

## ASX ANNOUNCEMENT

### Exopharm Shareholder Update

- Webinar 10:30am Friday 29 May at <https://exo.ph/May2020> open to all
- EEV intellectual property (IP) portfolio being expanded
- Exopharm's engineered EVs (EEVs) generating data and news
- First-in-human allogeneic (unmatched) Plexaris safety study aims at CY 2020 study start
- Exopharm moves into its new facility at the Baker Institute in Melbourne and is in full operation
- Operations now back to full pace

**28 May 2020, Melbourne, Australia:** Exopharm Limited (ASX:EX1) is a clinical stage Australian company using exosomes (extracellular vesicles (EVs)) from cells to generate a new class of cell-free medicines. Exopharm is a leader in the manufacture and experimental clinical use of EV medicines.

Exopharm is developing two main types of EV products:

- NEVs (naïve EVs) from stem cells and platelets as a new class of regenerative medicine; and
- EEVs (engineered EVs) designed as specific medicines to treat conditions such as viral infection, cancer and inherited conditions.

#### Webinar invitation

Shareholders and other interested people are invited to join our Webinar update 10:30am Friday 29 May at <https://exo.ph/May2020>. There will be a Q&A session as part of the Webinar.

#### EEV IP portfolio is being expanded

EEVs have generated sizeable commercial transactions between EV companies and pharmaceutical partners, but translating the promise of EEVs into the clinic has been slow due to manufacturing limitations.

Exopharm's strategy prioritised achieving clinical grade and scale manufacturing capabilities with naïve EVs. Exopharm became the leader in the field with its PLEXOVAL study in early CY 2020.

Exopharm will use its manufacturing capability and know-how in new EEV product areas, and is now progressing into proof-of-concept and then non-human studies with EEVs. In many cases EEV products leverage three key technologies to achieve unique potential medicines:

- Targeting – Ligands are added to the surface of the EV to maximise their uptake by specific cells;
- Enhanced cargo – Active components such as small molecules, RNA or proteins are loaded into EVs for delivery; and
- Production – A proprietary manufacturing technology is required to supply clinical-grade consistent products.

Exopharm is building its EEV program around these three technologies and has generated or is in the process of generating results from in-vitro testing in areas such as anti-cancer drug delivery (Plexodox) and EEVs to reduce viral replication (Fortrexo), as well as other important therapeutic areas as detailed below.

Over the past 12 months Exopharm has pursued additional intellectual property (IP) to complement its manufacturing leadership, including investigating and assessing various in-licensing IP activities from third parties, with some IP in-licensing activities progressing through to the due diligence phase.

In-licensing, along with other in-house developments, is aimed at growing the Exopharm patent and IP portfolio. Exopharm is actively seeking licenses to patents from third parties and know-how to strengthen its IP portfolio for EEVs and make Exopharm an attractive partner for pharmaceutical companies and biotechnology companies seeking innovative EEV products.

Exopharm is also in the process of lodging additional patent applications that cover IP related to it's EEV program.

#### *Application of Engineered Exosomes (EEVs) to Viruses and Targeted Diseases*

EEVs open the door to treatments that are new to medicine and use the unique properties of nanoparticle EVs, which include their naturally-designed capability for readily accessing all parts of the body such as crossing the blood brain barrier, targeting specific cells and passing across cell membranes to deliver their cargos.

Exopharm is seeking to demonstrate the utility of its EEVs in important therapeutic areas including:

- Delivery of anti-cancer drugs into cancer cells with significant dose reduction (and therefore likely toxicity/dose improvements) (Plexodox project) (Plexaris EVs loaded with the anti-cancer drug doxorubicin kills lung cancer cells at a dose considerably lower than doxorubicin alone, in vitro testing shows);
- Interruption of viral replication in infected cells – including COV, RSV and Dengue (Fortrexo project) (ongoing early stage development seeking proof of concept and utility);
- Targeted delivery across the blood brain barrier – including Huntington's disease and Glioblastoma (ongoing early stage development seeking proof of concept and utility); and

- Auto-immune conditions including Rheumatoid Arthritis (ongoing early stage development seeking proof of concept and utility).

Development seeking proof of concept and utility is subject to various limitations and subject to ongoing success would lead to pre-clinical animal studies and subsequent clinical programs.

EEV projects are particularly relevant to early-stage partnering and Exopharm has initiated preliminary partnership discussions. Partners with interests in specific medical areas are being sought to fund clinical trials through to registration and sales. These discussions are at an early stage and outcomes are uncertain with no guarantee that the Company will reach any suitable agreements or that these agreements may be dependent on additional in vitro, pre-clinical or clinical testing.

The potential of EEV projects was exemplified in the recent announcement about our “Plexodox” anti-cancer product. Exopharm’s Plexaris EVs were loaded with the generic anti-cancer drug doxorubicin – so the drug doxorubicin was the internal ‘cargo’ of the EVs. In an in vitro study the potency (cancer cell killing efficacy) of EVs loaded with doxorubicin (Plexodox) was greater than cells exposed to doxorubicin without EVs. Doxorubicin drug sales worldwide exceed \$1 billion annually, but patients treated with doxorubicin often suffer adverse side-effects due to the drug’s toxicity to healthy cells, so dosing is often restricted to levels that are less effective against targeted cancer cells. Plexodox has the potential to both increase the doxorubicin anti-cancer cell killing while reducing the toxicity (increasing the therapeutic window), making this early proof-of-concept in EEVs a potential candidate for partners. For more information on Plexodox please see ASX Announcement dated 25<sup>th</sup> May 2020.

#### PLEXOVAL Study Update – moving to allogeneic study in CY 2020

Exopharm’s commercial objective is to develop and partner off-the-shelf exosome/EV medicines. Exopharm continues to invest in its core business of making clinical grade NEVs and running studies to demonstrate safety, tolerability and efficacy.

Exopharm is planning the first-in-human allogeneic (off-the-shelf) Plexaris (Exopharm’s platelet-derived exosome product) safety study (PLEXOVAL II) in CY 2020. This proposed Phase 1 allogeneic (unmatched) Plexaris safety study is the next major clinical step to demonstrate product safety and tolerability of an off-the-shelf logistics chain. The Company has recently lodged an ethics approval for PLEXOVAL II. Exopharm expects to announce the start of subject enrolments and further study details in the coming months, subject to the necessary approvals and final study preparations.

#### Exopharm’s team moves into the Baker Institute

Exopharm now has its own main laboratory and manufacturing facility at the Baker Institute in Melbourne and is in full operation. This new main laboratory doubles Exopharm’s development footprint and supports the needs of our development and

innovation teams. Being located within the Alfred Medical Precinct provides access to a large public hospital, clinical trial possibilities and many important medical services.

Plans for an opening ceremony have been postponed due to COVID-19, but a virtual tour will be part of our Webinar tomorrow.

### COVID-19 Impact Update

The COVID-19 pandemic has illustrated the importance of developing and commercialising innovative medicines against new threats. Exopharm has been working hard over the past months to design EVs for fast response to viral infections.

During the COVID-19 situation Exopharm has implemented policies and procedures to protect the team. There have been no reductions in staff or work-levels.

At Exopharm COVID-19 influenced our work in a variety of ways including:

Impact of COVID-19	Exopharm Response
Halt of autologous PLEXOVAL I study (as previously reported)	Acceleration of allogeneic PLEXOVAL II study design and conduct Accelerate internal proof-of-concept work with EEVs
Reduced access to shared research facilities	Accelerated transfer of our staff to our new site at Baker Institute – access has been open
Interruption of suppliers	Focus on activities fully within Exopharm’s control
Reduced international travel for commercial and other meetings	Increased use of videoconferencing

## Glossary

COV	Coronavirus, a family of viruses responsible for the variant causing COVID-19
Dengue	A mosquito-borne virus causing approximately 60 million infections worldwide
Doxorubicin	Off-patent chemotherapy drug with known side-effects
Fortrexo product	An Exopharm product in early stage in vitro testing designed for the interruption of viral replication in infected cells – including COV, RSV and Dengue
Glioblastoma	An aggressive form of brain cancer that is difficult to treat
Huntington’s disease	An inherited disease that causes degeneration of nerve cells in the brain for which there is no effective treatment
In vitro	In vitro means studies performed with microorganisms, cells, or biological molecules outside their normal biological context.

Lung cancer cells	Refers to cells grown from the Calu-3 adenocarcinoma cell line
Plexaris	Exopharm's platelet-derived extracellular vesicle medicine currently in human safety trials.
Plexodox	Exopharm's formulation of doxorubicin within Plexaris.
RSV	Respiratory syncytial virus is the most common cause of respiratory infection in children
Rheumatoid Arthritis	A degenerative auto-immune disorder that causes pain and damage in major joints

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

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### **ABOUT EXOPHARM**

Exopharm Limited (ASX:EX1) is a clinical-stage Australian regenerative medicine company developing therapeutic exosome products as alternatives to stem-cell therapies.

Exosomes are small particles naturally produced by cells, which deliver therapeutic 'cargoes' to other cells to reduce inflammation and promote regeneration. Exosomes are plentiful in our youth but decline with age. Recent research points to exosomes as a way to extend the number of healthy, functional years (extending health span).

Exosomes secreted by stem cells could be used instead of stem-cell therapy with equal or greater benefit – and without the problems of stem-cell therapies. They could be used to deliver targeted 'novel' drugs and have potential as diagnostics.

While trillions of exosomes are produced by stem cells, the real challenge is to 'purify' them as drug products. Exopharm owns a purification technology called Ligand-based Exosome Affinity Purification (LEAP). LEAP technology and associated know-how places Exopharm at the forefront of this emerging field worldwide. Exopharm is at clinical stage with pending and current trials for wound healing, dry aged-related macular degeneration and osteoporosis.

Exopharm was founded in 2013 by Dr Ian Dixon, co-founder of the ASX-listed stem-cell therapy developer Cynata Therapeutics. He was also a director of Cell Therapies, which produced adult stem cells for ASX-listed stem cell company Mesoblast. Exopharm listed on the ASX in December 2018.

## **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.

## **INHERENT RISKS OF INVESTMENT IN BIOTECHNOLOGY COMPANIES**

There are a number of inherent risks associated with the development of biopharmaceutical products to a marketable stage. The lengthy clinical trial process is designed to assess the safety and efficacy of a drug prior to commercialisation and a significant proportion of drugs fail one or both of these criteria. Other risks include uncertainty of patent protection and proprietary rights, whether patent applications and issued patents will offer adequate protection to enable product development, the obtaining of necessary drug regulatory authority approvals and difficulties caused by the rapid advancements in technology. Companies such as Exopharm are dependent on the success of their research and development projects and on the ability to attract funding to support these activities. Investment in research and development projects cannot be assessed on the same fundamentals as trading and manufacturing enterprises. Therefore, investment in companies specialising in drug development must be regarded as highly speculative. Exopharm strongly recommends that professional investment advice be sought prior to such investments.