ASX Announcement

Melbourne, Australia, 28 September 2022

Study indicates Exopharm's exosomes and manufacturing technologies can make a safe drug-delivery vehicle

- Preliminary results from recently completed study do not detect immunogenicity or toxicity of exosomes manufactured by Exopharm
- This externally generated dataset shows the Exopharm product and the manufacturing process are suitable for clinical pursuit
- These results support Exopharm's forward clinical product development program and partnering
- This outsourced study evaluated immunogenicity and toxicology outcomes with repeat dosing of HEK293-derived naïve exosomes in healthy adult wild-type mice

Genetic medicine and exosome-based drug-delivery company Exopharm Limited (ASX:EX1) announces positive data from an expert animal study conducted by an external group to assess immunogenicity and toxicity of Exopharm's exosomes.

Validation of Exopharm's technology further progressed

As mentioned in the Company's Quarterly Activities Report (29 July 2022), a batch of exosomes had been manufactured and characterised to support Exopharm's testing of naïve exosomes – a prerequisite for later human studies. As planned, an animal study to test LEAP purified exosomes for safety and immunogenicity has now completed dosing.

The interim study results show that repeated dosing of the exosomes was safe and did not generate an immune response despite up to 10 doses of around 3.4 billion particles per dose over 23 days.

Exosomes as a drug-delivery 'chassis' hold the prospect of being seen by the person's immune system as harmless and could be dosed many times (i.e. they have low immunogenicity). These study results lend support to this thesis.

The positive results back the use of exosomes made from Exopharm's producer-cells and purified by its patented LEAP purification process as a safe and well-tolerated alternative to viral vectors (e.g. adeno-associated virus [AAV]) and lipid nanoparticles [LNPs].

Using exosomes as a carrier of the active pharmaceutical ingredient (API) is core to Exopharm's present strategy. Showing that the exosome carrier is 'silent' to the recipient's

immune system and non-toxic are important steps in that strategy. The results from this study indicate that Exopharm's exosomes have these all-important attributes.

Exopharm's founder and CEO Dr Ian Dixon said "The success of our own products and our partnering relies on our ability to demonstrate that Exopharm's inhouse developed exosomes are a potentially safe and highly effective way to deliver medicines with repeat dosing. The data coming out of this study are an important step in this journey."

Dr Dixon commented further "The exosomes tested in this pivotal immunogenicity and toxicology study showcase the significant progress we have made over the past 24 months. These exosomes come from our highly-scalable GMP HEK293 cells, which were produced and collected in our improved cell culture system and purified using our latest protocols of the patented LEAP purification step."

Key details and outcomes of the study

HEK-293 cells were cultured by Exopharm to produce naïve (*no engineering of the cells*) exosomes. These exosomes were then purified using Exopharm's LEAP technology at its research centre. At University of Queensland, around 3.4 billion particles in 100 millionths of a litre (100µL) liquid of solution were injected intravenous under anaesthetic into a cohort of healthy adult wild-type mice at each dosing. Other mice in the study received the same volume of a control substance PBS (phosphate-buffered saline). Another small cohort of mice were administered LPS (Lipopolysaccharide) systemically to create a positive control and for assay validation.

Dosing was over 23 days and there was a total of 10 doses per mouse. Preliminary data obtained included body and organ mass, gross necropsy, haematology, and spleen-cell immunophenotyping – all of which confirmed the absence of an immune response or detectable toxicity levels. The study was performed under ethics approval (University of Queensland Animal Ethics Committee (AE000938)) and animals were monitored for changes in behaviour and health.

In the context of this study, immunogenicity is the ability of the animal's immune system to detect and mount an adverse immune response against the foreign exosomes that were administered. For a drug-delivery technology for therapeutic products, the ideal outcome from such a test is that the exosomes are not subject to an adverse host immune response – which is the outcome seen in these preliminary results.

The key conclusion from the preliminary data from this study is that the exosomes are not immunogenic or toxic and the product and the manufacturing process are suitable for clinical pursuit.

This study is a further important step towards the successful development of engineered exosome products.

Exopharm's founder and CEO Dr Ian Dixon said "Since its formation in 2013, Exopharm has been developing a portfolio of technologies to enable the commercialisation of exosome-based medicines. This collection of exosome-related technologies, our '*tool chest*', places Exopharm in a leadership position in exosome product development, manufacture and research. Now, for the first time, naive (*un-engineered*) exosomes from Exopharm's own master cell bank (MCB) have been manufactured using LEAP at a scale and quality suitable to confirm their safety profile in a repeat-dose immunogenicity and toxicology study. This study indicates that the chassis for our future engineered exosome products is safe in the test animals."

With Exopharm's exosome products intended to be used in human trials, this study represents a further positive step to show that the exosomes could be safe for use and that the manufacturing process produces a non-immunogenic and non-toxic product. Potential partners also want to see these data points.

This study adds to existing evidence that exosomes could be used as a safe and well-tolerated drug-delivery technology for Genetic Medicines and other exosome-based medicines.

Ahead of this safety validation process being completed, Exopharm already has in place a collection of exosome-related technologies (the '*tool chest*'), which comprise the key components necessary for the development and manufacture of commercial-scale, exosome-based medicines.

For Exopharm's future products, the manufacture of clinical-grade engineered exosomes begins with a MCB of cells that is compliant with strict current Good Manufacturing Practice (cGMP) quality requirements. A GMP cell line and the exosomes derived from it were selected to provide the chassis for future engineered exosome production.

By the Managing Director – this release has been authorised by the Managing Director.

COMPANY AND MEDIA ENQUIRIES:

Join our mailing list to receive updates:
http://exo.ph/ExoMails
www.exopharm.com
P: +61 (0)3 9111 0026

Ian Dixon
Managing Director
Tel: +61 418 561 907
ian.dixon@exopharm.com

ABOUT EXOPHARM

Exopharm (ASX:EX1) is a leader in advancing Genetic Medicines and other exosome-based medicines using exosomes or extracellular vesicles (EVs) as a chassis for improved and non-viral drug-delivery.
Exopharm (ASX:EX1) 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. Exosomes can be used to deliver small molecule drugs, mRNA, DNA and other types of APIs.
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.
Exosome-based medicines could improve the treatment of many chronic or inherited medical conditions.
Exopharm is making its proprietary technologies available to pharmaceutical and biotechnology companies that want to harness exosome-delivery for their own products.
In addition, Exopharm is using its technology platform to enable its own product development programs - 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.