FINAL PHASE 1 CLINICAL TRIAL REPORT CONFIRMS ARGENICA SUCCESSFULLY PASSES CRITICAL MILESTONE

Highlights:

- *All doses of ARG-007 administered were **safe and well tolerated** with no dose related findings noted for any of the evaluated safety parameters.*
- *The pharmacokinetic profile seen in humans aligns with the pharmacokinetic profile seen at the effective doses tested in animals, giving Argenica confidence in its dose selection for the Phase 2 trial.*
- *The rapid uptake of ARG-007 indicates the **fast-acting** nature of the drug, a critical requirement for neuroprotective drugs delivered in acute indications such as ischaemic stroke and hypoxic ischaemic encephalopathy (HIE).*
- *ARG-007 also shown to have an extended half-life (time in which the drug remains in the body) suggesting **prolonged efficacy** at the effect site, also important for acute conditions such as ischaemic stroke and HIE.*
- *The final clinical trial report is a critical component of Argenica's ethics submission for initiating a Phase 2 trial in ischaemic stroke patients. It is anticipated that the ethics submission will be lodged in Q3 CY2023.*

Perth, Australia; 15 May 2023 - Argenica Therapeutics Limited (ASX: AGN) ("Argenica" or the "Company"), a biotechnology company developing novel therapeutics to reduce brain tissue death after brain injury, is pleased to announce the receipt of the Final Phase 1 Clinical Trial Report provided by clinical research organisation Linear Clinical confirming ARG-007 is safe, well tolerated and has a favourable pharmacokinetics profile.

SAFETY & TOLERABILITY OUTCOMES:

The clinical trial report concluded that single intravascular (IV) doses of ARG-007 at 0.03, 0.10, 0.20 and 0.30 mg/kg were safe and well tolerated with no dose related findings noted for any of the evaluated safety parameters.

Safety and tolerability were evaluated from the analysis of:

- Incidence and severity of adverse events (AE);
- Incidence of serious adverse events (SAE) and suspected unexpected serious adverse reactions;
- Clinically significant changes from baseline in:
  - Laboratory evaluations (hematology, chemistry, urinalysis);
  - Electrocardiograms;
  - Vital signs;
  - Physical examinations.

There have been no changes in the nature and extent of adverse events from those previously announced on 6 March 2023. Details of all safety data are presented in Appendix 1.

PHARMACOKINETIC OUTCOMES:

Pharmacokinetic (PK) analysis measured concentrations of ARG-007 in blood plasma over time. This is an important measure because, together with protein binding data generated for ARG-007, it indicates the amount of drug in the blood stream that can elicit an effect at various points in time following administration. Further, the PK data confirms the link between the PK profile for effective doses seen in animal models to the PK profile in humans. It also provides data on the half-life and clearance rate of ARG-007 from the body (outlined further below).

In the Phase 1 study blood samples were collected over various time points from the time of initiation of ARG-007 administration through to 48 hours. Each blood sample collected was used to analyze the concentration of ARG-007 in the blood plasma (drug concentration) at each specific timepoint.

Importantly, the human PK data showed exposure levels and timing of concentration of drug in the plasma aligned with the animal PK data on the efficacious doses tested in animal models of stroke (see previous announcement on 19 May 2022). This gives Argenica confidence that the doses tested in the Phase 1 trial align with the efficacious doses seen in animals, and provides the data needed for appropriate dose selection for the Phase 2 trial.

From the graphs shown in Appendix 1, the PK findings demonstrate that ARG-007 is rapidly taken up by the body, with the highest concentration of ARG-007 in the plasma observed at the end of infusion (10 minutes). Concentrations then decrease sharply at 30 minutes post initiation of infusion. Most of the drug has left the bloodstream at 24 hours post initiation of infusion, however there is a trailing concentration of ARG-007 that remains in the bloodstream, resulting in an extended half-life. The concentration of ARG-007 in plasma was also directly related to dose, with the highest dose having the greatest plasma concentration.

This PK data indicates that ARG-007 will be at its maximum concentration at the effect site shortly after the drug administration is initiated, however the extended half-life of the drug

also means that it remains in the body for a period of time (half-life of 12.4 to 15.8 hours), being available to provide continued protection to neurons. For acute neurological conditions, including acute ischaemic stroke and hypoxic ischaemic encephalopathy (HIE), the ability for ARG-007 to quickly reach maximum concentration in the blood, whilst also maintaining an extended half-life, will provide fast acting but prolonged efficacy at the effect site. This aspect of the PK profile of ARG-007 is critical in reducing the extent of neuronal cell death following ischaemia.

Further data on the PK analysis can be found in Appendix 1.

Argenica's Managing Director, Dr Liz Dallimore said: "The receipt of the Final Phase 1 Clinical Trial Report is a huge milestone for Argenica. We now have quality assured data showing ARG-007 is safe and well tolerated in humans, and is fast acting, reaching its maximum concentration in the blood at 10 minutes but with a relatively long half-life to exert its action for longer. With 1.9 million brain cells dying every minute after stroke, time to maximum drug concentration is critical."

NEXT STEPS

Argenica is now working towards finalising an application to a Human Research Ethics Committee requesting approval to commence a Phase 2 clinical trial in acute ischaemic stroke patients. It is anticipated that this ethics submission with be made in Q3 CY2023.

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 is now progressing towards a Phase 2 clinical trial in ischaemic stroke patients, as well as continuing to generate preclinical data in other neurological conditions, including in TBI, HIE and Alzheimer's Disease.

APPENDIX 1 – PHARMACOKINETIC DATA

A total of 24 subjects (6 subjects in 4 cohorts) who received ARG-007 were included in the PK analysis. The analysis of ARG-007 PK data demonstrated quantifiable concentrations from 5 minutes after the start of infusion up to 48 hours after start of infusion for all ARG-007 dose groups.

The pharmacokinetic data presented below outlines the concentration of ARG-007 in blood plasma over time. The first graph shows the blood plasma concentrations in nanograms (ng) per millilitre (mL) out to 60 minutes post initiation of ARG-007 infusion. This data shows each dose of ARG-007 peaks at 10 minutes post initiation of the infusion, with a decrease at 30 minutes.

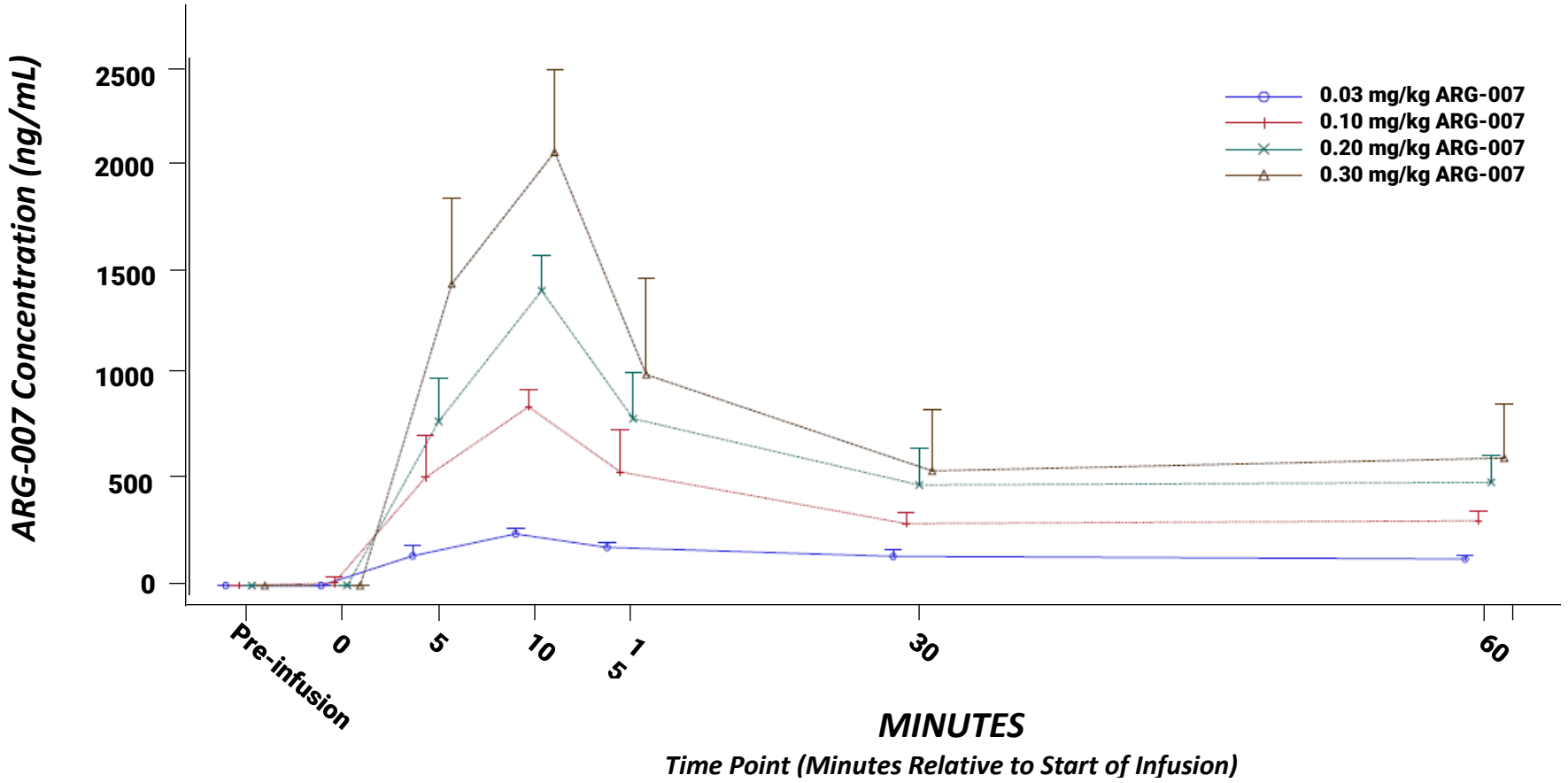
The second graph shows the blood concentrations in nanograms (ng) per millilitre (mL) out to 48 hours post initiation of ARG-007 infusion. This data shows each dose of ARG-007 peaks at 10 minutes with a sharp decrease in concentration, but that there are still detectable levels of ARG-007 in the blood plasma out to 48 hours post initiation of drug infusion. Having a longer clearance rate means the ARG-007 has a longer time to exert its action.

Review of the individual PK concentrations per dose group demonstrated that the highest concentrations for ARG-007 were observed immediately at the end of infusion. The distribution and elimination profile for ARG-007 was observed to be complex with a local decrease in concentration shortly followed by secondary minor blunted peak.

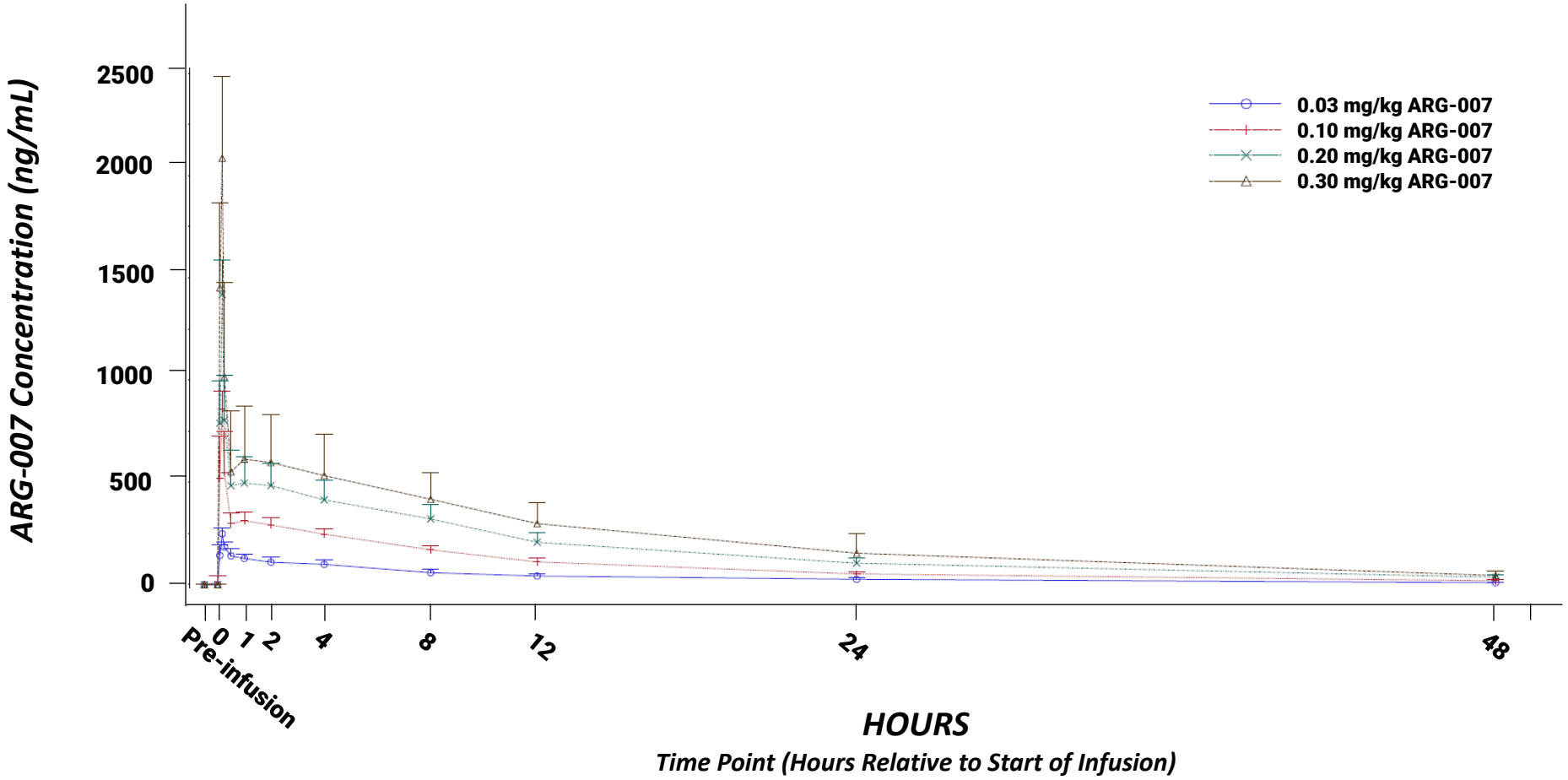
Review of the mean plots in the figures below reconfirmed the findings from the analysis of individual data. At the higher doses (0.2 mg/kg and 0.3 mg/kg) local decreases of concentrations at around 30 minutes from the start of infusion followed by a secondary peak at around 2 hours from the start of infusion were observed. The elimination phase after that featured faster elimination of up to approximately 12 hours from the start of infusion and a second slower phase after that. Elimination was not complete at the time of the last PK sample at 48 hours post start of infusion with all subjects at all dose levels exhibiting small quantifiable concentrations meaning there was still availability of drug in the system to exert an effect.

ARGENICA THERAPEUTICS

Mean Plasma ARG-007 Concentrations After Start of Infusion (MINUTES)



Mean Plasma ARG-007 Concentrations After Start of Infusion (HOURS)



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