

## ASX ANNOUNCEMENT

## **Quarterly Activities Report and Appendix 4C**

## **Highlights**

## • First payment from Astellas research collaboration:

- First payment of AU\$77K received from the Astellas Institute for Regenerative Medicine (AIRM) under the agreement announced in January 2022 – as part of potentially up to US\$481,000.
- Validation work is progressing well.

## • Significant progress on Exopharm's technology to support partnering and products:

- Further progress on Exopharm's Master Cell Bank of HEK293 cells.
- o EVPS exosome engineering demonstrated with two versions.
- Successful LOADing of DNA, mRNA and siRNA into exosomes demonstrated to support partnering and products.
- o Batch of exosomes made for an animal study planned to commence in Q1 FY23.

## • Increased industry interest in exosomes:

- Discussions currently underway with more potential partners on new research collaboration agreements and potential additional revenue in FY23.
- Many biotechnology and pharmaceutical companies could benefit from using exosomes to overcome delivery challenges with their genetic medicines which require delivery of DNA, RNA, CRISPR or AAV cargos.
- Exopharm's presentation "How Exosomes are Igniting Modern Medicine Delivery" was given at the 2022 BIO Convention in the US in June 2022.

## Exopharm's genetic medicines may be supported by non-dilutive funding

- Exopharm has identified some particular opportunities for its exosome medicines.
- Non-dilutive funding may be sought to support development of some key products.

#### Cashflow helped by non-dilutive R&DTI receipts, revenue and cost reductions

- \$2.7 million in non-dilutive R&DTI based funding received.
- Additional R&DTI-based funding of \$482,602 was announced on 28 July 2022.
- Further R&DTI rebate cash expected to be received in Q1 and Q2 FY23.
- Revenue from existing and new research collaboration agreements is anticipated and may build in FY23.
- Cost reductions announced in May 2022 are being implemented in non-core areas of the business.
- Exopharm is managing the business costs and incoming cash carefully.

29 July 2022

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

Exopharm provides this update on activities and the Appendix 4C for the quarter ended 30 June 2022.

Dr Ian Dixon, founder and CEO, said, "We have made significant progress over the past quarter and expect more commercial and technology newsflow in the coming quarter. We are well positioned to benefit from the increased industry interest in exosomes as transformational genetic medicines. We continue to invest in our commercial activities and to further validate our proprietary technology platform, with a clear focus on revenue generation. Commercial revenues are starting to build, and we anticipate further revenue over the next year. We are currently in discussions with several potential partners on further research collaboration agreements and associated additional potential revenue."

## First payment from Astellas research collaboration

In January 2022, Exopharm announced the Master Collaborative Services Agreement (MSA) with Astellas Institute for Regenerative Medicine (AIRM), which is a subsidiary of Astellas Pharma Inc., a top 20 global pharmaceutical company.

The initial research projects are designed to validate Exopharm's LEAP, LOAD and EVPS technology platform to manufacture exosomes for Astellas, initially at Exopharm's facilities in Melbourne, followed by the Astellas facilities in Massachusetts, USA.

In Q4 FY22, Exopharm received the first payment of AU\$77K under this collaboration agreement. Under the terms of the MSA, AIRM will potentially pay Exopharm fees of up to US\$481,000.

#### Significant progress on Exopharm's technology

Exopharm continues to make significant progress in its proprietary technologies, including the LEAP based manufacturing process, EVPS engineering and LOAD capabilities.

Exopharm's exosomes are produced from human cells cultured in a bioreactor and purified using Exopharm's patented LEAP technology. The manufacture of clinical-grade exosomes in large-scale requires a Master Cell Bank (MCB) of cells that is secure and compliant with strict quality requirements.

In March 2022, Exopharm successfully developed and validated a HEK293 cell culture to research standards for a second time, an important milestone towards the establishment of a Current Good Manufacturing Practice (cGMP) MCB for clinical product manufacture.

In Q4, Exopharm completed its manufacturing quality framework and established a Good Laboratory Practice (GLP)-compliant Master Cell Bank for exosome production. GMP compliance is the next step on from GLP compliance.

In the last quarter, Exopharm advanced its tissue-specific delivery EVPS technology by demonstrating the engineering of two different proteins into exosomes and demonstrated tissue tropism. Tissue tropism can be a useful feature of exosome medicines and supports partnership discussions.

Successful LOADing of DNA, mRNA and siRNA into exosomes enables the development of therapeutics for multiple complex diseases and is of particular interest to potential partners seeking to overcome the delivery challenges with nucleic acid cargos. To date, the loading of these nucleic acid cargos into exosomes has been challenging. Improved LOADing of DNA, mRNA and siRNA into exosomes has now been demonstrated in our research facility.

A batch of exosomes has been manufactured and characterised to support Exopharm's future animal testing of naïve exosomes – a prerequisite for later human studies. An animal study to test LEAP purified exosomes for safety and immunogenicity is planned to commence dosing in Q1 FY23.

In June 2022, the first article on the benefits of Exopharm's proprietary Exoria product for exosome analysis was published in a peer-reviewed journal. <sup>1</sup> A presentation on the advantages of Exoria was given by one of Exopharm's collaborators at the International Society for Extracellular Vesicles (ISEV) conference in France in May 2022.

The Finnish Red Cross Blood Service and Exopharm are currently exploring potential licensing structures, following an evaluation of our LEAP technology to produce blood-cell derived exosomes.

Leading international chemical manufacturing company Showa Denko Materials continues its evaluation of exosome purification technologies that includes our LEAP platform under a feasibility study agreement.

## **Increased industry interest in exosomes**

Discussions are currently underway with numerous potential partners on new research collaboration agreements and licensing. Exopharm is offering partners non-exclusive access to its evolving 'toolchest' of exosome technologies – including patented LEAP for purification in large-scale, LOAD to load active pharmaceutical ingredient (API) into exosomes, and EVPS to provide tissue-specific delivery ('tissue tropism') inside the body.

Many biotechnology and pharmaceutical companies could benefit from using exosomes to overcome delivery challenges with their genetic medicine APIs such as DNA, RNA, CRISPR, and AAVs.

<sup>&</sup>lt;sup>1</sup> https://doi.org/10.1016/j.jcyt.2022.02.003 Tertel et. al., Cytotherapy, 24(6) pp619-628, June 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

Exopharm's presentation "How Exosomes are Igniting Modern Medicine Delivery" was well received at the 2022 Biotechnology Innovation Organisation's (BIO) International Convention in the US in June 2022.

In June at the BIO Convention, Exopharm met with more than fifty different international biotechnology and pharmaceutical companies that are advancing RNA, DNA, CRISPR, and AAV products.

## **Exopharm's genetic medicines may be supported by non-dilutive funding**

Exopharm invested in a detailed review of potential product opportunities and has identified some particular exosome medicines that potentially show promise and fit with Exopharm's focus on genetic medicines. Further assessment of technological and business feasibility is underway.

Exopharm is uniquely positioned to apply its 'toolchest' of exosome technologies to transformative genetic medicines to address areas of particular unmet medical needs.

Non-dilutive funding is being sought to support the development of some key products that are attractive to industry partners and Patient Advocacy Organisations (PAOs).

## **Finance and Appendix 4C commentary**

Exopharm ended the quarter with cash of \$4.8 million (\$5.6 million at 31 March 2022).

Quarterly operating net cash outflows for the period was higher than the average for the financial year at \$3.2 million (\$3.1 million outflow in the prior quarter).

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

During the quarter, Exopharm entered into a non-dilutive funding agreement with Radium Capital, providing \$2.7 million in prepayment of the Company's FY22 R&D tax incentive R&DTI) claim.

Additional R&DTI funding of \$482,602 for May and June FY22 R&D expenses was announced on 28 July 2022, and further R&DTI rebate amounts are also planned to be received in Q1 and Q2 FY23.

Since the start of CY 2022 various cost-reduction initiatives have been implemented, including those as announced on 30<sup>th</sup> May 2022, in non-core areas of the business and some of these changes are still taking effect whilst preserving core operations.

Revenue from the existing Astellas research collaboration agreement is scheduled to build in Q1 and Q2 FY23 and revenue from new research collaboration agreements is planned to build in FY23.

Exopharm is managing the business costs and incoming cash carefully.

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: \$184,201 (including superannuation and advisory panel fees)
- Total payments to related parties and their associates included in items 6.1: \$184,201

This announcement has been authorised for release by the Board.

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#### **GLOSSARY**

A A \ /				• • •	\ /·
A A A A A	^ ^	$\alpha \alpha \alpha \alpha$	-	こっきへつ	1/1/1/1/
AAV	Au		ハララいい	เลเษน	Virus

CRISPR clustered regularly interspaced short palindromic repeats - a gene editing

technology

DNA Deoxyribonucleic acid

mRNA messenger Ribonucleic acid

R&DTI Research & Development Tax Incentive

siRNA silencing Ribonucleic acid

tropism tissue tropism means selective to certain cells, tissue or organs

#### **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

Quarter ended ("current quarter")

78 163 765 991

30 June 2022

Con	solidated statement of cash flows	Current quarter \$A'000	Year to date (12 months) \$A'000
1.	Cash flows from operating activities		
1.1	Receipts from customers	77	98
1.2	Payments for		
	(a) research and development	(490)	(2,506)
	(b) product manufacturing and operating costs	-	-
	(c) advertising and marketing	(71)	(424)
	(d) leased assets	-	-
	(e) staff costs	(1,716)	(6,809)
	(f) administration and corporate costs	(826)	(3,195)
1.3	Dividends received (see note 3)	-	-
1.4	Interest received	-	4
1.5	Interest and other costs of finance paid	(13)	(64)
1.6	Income taxes paid	-	-
1.7	Government grants and tax incentives	13	3,963
1.8	Other (provide details if material)	(157)	314
1.9	Net cash from / (used in) operating activities	(3,183)	(8,619)

2.	Cash flows from investing activities		
2.1	Payments to acquire:		
	(a) entities	-	-
	(b) businesses	-	-
	(c) property, plant and equipment	(158)	(1,125)
	(d) investments	-	-
	(e) intellectual property	-	-
	(f) other non-current assets	-	-

ASX Listing Rules Appendix 4C (17/07/20)

Cons	solidated statement of cash flows	Current quarter \$A'000	Year to date (12 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	(158)	(1,125)

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	2,729	2,729
3.6	Repayment of borrowings	-	-
3.7	Transaction costs related to loans and borrowings	(1)	(1)
3.8	Dividends paid	-	-
3.9	Other (repayment of lease liability)	(189)	(749)
	Other (bank guarantee and security deposit)		(110)
3.10	Net cash from / (used in) financing activities	2,539	1,869

4.	Net increase / (decrease) in cash and cash equivalents for the period		
4.1	Cash and cash equivalents at beginning of period	5,648	12,723
4.2	Net cash from / (used in) operating activities (item 1.9 above)	(3,183)	(8,619)

ASX Listing Rules Appendix 4C (17/07/20)

Con	solidated statement of cash flows	Current quarter \$A'000	Year to date (12 months) \$A'000
4.3	Net cash from / (used in) investing activities (item 2.6 above)	(158)	(1,125)
4.4	Net cash from / (used in) financing activities (item 3.10 above)	2,539	1,869
4.5	Effect of movement in exchange rates on cash held	1	(1)
4.6	Cash and cash equivalents at end of period	4,847	4,847

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	4,847	5,648
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)	4,847	5,648

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	184
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

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.

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## 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.

- 7.1 Loan facilities
- 7.2 Credit standby arrangements
- 7.3 Other (please specify)
- 7.4 Total financing facilities

Total facility amount at quarter end \$A'000	Amount drawn at quarter end \$A'000
2,729	2,729
-	-
-	-
-	-

## 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.

#### Financing facilities – additional notes 7.1

The loan facility in 7.1 is with Radium Capital and is an advance on 80% of the Company's estimated R&D Tax Incentive (RDTI) for the for the period 1 July 2021 – 30 April 2022 (Tranche 1). The interest rate for the loan facility is 15% per annum. The facility is secured. Repayment is timed to coincide with receipt of Exopharm's 2022 FY RDTI refund. The facility has been in place since 16 June 2022 and a facility amounting to \$2,729,305 has been received (total amount borrowed: \$2,729,305).

#### Additional financing facilities available after quarter end

Further loan facilities are planned to be entered into <u>after</u> quarter end and would bring in extra cash in 2 tranches:

- Tranche 2 in Q1 FY23. Loan advance on the estimated RDTI amount for the period 1 May 2022 – 30 June 2022. The amount was announced on 28<sup>th</sup> July 2022 as \$482,602.
- Tranche 3 in Q2 FY23. Loan advance on the estimated RDTI amount for the period 1<sup>st</sup> July 2022 – 30 September 2022. The amount received will be calculated at the time.

#### Additional cash receipts expected after quarter end from FY22 expenditure

Further cash is expected to be received in Q2 FY23 based upon the FY22 RDTI amount that has not been advanced in tranches 1 to 2. i.e. around 20% of the FY22 RDTI amount less interest costs. The amount received will be calculated at the time.

8.	Estimated cash available for future operating activities	\$A'000
8.1	Net cash from / (used in) operating activities (Item 1.9)	(3,183)
8.2	Cash and cash equivalents at quarter end (Item 4.6)	4,847
8.3	Unused finance facilities available at quarter end (Item 7.5)	-
8.4	Total available funding (Item 8.2 + Item 8.3)	4,847
8.5	Estimated quarters of funding available (Item 8.4 divided by Item 8.1)	1.5

- 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?

ASX Listing Rules Appendix 4C (17/07/20)

Answer: No, the Company expects to have improving net operating cashflows going forward.

There are two components to this expectation:

- On the cost-side, the Company has implemented some cost reduction measures in non-core areas of the business commencing in May 2022, as announced on 30 May 2022. Some of these reductions in expenditure are yet to take full effect, and will have a beneficial effect on net operating cash going forward.
- On the income-side, the Company recorded its first income from the Astellas agreement in Q4 FY22 and that contract is expected to generate further income in FY23, which will have a beneficial effect on net operating cash flow going forward. As the company builds operating income from additional collaborative research agreements and other non-dilutive cash sources, operating revenue is expected to lift in H1 FY23, and improve net operating cash going forward. Some agreements for collaborative research agreements may include upfront payments. The amounts received will be disclosed at the time.
- 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?

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Answer: Yes, further cash is anticipated and this may come from sources which can also include capital raising.

There are a number of sources of additional cash potentially available to the Company.

These include:

- RDTI rebates and loans on RDTI rebates
  - The Company has a strong track-record in receiving Research & Development Tax Incentive (RDTI) cash rebates. More recently the Company has brought cashflow forward by securing loans on estimated future RDTI cash rebates, to fund its operations. More details on page 4 of this Report.
- Operating income from existing collaboration agreement
   As reported on 31 January 2022, the Company has a Master Collaborative Services Agreement (MSA) with Astellas under which the Company received its first payment of AU\$77K in Q4 FY22. The total potential fees are up to U\$\$481,000, so these further potential payments, if received, would improve net operating cash going forward.
- Operating income from new potential collaboration agreements
   If the company builds operating income from additional collaborative research agreements, operating revenue could lift in H1 FY23, and provide additional cash to improve net operating cash going forward. Agreements for collaborative research may include upfront payments in US\$. These payments, if received, could improve net operating cash going forward.
- Operating income from potential licensing deals
  The Company has a number of proprietary technologies and is engaged in
  discussions with organisations seeking to use exosome technologies for
  their own operations. In biotechnology it is not unusual to license
  technologies for a mixture of upfront fees, milestone fees and then backended income sharing. These payments, if received, could improve net
- Other non-dilutive funding sources that may support product development Exopharm invested in a detailed review of potential product opportunities and has identified some particular exosome medicines that show promise and fit with Exopharm's focus on genetic medicines.
  - Exopharm is uniquely positioned to apply its 'toolchest' of exosome technologies to transformative genetic medicines to address areas of particular unmet medical needs.
  - Non-dilutive funding is being sought to support the development of some key products that are attractive to industry partners and Patient Advocacy Organisations (PAOs). These payments, if received, could have the benefit of improving net operating cash going forward.
- Capital raising

operating cash going forward.

- The Company may be able to raise cash by the issue of shares. The Company may be able to add to its working capital by the issuance of shares under its existing Capacity. The Company could also seek to issue shares subject to shareholder approval.
- 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 business activities to support its business objectives.

As described above, the commercial activities of the Company have started to generate operating income, and the plan is that this operating income and net cashflow could improve and grow into the future if more agreements are entered into.

Since listing in December 2018 the Company has invested into its technologies and capabilities to meet its business objectives – namely enabling exosome medicines to become a reality and generating operating revenue from partnering agreements. The present plan is that this prior investment may convert into further potentially revenue-generating research collaboration agreements and other cashflow in FY23.

There is a range of options to address funding needs, to support operations and to meet its business objectives. See answers to item 8.6 question 2.

## **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 2022

Authorised by order of the Board

(Name of body or officer authorising release – see note 4)

#### Notes

- 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.
- 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.