PRELIMINARY PRE-CLINICAL TOXICOLOGY STUDIES SUCCESSFULLY COMPLETED

Highlights:

- *Argenica has completed preliminary pre-clinical toxicology studies and genotoxicity studies of ARG-007 under non-Good Laboratory Practice (non-GLP) conditions.*
- *The toxicology studies have identified the parameters for the no observed adverse effect levels (NOAELs) required for the Good Laboratory Practice (GLP) toxicity studies, estimating the safe starting dose for ARG-007 for the Phase 1 clinical trial.*
- *The preliminary genotoxicity studies have been successfully completed and toxicity parameters identified, which has allowed Argenica to initiate the final GLP genotoxicity studies.*
- *GLP studies for genotoxicity, pharmacokinetics and toxicology have now been initiated, with GLP safety studies to commence shortly. Results from these studies will be reported throughout Q1 CY22.*

Perth, Australia; 24 JANUARY 2022 - 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 the completion of the preliminary pre-clinical toxicology studies in both rat and non-human primates (NHPs), and preliminary *in vitro* genotoxicity studies.

These studies, carried out under non-Good Laboratory Practice (non-GLP) conditions, are necessary to identify the suitable dose ranges for further testing under the principles of Good Laboratory Practice (GLP) and provide an indication of the no observed adverse effect level (NOAEL) of ARG-007 required for determining the doses for the Phase 1 clinical trial.

Through these studies, Argenica has successfully identified the safe dosing range, which importantly exceeds the efficacious dose range, allowing the company to confidently progress to the full GLP studies required to initiate our Phase 1 clinical trial. Argenica can also confirm that ARG-007 administered at doses that are not bactericidal, does not appear to cause mutations in the DNA of the test organism – the "mutagenic potential".

Argenica's CEO, Dr Liz Dallimore said: "The results of these non-GLP studies have provided us with great confidence as we finalise our GLP preclinical studies. Identifying the dose ranges for our critical toxicity studies and estimating ARG-007's no observed adverse effect level,

which is importantly above our efficacious dose, is a vital step in achieving Human Research Ethics Committee approval and commencing our Phase 1 clinical trial."

NEXT STEPS

Given Argenica has completed the non-GLP studies necessary for the progression of the required GLP studies, the Company has now begun the final GLP studies for pharmacokinetics (PK) and toxicity, and safety studies will follow shortly after. These GLP studies will confirm the safety and tolerability of single doses of ARG-007 prior to commencement of the Phase 1 clinical trial. The results of these pre-clinical studies will be reported throughout Q1 CY22.

The GLP genotoxicity studies are nearing completion and the results will be reported within Q1 2022.

The data collected in both the non-GLP and GLP studies will be available for the Human Research Ethics Committee (HREC) review for approval of the Phase 1 clinical trial. Engagement with the HREC and submissions of data packages will commence in Q1 2022.

FURTHER INFORMATION ABOUT NON-GLP AND GLP STUDIES

To progress the further development of ARG-007, and administration of ARG-007 into humans in the upcoming Phase 1 clinical trial, the drug is required to undergo rigorous pre-clinical testing to understand the drug's non-toxic dosing levels and ensure the compound is considered safe to administer to humans. Studies are carried out under both non-GLP and GLP conditions. Regulatory bodies, such as the FDA, require data to be collected under GLP conditions, which are a set of principles to ensure quality assurance is achieved during pre-clinical studies. The principles largely cover the way in which study data is generated, handled, reported, retained and archived. Laboratories must have the required management systems, record storage, test article storage and tracking, laboratory materials and equipment tracking and maintenance in place to meet GLP principles.

Preliminary, non-GLP, studies are undertaken prior to the regulatory required GLP studies to identify any issues with toxic effects of the drug without the costly GLP quality assurance processes. Conducting these non-GLP studies have allowed Argenica to collect data on the safe dose range of ARG-007 so the Company can quickly and easily progress the assessment under GLP conditions, thereby mitigating the potential technical risk of not attaining the appropriate toxicology data under GLP conditions. The non-GLP data may also be included in the ethics submission for the Phase 1 clinical trial to strengthen the overall data package presented.

RAT AND NHP TOXICOLOGY STUDIES

Conducting toxicology studies is vital to characterise potential adverse effects that may occur at specified dosing levels, and to estimate a safe starting dose and dosage regimen in humans.

The non-GLP toxicology studies have confirmed the parameters in which Argenica can identify the maximum safe starting dose and have determined ARG-007s NOAEL (no observed adverse effect levels). The Company will now do the same studies under GLP conditions to confirm the maximum recommended starting dose (MRSD) for the Phase 1 clinical trial.

Through the company's contracted preclinical research organisation, Medicilon, Argenica has performed the non-GLP toxicity dose range finding studies in the two most relevant and sensitive animal species, being rats and NHPs, to provide an estimate of the NOAEL. In addition, through these studies, Argenica has identified the safe dosing range, which importantly exceeds the efficacious dose range, allowing the company to confidently progress to the full, GLP studies required by the regulatory authorities (FDA, TGA etc).

***IN VITRO* GENOTOXICITY**

During development of new pharmaceuticals, the assessment of genotoxicity is an important part of non-clinical safety evaluation. Genotoxicity is the ability for substances to damage the DNA and/or chromosomes within cells. Whilst peptides are generally not expected to interact directly with DNA or other chromosomal material[1] it is an important step in the pre-clinical assessment process to determine whether ARG-007 induces any mutations in genetic material within the cells.

Argenica has now completed the non-GLP bacterial reverse gene mutation (Ames) studies and shown that, at doses that are not bactericidal, it does not appear that ARG-007 is mutagenic. The Ames test used in these studies is a widely employed method that uses bacteria to test whether a given chemical can cause mutations in the DNA of the test organism – the "mutagenic potential".

Further, the Company has conducted the *in vitro* mammalian chromosomal aberration test (OECD 473) which is used to identify substances that cause structural chromosomal aberrations in cultured mammalian cells. In non-GLP studies the Company has determined the cytotoxicity of ARG-007 in cultured mammalian cells with or without rat liver S9 metabolic activation, so as to provide the basis for the selection of the concentration range of the formal GLP test.

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 improve patient outcomes. Our lead neuroprotective peptide candidate, ARG-007 has been successfully demonstrated to improve outcomes in pre-clinical stroke models and is in the process of being verified for its safety and toxicity before commencing Phase 1 clinical trials in humans. The aim is for our therapeutic to be administered by first responders to

protect brain tissue against damage during a stroke with further potential to enhance recovery once a stroke has taken place.

Reference:
1. Thybaud, et al., 2016. Genotoxicity assessment of peptide/protein-related biotherapeutics: points to consider before testing. Mutagenesis, Volume 31, Issue 4, Pages 375–384.