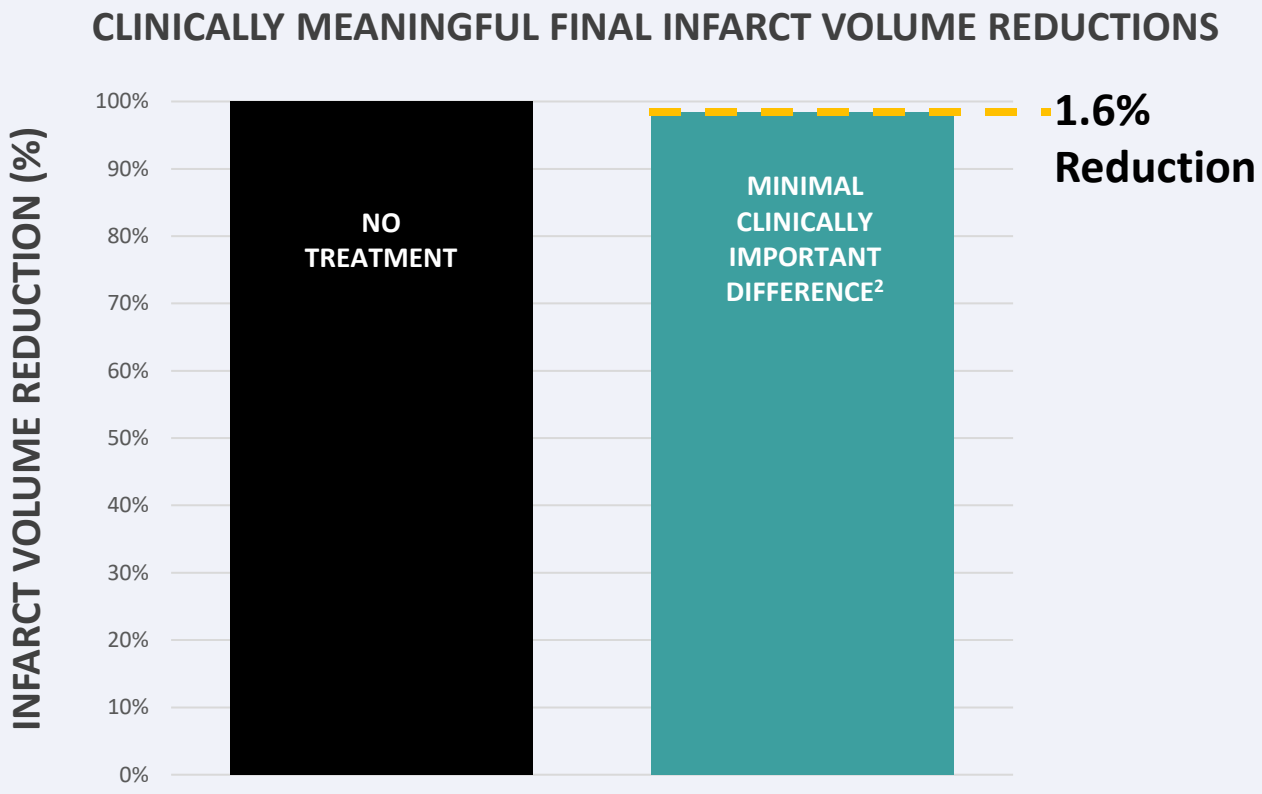



- Patients with slow/poor collaterals have highly vulnerable brain tissue that is not yet dead
- This vulnerable tissue is where injury cascades are most active, such as excitotoxicity and oxidative stress
- This makes these patients a good target for ARG-007

**15% INFARCT VOLUME REDUCTION IN ARG-007 TREATED PATIENTS WITH SLOW COLLATERALS**

*1. Referencing provided at Appendix 1*

# HOW MUCH BRAIN DO YOU NEED TO SAVE?




- A 0.6 mL, which equates to a 1.6% decrease in infarct volume (decrease in brain cell death), is **the minimum amount** of decrease deemed to be clinically important[1]. This decrease, on average, results in **1.3 more patients** out of 100 achieving functional independence (mRS 0-2).

- Studies have shown a decrease of **5%, 11.5% and 17%** would result in **5, 10 and 15** more patients out of **100**, respectively, achieving functional independence (mRS of 0-2). This means 5, 10 and 15 more patients per 100 who would move from being severely or moderately disabled to having no or only a slight disability[1].

- **SIGNAL OF EFFICACY IN SLOW COLLATERAL PATIENTS SHOWS 15% MEAN INFARCT VOLUME REDUCTION IN ARG-007 TREATED PATIENTS[3]**

***EVEN A SMALL REDUCTION IN INFARCT VOLUME INCREASES THE CHANCE A PATIENT WILL WALK, TALK & CARE FOR THEMSELVES***

1. *Liao NC, Bahr Hosseini M, Saver JL. Clinically important effect sizes for clinical trials using infarct growth reduction as the primary outcome: a systematic review. J Neurointerv Surg. 2023 Oct 31 – average final infarct volume across all studies is 38.4mL.*
2. *From Liao et al 2023 - Minimal clinically important difference-outcome specific is defined as the smallest change in a treatment outcome measure that a patient would consider of value, if the treatment producing the outcome was simply implemented, safe and inexpensive.*

# SUMMARY

- **The 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.**

- **Together with the robust, validated preclinical animal data which has consistently demonstrated significant treatment outcomes, we have 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[1].**



1. *See ASX Announcement dated 3 September 2025 – Topline Data in Phase 2 Trial*

# APPENDIX 1
# REFERENCES

# REFERENCES


SLIDE 8 REFERENCES:

- **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**. **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. *Interventional Neuroradiology*. 2023;29(5):615–622. doi:10.1177/15910199231166739.
- **Jansen IGH, Mulder MJHL, Goldhoorn RB, et al.** Impact of single-phase CT angiography collateral status on functional outcome over time: results from the MR CLEAN Registry. *Journal of NeuroInterventional Surgery*. 2019;11(9):866–873

SLIDE 11 REFERENCES:

- **Ospel, Johanna & Cimflová, Petra & Volny, Ondrej & Qiu, Wu & Hafeez, Moiz & Mayank, Arnuv & Najm, Mohamed & Chung, Kevin & Kashani, Nima & Almekhlafi, Mohammed & Menon, Bijoy & Goyal, Mayank**. (2021). Utility of Time-Variant Multiphase CTA Color Maps in Outcome Prediction for Acute Ischemic Stroke Due to Anterior Circulation Large Vessel Occlusion. Clinical Neuroradiology. 31

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