FDA GRANTS ORPHAN DRUG & RARE PEDIATRIC DISEASE DESIGNATIONS FOR ARGENICA'S SECOND DRUG, ARG-006, IN TREATMENT OF HIE

Highlights:

- *Argenica has been granted* ***Orphan Drug*** *and* ***Rare Pediatric Disease Designations*** *for its second drug candidate, ARG-006, for the treatment of Hypoxic Ischaemic Encephalopathy (HIE) in term newborn infants.*

- *ARG-006 is a stereoisomer, or mirror image, of Argenica's lead neuroprotective drug candidate ARG-007, and because they have different biological activity, they are* ***deemed different chemical entities and therefore different drugs.***

- ***Both ARG-006 and ARG-007 are being investigated for their respective safety and efficacy profiles in neonatal term HIE, offering the Company different therapeutic options for the treatment of HIE.***

- *These new designations will ensure ARG-006 has the* ***same regulatory incentives*** *granted to ARG-007 in the event Argenica determines it is more favourable to progress ARG-006 into the clinic in HIE.*

Perth, Australia; 30 OCTOBER 2024 - Argenica Therapeutics Limited (ASX: AGN) ("Argenica" or the "Company"), a biotechnology company developing novel therapeutics to reduce brain tissue death after brain injury and other neurological conditions, is pleased to announce the United States Food and Drug Administration (FDA) has granted its second neuroprotective drug candidate, **ARG-006, Orphan Drug Designation (ODD) and Rare Pediatric Disease Designation (RPDD**) for the treatment of Hypoxic Ischaemic Encephalopathy (HIE) in newborn term infants.

ARG-006 is the L-isomer (stereoisomer, or mirror image) of ARG-007 (the D-isomer) and is considered a different chemical entity and therefore a different drug by regulatory authorities. Argenica has begun exploring the safety, pharmacokinetics and therapeutic potential of ARG-006, along with ARG-007, in its HIE piglet studies to determine which drug may present the more favourable target product profile. The progression of brain injury in HIE typically occurs in several stages, each involving different mechanisms that lead to neuronal damage and brain dysfunction. This brain injury typically occurs over several days to weeks, unlike acute ischaemic stroke where

the brain injury (initial injury and brain reperfusion injury) often occurs within a fairly short time period i.e. hours to a day. Therefore, Argenica is investigating the drug target product profile of both ARG-006 and ARG-007 and how this aligns best with brain injury seen in HIE.

Supporting the development and evaluation of new treatments for rare diseases such as HIE is a key priority for the FDA. The FDA has authority to grant ODD and RPDD to a drug or biological product to prevent, diagnose or treat a rare disease or condition.

Orphan Drug Designation (ODD)

ODD qualifies companies for significant incentives including:

- Tax credits for qualified clinical trials
- Exemption from user fees
- Potential seven years of market exclusivity after approval

Rare Pediatric Disease Designation (RPDD)

Supporting the development and evaluation of new treatments for rare diseases in children is also a key priority for the FDA. The FDA has authority to grant a RPDD to a drug or biological product that shows promise in preventing, diagnosing or treating a rare disease or condition in the pediatric population (children 18 years and younger). The granting of the RPDD may provide a key substantial benefit to Argenica, being, that upon approval of a New Drug Application (NDA) for either ARG-006 or ARG-007 in HIE, the FDA may award a **Priority Review Voucher (PRV)** provided that HIE is the first indication for which the drug is approved.

Under the current scheme, the PRV can be redeemed to accelerate the review of a subsequent marketing application or may be sold or transferred to a third party. The sale price of a PRV is often in the tens of millions of dollars[1]. It should be noted, however, as of 27th September 2024, the US Congress decided to revise the scheme such that the PRV program will begin to sunset after December 20, 2024, and any drug with a RPDD must be approved by September 30, 2026, to be eligible to apply for a PRV. Whilst this decision and timeline may be revised, based on the current situation with the PRV program, Argenica deems the greatest value to be in the ODD designation.

Dr Liz Dallimore, **Argenica's Managing Director**, said: "Argenica has made the strategic decision to seek ODD and RPDD for its experimental drug ARG-006 in HIE to ensure the Company has the option to progress this drug asset through clinical development should it make scientific, clinical and commercial sense to do so. Our CSO, Prof Bruno Meloni and his team, have collected compelling efficacy data on ARG-006 and Dr Adam of the Perron Institute is collaborating with the Aarhus University in Denmark, to investigate the attributes of both ARG-007 and ARG-006 in a piglet study in HIE."

[1] https://www.gao.gov/products/gao-20-251

HIE occurs when the brain does not receive enough oxygen or blood flow for a period of time. It may occur at any time prior to labour, during labour and delivery, or immediately following delivery. The initial injury that is caused by a loss or reduction of oxygen supply is followed by progressive brain cell death due to excitotoxicity, oxidative stress, and inflammation[2,3]. The physiological effects resulting from the interruption to blood flow and/or oxygen in the brain can vary greatly depending on the length of time the disruption occurs as well as the location of the disruption. Some children may only display mild effects whilst others will have severe permanent disability including cerebral palsy, cognitive impairment, or developmental delay. The addressable market for HIE is expected to be USD$1.9 Billion by 2030.[4]

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 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 is progressing its a Phase 2 clinical trial in ischaemic stroke patients, as well as continuing to generate preclinical data in other neurological conditions, including in TBI.

[2] Leonardo CC, Pennypacker KR. Neuroinflammation and MMPs: potential therapeutic targets in neonatal hypoxic-ischemic injury. *J Neuroinflammation* (2009) 6:13

[3] Thornton C, Hagberg H. Role of mitochondria in apoptotic and necroptotic cell death in the developing brain. *Clin Chim Acta* (2015) 451:35–8

[4] Data Bridge Market Research Market Analysis Study 2023