APPENDIX 4C – 31 MARCH 2022

QUARTERLY ACTIVITIES & CASHFLOW REPORT

Highlights:

- *Pre-clinical studies required for the planned Phase 1 in-human clinical trial of the Company's lead candidate ARG-007 continued during the quarter, with final GLP genotoxicity and toxicology studies completed.*

- *Argenica anticipates completion of remaining pre-clinical studies, ethics submission to the Human Research Ethics Committee (HREC), and initiation of clinical trial site management setup in late Q2 CY22,*

- *Following HREC approval, the Company will commence recruiting patients for its Phase 1 clinical trial.*

- *During the quarter, the Company continued to progress pre-clinical work focussed on the potential application of ARG-007 in other types of brain injury. The Company was pleased to announce positive results from a preclinical study assessing the efficacy of ARG-007 in protecting brain cells following blood flow disruption to the brain (cerebral ischaemia), as seen following cardiac arrest and certain cardiac surgeries.*

- *Cash reserves of $4.37m as at 31 March 2022. Funds from the IPO available for the first Phase I in-human clinical trial.*

Perth, Australia; 29 APRIL 2022 - Argenica Therapeutics Limited (ASX: AGN) ("Argenica" or the "Company"), a biotechnology company developing novel therapeutics to reduce brain tissue death after stroke and other types of brain injury, is pleased to lodge the following update and attached Appendix 4C Quarterly Cashflow Report for the 9-month period ended 31 March 2022.

During the quarter, the Company continued to advance pre-clinical studies in preparation for its planned first-in-human Phase 1 clinical trial of the Company's lead candidate ARG-007 focussed on testing the safety and tolerability of the drug in healthy volunteers. Additional

activities undertaken during the quarter included pre-clinical studies on the application of ARG-007 for other types of brain injury.

Key activities undertaken are outlined below.

PHASE 1 CLINICAL TRIAL ROADMAP

Argenica's core focus during the quarter was on the preparatory work required to initiate its Phase 1 clinical trial which included the following required efficacy and safety studies:

- Final Pharmacokinetic (PK) Studies: These studies are critical in determining how ARG-007 is absorbed, distributed, metabolised, and excreted by the body and are essential for establishing appropriate dosing regimens for the Phase 1 trial. Argenica announced highly encouraging results from its Pilot PK study on 1 July 2021; and

- Safety & Toxicology Studies: These studies characterise the toxicity profile of ARG-007 by identifying its impact on genes and target organs. By understanding the potential toxic effect on genes, kidneys, the heart, muscles, and other vital organs, toxicology studies help to determine the margin of safety of a drug for its expected clinical dose when administered to humans. The results from these studies will be critical in guiding the parameters for Argenica's Phase 1 clinical trial to maximise safety and minimise risk.

During the quarter, the Company also successfully completed the final Good Laboratory Practice (GLP) genotoxicity studies of ARG-007. Regulatory bodies, such as the FDA, require data to be collected under GLP conditions, which are a set of principles to ensure quality assurance is achieved during pre-clinical studies. Data from two GLP genotoxicity studies showed ARG-007 will not likely pose a genetic or carcinogenic risk to patients and that it does not cause any structural damage to chromosomes in mammalian cells.

Following quarter end, Argenica completed dosing and data analysis in the final GLP toxicology studies to determine the maximum tolerated dose (MTD) of ARG-007. These GLP toxicology studies carried out in rats and non-human primates collected key data required for ethics approval of the upcoming Phase 1 clinical trial. The MTD determined in these studies is used to establish the safe starting dose in the Phase 1 clinical trial. Importantly, the MTD is significantly higher than the previously determined efficacious doses, thereby reducing the likelihood of an adverse event occurring during the Phase 1 trial.

The Company is now completing the final pre-clinical activities required for ethics submission, including the final pharmacokinetics (PK), final GLP safety, and pathology assessments. The Company's PK studies have been delayed due to the Covid lockdown in Shanghai, where the Company's clinical research organisation (CRO) is based. However, the CRO has recently informed Argenica that they have now been given priority to resume business operations and they expect their operations to commence shortly. Given the PK study is a short study of only

a few days duration, and only in rats, the delay is not expected to impact timing of ethics submission in Q2 CY22.

The GLP safety studies have progressed with only minimal delay caused by the Shanghai lockdown. These studies are conducted in rats and monkeys and assess the safety of ARG-007 in the cardiovascular, respiratory, and central nervous systems. It is anticipated these studies will be completed in the coming weeks.

Following completion of these pre-clinical studies, Argenica anticipates ethics submission to the Human Research Ethics Committee (HREC) and initiation of clinical trial site management setup in late Q2 CY22, enabling the Phase 1 clinical trial to begin recruiting patients immediately following ethics approval.

PHASE 1 CLINICAL TRIAL DESIGN

GLP toxicology studies completed have established ARG-007's MTD, which will inform the safe starting dose for Argenica's Phase 1 clinical trial. The Phase 1 trial will be conducted in healthy human volunteers to assess the safety, tolerability, and pharmacokinetics of single ascending doses of ARG-007. The trial is anticipated to be run as a double-blind, randomised, placebo-controlled, sequential-groups study. The trial has been designed to include a total of 32 participants enrolled in 4 groups of 8 people. Each participant will either receive a dose of ARG-007 or a placebo on Day 1, with safety pathology samples and data collected at multiple points over the following 8 days starting with the cohort receiving the lowest dose of ARG-007. Following the 8 days of data collection in the first cohort, the next cohort will then commence, receiving the next highest dose of ARG-007. The sequential staging of cohorts allows Argenica to determine whether any adverse reactions are seen in a cohort before progressing to the next highest dosed cohort.

The Phase 1 clinical trial will provide Argenica with critical data on the safety and tolerability of ARG-007. The purpose of the Phase 1 trial is to determine if ARG-007 is safe and well tolerated when administered in healthy human subjects. Data collected from the trial will also provide the required foundation to progress into a Phase 2 trial, where, assuming ARG-007 is safe and well tolerated in human subjects in its Phase 1 trial, ARG-007 will be administered to stroke patients to determine whether efficacy is seen in a small number of human patients.

POSITIVE PRECLINCAL DATA ON EFFICACY OF ARG-007 IN NEW INDICATION – GLOBAL CEREBRAL ISCHAEMIA

Argenica also continued to progress pre-clinical work focussed on the potential application of ARG-007 for other types of brain injury.

During the quarter, the Company was pleased to announce positive results from a preclinical study assessing the efficacy of ARG-007 in protecting brain cells following blood flow

disruption to the brain (cerebral ischaemia), as seen following cardiac arrest and certain cardiac surgeries.

The preclinical study found that ARG-007, administered after disruption of blood flow to the brain utilising a four-vessel occlusion (4-VO) rat model, reduced cell death in hippocampal neurons (CA1 neurons) in the brain. The data was compared to un-injured (sham) animals and injured (4-VO) animals who received saline as the treatment (vehicle). These results provide further evidence of ARG-007's neuroprotective capabilities in a new therapeutic area of global cerebral ischaemia, which can occur following cardiac arrest or from certain cardiac surgeries where cardiac output is decreased.

Please refer to ASX announcement titled "Positive Preclinical Data On Efficacy Of ARG-007 In New Indication – Global Cerebral Ischaemia" released on 30 March 2022 for further details.

This study builds on the positive efficacy results achieved in other indications such as hypoxic ischemic encephalopathy (HIE). HIE is a type of brain dysfunction that occurs when the brain doesn't receive enough oxygen or blood flow for a period of time. It is one of the most serious birth complications for infants.

As released in the prior quarter, a preclinical study utilising a late pre-term animal model of HIE showed that ARG-007 reduced the volume of brain tissue death by 50% compared to groups which received a placebo saline injection. Importantly, ARG-007 also reduced the volume of brian tissue death by 40% compared to hyperthermia, the current standard of care for infants with HIE.

CASHFLOW COMMENTARY, CASH RESERVES OF $4.370 MILLION AS AT 31 MARCH 2022

The Company had net cash operating outflows for the quarter of $0.934 million and cash reserves of $4.370 million as at 31 March 2022.

Operating cash outflows in the quarter included expenditure on research and development activities ($0.661 million), staff costs (including research and development employees) ($0.197 million), corporate administration ($0.102 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 outflows for the quarter of $0.003 million being share issue costs on shares released from ASX escrow requirements during the quarter.

As required by ASX Listing Rule 4.7C3, the Company notes that $0.086 million was paid to related parties during the quarter (as noted in section 6 of the attached Appendix 4C) and these payments included (i) salary and superannuation paid to an Executive Director ($0.050 million) and (ii) Directors fees and superannuation paid to Non-Executive Directors ($0.036 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 31 March 2022 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 has and intends to apply for a cash rebate on eligible research and development (R&D) expenses under the Australian Commonwealth Government's R&D tax incentive program to assist funding its R&D activities. The 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
R&D tax incentive rebate	-	$259
Interest received	-	$2
Total funds available	**$8,034**	**$8,296**
Proposed use of funds		
Pre-clinical development activities	$2,175	$1,691
Clinical trial and safety assessment (phase 1)	$1,525	$388
Product development and planning activities for clinical trial (phase 2a)	$300	$101
Regulatory approval strategy and preparation	$550	$114
IP protection costs	$150	$104
Corporate administration	$2,000	$726

Working capital	$579	$32
Costs of the Offer	$755	$769
Total Expenditure	**$8,034**	**$3,926**
CLOSING CASH BALANCE	**-**	**$4,370**

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 2021[i] 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 MCAO[ii] 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.

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 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[iii] and perinatal hypoxic-ischaemic encephalopathy (HIE)[iv], the latter being a leading cause of mortality and morbidity in newborn infants.

[i] 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.

[ii] 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.

[iii] 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

[iv] 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	31 MARCH 2022

Consolidated statement of cash flows		**Current quarter $A'000**	**Year to date (9months) $A'000**
1.	**Cash flows from operating activities**		
1.1	Receipts from customers	-	-
1.2	Payments for		
	(a) research and development	(661)	(1,746)
	(b) product manufacturing and operating costs	-	-
	(c) advertising and marketing	-	-
	(d) leased assets	-	-
	(e) staff costs	(197)	(661)
	(f) administration and corporate costs	(102)	(370)
1.3	Dividends received (see note 3)	-	-
1.4	Interest received	1	2
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	-	259
1.8	Other (provide details if material)		
	- Net GST (paid) / received	25	25
	- IPO Expenses	-	(76)
1.9	**Net cash from / (used in) operating activities**	**(934)**	**(2,517)**

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

Consolidated statement of cash flows		Current quarter $A'000	Year to date (9months) $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)	-	-
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	(3)	(257)
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**	**(3)**	**(257)**

4.	**Net increase / (decrease) in cash and cash equivalents for the period**		
4.1	Cash and cash equivalents at beginning of period	5,307	7,144
4.2	Net cash from / (used in) operating activities (item 1.9 above)	(934)	(2,517)

Consolidated statement of cash flows		Current quarter $A'000	Year to date (9months) $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)	(3)	(257)
4.5	Effect of movement in exchange rates on cash held	-	-
4.6	**Cash and cash equivalents at end of period**	**4,370**	**4,370**

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	4,370	5,307
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)**	**4,370**	**5,307**

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	86
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 explanation for, such payments.

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 quarter 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)	(934)
8.2	Cash and cash equivalents at quarter end (item 4.6)	4,370
8.3	Unused finance facilities available at quarter end (item 7.5)	-
8.4	Total available funding (item 8.2 + item 8.3)	4,370
8.5	**Estimated quarters of funding available (item 8.4 divided by item 8.1)**	4.8

Note: if the entity has reported positive net operating cash flows in item 1.9, answer item 8.5 as "N/A". Otherwise, a 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

1 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 April 2022.....

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".

5. 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.