

# APPENDIX 4C – 30 JUNE 2021 QUARTERLY ACTIVITIES & CASHFLOW REPORT

#### Highlights:

- Advancement of pre-clinical research in preparation for the planned Phase 1 in-human clinical trial of the Company's lead candidate ARG-007:
  - Highly encouraging results from Argenica's pilot Pharmacokinetic (PK) study. No adverse effects were observed in the PK animal study, indicating that ARG-007 is potentially safe and well-tolerated at the relevant doses.
  - A further preliminary study showed ARG-007 has the potential to continue offering neuroprotection when co-administered with the clot dissolving drug Tissue Plasminogen Activator.
- Subsequent to quarter end Argenica's Chief Scientific Offer, Prof Bruno Meloni and his team at the Perron Institute, secured a A\$290,000 cash grant to advance animal studies which will assist in confirming the optimal effective dose of ARG-007 and confirm its effectiveness when co-administered with clot dissolving drugs.
- Successful listing on the ASX after \$7m capital raising at \$0.20 per share with strong support received from institutional, high net-worth and sophisticated investors.
- Cash reserves of \$7.1m as at 30 June 2021. Funds from the IPO will be directed towards the first Phase I in-human clinical trial.

**Perth, Australia; 29 JULY 2021** - Argenica Therapeutics Limited (ASX: AGN) ("Argenica" or the "Company"), a biotechnology company developing novel therapeutics to reduce brain tissue death after stroke, is pleased to lodge the following update and attached Appendix 4C Quarterly Cashflow Report for the 12-month period ended 30 June 2021.

During the quarter, the company advanced pre-clinical studies in preparation for the planned Phase 1 in-human clinical trial of the Company's lead candidate ARG-007. Key activities undertaken are outlined below:

#### COMMENCED TRADING ON THE ASX, WELL SUPPORTED IPO RAISING \$7.0 MILLION

During the quarter, Argenica was pleased to commence trading on the Australian Securities Exchange (ASX) following a well-supported Initial Public Offering (IPO). The Company raised AUD\$7 million before costs with strong support received from institutional, high net-worth and sophisticated investors.

The listing will allow the Company to develop its novel neuroprotective therapeutics that provide protection for brain cells that would otherwise potentially be irreparably damaged by stroke, and other types of brain injury. Development partners include world renowned Perron Institute for Neurological and Translational Science (Perron Institute) and The University of Western Australia.

Argenica's lead candidate, ARG-007, is being developed as a potential therapeutic for stroke, to be administered in the field by paramedics to provide neuroprotective treatment prior to a patient's arrival at the hospital. This approach could potentially reduce brain tissue death during the period before formal diagnosis and treatment of the underlying stroke condition, greatly enhancing clinical recovery outcomes.

Funds from the IPO will be directed towards a number of key development activities, which include building on Argenica's encouraging pre-clinical evidence and transitioning into a Phase 1 clinical trial planned to commence in Q4 CY21. The Company also intends to expand on its existing and future development collaborations, build a regulatory approval framework and explore additional applications of the technology in other neurological conditions.

#### POSITIVE INITIAL RESULTS FROM PILOT PK STUDY

During the quarter, Argenica released highly encouraging results from its pilot Pharmacokinetic (PK) study. The PK profile of a drug provides data to determine what happens to a drug in the body including a drug's absorption into the bloodstream, distribution to tissues, and how it is metabolised and/or excretion from the body.

An understanding of the PK of investigational drugs is essential for establishing appropriate dosing regimens and is an important element of the data package required to initiate the inhuman clinical development of ARG-007.

The PK data generated has indicated favourable PK profiles in the dose range of 0.3-10 mg/kg which includes ARG-007's efficacious dose of approximately 1 mg/kg, with a rapid time to reach maximum concentration in the blood, irrespective of sex or dose. Argenica has completed this pilot PK study to confirm that ARG-007 has adequate PK parameters prior to initiation of final preclinical PK studies required for the Phase 1 clinical trial.

These results expand ARG-007's PK profile, which includes previous data from a radiolabelled Positron Emission Tomography (PET) imaging study showing ARG-007 is rapidly taken up by the kidneys - the standard route of peptide clearance from the body.

In addition to the measured PK data, no adverse effects were observed in the animals in each arm of the study, indicating that ARG-007 is potentially safe and well-tolerated at the administered, pharmacodynamically relevant doses.

These results are necessary for the upcoming toxicology studies required for the clinical trial regulatory submission and will also provide insights into how ARG-007 could be clinically administered in stroke and other therapeutic applications.

Please refer to ASX announcement titled "Argenica Completes Pilot Pre-Clinical Pharmacokinetics Study" released on 1 July 2021 for further details.

# STUDY SHOWS ARG-007 DOES NOT DEGRADE WHEN CO-ADMINISTERED WITH ISCHEMIC STROKE THERAPEUTICS

The Company was also pleased to provide positive preliminary results from a study showing ARG-007 has the potential to continue offering neuroprotection when co-administered with Tissue Plasminogen Activator (tPA). tPA, or alteplase, is an intravenous medicine given to ischemic stroke victims that can dissolve the stroke-causing clot. tPA is administrated after imaging diagnosis confirms an ischemic stroke, which can occur many hours after the initial stroke and does not prevent or reverse neuronal damage and cell death, but rather dissolves the clot causing the stroke.

Results from studies with other potential competitive neuroprotective peptides have suggested that the active peptide can get degraded following administration of tPA, which reduces the efficacy after tPA administration. This limitation would significantly impact the applicability of the neuroprotective agent in cases where tPA is expected to be administered as an acute ischemic stroke treatment.

In an in vitro neuronal excitotoxicity model, the ARG-007 peptide is resistant to proteolytic degradation when incubated with tPA and maintains its neuroprotective properties post tPA exposure. A previous study also confirmed the neuroprotective stability of ARG-007 when incubated with plasmin, an enzyme activated by tPA that dissolves the clot causing the stroke. These results suggest that ARG-007 could potentially continue to provide neuroprotective benefits after clot dissolving drugs are administered to stroke patients.

The Company is currently undertaking further pre-clinical trials to confirm these results in an animal model of stroke. These subsequent trials, to be undertaken by Prof Meloni, will examine the in vivo neuroprotective efficacy of ARG-007 when administered with tPA following stroke in animals.

Please refer to ASX announcements titled "Study Shows ARG-007 Does Not Degrade" released on 12 July 2021 and "Study Additional Information" released on 13 July 2021 for further details.

#### GRANT SECURED TO ADVANCE PRE-CLINICAL STUDIES OF ARG-007

Subsequent to quarter end, Argenica's Chief Scientific Offer, Prof Bruno Meloni and his team at the Perron Institute for Neurological and Translational Science, secured a A\$290,000 cash grant from MSWA to advance additional pre-clinical research of its lead therapeutic candidate ARG-007.

The grant has been awarded to ascertain ARG-007's ideal dose amount for neuroprotective response effectiveness when administered alone, or with clot dissolving tissue plasminogen activator (tPA) drug, in an experimental stroke model. The intellectual property arising from this grant will be assigned to Argenica under the company's Intellectual Property Assignment Agreement for ARG-007.

The findings from this funded project will assist Argenica in confirming the most appropriate escalating dose profile for the upcoming Phase 1 clinical trial.

#### **OUTLOOK, CLINICAL TRIAL REMAINS ON TRACK FOR Q4 2021**

Argenica is now focused on optimisation of the manufacturing processes and has formally initiated the studies required by the regulators for the Phase 1 clinical trial, including the full PK, genotoxicity, safety pharmacology and toxicokinetic studies.

The Phase 1 clinical trial will provide critical data related to the safety of ARG-007 in healthy subjects, which is required for a more comprehensive Phase 2 study in stroke patients.

# CASHFLOW COMMENTARY, CASH RESERVES OF \$7.1 MILLION AS AT 30 JUNE 2021 FOLLOWING WELL SUPPORTED IPO

The Company had net cash operating outflows for the quarter of \$0.774 million and cash reserves of \$7.144 million as at 30 June 2021 following the completion of a \$7.0 million (before costs) IPO capital raising. A total of 35,000,000 fully paid ordinary shares at \$0.20 per share were issued under the IPO.

Operating cash outflows in the quarter totalled \$0.774 million and included expenditure on research and development activities (\$0.259 million), staff costs (including research and development employees) (\$0.066 million), corporate administration (\$0.144 million) and non-recurring costs associated with the IPO (\$0.266 million). Research and development expenditure included payments to third party contractors undertaking the required studies to progress to the Phase 1 clinical trial and manufacture of ARG-007.

The Company had net financing cash inflows for the quarter of \$6.819 million from the IPO capital raising net of transactions costs. Capital raising fees of \$0.293 million due to the lead manager of the IPO were outstanding as at 30 June 2021 and will be paid in the following quarter.

As required by ASX Listing Rule 4.7C3, the Company notes that \$0.035 million was paid to related parties during the quarter (as noted in section 6 of the attached Appendix 4C) and these payments included salary and superannuation paid to an Executive Director (\$0.020 million) and for corporate services (including office space, utilities and executive management and administrative support) provided by Polaris Consulting Pty Ltd, a director-related entity of Geoff Pocock (\$0.015 million).

#### IPO PROSPECTUS USE OF FUNDS COMPARED TO ACTUAL EXPENDITURE

In accordance with ASX listing rule 4.7C.2, the Company provides below a use of funds comparison table showing actual spend for the period 23 April 2021 to 30 June 2021 compared to the intended use of funds table provided in the Company's IPO prospectus lodged with ASIC on 23 April 2021.

The use of funds table in the Prospectus outlined the Company's intended use of funds in the two year period following Admission of the Company to the Official List of the ASX. It should be noted that these are estimates and will be subject to modification on an ongoing basis depending on the results obtained from the Company's activities.

It should also be noted Argenica intends to apply for research and development (R&D) tax funding from the Australian Commonwealth Government to assist funding its R&D activities. A current scheme provides a refundable tax offset for expenditure on certain eligible R&D activities. As this funding is uncertain it was not included in the use of funds in the Prospectus.

Source of funds	Prospectus \$'000	Actual \$'000
Approximate cash as at the date of Prospectus / Opening cash balance	\$1,034	\$1,034
Proceeds from the Public Offer	\$7,000	\$7,000
Total funds available	\$8,034	\$8,034
Proposed use of funds		
Pre-clinical development activities	\$2,175	\$223
Clinical trial and safety assessment (phase 1)	\$1,525	\$5
Product development and planning activities for clinical trial (phase 2a)	\$300	\$5
Regulatory approval strategy and preparation	\$550	\$5

CLOSING CASH BALANCE	-	\$7,144
Total Expenditure	\$8,034	\$890
Costs of the Offer	\$755	\$444
Working capital	\$579	\$48
Corporate administration	\$2,000	\$118
IP protection costs	\$150	\$41

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 improve patient outcomes. Our lead neuroprotective peptide candidate, ARG-007 has been successfully demonstrated to improve outcomes in pre-clinical stroke models and is in the process of being verified for its safety and toxicity before commencing Phase 1 clinical trials in humans. The aim is for our therapeutic to be administered by first responders to protect brain tissue against damage during a stroke with further potential to enhance recovery once a stroke has taken place.

#### **ABOUT ARG-007**

Argenica's lead drug candidate, ARG-007, is a cationic arginine-rich peptide which has been in preclinical development by the company's Chief Scientific Officer Prof Bruno Meloni for over 6 years. ARG-007 has shown preclinical evidence of induced neuroprotection in animal models of stroke. Most recently data published in May 2021¹ utilising a rodent model of a middle cerebral artery occlusion (MCAO) type stroke showed ARG-007 administration at a dose of 300 nmol/kg resulted in slowing of the infarct core growth and preservation of penumbral tissue. Data gathered in non-human primate animal models of MCAO² showed ARG-007 treatment reduced infarct lesion volume by up to 65.2% and 69.7% at 24 hours and 28 days poststroke, respectively. In this study animals receiving ARG-007 also displayed reduced functional deficits.

<sup>1</sup> 

<sup>&</sup>lt;sup>1</sup> Milani, D., Clark, V. W., Feindel, K. W., Blacker, D. J., Bynevelt, M., Edwards, A. B., Anderton, R. S., Knuckey, N. W., & Meloni, B. P. (2021). Comparative Assessment of the Proteolytic Stability and Impact of Poly-Arginine Peptides R18 and R18D on Infarct Growth and Penumbral Tissue Preservation Following Middle Cerebral Artery Occlusion in the Sprague Dawley Rat. Neurochemical research, 46(5), 1166–1176.

<sup>&</sup>lt;sup>2</sup> Meloni, B. P., Chen, Y., Harrison, K. A., Nashed, J. Y., Blacker, D. J., South, S. M., Anderton, R. S., Mastaglia, F. L., Winterborn, A., Knuckey, N. W., & Cook, D. J. (2020). **Poly-Arginine Peptide-18 (R18) Reduces Brain Injury and Improves Functional Outcomes in a Nonhuman Primate Stroke Model.** *Neurotherapeutics : the journal of the American Society for Experimental NeuroTherapeutics*, *17*(2), 627–634.

ARG-007 has also been shown to be resistant to proteolytic degradation by tissue plasminogen activator (tPA) *in vitro* as described in the company's ASX announcement of 12 July 2021. Argenica believes ARG-007 may have applications beyond stroke with preclinical evidence of efficacy in animal models of traumatic brain injury<sup>3</sup> and perinatal hypoxic-ischaemic encephalopathy (HIE)<sup>4</sup>, the latter being a leading cause of mortality and morbidity in newborn infants.

<sup>&</sup>lt;sup>3</sup> Chiu, L. S., Anderton, R. S., Clark, V. W., Cross, J. L., Knuckey, N. W., & Meloni, B. P. (2020). **Effect of Polyarginine Peptide R18D Following a Traumatic Brain Injury in Sprague-Dawley Rats.** *Current therapeutic research, clinical and experimental, 92,* 100584

<sup>&</sup>lt;sup>4</sup> Edwards, A. B., Anderton, R. S., Knuckey, N. W., & Meloni, B. P. (2018). **Assessment of therapeutic window for poly-arginine-18D (R18D) in a P7 rat model of perinatal hypoxic-ischaemic encephalopathy.** *Journal of neuroscience research*, *96*(11), 1816–1826.

### **Appendix 4C**

# Quarterly cash flow report for entities subject to Listing Rule 4.7B

#### Name of entity

ARGENICA THERAPEUTICS LIMITED	
ABN	Quarter ended ("current quarter")
78 637 578 753	30 JUNE 2021

Con	solidated statement of cash flows	Current quarter \$A'000	Year to date (12months) \$A'000
1.	Cash flows from operating activities		
1.1	Receipts from customers	-	145
1.2	Payments for		
	(a) research and development	(259)	(733)
	(b) product manufacturing and operating costs	-	-
	(c) advertising and marketing	-	-
	(d) leased assets	-	-
	(e) staff costs	(66)	(123)
	(f) administration and corporate costs	(144)	(259)
1.3	Dividends received (see note 3)	-	-
1.4	Interest received	-	-
1.5	Interest and other costs of finance paid	-	-
1.6	Income taxes paid	-	-
1.7	Government grants and tax incentives - R&D tax rebate	-	151
1.8	Other (provide details if material)		
	- Net GST (paid) / received	(39)	(48)
	- IPO Expenses	(266)	(287)
1.9	Net cash from / (used in) operating activities	(774)	(1,154)

2. (	Cash flows from investing activities	
2.1 I	Payments to acquire or for:	
(	(a) entities	-
(	(b) businesses	-
(	(c) property, plant and equipment	-

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Con	solidated statement of cash flows	Current quarter \$A'000	Year to date (12months) \$A'000
	(d) investments	-	-
	(e) intellectual property	-	-
	(f) other non-current assets	-	-
2.2	Proceeds from disposal of:		
	(a) entities	-	-
	(b) businesses	-	-
	(c) property, plant and equipment	-	-
	(d) investments	-	-
	(e) intellectual property	-	-
	(f) other non-current assets	-	-
2.3	Cash flows from loans to other entities	-	-
2.4	Dividends received (see note 3)	-	-
2.5	Other (provide details if material)	-	-
2.6	Net cash from / (used in) investing activities	0	0

3.	Cash flows from financing activities		
3.1	Proceeds from issues of equity securities (excluding convertible debt securities)	7,000	8,137
3.2	Proceeds from issue of convertible debt securities	-	-
3.3	Proceeds from exercise of options	-	-
3.4	Transaction costs related to issues of equity securities or convertible debt securities	(181)	(181)
3.5	Proceeds from borrowings	-	-
3.6	Repayment of borrowings	-	-
3.7	Transaction costs related to loans and borrowings	-	-
3.8	Dividends paid	-	-
3.9	Other (provide details if material)	-	-
3.10	Net cash from / (used in) financing activities	6,819	7,956

4.	Net increase / (decrease) in cash and cash equivalents for the period		
4.1	Cash and cash equivalents at beginning of period	1,099	342
4.2	Net cash from / (used in) operating activities (item 1.9 above)	(774)	(1,154)

Con	solidated statement of cash flows	Current quarter \$A'000	Year to date (12months) \$A'000
4.3	Net cash from / (used in) investing activities (item 2.6 above)	-	-
4.4	Net cash from / (used in) financing activities (item 3.10 above)	6,819	7,956
4.5	Effect of movement in exchange rates on cash held	-	-
4.6	Cash and cash equivalents at end of period	7,144	7,144

5.	Reconciliation of cash and cash equivalents at the end of the quarter (as shown in the consolidated statement of cash flows) to the related items in the accounts	Current quarter \$A'000	Previous quarter \$A'000
5.1	Bank balances	7,144	1,099
5.2	Call deposits	-	-
5.3	Bank overdrafts	-	-
5.4	Other (provide details)	-	-
5.5	Cash and cash equivalents at end of quarter (should equal item 4.6 above)	7,144	1,099

6.	Payments to related parties of the entity and their associates	Current quarter \$A'000	
6.1	Aggregate amount of payments to related parties and their associates included in item 1	35	
6.2	Aggregate amount of payments to related parties and their associates included in item 2	-	
	Note: if any amounts are shown in items 6.1 or 6.2, your quarterly activity report must include a description of, and an		

7.	Financing facilities  Note: the term "facility' includes all forms of financing arrangements available to the entity.  Add notes as necessary for an understanding of the sources of finance available to the entity.	Total facility amount at quarter end \$A'000	Amount drawn at quarter end \$A'000
7.1	Loan facilities	-	-
7.2	Credit standby arrangements	-	-
7.3	Other (please specify)	-	-
7.4	Total financing facilities	-	-
7.5	Unused financing facilities available at qu	uarter end	
7.6	Include in the box below a description of each facility above, including the lender, interest rate, maturity date and whether it is secured or unsecured. If any additional financing facilities have been entered into or are proposed to be entered into after quarter end, include a note providing details of those facilities as well.		

8.	Estimated cash available for future operating activities	\$A'000
8.1	Net cash from / (used in) operating activities (item 1.9)	(774)
8.2	Cash and cash equivalents at quarter end (item 4.6)	7,144
8.3	Unused finance facilities available at quarter end (item 7.5)	-
8.4	Total available funding (item 8.2 + item 8.3)	7,144
8.5	Estimated quarters of funding available (item 8.4 divided by item 8.1)	10.8
	Note: if the entity has reported positive net operating cash flows in item 1.9, answer item 8.5 as "N/A". Otherwise, a	

Note: if the entity has reported positive net operating cash flows in item 1.9, answer item 8.5 as "N/A". Otherwise, a figure for the estimated quarters of funding available must be included in item 8.5.

8.6 If item 8.5 is less than 2 quarters, please provide answers to the following questions:

8.6.1 Does the entity expect that it will continue to have the current level of net operating cash flows for the time being and, if not, why not?

Answer: N/A

8.6.2 Has the entity taken any steps, or does it propose to take any steps, to raise further cash to fund its operations and, if so, what are those steps and how likely does it believe that they will be successful?

Answer: N/A

8.6.3 Does the entity expect to be able to continue its operations and to meet its business objectives and, if so, on what basis?

Answer: N/A

Note: where item 8.5 is less than 2 quarters, all of questions 8.6.1, 8.6.2 and 8.6.3 above must be answered.

#### **Compliance statement**

- This statement has been prepared in accordance with accounting standards and policies which comply with Listing Rule 19.11A.
- 2 This statement gives a true and fair view of the matters disclosed.

Date:	29 July 2021
Authorised by:	By the Board of the Company(Name of body or officer authorising release – see note 4)

#### Notes

- 1. This quarterly cash flow report and the accompanying activity report provide a basis for informing the market about the entity's activities for the past quarter, how they have been financed and the effect this has had on its cash position. An entity that wishes to disclose additional information over and above the minimum required under the Listing Rules is encouraged to do so.
- 2. If this quarterly cash flow report has been prepared in accordance with Australian Accounting Standards, the definitions in, and provisions of, AASB 107: Statement of Cash Flows apply to this report. If this quarterly cash flow report has been prepared in accordance with other accounting standards agreed by ASX pursuant to Listing Rule 19.11A, the corresponding equivalent standard applies to this report.
- 3. Dividends received may be classified either as cash flows from operating activities or cash flows from investing activities, depending on the accounting policy of the entity.
- 4. If this report has been authorised for release to the market by your board of directors, you can insert here: "By the board". If it has been authorised for release to the market by a committee of your board of directors, you can insert here: "By the [name of board committee eg Audit and Risk Committee]". If it has been authorised for release to the market by a disclosure committee, you can insert here: "By the Disclosure Committee".
- If this report has been authorised for release to the market by your board of directors and you wish to hold yourself out as complying with recommendation 4.2 of the ASX Corporate Governance Council's *Corporate Governance Principles and Recommendations*, the board should have received a declaration from its CEO and CFO that, in their opinion, the financial records of the entity have been properly maintained, that this report complies with the appropriate accounting standards and gives a true and fair view of the cash flows of the entity, and that their opinion has been formed on the basis of a sound system of risk management and internal control which is operating effectively.