FDA FEEDBACK RECEIVED, REQUESTS ADDITIONAL RAT STUDY

Key Points:

- *The US FDA has advised that the clinical hold on Argenica's IND for xaranetide in acute ischaemic stroke remains in place, requesting an additional rat study.*
- *The FDA has requested additional non-clinical data, specifically a GLP non-clinical neurotoxicity study assessing whether xaranetide forms toxic Olney lesions in rats. Olney lesions can form in rats following administration of NMDA receptor antagonist drugs. There is no evidence that Olney lesions exist in humans. The FDA has requested this study be completed before commencement of clinical dosing in the US. No microscopic damage to the brain has been identified in non-clinical animal studies of xaranetide conducted to date.*
- *FDA has also revised downward the permitted clinical exposure limit, below the doses in the Company's proposed trial design. The Company does not agree with this view and has identified issues with the data on which this decision has been made.*
- *The Company is reviewing the feedback and assessing next steps, including requesting a Type A meeting with the FDA, however, will continue to progress regulatory submissions in other jurisdictions.*

Perth, Australia; 19 November 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, advises that the United States Food and Drug Administration (FDA) has completed its review of the Company's clinical hold complete response, submitted on 23 September 2026, and has advised that removal of the clinical hold is not warranted at this time, pending additional information.

The Company submitted a complete response on 23 September 2026 addressing the matters raised in the FDA's August 2025 letter, the FDA's feedback maintaining the hold was provided over 4 weeks after the mandatory 30-day deadline.

The key matters required to be addressed are outlined below:

Nonclinical neurotoxicity study. Recent mechanism-of-action studies show that xaranetide is a non-competitive, voltage-dependent, partial, NMDA receptor inhibitor[1]. This is important for neuroprotection as NMDA receptors are the key channels implicated in neuronal cell death following stroke. However, they also play an important role in normal brain functioning. Olney lesions arise in rats given high-affinity NMDA channel blockers that produce sustained, complete receptor blockade[2], and lesion severity is dose and exposure dependant[3,4]. Xarandetide is not a complete NMDA receptor blocker, is reversible and not administered chronically in stroke, therefore does not align with many of the requirements to produce Olney lesions in rats. However, given there is NMDA receptor interaction the FDA has requested an Olney lesion neurotoxicity study in rats, to be completed before further human dosing under the IND. Argenica will seek quotes from clinical research organisations to an indication of investment required. FDA has offered to review the study protocol in advance. It should be noted that no microscopic damage to the brain has been identified in non-clinical animal studies to date.

Clinical exposure limit. The FDA has stated they require a ten-fold margin to the rat exposure at the no-effect level for dosing in the Phase 2b trial. The FDA has revised downward the limit on permitted plasma exposure, derived from non-GLP toxicokinetic data in a single rat cohort within a specific non-clinical study conducted by Argenica. The revised limit sits below the doses in the trial design submitted in September 2026, so any future US study would need to commence at a lower dose, with a clear plan for dose escalation. However, a preliminary review by the Company has identified substantially greater variability in the data being relied upon by the FDA. Further, it does not align with previously provided GLP toxicokinetic data. The Company will now work with its nonclinical contract research organisation to verify the variability and intends to seek further discussion with FDA regarding the basis for the revised limit.

Given the above identified points, the Company now plans to request a Type A meeting to discuss further with FDA.

The Company maintains a strong conviction on the potential benefit of xaranetide to stroke patients given the extensive efficacy demonstrated in many preclinical studies, and the signal shown in severe stroke patients in the Phase 2 trial. In light of this, the Company will continue to progress regulatory submissions in other jurisdictions.

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[1] ASX Announcement dated 20 October, 2026 “New Mechanism Findings Offer Insights Into Xaranetide’s Phase 2 Signal in More Severe Stroke.

[2] Olney JW, Labruyere J, Price MT. Pathological changes induced in cerebrocortical neurons by phencyclidine and related drugs. *Science* 1989;244:1360–1362.

[3] Fix AS, Horn JW, Wightman KA, et al. Neuronal vacuolization and necrosis induced by the noncompetitive N-methyl-D-aspartate (NMDA) antagonist MK(+)801 (dizocilpine maleate): a light and electron microscopic evaluation of the rat retrosplenial cortex. *Experimental Neurology* 1993;123:204–215.

[4] Morris PJ, Burke RD, Sharma AK, et al. A comparison of the pharmacokinetics and NMDAR antagonism-associated neurotoxicity of ketamine, (2R,6R)-hydroxynorketamine and MK-801. *Neurotoxicology and Teratology* 2021;87:106993.

Argenica will continue to provide updates to the market as it looks to work with the FDA to have these issues resolved.

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

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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.