ARGENICA ADVANCES IND APPLICATION WITH SUCCESSFUL COMPLETION OF REQUESTED GENOTOXICITY ASSAY

Highlights:

- *Argenica has directly addressed the FDA's request in its clinical hold letter related to genotoxicity[1] by* ***completing a fully GLP-compliant in vitro Mouse Lymphoma Assay (MLA), with no evidence of genotoxicity seen.***

- *The FDA identified that a previously submitted Ames genotoxicity assay was inadequate and specifically directed Argenica to conduct a follow-up mammalian cell gene mutation assay, naming the mouse lymphoma thymidine kinase (TK) assay as an acceptable approach. This study has now been successfully conducted with ARG-007 showing* ***no evidence of gene mutation or chromosomal aberrations****, with no concentration of ARG-007 exceeding the regulatory threshold for a positive genotoxicity result.*

- ***Two of the three FDA-requested assays are now complete****, with the positive outcome of the Tenecteplase assay previously reported[2], and the GLP hERG cardiac safety assay currently in progress as the third and final required study.*

- *Completion of all three assays will position Argenica to compile and submit a comprehensive response, along with the updated Phase 2b protocol, to the FDA clinical hold and seek approval of the investigational new drug (IND) application for ARG-007,* ***allowing Argenica to conduct its Phase 2b trial in the United States.*** *Argenica is also progressing regulatory approvals to establish trials sites in Australia.*

Perth, Australia; 21 MAY 2026- Argenica Therapeutics Limited (ASX: AGN) ("Argenica" or the "Company"), a biotechnology company developing novel therapeutics to reduce brain tissue death after stroke and other acute neurological conditions, is pleased to announce results of the *in vitro* Mouse Lymphoma Assay (MLA) under good laboratory practice (GLP), with results confirming ARG-007 showed no signs of causing genetic mutations, with no concentration of ARG-007 exceeding the regulatory threshold for a positive genotoxicity finding. These results

[1] ASX Announcement dated 14 August, 2025 "Argenica Receives IND Feedback from FDA"
[2] ASX Announcement dated 4 December, 2025 "Positive Tenecteplase Study Results Fulfil a Key FDA Requirement"

support a clean genotoxicity profile for ARG-007 and directly address the FDA-requested mammalian cell gene mutation component of the clinical hold response.

Dr Liz Dallimore, Managing Director of Argenica, commented: " *The successful completion of the FDA-requested GLP mouse lymphoma assay is an important step in addressing the clinical hold requirements for ARG-007. The study showed no evidence of gene mutation or chromosomal damage, directly addressing the genotoxicity requirements identified by the FDA. With two of three FDA-requested studies now complete and the hERG assay currently in progress, we are in the final stages of assembling the safety package required for our comprehensive clinical hold response and look forward to updating the market on progress shortly."*

BACKGROUND TO THE FDA CLINICAL HOLD

As previously disclosed to the market, Argenica received an IND clinical hold letter from the US Food and Drug Administration (FDA) in relation to ARG-007[3]. The FDA's letter highlighted additional data to be generated related to interaction with clot dissolving drug Tenecteplase (TNK), impact on cardiac activity using a hERG assay, and genotoxicity. In relation to genotoxicity, the FDA requested a follow-up in vitro mammalian cell gene mutation assay, such as the mouse lymphoma thymidine kinase (TK) assay, to be conducted.

Argenica has now completed that assay under GLP conditions, with ARG-007 showing no evidence of gene mutation or chromosomal aberrations.

The Company previously announced the completion of the first of the three FDA-requested assays, the TNK assay with positive results[4]. The MLA represents the second of the three required assays. The third study, the GLP hERG cardiac safety assay, is currently in progress.

Upon completion of the hERG study, Argenica will be in a position to compile a comprehensive response to the FDA clinical hold, incorporating the results of all three completed assays, with the aim of seeking reinstatement of the IND for ARG-007. This will allow Argenica to conduct it's proposed Phase 2b trial in moderate to severe stroke patients in the United States. The Company is also preparing its Human Research Ethics Committee (HREC) submission to seek approval to commence the Phase 2b trial in Australian.

WHY THE FDA REQUESTED THE MOUSE LYMPHOMA ASSAY

Before any new drug can be tested in humans, regulators require safety tests to check whether it could damage DNA. Argenica had already completed two such tests for ARG-007, with both confirming no evidence of DNA damage. A third bacterial DNA test produced an inconclusive result, not due to any safety concern, but because ARG-007's cell-penetrating properties

[3] ASX Announcement dated 14 August, 2025 "Argenica Receives IND Feedback from FDA"
[4] ASX Announcement dated 4 December, 2025 "Positive Tenecteplase Study Results Fulfil a Key FDA Requirement"

interfered with the bacteria used in the test. International guidelines specifically provide for this situation, recommending a follow-up test using mammalian cells. The FDA directed Argenica to complete the MLA in order to comply with this recommendation.

The MLA uses mammalian cells (mouse lymphoma L5178Y cells) which are considerably more tolerant of cationic peptide compounds than bacterial strains (as previously conducted by Argenica), and which more closely reflect the biology of human cells. The MLA detects both gene mutations and chromosomal aberrations simultaneously through the "tk" locus system, making it a comprehensive and sensitive genotoxicity assessment tool.

Critically, the FDA specifically named this assay as an acceptable follow-up study for ARG-007, confirming that a clean MLA result will directly address the genotoxicity deficiency identified in the clinical hold letter.

The study was conducted by Labcorp Early Development Laboratories Ltd (Huntingdon, UK), an internationally accredited GLP laboratory, under full compliance with OECD Guideline 490 and ICH S2(R1).

STUDY RESULTS

The study evaluated the potential of ARG-007 to induce forward mutation at the thymidine kinase (tk) locus in mouse lymphoma L5178Y cells in the absence and presence of a rat liver metabolizing system (S-9). Both 3-hour and 24-hour treatment periods were assessed, tested at concentrations up to the maximum achievable concentration with the highest analysable concentrations limited by precipitation of the compound. A preliminary cytotoxicity range-finder experiment was conducted, to establish an appropriate concentration range for the Mutation Experiment.

Across all test conditions, the mutant frequency at every tested concentration of ARG-007 remained below the sum of the mean vehicle control mutant frequency plus the Global Evaluation Factor (GEF) of 126 mutants per 10^6 viable cells; the regulatory threshold above which a result is considered positive. ARG-007 did not induce gene mutation or chromosomal aberrations under any test condition.

The linear trend test for mutant frequency was non-significant with a negative slope under all three test conditions, providing additional statistical confirmation that there is no dose-dependent increase in mutation frequency attributable to ARG-007.

PATH TO LIFTING THE FDA CLINICAL HOLD

With two of three required assays now complete, both demonstrating clean and favourable safety profiles, Argenica is progressing toward the completion of the final FDA-required study, the hERG cardiac safety assay, which assesses whether ARG-007 inhibits the cardiac potassium channel associated with drug-induced arrhythmia risk. The Company will provide a further update to the market upon completion of this final study.

Upon completion of all three studies, Argenica intends to compile and submit a comprehensive response to the FDA clinical hold as expeditiously as possible. This will include an updated Phase 2b protocol reflecting the focus on moderate to severe stroke patients.

Under FDA regulations, the FDA has 30 days from receipt of a complete clinical hold response to advise the sponsor whether the hold has been lifted.

A successful FDA response would result in the lifting of the clinical hold and approval of the IND, enabling Argenica to progress ARG-007 into human clinical trials in the United States.

This announcement has been approved for release by the Board of Argenica.

For more information please contact: info@argenica.com.au

ABOUT ARGENICA

Argenica Therapeutics Limited (ASX: AGN) is a clinical-stage biotechnology company developing innovative neuroprotective therapeutics to improve outcomes for patients following stroke and other acute neurological injuries. The Company's lead drug candidate, ARG-007, is designed to protect vulnerable brain tissue by reducing cell death and limiting secondary damage after an ischemic event. With a strong scientific foundation and a clear clinical development pathway, Argenica is focused on advancing novel treatments that have the potential to significantly improve patient recovery and transform the standard of care in acute neurology.