ARG-007 (XARANETIDE) SHOWS SIGNIFICANT NEUROPROTECTION IN PRECLINICAL CONCUSSION STUDY

Highlights:

- *ARG-007 (xaranetide) has **shown significant efficacy in reducing the secondary injury effects** in a repeated mild traumatic brain injury (mTBI), or **concussion**, preclinical animal model. Xaranetide demonstrated broad neuroprotective activity by **attenuating multiple pathological processes implicated in concussion**, including neuroinflammation (reduced astrocyte and microglial activation), oxidative stress, and axonal injury.*

- *The preclinical study, undertaken by Curtin University, showed a single low-dose of xaranetide (1 mg/kg IV) administered 30 minutes after a repeated mTBI significantly reduced neuroinflammation, oxidative stress and axonal damage, three of the most significant components of the secondary injury cascade seen following concussion. Importantly, this effect was enduring, **lasting up to 11 days post-injury.***

- *Xaranetide **significantly reduced neuroinflammation** — driven by overactive immune cells (astrocytes and microglia) — across multiple brain regions involved in memory and cognition (hippocampus, cortex, corpus callosum). It also **lowered markers of cellular damage** (oxidative stress) and **reversed structural damage to nerve fibers** in the ventral tegmental area (VTA), a region tied to mood and motivation.*

- *These findings suggest the therapy may not simply alleviate symptoms but may modify the underlying biological response to concussion. Importantly, these findings are **consistent with previously reported efficacy** in multiple moderate and severe traumatic brain injury models, demonstrating biological activity across the spectrum of traumatic brain injury severity[1,2,3,4] **increasing confidence that xaranetide is targeting fundamental pathways of brain injury**.*

Perth, Australia; 16 July, 2026 - 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 positive preclinical efficacy data for its lead drug candidate ARG-007 (xaranetide) in a rodent repeated mild traumatic brain injury (rmTBI), or **concussion**, model. This study was undertaken in collaboration with researchers from Curtin University and the Perron Institute for Neurological and Translational Science and

[1]ASX Announcement - 22 June 2023 – ARG-007 Protects Brain Cells in Moderate Traumatic Brain Injury Model
[2] ASX Announcement - 15 May 2024 – ARG-007 Significantly Reduces Effects of Traumatic Brain Injury in Preclinical Study
[3] ASX Announcement - 4 February 2025 – ARG-007 Shows Significant Neuroprotection in Main Traumatic Brain Injury Study
[4] ASX Announcement - 18 June 2025 – Argenica to Progress Clinical Development of ARG-007 in Traumatic Brain Injury

showed xaranetide reduced multiple key drivers of secondary brain injury following repeated mTBI, including neuroinflammation, oxidative stress and axonal damage. These processes are believed to contribute to ongoing neuronal dysfunction and persistent post-concussive symptoms[5].

Dr Liz Dallimore, Managing Director, commented *"These findings show that a single dose of xaranetide, given soon after repeated mild brain injury, reduced inflammation, oxidative stress, and cellular damage across multiple regions of the brain — processes believed to drive prolonged concussion symptoms and delayed recovery. This is another independent demonstration of xaranetide's efficacy in TBI, adding to a growing body of evidence across mild, moderate, and severe injury models, and reinforcing its potential as a disease-modifying therapy for repeated concussion. Based on these results, Argenica is now considering next steps to advance xaranetide's development in this indication."*

Key Findings

Xaranetide reduced multiple key drivers of secondary brain injury following repeated mTBI, including neuroinflammation, oxidative stress and axonal damage. These processes are believed to contribute to ongoing neuronal dysfunction and persistent post-concussive symptoms[5].

A single intravenous dose of xaranetide (1 mg/kg) administered following two mild traumatic brain injuries (mTBIs) given 24 hours apart reduced GFAP-positive astrocyte reactivity in the dentate gyrus of the hippocampus to levels comparable with sham animals. GFAP is a well-established marker of astrocyte activation and neuroinflammation following brain injury.

The study also evaluated Iba1, a marker of activated microglia. Xaranetide significantly reduced Iba1-positive microglial reactivity across the cortex, corpus callosum and dentate gyrus, with all three brain regions returning to sham levels by Day 11 following injury.

Astrocytes and microglia are the brain's principal inflammatory cells. While they play an important role in the acute response to injury, persistent activation following concussion is believed to contribute to ongoing neuronal dysfunction, impaired synaptic signalling and axonal injury, processes associated with persistent post-concussive symptoms and delayed neurological recovery. The ability of xaranetide to normalise both GFAP and Iba1+ suggests it may interrupt this secondary injury cascade rather than simply suppress inflammation.

Importantly, these anti-neuroinflammatory effects were sustained for at least 11 days following injury, demonstrating durable modulation of the inflammatory response during a critical period of brain recovery.

[5] Ahmed Z, Chaudhary F, Fraix MP, Agrawal DK. Epidemiology, Pathophysiology, and Treatment Strategies of Concussions: A Comprehensive Review. *Fortune Journal of Health Sciences*. 2024;7:197–215

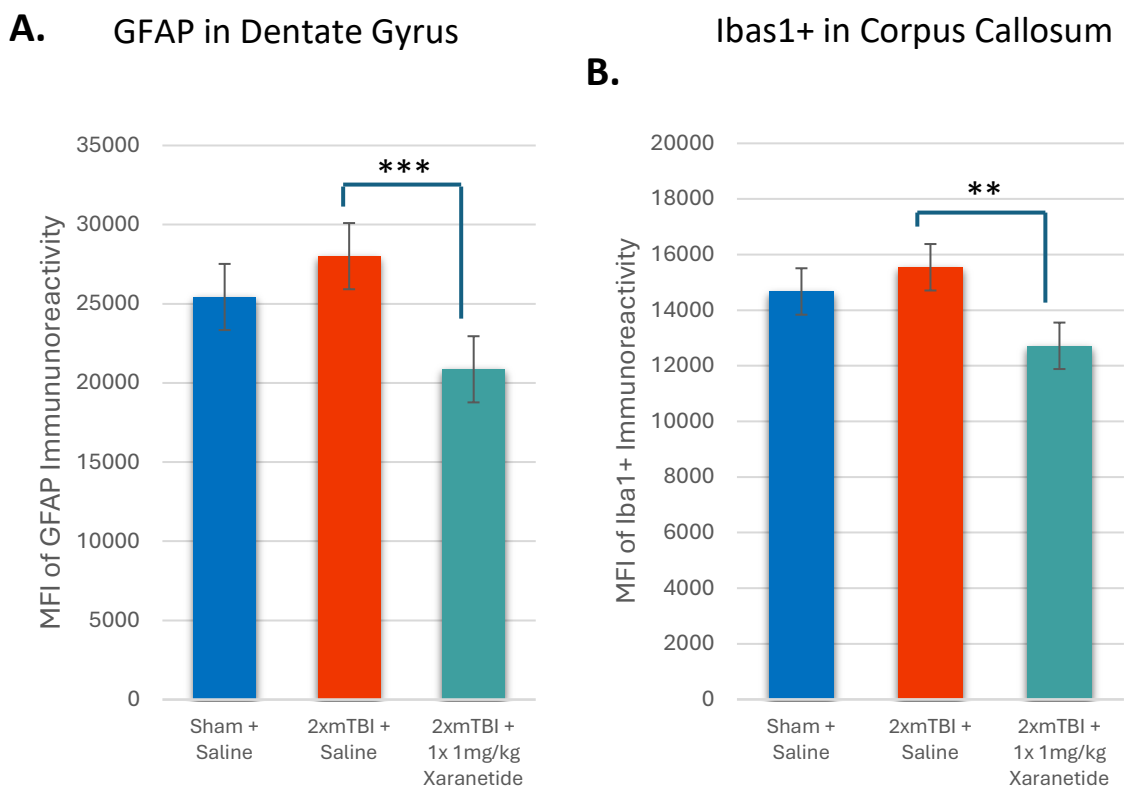

Figure 1. Xaranetide reduced neuroinflammation in the dentate gyrus (A) and the corpus callosum (B) of the brain as shown by a significant reduction in GFAP density (*p = < 0.001), and Iba1+ density respectively (**p = < 0.01). Both neuroinflammation markers were reduced to non-injury (sham) controls when analysed at day 11 post injury.**

This single low dose of xaranetide also reduced MnSOD immunoreactivity, a marker of oxidative stress, back down to normal levels as measured 11 days post injury in both the cortex and ventral tegmental area (VTA), brain regions critical for cognition, attention and motivation. A significant reduction in neurofilament light, a marker of neuroaxonal injury, was also seen in the VTA.

The VTA is a relatively small structure located in the midbrain, but it has a disproportionately important role in regulating motivation, reward, attention, learning and cognition. It contains dopamine-producing neurons that project to multiple brain regions, including the prefrontal cortex, nucleus accumbens, hippocampus and amygdala. In the context of concussion, the VTA is becoming increasingly recognised as an important region because disruption of dopaminergic signalling is thought to contribute to many of the cognitive and neuropsychiatric symptoms experienced after mild TBI.

The study utilised sham animals as the control arm in the experiments. Sham animals underwent the exact same surgical and experimental procedures as the injured animals — including anesthesia and handling — but did not receive the actual brain injury, allowing researchers to isolate effects caused specifically by the mTBI itself rather than by the

surrounding procedures. The biomarker levels seen in sham animals is therefore what is expected in normal non-injured animals.

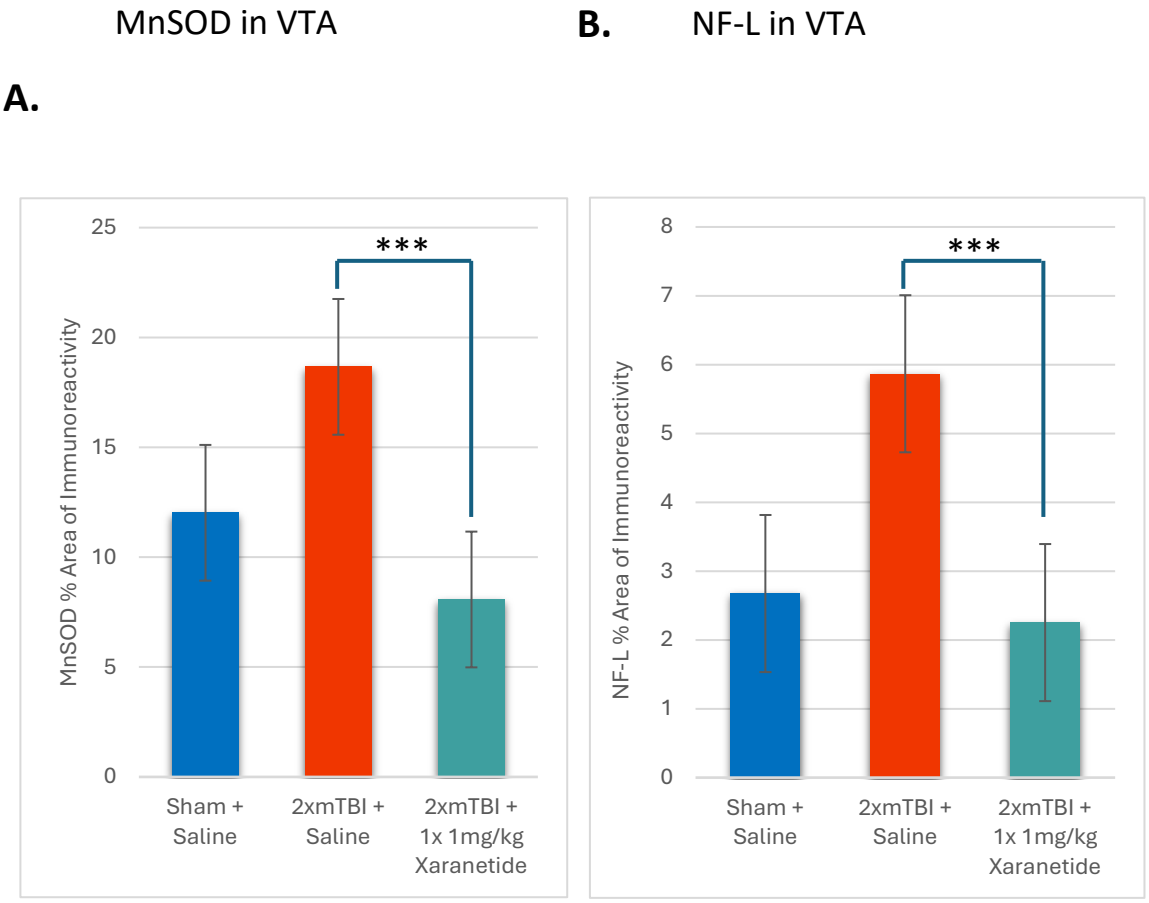

Figure 2. Xaranetide reduced key biomarkers of neurological dysfunction following concussion in the VTA region of the brain, specifically (A) a significant reduction in MnSOD immunoreactivity (*p = < 0.001) and (B) a significant reduction in NF-L levels (***p = < 0.001). Both markers were reduced to non-injury (sham) controls when analysed at day 11 post injury.**

The simultaneous modulation of neuroinflammation, oxidative stress and axonal damage back to normal levels as reference by the sham animal data supports xaranetide's potential as a disease-modifying neuroprotective therapy rather than one targeting a single downstream pathway.

PLATFORM POTENTIAL

These results extend the evidence base for xaranetide beyond its lead acute ischaemic stroke program, demonstrating a consistent, mechanistically-aligned protective effect, reducing neuroinflammation, oxidative stress and axonal damage, across three distinct preclinical injury models: single moderate-to-severe TBI, ischaemic stroke, and now repeated mild TBI. Repeated mild TBI and concussion represent a large, currently underserved population, including contact-sport athletes, military personnel and survivors of domestic violence, for

which no approved pharmacological neuroprotective therapy exists. This data provides a scientific basis to explore mTBI/concussion as a complementary indication for xaranetide, broadening the Company's potential addressable markets alongside its core stroke program.

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.