ASX Announcement

Melbourne, Australia, 27 October 2022

UPCOMING WEBINAR

- Webinar: Genetic Medicines and exosomes: Recent testing provides supporting validation

Genetic medicine and exosome-based drug-delivery company Exopharm Limited (ASX:EX1) releases notice of, and information to be covered in an upcoming webinar.

Title: Genetic Medicines and exosomes: Recent testing provides supporting validation
Time: 8:00 (Melbourne, Victoria, Australia), 28 October 2022
Registration: https://exo.ph/Genetic-Medicines-and-exosomes

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.

V1.3

exopharm

Webinar:

Genetic Medicines and exosomes:
Recent testing provides supporting validation

Exo-webinar series : part 3

Thu 27 October 2022 – 17:00 (Boston) / 14:00 (San Francisco)

Fri 28 October 2022 – 08:00 (Melbourne)

Registration: https://exo.ph/Genetic-Medicines-and-exosomes

Legal Disclaimer

Purpose of presentation: This presentation (including this document, any related video or oral presentation, any question and answer session and any written or oral material discussed or distributed in relation to this presentation) has been prepared by Exopharm Limited (ACN 163 765 991) (Exopharm or Company).

Not an offer or solicitation: This presentation is not investment advice nor an offer to subscribe for securities or otherwise invest in Exopharm, and it should not be relied upon to make any investment decision.

Nature of presentation: This presentation is not a prospectus, product disclosure statement or other investment disclosure document, and the level of disclosure in this presentation is less than such disclosure documents. This presentation does not purport to contain all of the information that a prospective investor may require to make an evaluation of Exopharm or its business activities and nothing in this presentation is, or is intended to be, a recommendation to invest in Exopharm. Exopharm does not purport to give financial or investment advice. No account has been taken of the objectives, financial situation or needs of any recipient of this presentation.

Forward-looking statements: This presentation may contain forward-looking statements which may be predictive in nature and incorporate an element of uncertainty or risk, such as 'intends', 'may', 'could', 'believes', 'estimates', 'targets' or 'expects'. These statements are based on an evaluation of current economic and operating conditions, as well as assumptions regarding future events. These events are, as at the date of this presentation, expected to take place, but there cannot be any guarantee that such will occur as anticipated, or at all, given that many of the events are outside Exopharm's control. The stated events may differ materially from results ultimately achieved. Accordingly, neither Exopharm nor any of its directors, employees, contractors or advisors make any warranty or assurance that the results, performance or achievements expressed or implied by the forward-looking statements contained in this presentation will actually occur. Further, other than as required by law, Exopharm may not update or revise any forward-looking statement if events subsequently occur or information subsequently becomes available that affects the original forward-looking statement.

Disclaimer: Neither Exopharm nor its officers, employees, contractors or advisors give any warranty or make any representation (express or implied) as to the accuracy, reliability, relevance or completeness of the material contained in this presentation. Nothing contained in this presentation is, or may be relied upon as a promise, representation or warranty, whether as to the past or the future. Except for statutory liability which cannot be excluded, Exopharm, its officers, employees, contractors and advisors expressly disclaim any responsibility for the accuracy or completeness of the material contained in this presentation and exclude all liability whatsoever (including in negligence) for any loss or damage which may be suffered by any person as a consequence of any information in this presentation or any error or omission therefrom.

Professional advice: Recipients of this presentation should consider seeking appropriate professional financial, taxation and legal advice in reviewing the presentation and all other information with respect to Exopharm and evaluating its business, financial performance and operations.

Recap: Exosomes for Genetic Medicines (GM)

Exosomes are an emerging GM **therapeutic product delivery chassis**

1. **GM therapeutic products** require specialised delivery uniquely suited for **Exosomes**

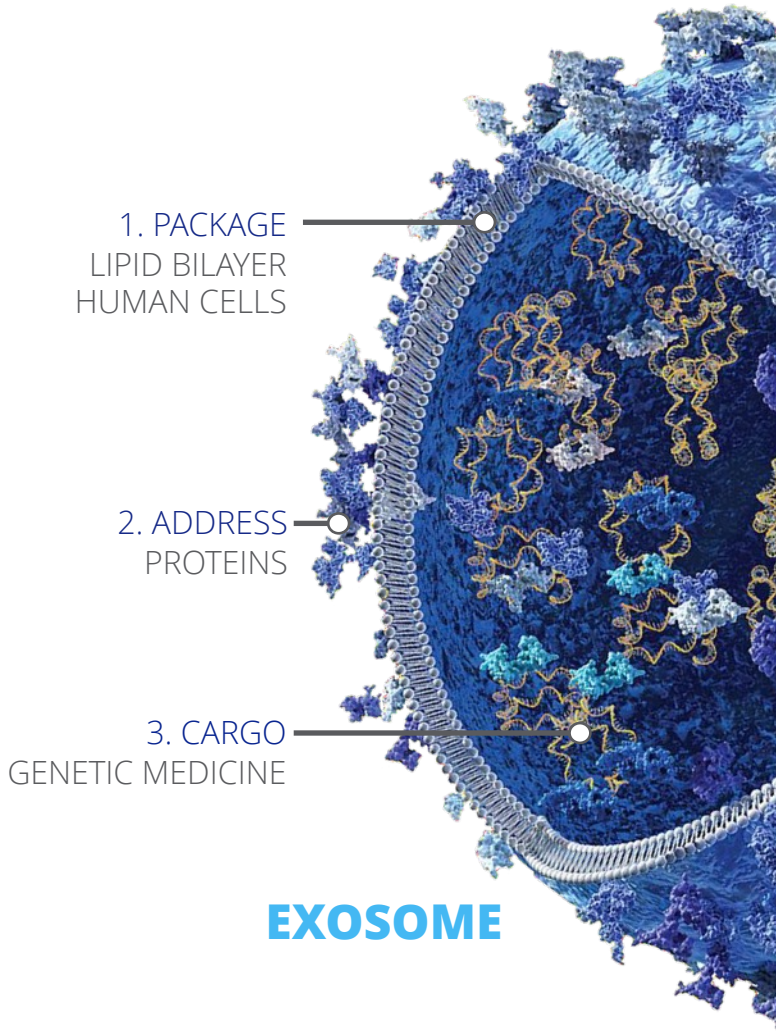
Types of GM products

Vaccine products

Therapeutic products

LNPs are suited to deliver vaccine products

Exosomes are suited to deliver therapeutic products



Recap: Exosomes for GMs

To be effective GM **therapeutic products** have **specific delivery requirements**

3. **GM therapeutic products** require **immune-silent** delivery, **re-dosing** flexibility, and may require **biological barrier crossing** capability

Immune profile:
Given their natural origin, exosomes are considered immune silent

Re-dosing flexibility:
Immune-silence and absence of accumulation means exosomes enable repeat/multiple dosing

Cross biological barriers:
Exosomes exist throughout the entire body in nature, so exosomes carrying a GM cargo could cross tissue barriers such as blood-brain barrier

Elsharkasy et al. Adv Drug Deliv Rev, 2020 Murphy et al. Nano Lett, 2021 Cheng et al. Nat Rev Drug Discov, 2022

Highlighted difference between exosomes and LNPs for delivery

Membrane fusion is the start – what happens inside a target cell matters most

4. **Exosomes** are efficiently processed inside a cell – optimising the **GM therapeutic product delivery efficiency**

   - **Exosomes are taken up by cells through 3 processes**, releasing the GM cargo into the cytoplasm
   - Inherently natural, exosomes are efficiently processed inside the target cell, leading to **higher delivery efficiency over synthetic LNPs**
   - **LNPs** and their synthetic components exhibit **immunogenicity** and **toxicity,** can trigger immune activation and have **impaired GM cargo delivery**

LNP = Lipid Nanoparticle, **GM** = Genetic Medicine (e.g., RNA, DNA, AAV, CRISPR technologies)

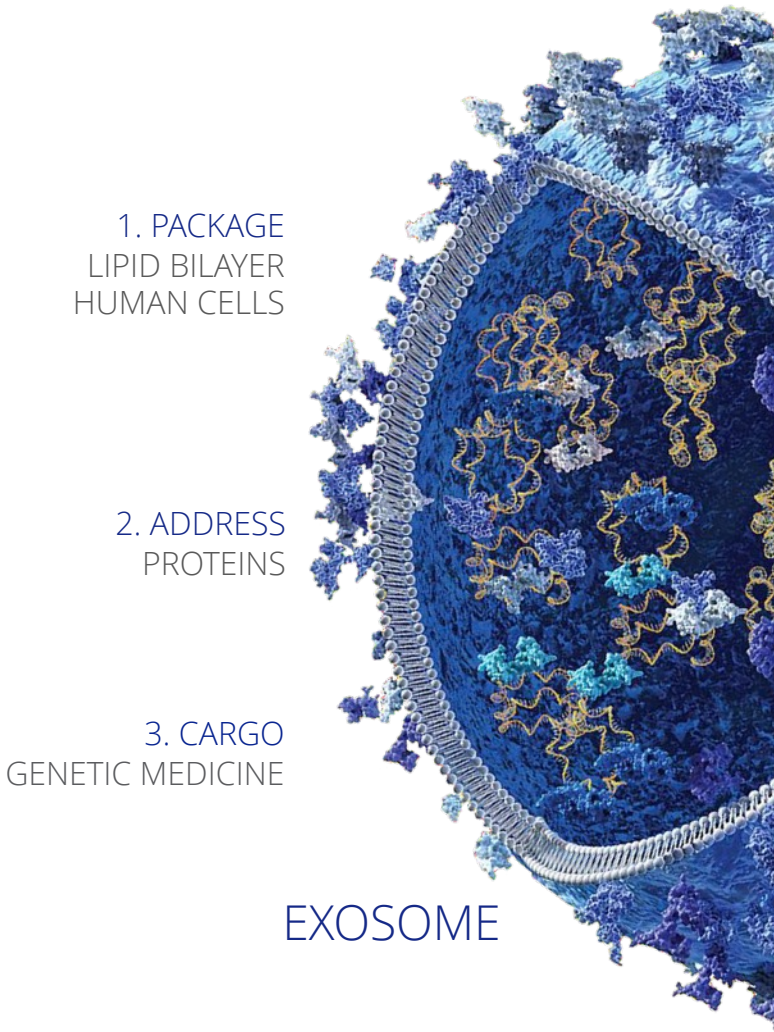
Pedrioli & Paganetti ***Front Cell Dev Biol***, 2021 Patel et al. ***Nat Commun***, 2020 Maugeri et al. ***Nat Commun***, 2019 Gilleron et al. Nat Biotechnol, 2013
Mulcahy et al. ***J Extracell Vesicles***, 2014 Heusermann et al. The Journal of Cell Biology, 2016 Rennick et al. Nat Nanotechnol, 2021 Joshi et al. ***ACS Nano***, 2020

Exosomes and safety as a drug-delivery chassis

Exosomes represent an ideal GM **therapeutic product delivery chassis**

Today's topics and themes:

1. Why the characteristics of the drug-delivery chassis are **vital for GM success**:
    - Safety in the patient is critical
    - Safety is made up of:
        - **toxicity**; and
        - **immunogenicity**
2. The safety of **Exopharm's exosomes have now been demonstrated**: successful *in vivo* study outcomes reported



The importance of toxicity

Toxicity of the GM carrier is critical for product success and safety

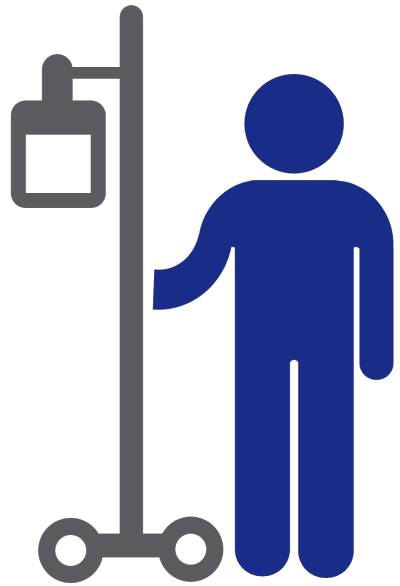
Most new drugs fail due to poor safety, and toxicity is the main problem

Toxicity means that the drug makes the patient sick or the patient dies

In GMs, toxicity can come from:

- the carrier (e.g. LNP, AAV); and
- the cargo (e.g. mRNA)

In GMs the toxicity is sometimes associated with the carrier



The lipids and fats from LNPs can accumulate in cells and become toxic

The empty capsids of AAVs have been shown to be toxic and deadly

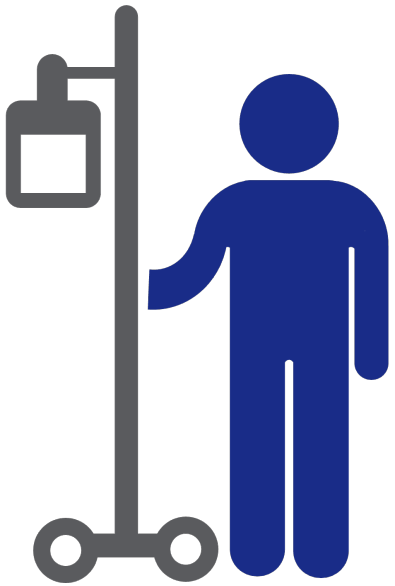
Exosomes enable non-toxic and safe GM delivery

The importance of immunogenicity

Inherently natural, exosomes are ideal for GM **therapeutic product delivery**

Delivering **GM therapeutic products** multiple times whilst avoiding an adverse immune response is paramount:

- Immunogenicity of a material is a measure of the extent that the body's immune system 'sees' it as 'danger' or 'foreign'
- **Immunogenicity of the carrier will** accelerate its clearance by the immune system
- Multiple doses of high immunogenicity material will lead rapid clearance and failure to deliver the GM *
- Immunogenicity can trigger **allergic reactions** or **severe adverse events**



Exosomes enable non-immunogenic and safe GM delivery

*Ability of the immune system to detect the GM and immediately mount an "attack" posture against the foreign object

Exopharm's immunogenicity and toxicology questions

Preclinical study to test if HEK293 **exosomes** are safe – preliminary results

- Preclinical study to demonstrate exosomes are non-immunogenic, non-toxic, and safe

- HEK293 exosomes are:
  - Produced by highly-scalable GMP HEK293 cells
  - Collected by our proprietary cell culture system: ***Hexocollect***
  - Purified using our proprietary technology: LEAP

GMP = good manufacturing practice; HEK293 = human embryonic kidney cells
Preliminary data, published on 28.09.2022 ASX Announcement Titled "Study results indicate exosomes safe for clinical pursuit"

in vivo safety of Exopharm's exosomes

Study scope and design

Objective

Understand the immunogenicity and toxicology of repeat dosing of HEK293-derived exosomes in healthy adult mice

Exopharm proprietary suite of technologies that underpin the study

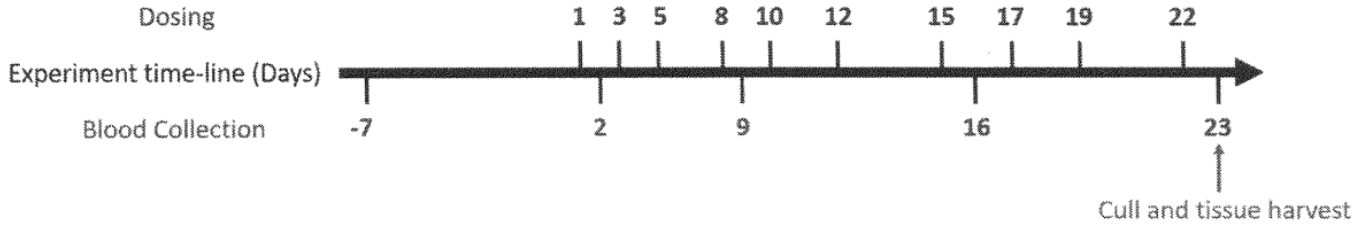
Ethics approval: University of Queensland Animal Ethics Committee (AE000938)
Preliminary data, published on 28.09.2022 ASX Announcement Titled "Study results indicate exosomes safe for clinical pursuit"

in vivo safety of Exopharm's exosomes

Study protocol and measures

Key details of the study

- Dosing over 23 days and a total of 10 doses per mouse



- At the end of treatment, mice were assessed for the following: body and organ mass, gross necropsy, hematology, blood chemistry, histology, spleen cell immunophenotyping and cytokine stimulation

Ethics approval: University of Queensland Animal Ethics Committee (AE000938)
Preliminary data, published on 28.09.2022 ASX Announcement Titled "Study results indicate exosomes safe for clinical pursuit"

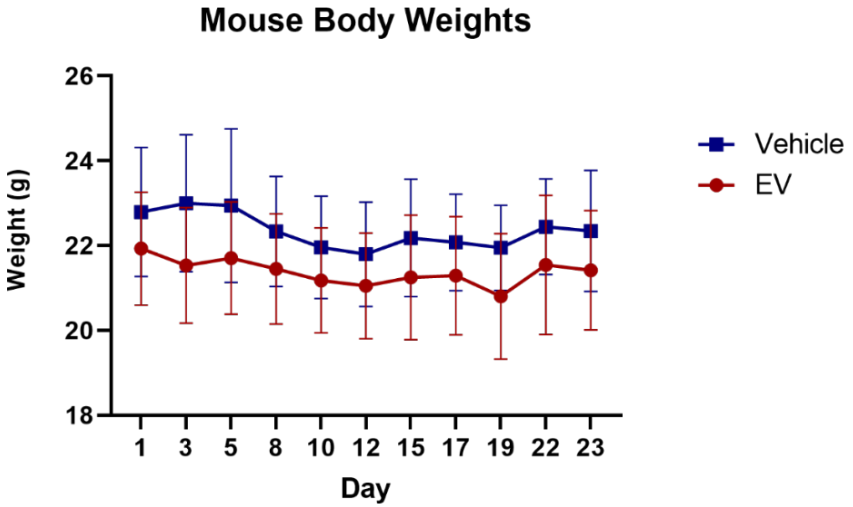
in vivo safety testing of Exopharm's exosomes

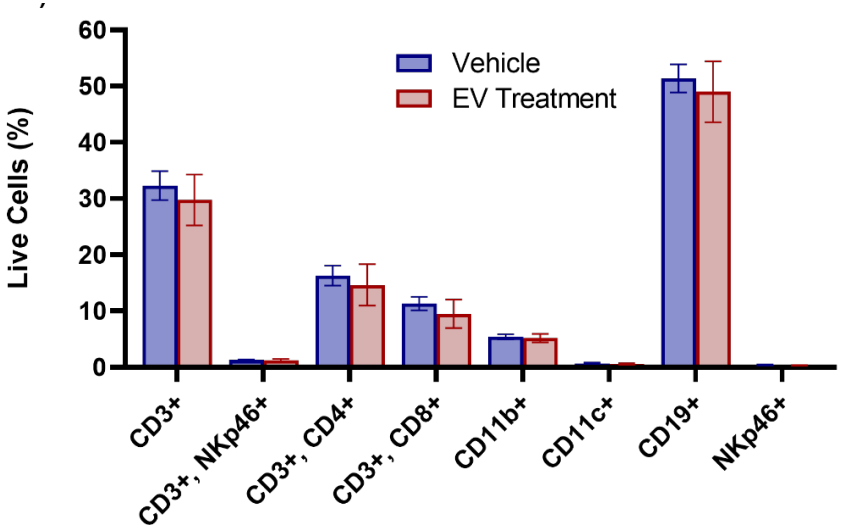
Preliminary study outcomes

After 23 days of dosing, the study observed:

- No significant changes in body weight or behaviour
- No gross lesions or significant changes in organ weight
- Little to no effect on the measured haematology parameters, including, white blood cells, red blood cells, platelets, monocytes, lymphocytes
- No abnormalities in immune cell populations in the spleen

These preliminary data indicate the absence of an immune response and no detectable toxicity levels.





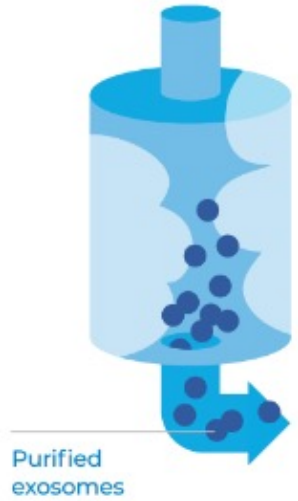
Vehicle: Control PBS; **EV treatment:** HEK293 exosomes

Ethics approval: University of Queensland Animal Ethics Committee (AE000938)
Preliminary data, published on 28.09.2022 ASX Announcement Titled "Study results indicate exosomes safe for clinical pursuit"

in vivo immunogenicity of Exopharm's exosomes

Key takeaways from the preliminary study results

- Exosomes demonstrated to be non-immunogenic and safe in an animal model
- Exopharm's proprietary exosome manufacturing process is suitable for clinical development, including validation of:
  - HEK293 cells compliant with strict current GMP quality requirements as an source of human exosomes
  - Advanced cell culture and exosome collection Hexocollect
  - Exosome purification technology LEAP
- Study outcome is an important step towards the successful development of future exosome products



Ethics approval: University of Queensland Animal Ethics Committee (AE000938)
Preliminary data, published on 28.09.2022 ASX Announcement Titled "Study results indicate exosomes safe for clinical pursuit"

Webinar key takeaways

- **Ensuring safety** early is an essential requirement for **GM therapeutic product** development success
- Preliminary study results support the use of Exopharm's exosomes and manufacturing technologies to make and develop exosome-encapsulated GM therapeutic products:
- Exopharm manufactured **HEK293 exosomes were successfully applied in multiple doses** and
- were **not immunogenic or toxic**

Preliminary data, published on 28.09.2022 ASX Announcement Titled "Study results indicate exosomes safe for clinical pursuit"

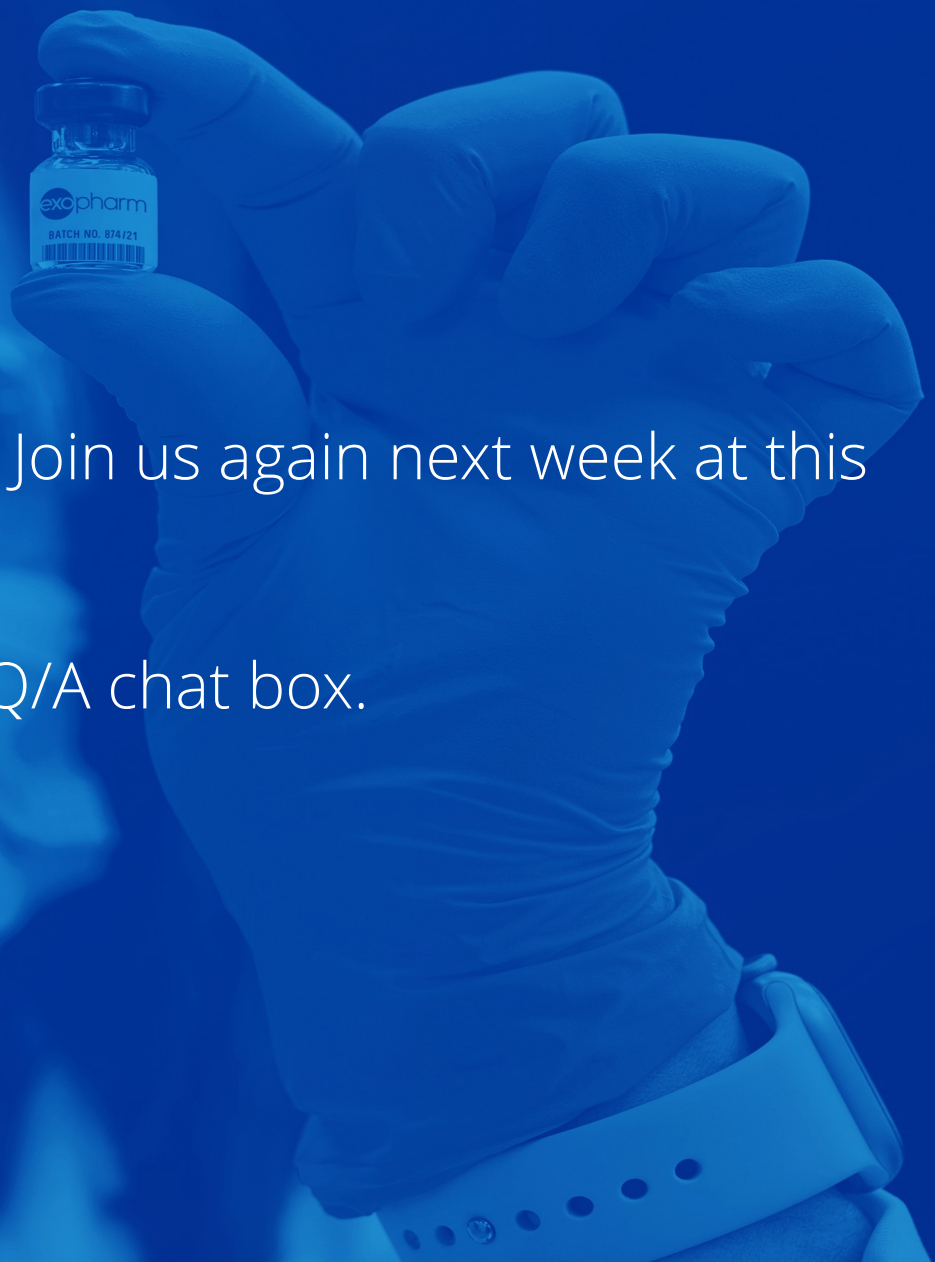
Exopharm is making things happen in medicine

Genetic Medicines (GMs) that are important

Exosome drug delivery to make new GMs work

based on Exosomes: Nature’s drug delivery chassis enabled by Exopharm’s manufacturing technologies

exopharm



Thank you for your participation. Join us again next week at this same time.

Please add your questions in the Q/A chat box.

webinar@exopharm.com

@Exopharm

Exopharm Ltd