

ASX ANNOUNCEMENT

Quarterly Activities Report and Appendix 4C

Highlights

- **Exopharm provides continued leadership to the exosome sector:**
 - Exosomes (also known as extracellular vesicles (EVs)) heralded as the 'next big thing' at the RNA Leaders World Congress.
 - Exopharm's **Exoria** dye identified as the best in class for labelling exosomes.
- **Product development activities progress:**
 - Advancements in Exopharm's GMP Master Cell Bank (MCB) continue.
 - Demonstrated loading of mRNA into exosomes using Exopharm's LOAD technology.
 - Exopharm's Pipeline Products Panel (PPP) make important developments.
- **Commercial collaborations build momentum**
 - Work with collaboration partners' progress.
 - Exopharm presenting and participating in multiple, global key conferences and partnering events.

29 April 2022

Melbourne, Australia: Exopharm Limited (ASX:EX1) is a company at the forefront of developing transformative exosome medicines.

Exopharm is pleased to provide this update on activities and the Appendix 4C for the quarter ended 31 March 2022.

Exosomes heralded as the 'next big thing' at the RNA Leaders World Congress

Exopharm's representation at the RNA Leaders World Congress in March was the perfect opportunity to turn up the conversation on exosomes with major pharmaceutical companies.

Dr. Johannes Mühl chaired the day 1 session focusing on formulation and biodistribution of RNA therapeutics.

The Congress was an international forum for dialog about the formulation and delivery challenges RNA-medicines face. These challenges include efficacy, immunogenicity, cytotoxicity, tissue tropism and crossing the blood-brain-barrier.

Representatives from most of the major pharmaceutical companies participated in the Congress.

Exopharm's exosomes could provide solutions to these formulation and delivery problems – and unlock the potential of mRNA-medicines to treat many medical problems.

Participation in the Congress has led to several new partnership and licensing discussions. Exopharm is offering partners access to its evolving 'toolchest' of exosome technologies – including patented LEAP for purification in large-scale, LOAD to load RNA into exosomes and EVPS to provide tissue-specific delivery.

Exopharm's Exoria dye identified as the best in class for labelling exosomes

Exosomes are invisible to the naked eye and are hard to count and track. Until now there has been no suitable and reliable way to solve this issue, which is an important limitation that holds back the development of exosome medicines and exosome research.

Labelling exosomes with fluorescent dyes has emerged as a potential solution to count and track exosomes using standard analytical equipment, but available dyes lacked specificity for exosomes, potentially leading to false or inaccurate data.

To overcome these limitations, Exopharm has developed **Exoria**, a dye specifically designed to allow researchers to count and track how exosomes migrate into cells and deliver their payloads. Exoria is now the subject of a patent application owned by Exopharm.

Exoria was compared with other dyes used in exosome research and was identified as the only dye that specifically labelled exosomes.¹ Importantly, it was also found that Exoria labelling did not interfere with the immunomodulatory properties of the mesenchymal stromal cell-derived extracellular vesicle (exosome) preparations as tested in a multi-donor mixed lymphocyte reaction assay.

This report positions Exopharm's Exoria to become the industry standard for correctly identifying and labelling exosomes.

Exoria is another important addition to the Exopharm 'toolchest' of exosomes technologies.

Advancements in Exopharm's Current Good Manufacturing Practice (cGMP) Master Cell Bank (MCB) continue

Exopharm's exosomes are produced from human cells cultured in a bioreactor and then purified using the patented LEAP technology.

¹ Article

Science Direct, March 2022, Imaging flow cytometry challenges the usefulness of classically used extracellular vesicle labeling dyes and qualifies the novel dye Exoria for the labeling of mesenchymal stromal cell-extracellular vesicle preparations

The manufacture of clinical-grade exosomes in large-scale requires a Master Cell Bank (MCB) of cells that are securely stored in large numbers and compliant with strict quality requirements.

In early March the MCB team reached an important milestone in the establishment of a Current Good Manufacturing Practice (cGMP) Master Cell Bank, successfully developing and validating a HEK293 cell culture to research standards for a second time.

The team are currently establishing and implementing the quality framework required for Exopharm to manufacture naïve, HEK-derived exosomes and load them with therapeutic cargo to cGMP standard.

Manufacturing products under cGMP assures the identity, strength, quality and purity of drug products, and certification in cGMP will bolster Exopharm's credibility and competitive advantage.

Demonstrated loading of mRNA into exosomes using Exopharm's LOAD technology

mRNA has gained enormous attention as a promising tool for the treatment of diseases. However, delivery of mRNA therapeutics is difficult, and a drug delivery system is required to protect the mRNA from degradation and enable it to reach and enter target cells.

Lipid nanoparticles (LNPs) have enjoyed recent clinical success in the formulation and delivery of mRNA-based vaccines. However, the broader success of mRNA therapeutics has additional and critical challenges that LNPs may not be able to overcome, including multiple-dosing, reduced toxicity of the carrier, avoiding being targeted by the human immune system (immunogenicity), targeting specific tissues/organs beyond the liver and maximising cytoplasmic delivery and bioactivity.

Exosomes have been proposed as highly efficient natural drug delivery vehicles that overcome these formulation and delivery challenges.

Early results from Exopharm's Technology group demonstrate loading mRNA into exosomes using Exopharm's LOAD technology. The combination of LOAD with the patented LEAP purification technology will enable the manufacture of mRNA-exosome medicines - advancing Exopharm as an ideal partner for pharmaceutical companies looking to advance mRNA for therapeutic treatments.

Exopharm's Pipeline Products Panel (PPP) make important advancements

Owning and developing its own exosome medicine products ('Pipeline Products') is a priority for Exopharm.

Implementation of this pipeline product strategy may result in a higher valuation commonly enjoyed by 'product' companies compared to 'platform technology' companies.

Exopharm's Pipeline Products will be selected to harness the unique features of exosomes, address truly unmet medical needs, and have strong commercial prospects. The aim is to

optimise the probability of technical and regulatory success whilst avoiding 'me-too' products.

In September '21 Exopharm formed the Pipeline Products Panel (PPP), which is headed up by Dr Johannes Mühl and includes Dr Jennifer King, Dr Mike West, Dr Sam Keenan, and Dr Ian Dixon. The charter of the PPP is to select the 'best' exosome medicine opportunities for Exopharm to invest in and develop.

Commencing with over 300 possible opportunities – including rare and common diseases and genetic disorders, the PPP are making good progress in the identification of the Pipeline Products. Product opportunities are assessed against objective scientific, medical, and commercial criteria. Key Opinion Leaders (KOLs) and scientific advisors have also been engaged in the process.

Once selected, *in vitro* and then *in vivo* testing will be carried out to confirm the product prospects. The present aim is to commence product testing in CY '22.

Commercial collaborations build momentum

Exopharm signed a collaboration agreement with the Astellas Institute for Regenerative Medicine (AIRM) to demonstrate the effectiveness of Exopharm's LEAP™, LOAD and EVPS technologies utilising AIRM's cell assets and technologies.

AIRM is a subsidiary of Astellas Pharma Inc., a top 20 global pharmaceutical company, with global sales of around US\$12 billion p.a. and strong investment in R&D to support the development of new treatments to address unmet medical needs.

"Astellas is keen to evaluate whether exosomes could become part of their future pipeline of innovative products. This collaboration services agreement defines how Astellas and Exopharm will work together in some important initial laboratory work" said Dr Ian Dixon, Managing Director and founder of Exopharm.

The project has commenced at Exopharm's laboratories in Melbourne and seeks to validate the use of Exopharm's LEAP technology platform to purify exosomes derived from two proprietary AIRM cell lines. A second phase of this project will involve transferring the LEAP technology to AIRM research headquarters located in Massachusetts USA for their further evaluation and use. Under the terms of the MSA, AIRM will pay Exopharm fees of up to US\$481,000 for both projects over a period of around 15 months.

Astellas cell lines have now been received at the Exopharm lab and work is underway to demonstrate Exopharm's LEAP technology for the purification of exosomes using two proprietary AIRM cell lines. This program of work is progressing according to plan.

Exopharm presenting and participating in multiple, global key conferences and partnering events.

In January '22, Exopharm presented at the 14th annual Biotech Showcase, a part of the 40th annual J.P. Morgan Health Care Conference, with a presentation focussing on delivering transformative medicine with exosomes. Exopharm also had a strong presence at the BIO CEO and Investor Digital Conference in February '22, and BIO-Spring Europe in March. The resultant interest in Exopharm and its technologies has been favourable, with several CDA-level partnership and licensing discussions now underway.

Looking forward, Exopharm has been invited to join an Australian Trade Mission to the '22 Biotechnology Innovation Organization's (BIO) International Convention, taking place in June in the U.S. Led by two Commissioners to the Americas, the Global Victoria Mission intends to showcase Victoria's best capabilities in the biotechnology sector.

The Global Victoria trade delegation will participate in site visits, attend pharmaceutical industry meetings, and be given opportunities to showcase their companies, which will culminate in a networking event at the end of week one.

This year, the BIO trade mission will have two components: a pre-BIO roadshow from 8 – 10 June, followed by participation and partnering activities at the BIO Convention, from 12 – 17 June. During week two, Pavilion Global Victoria will be supporting delegates at the Convention with a Victorian Government space at the Ausbiotech pavilion, where delegates will be showcased to the estimated 15,000 convention attendees from the pharmaceutical and biotechnology sectors from around the world. Exopharm will have its logo and marketing collateral on display at the State of Victoria space.

Exopharm President, International, David Oxley has been invited to speak during the BIO Convention. Mr Oxley's presentation will be entitled, "How Exosomes are Igniting Modern Medicine Delivery," and will showcase Exopharm and its technology platforms. A copy of Mr Oxley's presentation will be made publicly available on the day.

Appendix 4C commentary

Exopharm ended the quarter with cash of \$5.6 million (\$9.4 million at 31 December 2021). Quarterly operating cash outflows for the period was \$3.1 million (\$3.4 million outflow in the prior quarter).

Cash outflow for the period was predominately R&D costs – product development, manufacture and testing programs and R&D related salary costs – all aimed at supporting Exopharm's development and commercialisation activities.

In accordance with Listing Rule 4.7C, payments made to related parties and their associates included in items 6.1 of the Appendix 4C includes gross salaries, superannuation, fees to executive and non-executive directors and advisory panel fees, as follows:

- Total Gross salaries to directors: \$216,072 (including superannuation and advisory panel fees)

- Total payments to related parties and their associates included in items 6.1: \$216,072

By the Board - this announcement has been authorised for release by the Board.

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ABOUT EXOPHARM

Exopharm (ASX:EX1) is at the forefront of transformative medicines using exosomes or extracellular vesicles (EVs) and is pursuing a product pipeline-driven platform strategy. Exosomes can be loaded with a variety of active pharmaceutical ingredients (APIs) and can be targeted to selected cell-types and tissue types, improving the safety-profile of the APIs and providing better treatments. Exosome delivery of DNA and other gene therapies into the nucleus of the patient's cells can improve treatment of inherited medical conditions. Exosomes can also be used to deliver small molecule drugs, mRNA and other modern medicines.

Exosomes are an alternative means of drug delivery inside the body, alongside technologies such as lipid nanoparticles (LNP), cell- penetrating peptides, viral vectors and liposomes. Exopharm's exosome technologies solve important needs for the success of exosome medicines – **LEAP** manufacturing technology, **LOAD** API loading technologies and **EVPS** tropism technologies.

Exopharm technology platforms will underpin its own pipeline of exosome medicines – each aimed at delivering a transformative medicine for an unmet medical need.

FORWARD LOOKING STATEMENTS

This announcement contains forward-looking statements which incorporate an element of uncertainty or risk, such as 'intends', 'may', 'could', 'believes', 'estimates', 'targets', 'aims', 'plans' or 'expects'. These statements are based on an evaluation of current corporate estimates, economic and operating conditions, as well as assumptions regarding future events. These events are, as at the date of this announcement, expected to take place, but there cannot be any guarantee that such events will occur as anticipated or at all given that many of the events are outside of Exopharm's control or subject to the success of the Development Program. Furthermore, the Company is subject to several risks as disclosed in the Prospectus dated 6 November 2018.

Appendix 4C

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

Name of entity

EXOPHARM LIMITED

ABN

78 163 765 991

Quarter ended ("current quarter")

31 March 2022

Consolidated statement of cash flows	Current quarter \$A'000	Year to date (9 months) \$A'000
1. Cash flows from operating activities		
1.1 Receipts from customers	1	21
1.2 Payments for		
(a) research and development	(463)	(2,016)
(b) product manufacturing and operating costs	-	-
(c) advertising and marketing	(62)	(353)
(d) leased assets	-	-
(e) staff costs	(1,910)	(5,093)
(f) administration and corporate costs	(813)	(2,369)
1.3 Dividends received (see note 3)	-	-
1.4 Interest received	-	4
1.5 Interest and other costs of finance paid	(20)	(51)
1.6 Income taxes paid	-	-
1.7 Government grants and tax incentives	-	3,950
1.8 Other (provide details if material)	153	471
1.9 Net cash from / (used in) operating activities	(3,114)	(5,436)
2. Cash flows from investing activities		
2.1 Payments to acquire:		
(a) entities	-	-
(b) businesses	-	-
(c) property, plant and equipment	(353)	(967)
(d) investments	-	-
(e) intellectual property	-	-
(f) other non-current assets	-	-

Consolidated statement of cash flows		Current quarter \$A'000	Year to date (9 months) \$A'000
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	(353)	(967)
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	-	-
3.5	Proceeds from borrowings	-	-
3.6	Repayment of borrowings	-	-
3.7	Transaction costs related to loans and borrowings	-	-
3.8	Dividends paid	-	-
3.9	Other (repayment of lease liability)	(248)	(560)
	Other (bank guarantee and security deposit)	-	(110)
3.10	Net cash from / (used in) financing activities	(248)	(670)
4. Net increase / (decrease) in cash and cash equivalents for the period			
4.1	Cash and cash equivalents at beginning of period	9,365	12,723
4.2	Net cash from / (used in) operating activities (item 1.9 above)	(3,114)	(5,436)

Consolidated statement of cash flows		Current quarter \$A'000	Year to date (9 months) \$A'000
4.3	Net cash from / (used in) investing activities (item 2.6 above)	(353)	(967)
4.4	Net cash from / (used in) financing activities (item 3.10 above)	(248)	(670)
4.5	Effect of movement in exchange rates on cash held	(2)	(2)
4.6	Cash and cash equivalents at end of period	5,648	5,648

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	5,648	9,365
5.2	Call deposits	-	-
5.3	Bank overdrafts	-	-
5.4	Other	-	-
5.5	Cash and cash equivalents at end of quarter (should equal item 4.6 above)	5,648	9,365

6. Payments to related parties of the entity and their associates

- 6.1 Aggregate amount of payments to related parties and their associates included in item 1
- 6.2 Aggregate amount of payments to related parties and their associates included in item 2

Current quarter \$A'000
216
-

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

The payments to directors or their associates in 6.1 include gross salaries, superannuation, advisory panel fees, and fees and benefits to executive and non-executive directors.

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

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)	(3,114)
8.2 Cash and cash equivalents at quarter end (Item 4.6)	5,648
8.3 Unused finance facilities available at quarter end (Item 7.5)	-
8.4 Total available funding (Item 8.2 + Item 8.3)	5,648
8.5 Estimated quarters of funding available (Item 8.4 divided by Item 8.1)	1.8

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

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: Yes. The Company expects to have the current level of net operating cash flows for the time being.

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: Yes. The Company has activities underway to fund its operations. The Company is able to add to its working capital by the issuance of shares under its existing Capacity to raise capital. The Company also seeks to generate licensing revenues. The Company is presently debt free and could consider debt funding to cover short term cash flow needs.

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: Yes. The Company continues to manage its operations according to a detailed cash flow projection. The forecast indicates the Company can continue its operations and meet its business objectives.

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.

29 April 2022

Date:

Board of Directors

Authorised by:
(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.