ARGENICA RECEIVES IND FEEDBACK FROM FDA

Highlights:

- *Argenica has received further details from the US Food and Drug Administration (FDA) on the reasons for the imposed clinical hold and the information required to lift the hold in respect of the Company's IND application, which will enable clinical trials of ARG-007 in acute ischaemic stroke in the US.*

- *The FDA has requested additional information to provide assurance that the proposed trial dosing for a US trial can be achieved safely in humans. Argenica's Phase 2 acute ischaemic stroke trial safety data, which will be available in September, will be used as part of the Company's response to this request.*

- *The FDA has also requested Argenica conduct three additional in vitro cell culture studies with clinical research organisations (CROs) to address identified gaps in data. These are small studies that can be completed quickly and build on existing data already generated by Argenica.*

- *Argenica will work with the FDA to ensure the proposed approach to providing the additional information is adequate to lift the clinical hold.*

Perth, Australia; 14 August, 2025 - Further to its announcement to ASX dated 10 June 2025, Argenica Therapeutics Limited (ASX: AGN) ("Argenica" or the "Company"), a biotechnology company developing novel therapeutics to reduce brain tissue death after stroke, has now received the full clinical hold letter from the FDA outlining the additional information needed to resolve and lift the clinical hold currently in place the Company's investigational new drug application (IND).

In order to lift the clinical hold, the FDA has requested the following additional information:

- Additional information to demonstrate that the proposed clinical trial dose can be achieved safely in humans. The safety data generated in Argenica's Phase 2 clinical trial data will be used as part of the Company's response to this request.

- Conduct an *in vitro* study on the recently approved lysis drug Tenecteplase (TNK; required to be undertaken at a CRO) conducted in the same way as the alteplase (tPA) *in vitro* study using human blood clots. The FDA previously directed the Company to only conduct

this study for tPA due to TNK not being approved for use in humans in the US. Argenica's Chief Scientific Officer has previously conducted assays with TNK showing ARG-007 does not significantly inhibit TNK lysis[1], however Argenica will conduct an additional study with a reputable CRO.

- Conduct an *in vitro* study using an hERG assay which is designed to determine any potential effect on potassium channels related to the heart's electrical activity. Argenica monitored healthy volunteers' cardiac activity via electrocardiogram (ECG) during the Phase 1 trial and saw no impact on cardiac activity. Patients in the current Phase 2 acute ischaemic stroke study have also been monitored via ECG. This study will be conducted at a CRO to confirm the impact of ARG-007 on cardiac activity via this recommended assay.

- Conduct a follow up *in vitro* mammalian cell gene mutation assay, suggesting a mouse lymphoma TK assay, to determine genotoxicity in cells. Argenica will undertake this study as requested, however no genotoxicity was reported in either the AMES *in vitro* assay test or the *in vivo* micronucleus test conducted in rats.

- Include more detail on the Phase 1 data in the investigational brochure. This is a simple update which will be implemented immediately.

Argenica's Managing Director, Dr. Liz Dallimore commented: "*We are pleased to have received the clarification from the FDA as to the additional information required to progress the IND application. Importantly from a timing and cost perspective, the requested additional in vitro assays are standard assays which are straightforward and efficient to perform. Further, the important safety data results from the current Phase 2 clinical trial will soon be available in September to support our submission. Argenica will work with the FDA to ensure the proposed approach to providing the additional information is adequate to lift the clinical hold*."

Argenica will provide further updates as it works through the IND process with the FDA.

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

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

[1] Meloni BP, Blacker DJ, Edwards AB, Knuckey NW. Impact of poly-arginine peptides R18D and R18 on alteplase and tenecteplase thrombolysis in vitro, and neuroprotective stability to proteolysis. J Thromb Thrombolysis. 2022 Jul;54(1):172-182.

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 conducting a Phase 2 clinical trial in ischaemic stroke patients, as well as continuing to generate preclinical data in other neurological conditions.