

### **ASX ANNOUNCEMENT**

## INVESTOR DECK – to be presented at the Stockhead V-Con on Biotechs

30 June 2021

**Melbourne, Australia:** Exosome medicine company Exopharm Limited (ASX:EX1) advises that it will be presenting the attached Investor Deck at today's Stockhead V-Con on Biotechs.

This presentation provides updates on the exosome technology and exosome medicines programs at Exopharm.

This announcement has been approved by the Board for release to the ASX.

### **Company and Media Enquiries:**

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#### **ABOUT EXOPHARM**

Exopharm (ASX:EX1) is a clinical stage biopharmaceutical company using exosomes (extracellular vesicles (EVs)) from cells to generate a new class of precision medicines and regenerative medicines.

Various Exopharm EV products harness the powerful natural ability of EVs to efficiently target cells and transfer selected materials into cells and across barriers.

Exopharm has two exclusive proprietary technologies that extend the utility of EVs into engineered EV medicines (EEVs): the LOAD technology improves loading of nucleic medicines into EVs, and the EVPS technology allows EVs to be directed towards selected cell types. Exopharm uses combinations of LOAD and EVPS to develop a pipeline of EEV products aimed at treating a wide scope of medical problems including neurological diseases, infectious diseases, cancer, and fibrosis.

Exopharm's LEAP technology solves the challenge of purifying EVs at large scale. With LEAP, Exopharm is also developing naïve (or natural) EVs (NEVs) from adult stem cells and platelets as regenerative medicine products. NEVs have the potential to deliver the regenerative benefits of cells without the challenges of administering cells to patients. NEV products target a broad range of medical problems including osteoarthritis, autoimmune conditions, acute injury and chronic injury.

### 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.





### IMPORTANT INFORMATION

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). This presentation is intended for sophisticated or professional investors (as those terms are defined in the Corporations Act 2001 (Cth)), and their professional investment advisors and has been prepared for the sole purpose of providing general high-level information on Exopharm and its operations.

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## Exopharm Ltd

### Overview

- Australian clinical-stage company at the forefront of developing transformative medicines based upon exosomes (extracellular vesicles, EVs)
- 40 staff based in Melbourne, Australia; 1 based in Europe
- Publicly traded on the ASX (ASX:EX1) (listed Dec 2018)
   157.1 million shares on issue, current market cap.
   ~AU\$100 million
- A platform technology company with application to many exosome medicines – using our exclusive LEAP, LOAD and EVPS technologies

### **Priorities**

- Leading the emerging exosome field through our exosome technologies and exosome medicines
- Making exosome technologies available to established biopharmaceutical companies to empower the processes underpinning exosome manufacture
- Delivering existing and emerging drug candidates through precision exosome medicines



# Exosomes: Nature's Solution to Delivery in the Body



Exosomes (also referred to as extracellular vesicles or EVs) are natural, multifunctional and stable nanoparticles that transfer cargo and messages between cells.

Natural exosomes can be produced from cells in a bioprocessing facility.

Outer membrane that forms the

**1. PACKAGE** exosome (same membrane as human

cells)

External proteins that improve

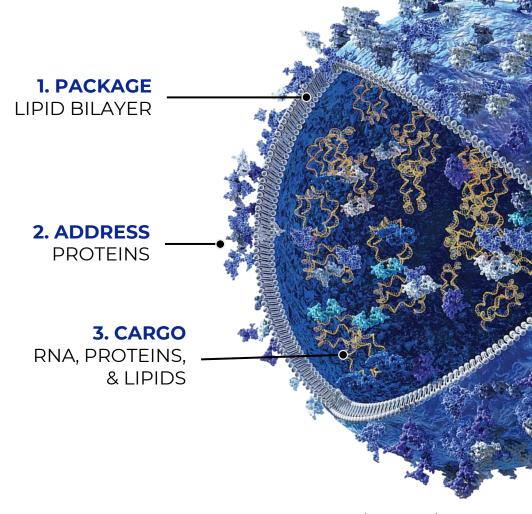
2. ADDRESS targeting of exosomes to specific cell

types

The materials delivered by exosomes,

**3. CARGO** including instructions (RNA) and building

materials (lipids, enzymes, proteins)



## Uncovered by Scientists in 2007, in 2021 Exosomes are Emerging as a New Frontier in Medicines Delivery



Exosomes represent a dynamically growing segment in life sciences with opportunities in research, diagnostics and therapeutic applications.

Dr Uwe Gottschalk, Chief Technology Officer for Lonza (2017) Targeted and nontargeted exosomes offer a highly differentiated platform with the potential to enhance tissue delivery for a variety of payloads like mRNA and proteins.

Dr Madhu Natarajan, Head of the Rare Diseases Drug Discovery Unit at Takeda (2020) Now is the time for researchers to usher in a new era of therapeutic possibilities using RNA-delivering, natural exosome vesicles.

Professor Phillip Askenase MD, Yale University School of Medicine (2020)

Exopharm is at the forefront of exosome medicines

# From Platform to Products,

Exopharm's EV Medicine Strategy

Establish EV Technology Platform

Design economical, scalable, and consistent processes for EV medicines from Day 1 Once established, leverage to drive EV medicines globally



**Build Clinical** Experience with Naïve EVs

Produce EVs from high-confidence sources (platelets, MSCs) for early human safety trials to credential manufacturing processes



Create Innovative Engineered EV Products

Customize EVs for cell-type specific delivery of precision medicines including nucleic acids and proteins

## Three Unique & Powerful Technologies Underpin our Partnering and Exosome Medicines



**Exclusivity** 



Scalable, economical GMP process for purifying exosomes

100% Exopharm



Tropism-conferring approach for engineering exosome surface proteins

100% Exopharm



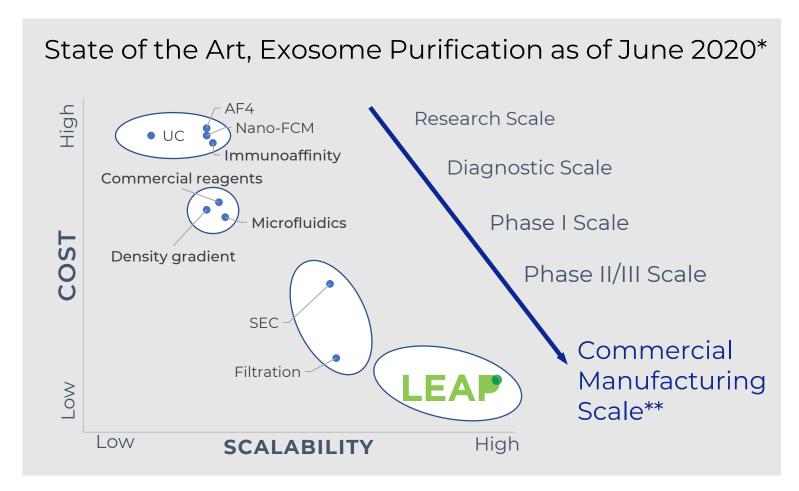
Activity enhancing method for delivering RNA by exosomes

100% Exopharm

EVPS US patent is granted, LOAD patent is progressing and LEAP patent is granted in Russia and progressing through national phase in USA under fast-track process.

# Exopharm Has the Only Known Technology for Commercial-scale Exosome Medicine Purification





Unlike all alternatives, LEAP technology:

- Uses industry-standard equipment/processes
- 2. Uses low-cost, reusable consumables
- 3. Scales economically beyond thousands of doses
- 4. Is proprietary (i.e. patent applied for)

LEAP unlocks the potential of Exosome Medicines

<sup>\*\*</sup> LEAP assessment from Exopharm, based on industrial use to date; LEAP Patents processing through National phases at present.

<sup>\*</sup> Adapted from <a href="https://doi.org/10.1016/j.tibtech.2020.05.012">https://doi.org/10.1016/j.tibtech.2020.05.012</a>

## SARS-CoV-2 RNA Vaccines Use "Artificial Exosomes"

Pfizer and Moderna SARS-2 vaccines package RNA into artificial synthetic lipid nanoparticles (LNPs)

However, LNPs have major limitations for drug delivery:

- Toxicity
- Anti-LNP immune response
- Inefficient cellular delivery

Naturally occurring exosomes from human cells have evolved an optimal composition over billions of years and have none of these limitations.





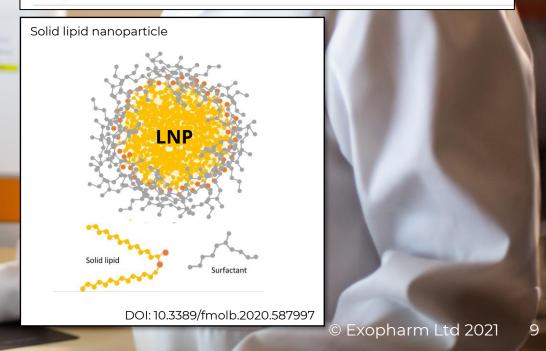
## nature

IEWS FEATURE · 12 JANUARY

## How COVID unlocked the power of RNA vaccines

The technology could revolutionize efforts to immunize against HIV, malaria, influenza and more.

Elie Dolgir





## LEAP Exosomes Overcome Significant Issues Associated with LNP Delivery

	Lipid Nanoparticles	Exosomes
Targeting	Yes	Yes
Stability	Yes	Yes
Efficient Uptake	No	Yes
Non-toxic	No	Yes
Frequent dosing	No	Yes
Scalability without LEAP (Manufacture/ Purification)	Yes	No
Scalability with Exopharm's LEAP Technology		YES



### **EVPS Construct**

**Cargo**: Cytoplasmic domain for reporter proteins (or anti-viral) carried as cargo

**VSVg**: Transmembrane domain passes through cell and exosome bilipid layers

**CTD**: Cell-targeting domain, a protein used by to enter cells (such as a viral coat protein, nanobody, cell-penetrating peptide, etc)

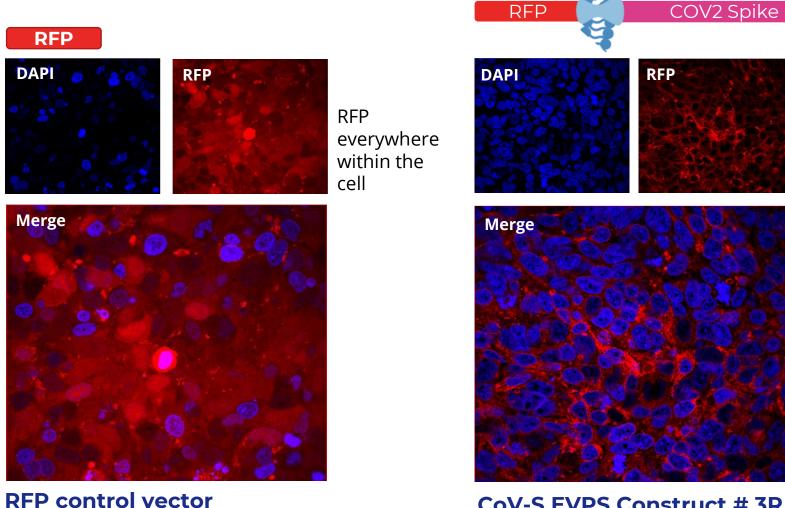
CTD Cell-targeting domain Cytoplasmic domain

Exosome from EVPS modified producer cell

Note: VSVg = vesicular stomatitis virus glycoprotein

## Confocal Imaging of Stable Spike-RFP Stable Cell line







'Membrane-

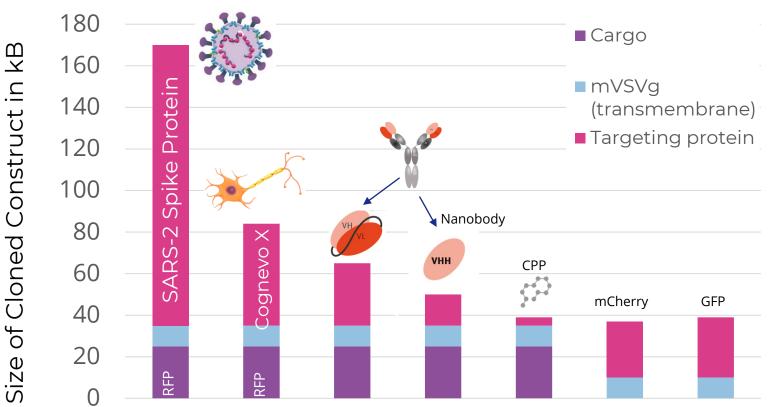
localized'

expression

**RFP** 

# EVPS Technology Proven with Large Targeting Moieties





Using EVPS construct, very large proteins can expressed by stable producer cell lines.

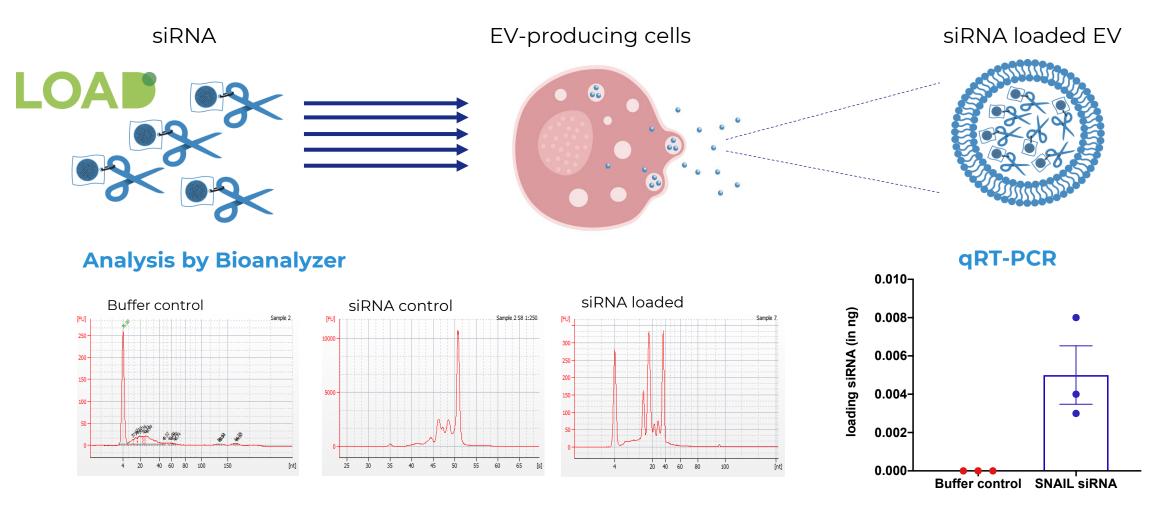
Technology can be applied to wide range of targeting proteins and/or large protein cargoes







## LOAD Creates High Copy-number EVs



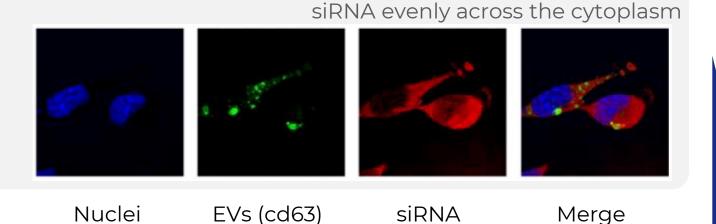
Depending on the conditions, siRNA copies per EV typically are between 500 – 1000



## LOAD Localizes RNA into EVs

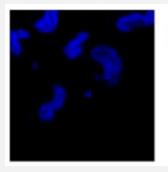
## Standard approach

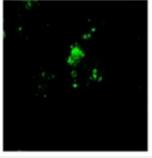
Producer cells electroporated with siRNA

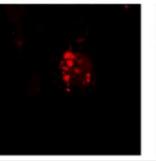


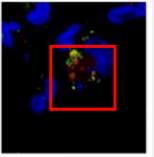
LOAD

Producer cells electroporated with LOAD powered siRNA









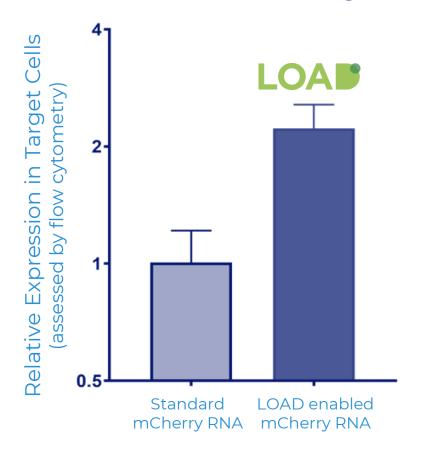
siRNA is localized within EVs; enrichment factor of 10 – 100x LOAD technology enriches RNAi near EV biogenesis sites

Therapeutic effect/cost of delivery improve substantially using LOAD technology



## LOAD Enhances Cargo Effect

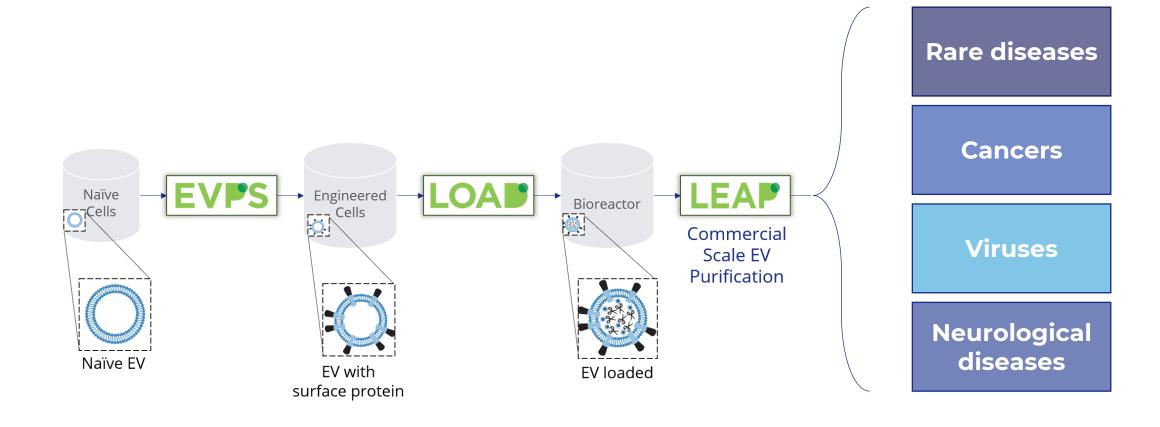
mCherry protein expression in cells treated with EVs containing mCherry RNA



RNA	Status	2021 Plans
siRNA (~20 bases)		Sars-COV2 siRNA
mCherry (~700 bases)		
CFTR-GFP (~6.5k bases)		Currently in progress
•••		

## Together these Technologies Create a Precision Medicine Factory





## Right Place, Right Time, Right People







McKinsey & Company

















## Thank you

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