# APPENDIX 4C – 31 DECEMBER 2021

# 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 are continuing with results from these studies expected throughout Q1 CY22.*

- *Argenica anticipates completion of preliminary study activities, preparation of ethics submission to the Human Research Ethics Committee (HREC), and initiation of clinical trial and site management setup in Q1 CY22, enabling the Phase 1 clinical trial to begin recruiting patients immediately following ethics approval.*

- *Positive efficacy results from a preclinical study of ARG-007 in a late pre-term animal model of hypoxicischaemic 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.*

- *Argenica granted patent protection in the United States, one of the world's largest healthcare markets.*

- *Appointment of experienced healthcare and clinical trials professional Dr Meghan Thomas, as Head of Clinical Development.*

- *Cash reserves of $5.3m as at 31 December 2021 after receipt of a $0.259 million R&D Tax Incentive Rebate for the financial year ended 30 June 2021. Funds from the IPO will be directed towards the first Phase I in-human clinical trial.*

**Perth, Australia; 27 JANAURY 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 6-month period ended 31 December 2021.

During the quarter, the Company continued to advance manufacturing and pre-clinical studies in preparation for the 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, and 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 has been on the preparatory work required to initiate its Phase 1 clinical trial including 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.

Subsequent to quarter end, Argenica completed preliminary pre-clinical toxicology studies and genotoxicity studies of ARG-007 under non-Good Laboratory Practice (non-GLP) conditions. The toxicology studies have identified the parameters for the no observed adverse effect levels (NOAELs) required for the Good Laboratory Practice (GLP) toxicity studies, estimating the safe starting dose for ARG-007 for the Phase 1 clinical trial. This has allowed Argenica to initiate the final GLP toxicity studies. The company also completed non-GLP genotoxicity studies. GLP studies for genotoxicity, pharmacokinetics and toxicology have now been initiated, with GLP safety studies to commence shortly. Please refer to the ASX announcement titled "Preliminary Pre-Clinical Toxicology Studies Successfully Completed" released on 24 January 2022.

Results from GLP pre-clinical studies are expected throughout Q1 CY22.

In addition to the completion of these pre-clinical studies, Argenica anticipates preparation of ethics submission to the Human Research Ethics Committee (HREC) and initiation of clinical trial and site management setup in Q1 CY22, enabling the Phase 1 clinical trial to begin recruiting patients immediately following ethics approval. Argenica has engaged Australian based drug development consultants Beyond Drug Development, and US based drug development and FDA regulatory consultants Ground Zero Pharmaceuticals, to provide input and advice on the Company's preclinical data package to ensure preclinical activities are

conducted in line with expectations of the HREC and FDA. Both consultants have been working closely with Argenica throughout the planning and execution of the pre-clinical activities and Phase 1 clinical trial planning.

Argenica released a presentation on 18 October 2021 titled "Phase 1 Clinical Trial Overview and Roadmap" which sets out further details on the trial.

Argenica's Phase 1 clinical trial will be conducted in healthy 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.

**POSITIVE PRECLINICAL DATA FOR ARG-007 NEUROPROTECTION IN HYPOXICISCHAEMIC ENCEPHALOPATHY**

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

During the quarter, the Company was pleased to share positive efficacy results from a preclinical study of ARG-007 in a late pre-term animal model of HIE. In an animal model of late pre-term HIE, ARG-007 reduced the volume of brain tissue death by 50% compared to groups which received a placebo saline injection. Importantly, ARG-007 reduced the volume of brain tissue death by 40% compared to hypothermia. Hypothermia is the current standard of care and the only approved treatment to improve neurological outcomes of HIE for late pre-term and term infants.

Reducing brain tissue death caused by HIE could make a significant difference to an infants' clinical outcome. It could mean the difference of walking, talking and thinking normally or being disabled for life. Findings from the study are currently being prepared for publication in a scientific journal and will become the foundation for additional efficacy studies of ARG-007 in additional animal models of HIE.

Please refer to an announcement released on 3 November 2021 titled "Positive Preclinical Data for Arg-007 Neuroprotection in Hypoxicischaemic Encephalopathy" for further details on the study.

**ARGENICA GRANTED PATENT PROTECTION IN THE UNITED STATES, ONE OF THE WORLD'S LARGEST HEALTHCARE MARKETS**

During the quarter Argencia announced that the United States Patent and Trademark Office (USPTO) had issued a Notice of Allowance for patent application number 16/041,483 relating to the use of ARG-007. The patent covers the use of ARG-007 as a therapeutic compound to prevent brain cell death in Argenica's lead applications of stroke, traumatic brain injury (TBI) and hypoxic ischaemic encephalopathy (HIE). This Notice of Allowance confirms that the patent application "Neuroprotective Peptides" is allowed for issuance as a patent. Argenica is pleased to advise that this patent was granted on 25 January 2022.

Argenica now has granted patents in the largest addressable markets of the EU (validated in 11 key countries), Japan, China and the US. Notably, these patents are 100% owned by Argenica and the Company's IP assignment is free of royalties or other encumbrances. A summary of patent coverage is provided below:

| Jurisdiction | Progress | Number | Protection coverage |
|---|---|---|---|
| Europe | Granted | EU3063168 | Exp: 30/10/2034 |
| Japan | Granted | Japan 6495270 | Exp: 30/10/2034 |
| China | Granted | ZL2014800719713 | Exp: 30/10/2034 |
| US | Granted | US16/041,483 | Exp: 30/10/2034 |

**APPOINTMENT OF DR MEGHAN THOMAS AS HEAD OF CLINICAL DEVELOPMENT**

Argencia was also pleased to recently advise of the appointment of experienced healthcare and clinical trials professional Dr Meghan Thomas, as Head of Clinical Development. Dr Thomas will join Argenica in its Perth office at the beginning of April and provide leadership, project management and program oversight for the timely preparation and execution of the Company's upcoming Phase 1 clinical trial program. Dr Thomas will also manage the Company's future clinical trials as Argenica moves into later stage clinical development.

## CASHFLOW COMMENTARY, CASH RESERVES OF $5.307 MILLION AS AT 31 DECEMBER 2021 AFTER RECEIPT OF $0.259 MILLION R&D TAX REBATE

The Company had net cash operating outflows for the quarter of $0.558 million and cash reserves of $5.307 million as at 31 December 2021.

Operating cash outflows in the quarter included expenditure on research and development activities ($0.582 million), staff costs (including research and development employees) ($0.216 million), corporate administration ($0.153 million) and non-recurring costs associated with the IPO ($0.076 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. Operating cash outflows in the quarter were partially offset by the receipt of an R&D Tax Incentive Rebate for the financial year ended 30 June 2021 of $0.259 million.

The Company had net financing cash outflows for the quarter of $0.005 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 $0.127 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 ($0.051 million) and (ii) Directors fees and superannuation paid to Non-Executive Directors ($0.047 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 December 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 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 | - | $1 |
| **Total funds available** | **$8,034** | **$8,294** |
| **Proposed use of funds** | | |
| Pre-clinical development activities | $2,175 | $1,020 |
| Clinical trial and safety assessment (phase 1) | $1,525 | $368 |
| Product development and planning activities for clinical trial (phase 2a) | $300 | $70 |
| Regulatory approval strategy and preparation | $550 | $75 |
| IP protection costs | $150 | $91 |
| Corporate administration | $2,000 | $540 |
| Working capital | $579 | $54 |
| Costs of the Offer | $755 | $769 |
| **Total Expenditure** | **$8,034** | **$2,987** |
| **CLOSING CASH BALANCE** | **-** | **$5,307** |

*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.

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[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 DECEMBER 2021 |

| **Consolidated statement of cash flows** | | **Current quarter $A'000** | **Year to date (6months) $A'000** |
|---|---|---|---|
| **1.** | **Cash flows from operating activities** | | |
| 1.1 | Receipts from customers | - | - |
| 1.2 | Payments for | | |
| | (a) research and development | (503) | (1,085) |
| | (b) product manufacturing and operating costs | - | - |
| | (c) advertising and marketing | - | - |
| | (d) leased assets | - | - |
| | (e) staff costs | (198) | (414) |
| | (f) administration and corporate costs | (115) | (268) |
| 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 | 259 | 259 |
| 1.8 | Other (provide details if material) | | |
| | - Net GST (paid) / received | - | 1 |
| | - IPO Expenses | - | (76) |
| **1.9** | **Net cash from / (used in) operating activities** | **(558)** | **(1,583)** |

| **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 (6months) $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 | (5) | (254) |
| 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** | **(5)** | **(254)** |

| **4.** | **Net increase / (decrease) in cash and cash equivalents for the period** | | |
|---|---|---|---|
| 4.1 | Cash and cash equivalents at beginning of period | 5,870 | 7,144 |
| 4.2 | Net cash from / (used in) operating activities (item 1.9 above) | (558) | (1,583) |

| Consolidated statement of cash flows | | Current quarter $A'000 | Year to date (6months) $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) | (5) | (254) |
| 4.5 | Effect of movement in exchange rates on cash held | - | - |
| **4.6** | **Cash and cash equivalents at end of period** | **5,307** | **5,307** |

| 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 | 5,307 | 5,870 |
| 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)** | **5,307** | **5,870** |

| 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**<br>*Note: the term "facility' includes all forms of financing arrangements available to the entity.*<br>*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) | (558) |
| 8.2 | Cash and cash equivalents at quarter end (item 4.6) | 5,307 |
| 8.3 | Unused finance facilities available at quarter end (item 7.5) | - |
| 8.4 | Total available funding (item 8.2 + item 8.3) | 5,307 |
| 8.5 | **Estimated quarters of funding available (item 8.4 divided by item 8.1)** | 9.5 |

*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: ....27 January 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.