ASX Announcement

Melbourne, Australia, 07 October 2022

SHAREHOLDER UPDATE

- Updated investor presentation

Genetic medicine and exosome-based drug-delivery company Exopharm Limited (ASX:EX1) announces the release of an updated investor presentation.

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

EXOPHARM LIMITED ACN: 163 765 991 ASX:EX1
Address: Level 17, 31 Queen Street Melbourne 3000
Telephone: 03 9111 0026 Email: info@exopharm.com Web: www.exopharm.com

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.

Investor presentation

October 2022

Ian Dixon
Founder and CEO

No-deal presentation

exopharm

ASX: EX1

Delivering transformative medicines

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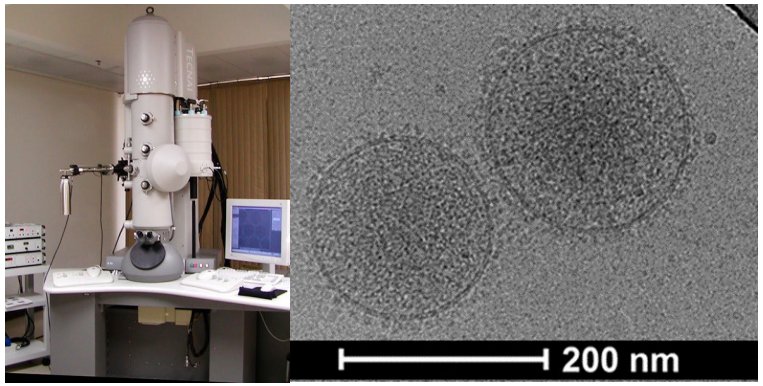
Exopharm (ASX:EX1)

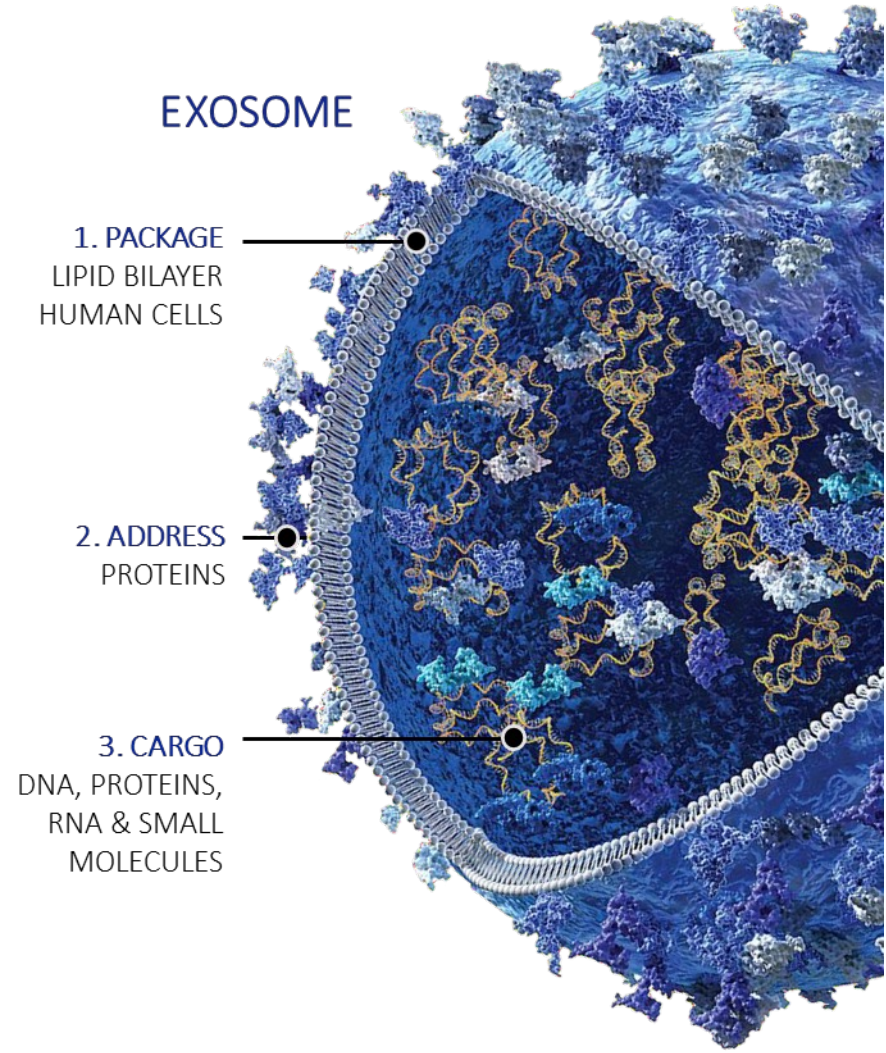
Enabling pharmaceutical companies to deliver drug candidates in novel ways

Exopharm (ASX:EX1) is a leader in the use of exosomes or extracellular vesicles (EVs) to enable improved drug-delivery in the body.

Exopharm is now developing a new class of transformative medicines that will use exosomes, ***Nature's drug-delivery vehicles***, to distribute drugs inside the body.

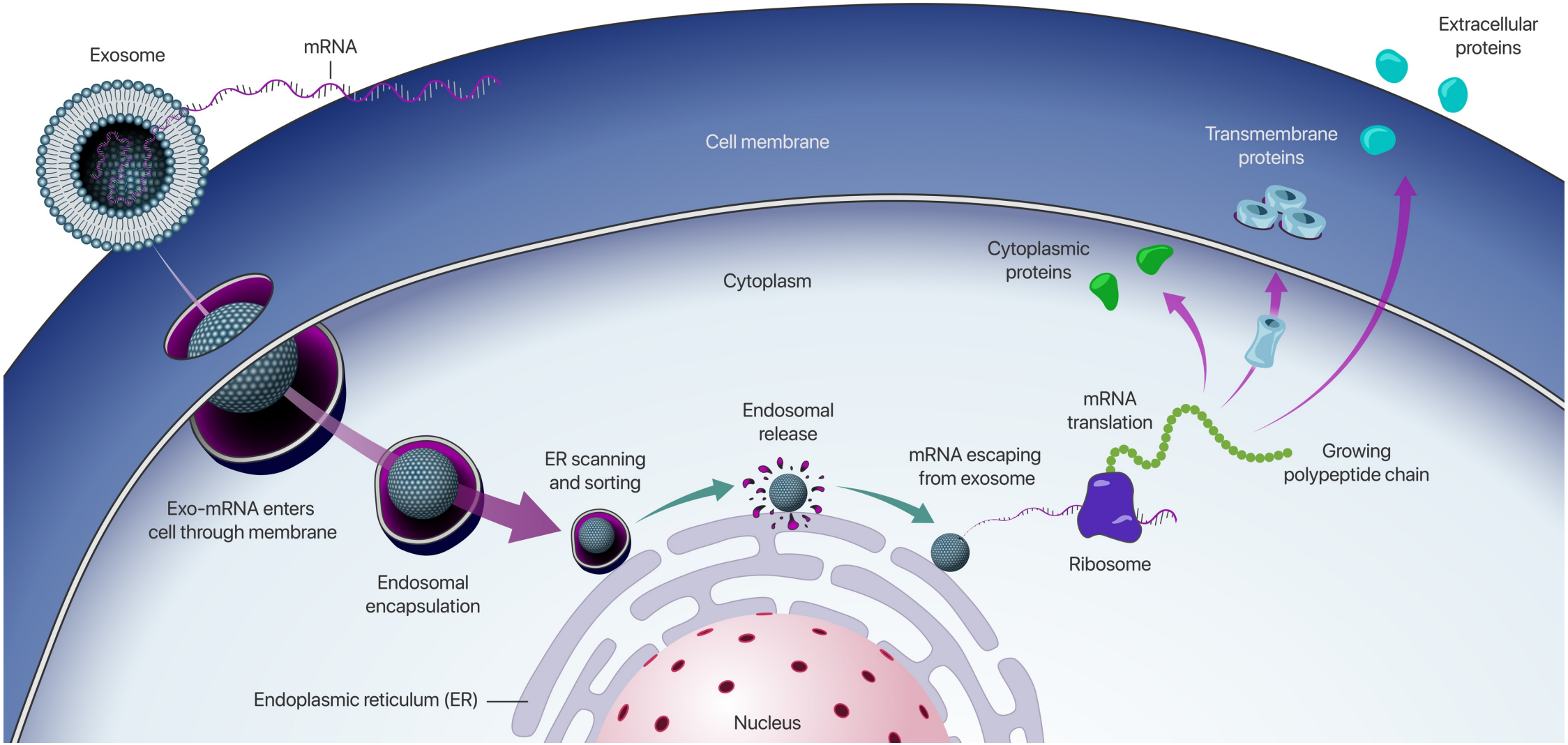


Exosomes as seen under a cryogenic electron microscope



DNA = deoxyribonucleic acid; **mRNA** = messenger ribonucleic acid (RNA)

EXO-RNA – exosomes as a nanoparticle RNA delivery chassis



mRNA = messenger ribonucleic acid (RNA)

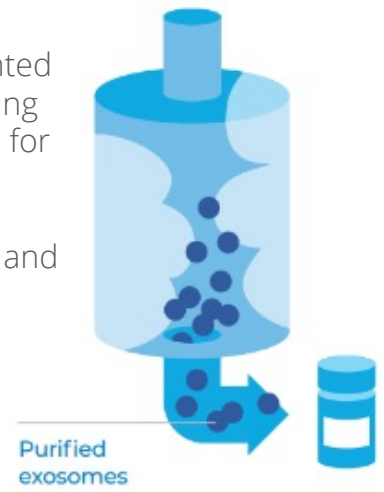
Exopharm's three core technologies

Technologies that enable entirely new exosome medicines

Purification technology

LEAP

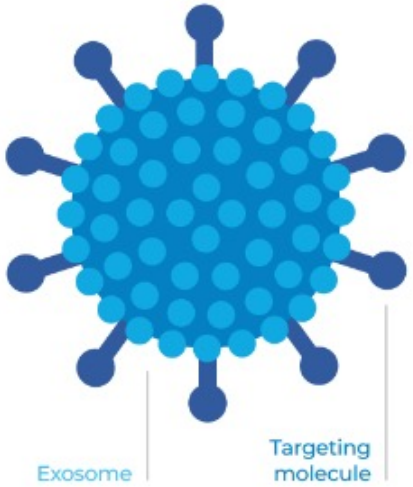
Exopharm's patented LEAP manufacturing technology allows for exosomes to be readily purified at commercial scale and low cost



Tissue tropism technology

EVPS

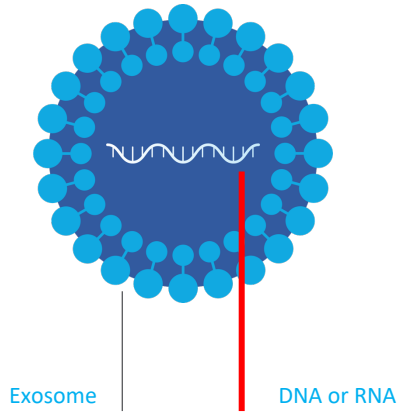
Exopharm's EVPS technology platform targets exosomes to specific tissues



API loading technology

LOAD

With Exopharm's LOAD technology exosomes can be loaded with a variety of genetic medicine active pharmaceutical ingredients (APIs), including DNA, mRNA, antisense oligonucleotides (ASOs), CRISPR gene editing constructs and more



CRISPR = Clustered Regularly Interspaced Short Palindromic Repeats

Corporate Overview

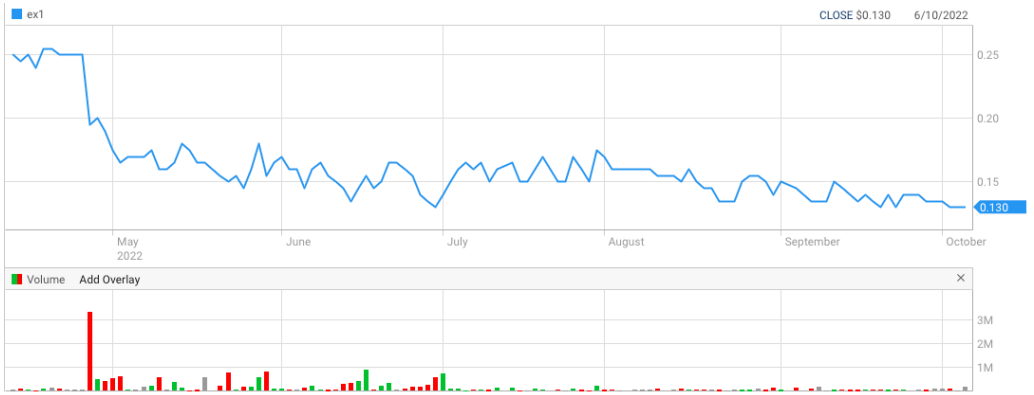
Capital structure

ASX Code	EX1
Share price[1]	$0.13
Ordinary shares outstanding[1,2]	157,211,533
Market cap[1,2]	$20.43M
Net cash (as at 30 June 2022)	$4.8m

Substantial shareholders

Shareholder	Shareholding % [2,4]
Dr Ian Dixon (Founder)[3]	17.97
Carl Charalambous and associated entities	10.81

Share trading



6 months up to closing on 06 Oct 2022

Other information

- Listed on ASX in December 2018 at 20 cents
- 4.5m options expiring 9th November 2025, 1.5m at $0.40, 1.5m at $0.60 and 1.5m @ $0.90
- Around $34m raised by the issue of shares
- The only pure-play exosome company listed on the ASX
- Exopharm has a 2018 Royalty Deed with Altnia Operations Pty Ltd (*Altnia*) which Exopharm (now LEAP Biotechnology Pty Ltd) [*a company owned by I Dixon FT*) under is obliged to pay Altnia a sales-based royalty of 3% of net sales from product made using the LEAP technology plus a 10% share of non-sales payments Exopharm receives from 3rd parties (e.g. milestone fees) – further detail disclosed in the 2018 Prospectus and released to ASX on 14th December 2018.

Notes:
[1] closing price as at 06 October 2022, [2] excluding 4.5m options expiring 9th November 2025, [3] through Family Trust, [4]as at 05 October 2022

People

Dr Ian Dixon
Founder, CEO & Main Shareholder

Ian is an experienced inventor (two US patents granted in 2021), serial bioentrepreneur (Cynata, Nyrada, EX1), technologist, biomedical engineering PhD (Monash University) and MBA. Ian's focus is on product innovation, technology development and building the team.

David Oxley
President - International

David heads up partnering and Business Development activities as well as being a senior member of the executive team. David brings deep commercial experience and an extensive network in the international pharmaceutical, biotech and life sciences sectors.

Dr Mike West
Chief Technology Officer

Mike holds a PhD in Chemistry and qualifications in patent law and management. Mike brings industry experience in drug development and worked at SmithKline Beecham Pharmaceuticals (now GSK) and other biotechnology companies.

Dr Gregor Lichtfuss
Co-founder and Head of Business Services Group

Gregor is focused on developing the business to enable further growth. Gregor is a leader in innovation with professional experience in applied science, R&D, tech transfer, investment, and entrepreneurship.

Board of Directors and Company Secretary

Jason Watson
Chair

David Franks
Company Secretary

Elizabeth McGregor & Dr Jennifer King
Non-executive Directors

Dr Ian Dixon
Managing Director

Other staff

47 people based in Melbourne Australia

Investment opportunity

Exopharm's proprietary exosome technologies

Global problem: Genetic disorders

There are more than 7,000 known but currently untreated genetic disorders
Many prevalent medical problems have genetic causes

Genetic Medicines (GMs) solution

Some new GMs need exosomes to solve the drug-delivery problem to make them work – ***like a letter needs an envelope***

Challenges

But using exosomes has been held back until now due to manufacturing challenges

Exopharm's solution

Exopharm's proprietary exosome technologies seek to overcome the manufacturing challenges

Exopharm is uniquely positioned as a technology leader & the pioneer in therapeutic exosomes

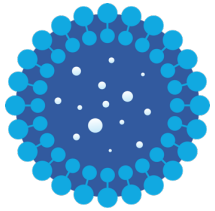
Industry opportunity

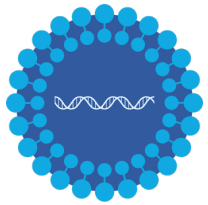
Genetic Medicines (GMs): significant uplift potential

The global addressable market for DNA-based gene therapy is expected to reach **$15B by 2030**[1]

> 400 million patients with > 7,000 rare diseases worldwide - less than 5% of which have an approved treatment[3]

The RNA-based therapeutics market alone is projected to see accelerated growth reaching a global addressable market in excess of **US$25B by 2030**[2]





**** Genetic Medicines include DNA, mRNA, siRNA, gene editing & transcription control, as either therapeutics or vaccines***

- Drug delivery and drug formulation will be minor components of these global markets
- The proportion of the demand for drug-delivery in GMs that exosomes will capture is as yet unknown
- The proportion of the demand for exosomes that Exopharm can capture is as yet unknown
- Other risks and uncertainties listed in slide #24

1. " Gene Therapy Market Size, Growth, Trends, Report 2021-2030" 2021 www.precedenceresearch.com/gene-therapy-market
2. "RNA based therapeutic market forecast 2021-2030" https://www.alliedmarketresearch.com/rna-based-therapeutics-market Dec 2021
3. Global Genes https://globalgenes.org/rare-disease-facts

Industry opportunity

Genetic Medicines (GMs) at the cusp of breakthrough

Present-day Genetic Medicines examples
mRNA in the vaccine encodes the virus antigen, loaded into LNPs (e.g. Pfizer's ***Comirnaty*** COVID-19 vaccine FDA registered **2020**)
DNA plasmid in the vaccine encodes the virus antigen (e.g. ZyCoV-D approved in India in **late 2021**)
AAV viral vector used to deliver DNA (e.g. ***Luxturna*** approved in **2017** and ***Zolgensma*** approved in **2019**
Gene silencing technologies (e.g. Vitravene, approved by the Food and Drug Administration (FDA) in **1998**)

Key points

- Few GMs have reached sales – despite the promise and needs
- GM is a very active area of development after the success of COVID-19 mRNA vaccines
- The largest pharmaceutical companies (and many biotechs) have adopted GM programs
- AAV GMs have progressed to recent approvals, however there are safety concerns flagged by the FDA
- ***mRNA vaccines*** are having an impact today but ***mRNA & DNA therapeutics*** are at an early-stage and have problems with drug-delivery
- There is a real sense of urgency and large investments are being made

API = active pharmaceutical ingredient ('exosome "cargo"', or payload); ; **AAV** = adeno-associated virus; **ASO** = antisense oligonucleotide **DNA** = deoxyribonucleic acid; **FDA** = Food and Drug Administration; **LNP** = lipid nanoparticle; **mRNA** = messenger ribonucleic acid (RNA)

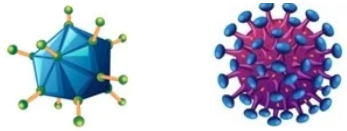
Industry opportunity

Genetic Medicines = delivery 'vehicles' + API 'cargo'

DNA and mRNA ***cannot*** be administered 'naked' into the body – they need to be packaged and delivered into cells – ***like a letter needs an envelope***.

Today, there are two main types of GMs ***by the type of delivery***:

- **viral vectors** – where a ***virus*** (e.g. AAV, lentivirus or herpes virus) is modified and then used to deliver a designer gene ***cargo*** into cells via 'infectious' pathways
- **non-viral vectors** – where a ***nanoparticle*** is engineered to deliver the API cargo

Viral vector GM components	
Encapsulation and delivery vehicles	The virus envelope is used as the delivery 'vehicle' for the GM 
Nucleic acid Active Pharmaceutical Ingredients (APIs)	DNA in DNA virus (e.g. AAV) RNA in retrovirus (e.g. lentivirus) that is converted into DNA in the patient's cells

Non-viral vector GM components	
Nanoparticle encapsulation and delivery vehicles	• **Exosomes** from human cells • **Synthetic** Lipid Nanoparticles (LNPs), Liposomes & Hybridosomes
Nucleic acid Active Pharmaceutical Ingredients (APIs)	• DNA; or • RNA

Image Credit: GraphicsRF.com / Shutterstock.com

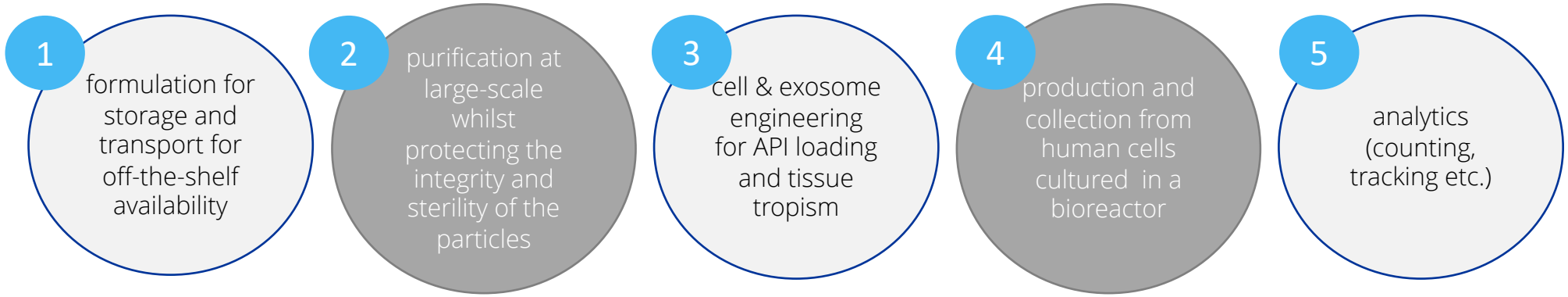
API = active pharmaceutical ingredient ('exosome "cargo"', or payload); ; **AAV** = adeno-associated virus; **DNA** = deoxyribonucleic acid; **mRNA** = messenger ribonucleic acid (RNA)

Technology opportunity

Exosome challenges & Exopharm's opportunity

Manufacturing challenges

The industrial-scale application of exosomes for drug-delivery has been held back by some key manufacturing challenges:



Exopharm has been solving these manufacturing problems

Technology opportunity

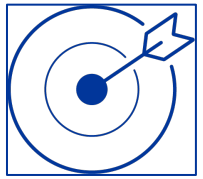
Exopharm's manufacturing technologies for exosome-medicines

Exopharm has been building an integrated suite of exosome-related manufacturing technologies since 2013

LEAP

To purify exosomes at commercial scale

US Patent granted in 2021



EVPS

To target exosomes to selected cells and tissues

Knowhow and future patent applications

LOAD

To load DNA and RNA into exosomes

Knowhow and future patent applications

Engineered Master Cell Banks

Supporting manufacture of engineered exosomes

Knowhow and core capability

Hexocollect

Efficient collection of exosomes from cells in culture

Knowhow and future patent applications

Formulation H

To allow transport and storage for off-the-shelf use

Patent applied for 16th June 2021

EXORIA reagent

Reagent to tag, count and track exosomes

Patent applied for 24th December 2020

Exosome manufacturing technologies are the key to unlocking the potential of exosome-based Genetic Medicines

Commercialisation strategy

Building financial value through a dual strategy

In-house product development

Exopharm developing its **own** exosome-medicine products

Objectives:

Early-stage partnering of some products

- Upfront fees, milestones and royalties on sales

Taking a small number of products forward

- Later partnering or other options

+

Technology and product partnerships/ licensing

Enabling **other** companies to adopt exosome products into their programs for any type of product

Objectives:

Partnering and licensing technology and knowhow

- Paid-for feasibility programs
- Upfront fees, milestones and royalties on sales

Mix of near-term and longer-term financial value

Strategy underpinned by a suite of proprietary technologies

In-house program and product selection

Maximise benefits of exosomes

Improved delivery of API

Multiple dosing

Cell targeted delivery

Rigorous survey over 12 months

Looked at over 400 possible products

Initial product focus

Localised and improved delivery of mRNA for additive gene therapy

Exosome loaded with mRNA API

API is Active Pharmaceutical Ingredient, ***mRNA*** is messenger RNA, ***RNA*** is Ribonucleic acid

2 Lead programs selected

- Localised (skin or lungs) delivery for early products
- Focus on mRNA as the API initially
- Potential of more than one product per program (e.g. skin and lungs)

Lead programs

1. Treating Cystic Fibrosis (CF) using exosome-based additive ***CFTR*** gene therapy and nebuliser delivery to lungs for monthly treatment

2. Treating elastin-deficiency in skin and lungs using exosome-based additive ***ELN*** gene therapy

Initial APIs
- ***mRNA as additive gene therapy***

Localised delivery
- ***Lungs***
- ***Skin***

CFTR = cystic fibrosis transmembrane conductance regulator

Development program outline

CY 2023

Proof of concept (POC) studies in animal models for validation

Clinical trials of up to 4 products following POC validation:

- Australian studies under CTN or CTA; or
- US studies under FDA IND regime

Final products will determine study designs, size of trials, trial costs and timing

IND = Investigational New Drug; ***CTN*** = Clinical Trial Notification; ***CTA*** = Clinical Trial Approval

Exopharm's partnering models

Enabling others to use exosomes and build near-term revenue for Exopharm

To enable others to use exosomes for their products and build near-term revenue for Exopharm

1

Feasibility Study Agreements – where Exopharm is paid to demonstrate the feasibility of a Partner's exosome medicine

Paid as a research contract with staged payments and defined outcomes

Upon conclusion the product has been derisked

Partner can negotiate a License to use Exopharm's technologies

2

Feasibility Study Agreements – where Exopharm is paid to demonstrate the feasibility of a Partner's exosome medicine

Paid as a research contract with staged payments and defined outcomes

Plus
Pre-agreed license terms if the Partner exercises their option to a full license

Partner can seek a full License to use Exopharm's technologies on the pre-agreed terms

3

Licensing LEAP technology – non-exclusive licenses and technology transfer

Upfront fees, milestone fees and royalties on sales

4

Licensing Exopharm's Product Candidates and exclusive license and technology licenses

Upfront fees, milestone fees and royalties on sales

1 2 3 4

Multiple approaches to build revenue streams, each underpinned by Exopharm's unique technologies

Partnership validation

Third party validation of Exopharm is building

Exopharm has active global and regional partnership discussions underway – supported by growing data that is underpinned by proprietary technology platforms and extensive exosomes know-how

Finnish Red Cross Blood Service

Signed June 2021

- One of Europe's leading Blood Banks
- LEAP technology evaluation of blood-cell-derived exosomes
- Exploring potential licensing structures

SHOWA DENKO

Signed September 2021

- Leading regional CDMO and regenerative medicine company
- On-going evaluation of exosome purification technologies, including LEAP platform

astellas

Signed January 2022

- Top 20 global pharma company
- Paid research agreement to assess exosomes from proprietary cells
- Validation work progressing well & revenue being received

CDMO = contract development and manufacturing organisation

Successful track record

Exopharm has a history of innovation and achievement

1. Granted US patent for 1st family of LEAP technology in December 2021
2. Industry collaborations:
   - Finnish Red Cross Blood Service in June 2021
   - Showa Denko in September 2021
   - Astellas Institute for Regenerative Medicine in January 2022
3. First commercial revenue in May 2022
4. Early in vitro data validating loading nucleic acids (RNA, siRNA and DNA) generated
5. Progress on other inventions and innovations:
   - EVPS
   - Exoria
   - Formulation H
   - Hexocollect
   - Master Cell Bank generated for engineered exosomes

Strategic growth initiatives

Exopharm is advancing its near- and longer-term growth objectives

Near-term objectives

1. Data from animal studies of immunogenicity, biodistribution and safety
2. Additional corporate transactions, generating upfront and milestone fees
3. Revenue growth from existing corporate agreements and workflow
4. Data on DNA and RNA loading & bioactivity tests
5. Lead product program: ***in vitro*** and ***in vivo*** results

Longer-term objectives

1. Bringing new GMs to patients
2. Additional paid research agreements & non-exclusive licensing agreements, including upfront, development, regulatory, and sales milestones, and escalating royalties on net sales
3. Further patents granted from the existing patent application pipeline & new patent applications pending
4. On-going internal research news flow from product candidate development
5. Master Cell Bank validation supporting GMP requirements

Exopharm Ltd (ASX:EX1)

Ian Dixon, PhD, MBA
Founder and CEO

www.exopharm.com

Supportive information

Risk management
General and specific influences

The operations and future prospects of Exopharm are potentially affected by a range of factors, some of which are outside of the control of the Company.
The field of biotechnology and pharmaceutic product development has inherent risks and uncertainty.

Such uncertainties include, but are not limited to:

General influences

- The influence of the present and future pandemics and associated restrictions or limitations;
- Settings in the broader economic and financial markets, including access to debt and/or equity markets, cost of capital and other factors;
- Geopolitical risks and potential broader affects, including the Ukraine/Russia conflict;
- Changes in the Australian government R&D Tax Incentive tax arrangement and the general availability of R&DTI cash rebates;
- Availability of international travel to facilitate business and technical meetings;
- Availability of research materials; and
- The cost and availability of skilled staff and expertise.

More specific influences

- The regulation and acceptance of Genetic Medicines and associated risks could increase the duration of development programs, delay approvals or increase the costs of development;
- Availability of onshore and offshore testing services and clinical trials, and their duration and costs;
- The suitability of exosomes derived from human cells as drug-delivery technology;
- The actual cost of exosome products compared with alternative technologies;
- Exopharm has a small management team and responsibilities are consolidated onto a small number of people – so there is key-person risk; and
- There are Intellectual Property risks, including that Exopharm may have unforeseen restrictions on its technologies.

Industry overview

Companies with nanoparticle drug-delivery options for GMs

Nanoparticle technologies	Commentary	Nanoparticle companies *
Exosomes	**Very few clinical trials so far due to manufacturing technology limitations** The most recent technology. No approved exosome products	**Exopharm ** *** (formed 2013) **Codiak Biosciences ** *** (formed 2015) Evox Therapeutics (formed 2016) AEGLE Therapeutics (formed 2013) EXOCOBIO (formed 2017) ReNeuron** (originally a cell therapy company)
Lipid Nano Particles (LNPs)	A combination of generic & proprietary technologies originating from 1990's	Acuitas Therapeutics (formed 2009)
Hybridosomes	A more complicated hybrid of exosomes and LNPs	Anjarium Biosciences (formed 2017)

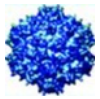
* Not an exhaustive list
** Listed on a public stock exchange
*** Have run early clinical trials with exosomes

Exosomes compared with AAV Viral Vectors

Simple comparison

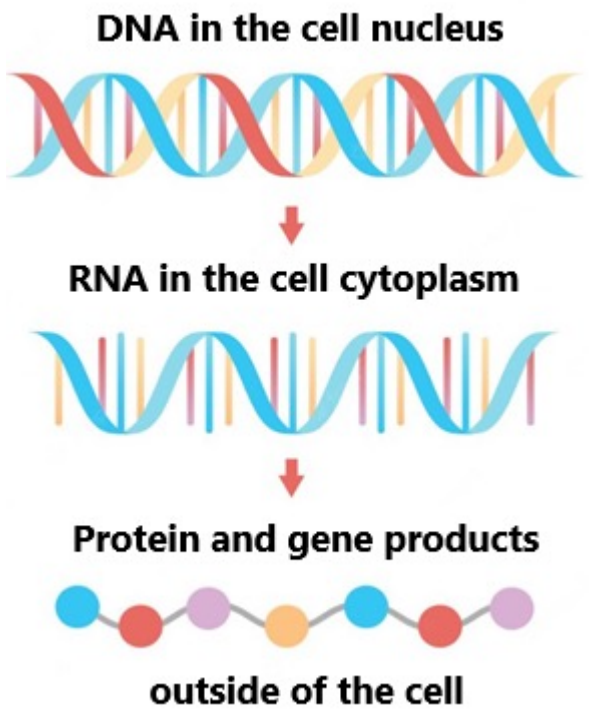
1. The use of viral vectors seeks to harness the 'infectivity' of viruses and transfer of DNA/RNA by viruses
2. But viruses have numerous problems as a GM drug-delivery vehicle:
    i. innate and adaptive immune responses incl. anti-viral inflammation
    ii. limited numbers of times they can be used in a person due to immune memory (after the first exposure)
    iii. toxicity of viral envelopes themselves e.g. AAV capsids
3. Exosomes are non-viral and of human origin

Comparison

	First clinical use	Non viral	Advantages	Disadvantages
Adeno associated virus AAV 	1990s	✗	• Recognised and established technology • Some tropism • Uses the natural 'infectivity' of virus	• Immunogenic • Toxicity and safety problems with FDA • Poor delivery efficiency (due to many empty capsids) • Limited to <4.7kbp gene size
Exosome 	2020s	✓	• Promising technology & Nature's delivery mechanism • Engineered tissue tropism can be built-in • Delivery of large genes • Good delivery efficiency • Can cross tissue barriers • Non-toxic	• Requires proprietary technology to manufacture • Needs more validation by clinical trials

Genetic Medicines (GMs)

The power of utilising Genetic Medicines



Type of GMs

Additive gene API
Gene editing
Base Pair Editing
(DNA)

siRNA, ASOs, RNAi

mRNA, Splice-switching oligonucleotides (SSOs)

Genetic Medicines may fix many medical problems rather than just treating the symptoms

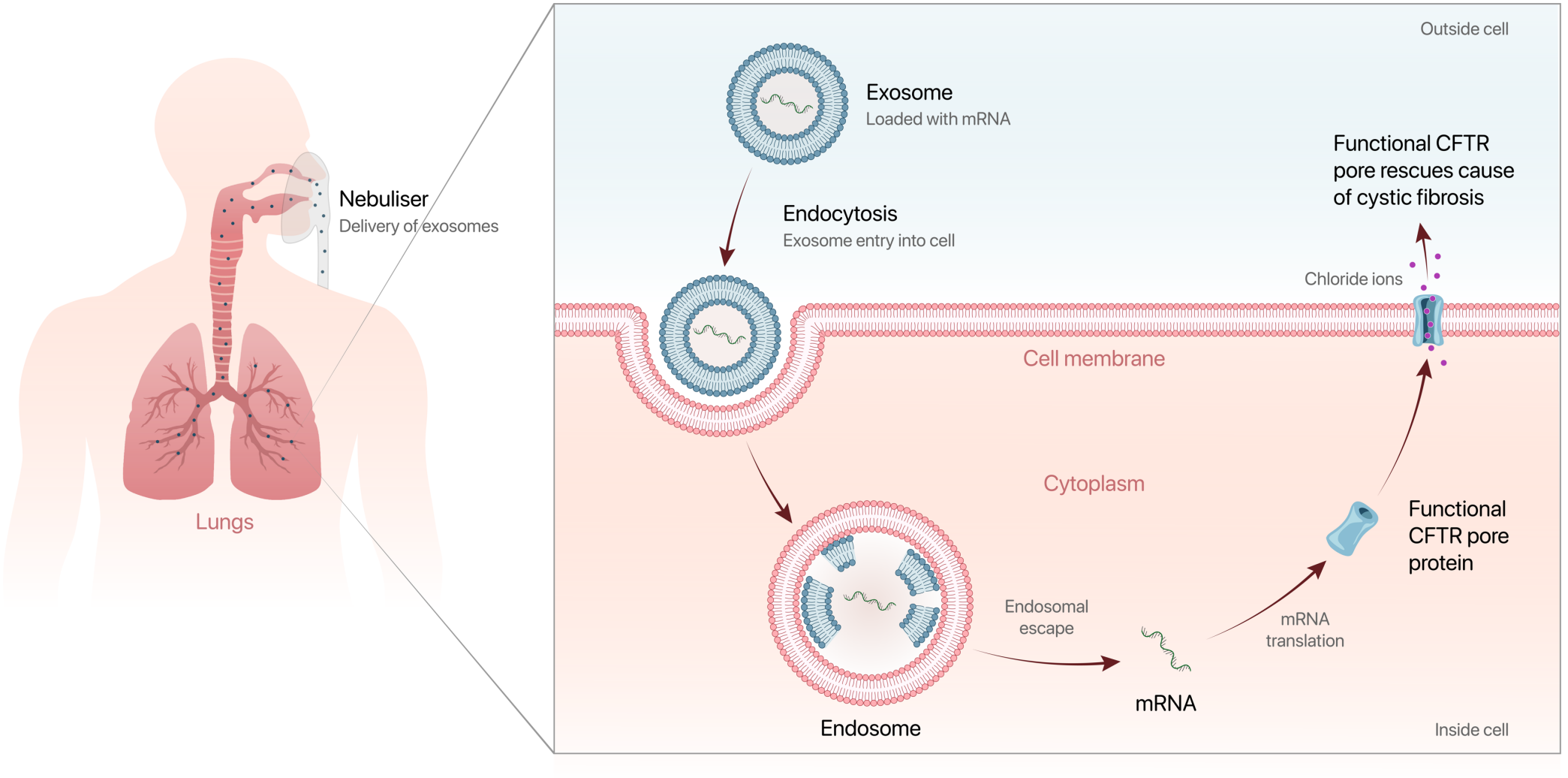
Inside every cell in our body there is biological machinery that normally works to produce the right protein (gene product) in the right cells, at the right time and in the right amount

Many diseases occur when this machinery is not working properly or the initial programming (DNA) is faulty

Genetic Medicines can now alter how this biological machinery works inside the patient's cells and to act at the root cause

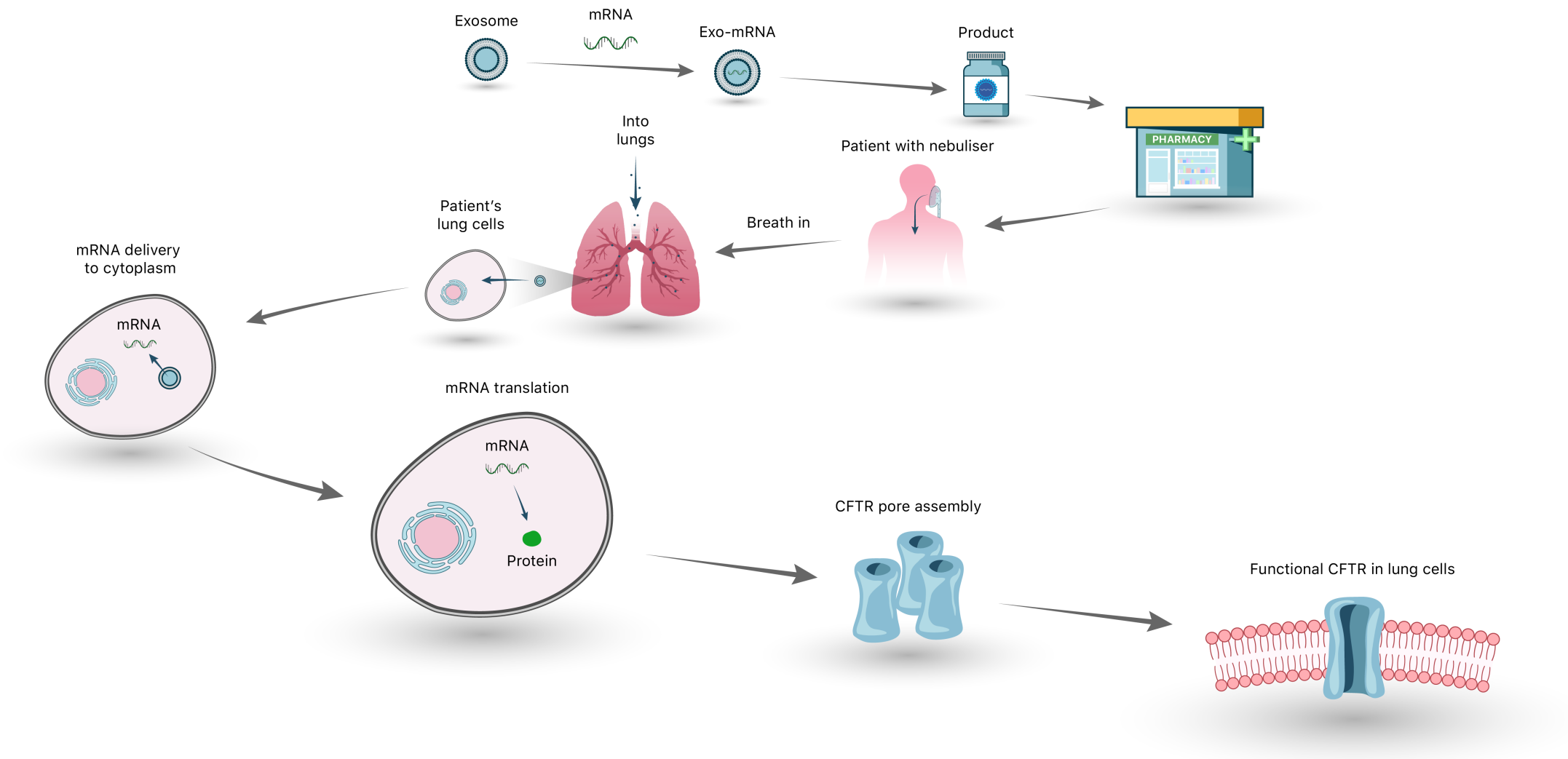
EXO-RNA for Cystic Fibrosis

An example exosome-based Genetic Medicine



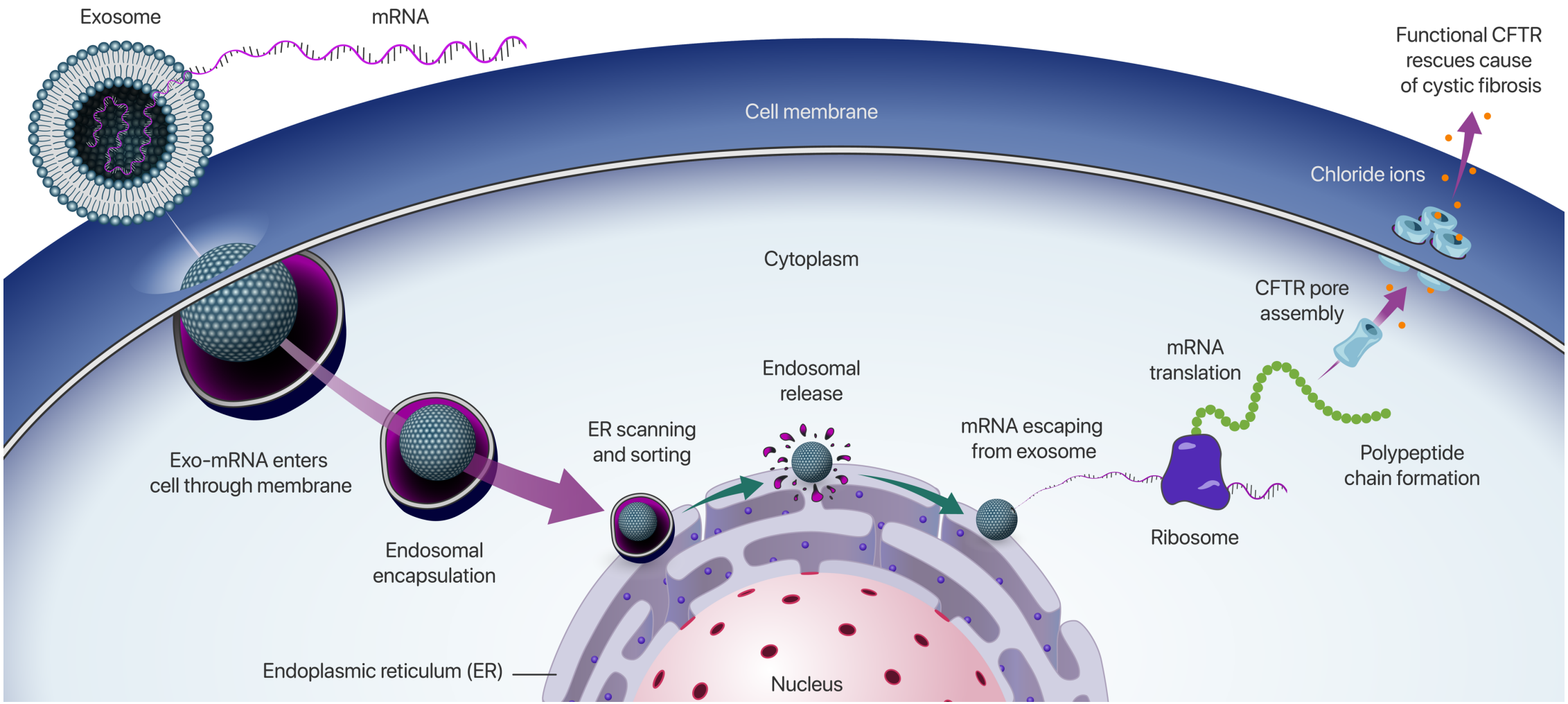
EXO-RNA for Cystic Fibrosis

An example exosome-based Genetic Medicine (II)



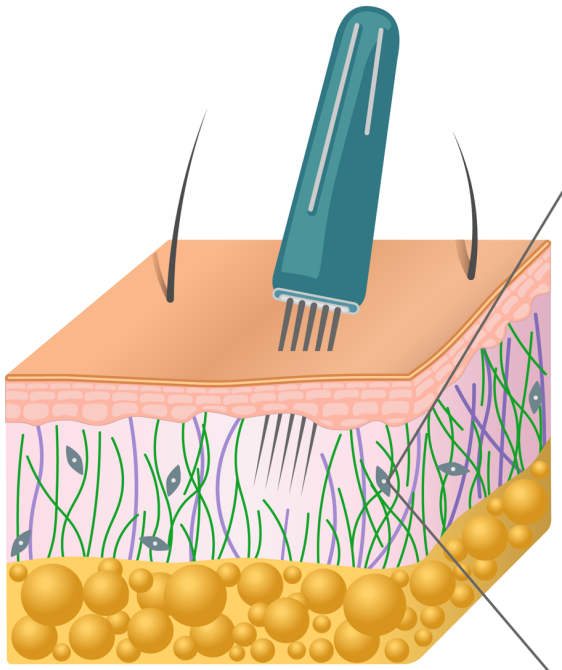
EXO-RNA for Cystic Fibrosis

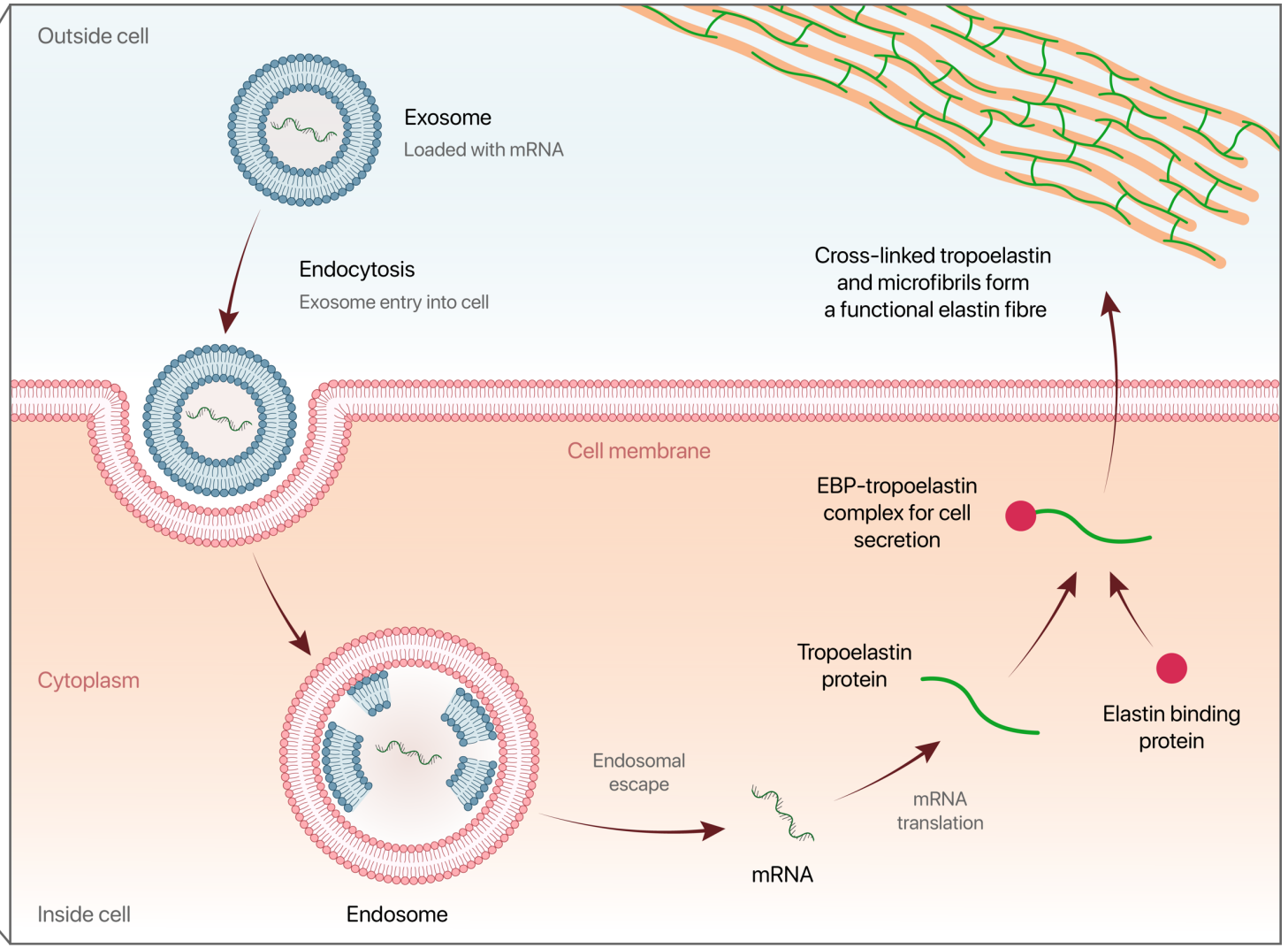
An example exosome-based Genetic Medicine (III)



EXO-RNA for Elastin deficiency

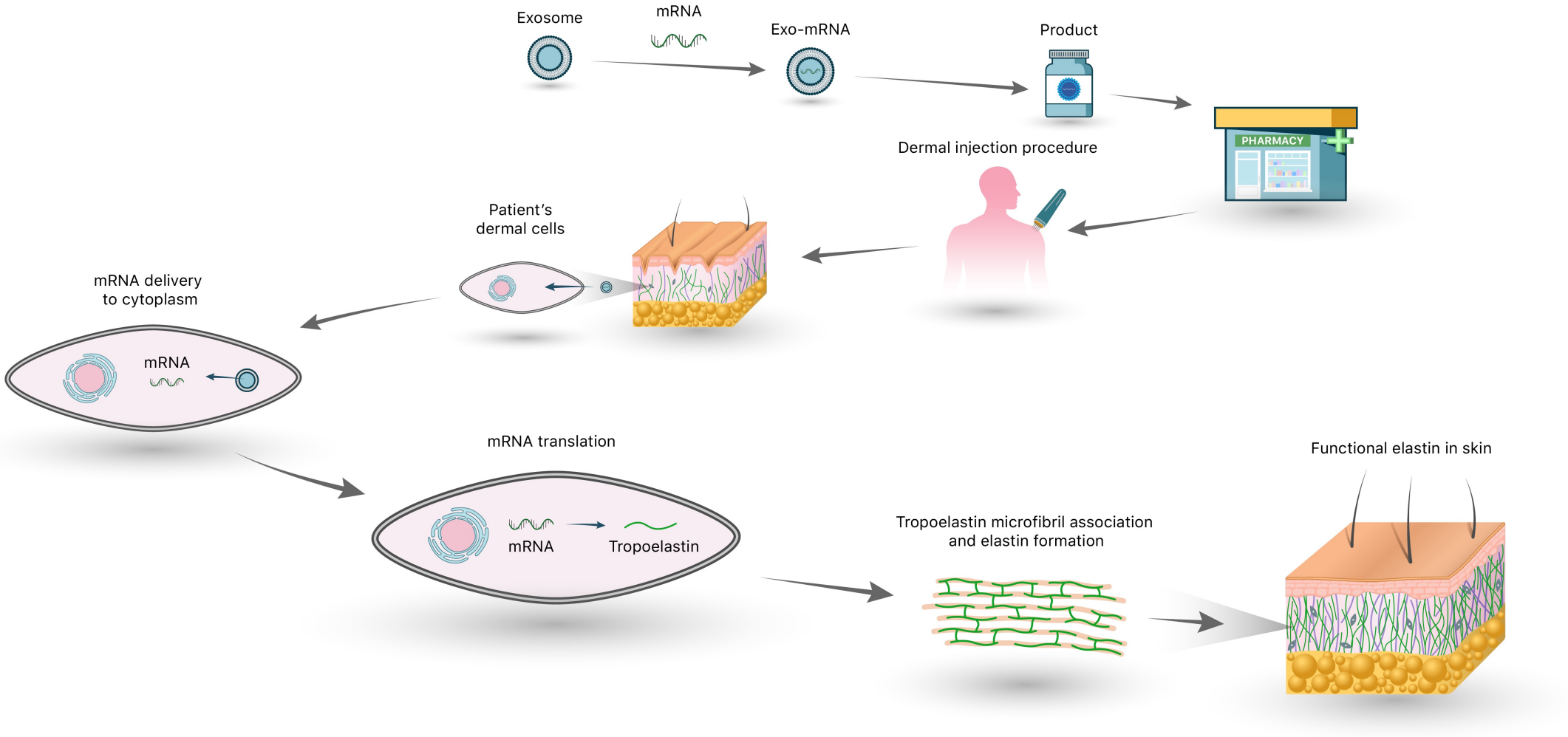
An example exosome-based Genetic Medicine





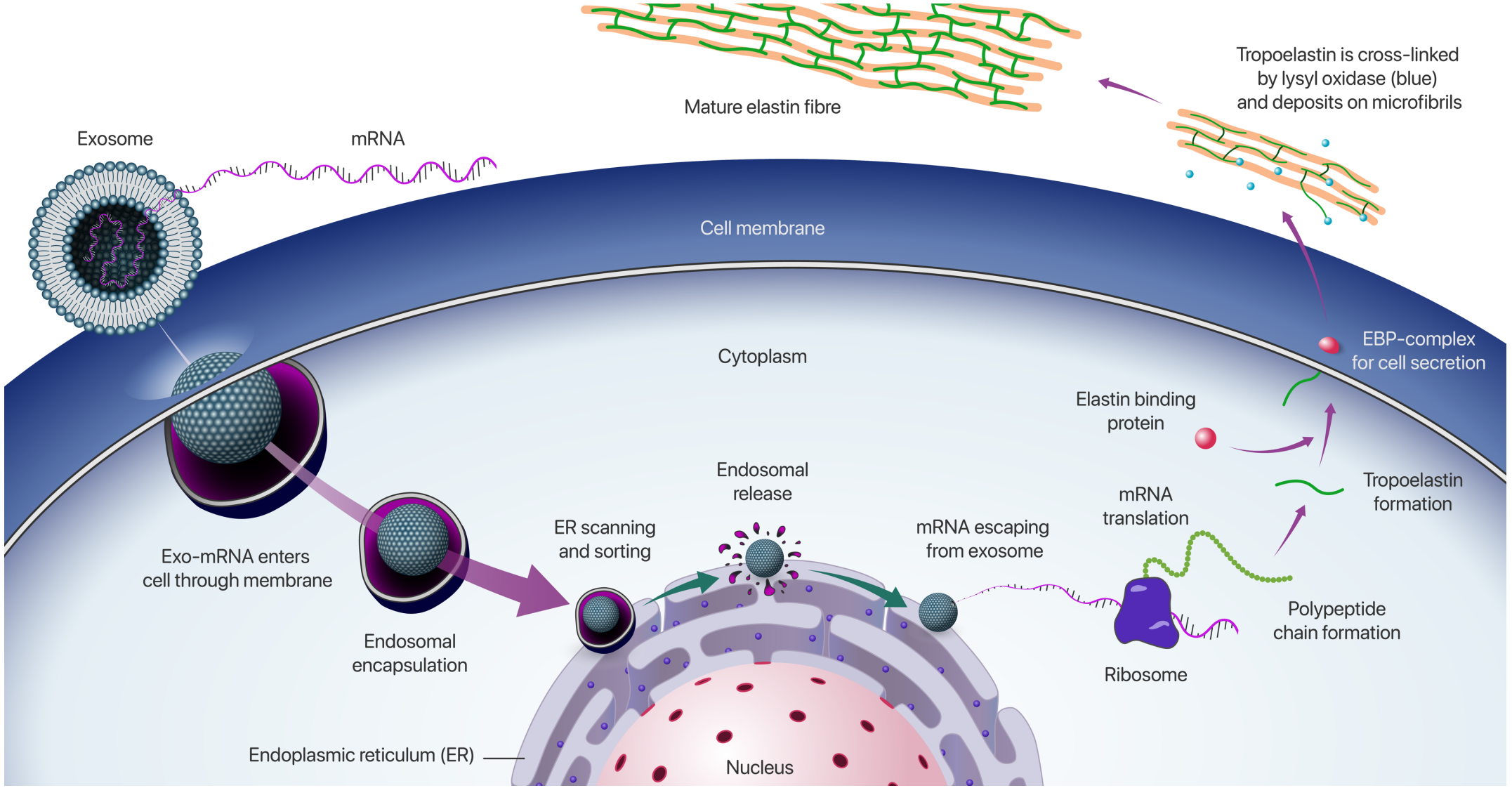
EXO-RNA for Elastin deficiency

An example exosome-based Genetic Medicine (II)



EXO-RNA for Elastin deficiency

An example exosome-based Genetic Medicine (III)

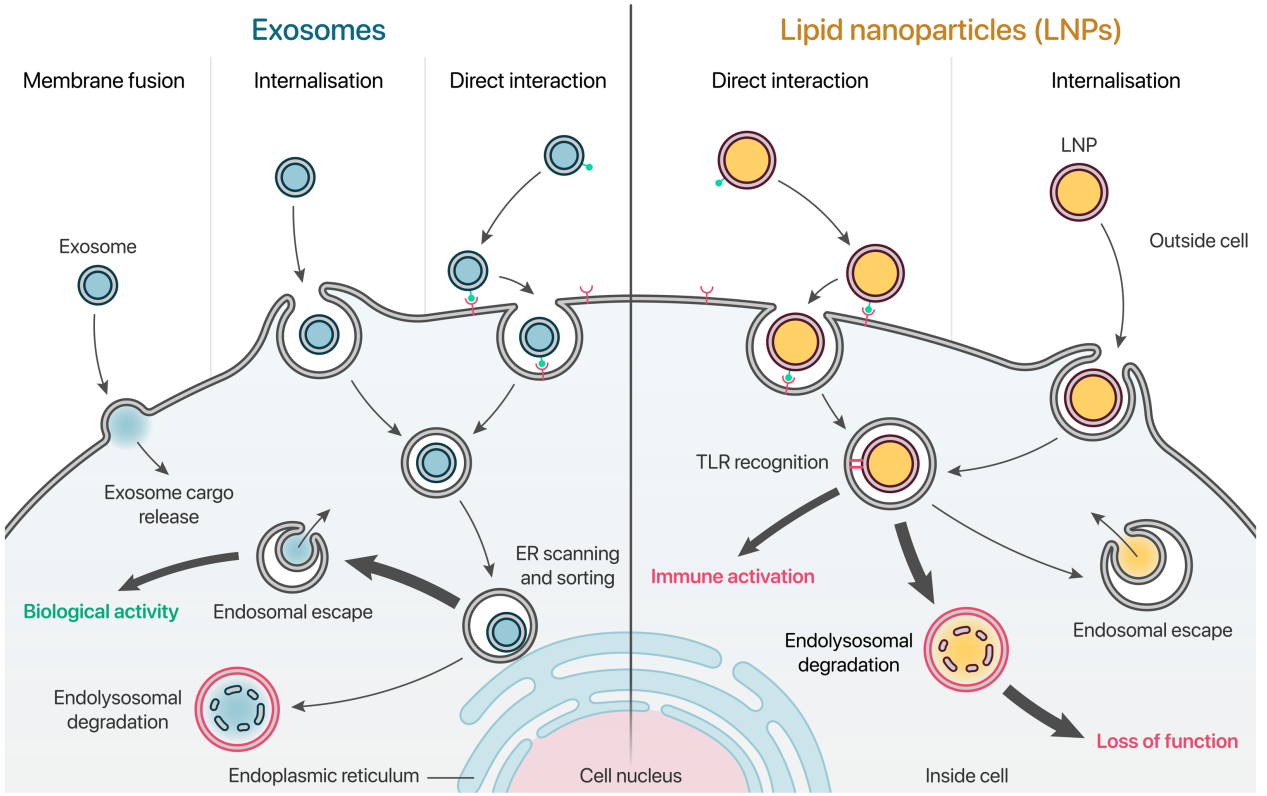


Exosomes compared with Lipid Nanoparticles (LNPs)

Simple comparison

1. Synthetic LNPs, once inside the cell may activate the immune system via TLR recognition in the endosome
2. In addition, the majority of the LNPs (along with their payload) are degraded in the endosome – only a small percentage of the administered dose is released into the cytoplasm of the cell
3. In contrast, exosomes can enter the cell through membrane fusion, by-passing the endosome altogether
4. Since the LNP payload is released into the cytoplasm, not the cell nucleus, additional engineering steps are required if DNA modification is the end goal
5. Exosomes are well-suited for delivery of DNA API into the cell nucleus – which is essential for DNA GMs

How they work inside cells differently for RNA APIs



Exosomes are Nature's way to deliver nucleic acids into cells via multiple internalization pathways

Genetic Medicines and delivery options

	Viral Delivery			Non-Viral Delivery	
Technology characteristic	AAVs	Herpesvirus (HSV)	Lentivirus (Lenti)	LNPs	Exosomes
Pre-existing immunity (none is good)	Yes	Yes	Yes	None	None
Suitable for repeat dosing without limit	No	No	No	Yes	Yes
Lacking toxicity of carrier	No	No	No	Potential for liver toxicity	Yes
Payload type	DNA	DNA	DNA	Universal *	Universal*
Processed inside cell efficiently	Yes	Yes	Yes	Not as efficient as AAV/Exosomes	Yes
Taken up by cells efficiently	Yes	Yes	Yes	Via LDL-R	Yes
Inflammatory potential	Yes	Yes	Yes	Less than viral delivery	No
Tropism (can target specific cells)	Yes	Yes	Yes	Yes	Yes
Efficient delivery across BBB	?	Yes	?	No	Yes
Manufacturing scale	Challenging	Challenging	Challenging	Yes	Emerging
Status on commercial prospects	Recent clinical challenges including toxicity (AAV), immunogenicity (AAV) and insertion related clonal expansion (Lenti) leading to increased regulatory scrutiny			Massive uplift form mRNA vaccine delivery over the past 3 years	Starting to take off in Tx uses, safety is clear

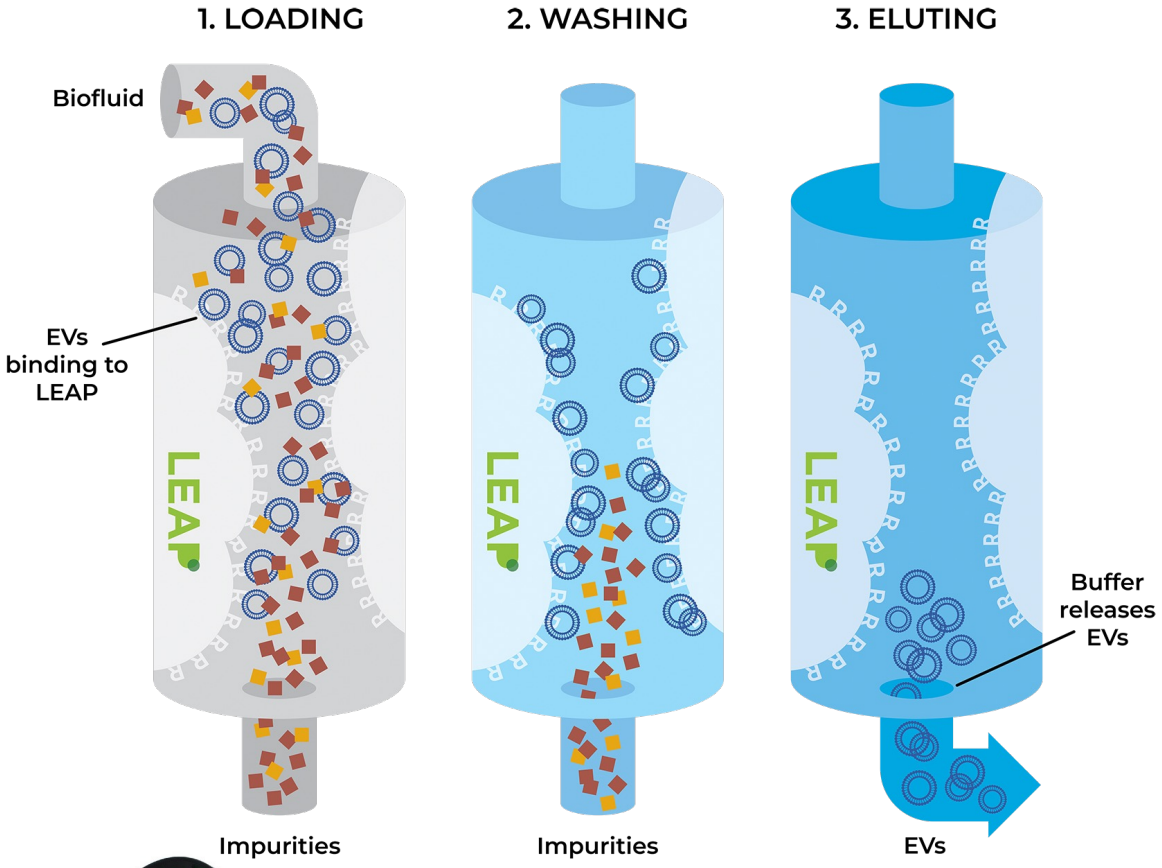
Tx therapeutic product, LNP lipid nanoparticle, BBB blood-brain barrier,
*Universal means DNA, RNA, siRNA, peptides, proteins, small molecules etc.

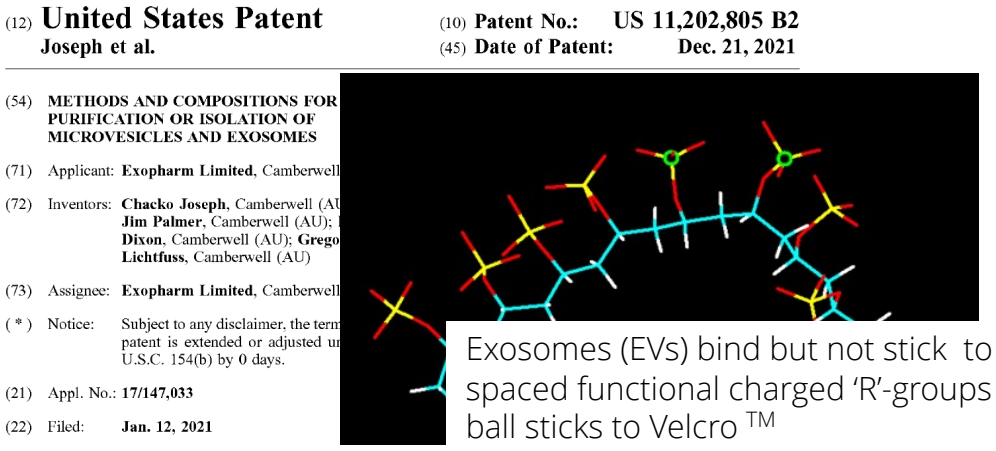
Colour code: Green means functional, red means non-functional, yellow means 'maybe'

LEAP purification technology explained – 1, 2 & 3

Understanding the internal workings of LEAP (step-by-step)

1. **Loading** – Biofluid is added to LEAP affinity chromatography column
   - EVs bind to the LEAP matrix
   - Most impurities fail to bind to the LEAP matrix and pass through
2. **Washing** – EVs are retained while residual impurities are washed out
3. **Eluting** – Simple buffer releases EV binding from LEAP ligand
   - EVs are now ready for formulation
   - Column is re-sterilized and prepared for the next batch





(12) **United States Patent**
Joseph et al.

(10) **Patent No.: US 11,202,805 B2**
(45) **Date of Patent: Dec. 21, 2021**

(54) **METHODS AND COMPOSITIONS FOR PURIFICATION OR ISOLATION OF MICROVESICLES AND EXOSOMES**

(71) Applicant: **Exopharm Limited**, Camberwell

(72) Inventors: **Chacko Joseph**, Camberwell (AU); **Jim Palmer**, Camberwell (AU); **Dixon**, Camberwell (AU); **Grego Lichtfuss**, Camberwell (AU)

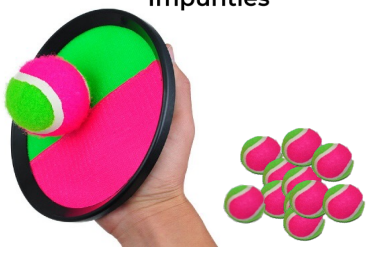
(73) Assignee: **Exopharm Limited**, Camberwell

(*) Notice: Subject to any disclaimer, the term patent is extended or adjusted u U.S.C. 154(b) by 0 days.

(21) Appl. No.: **17/147,033**

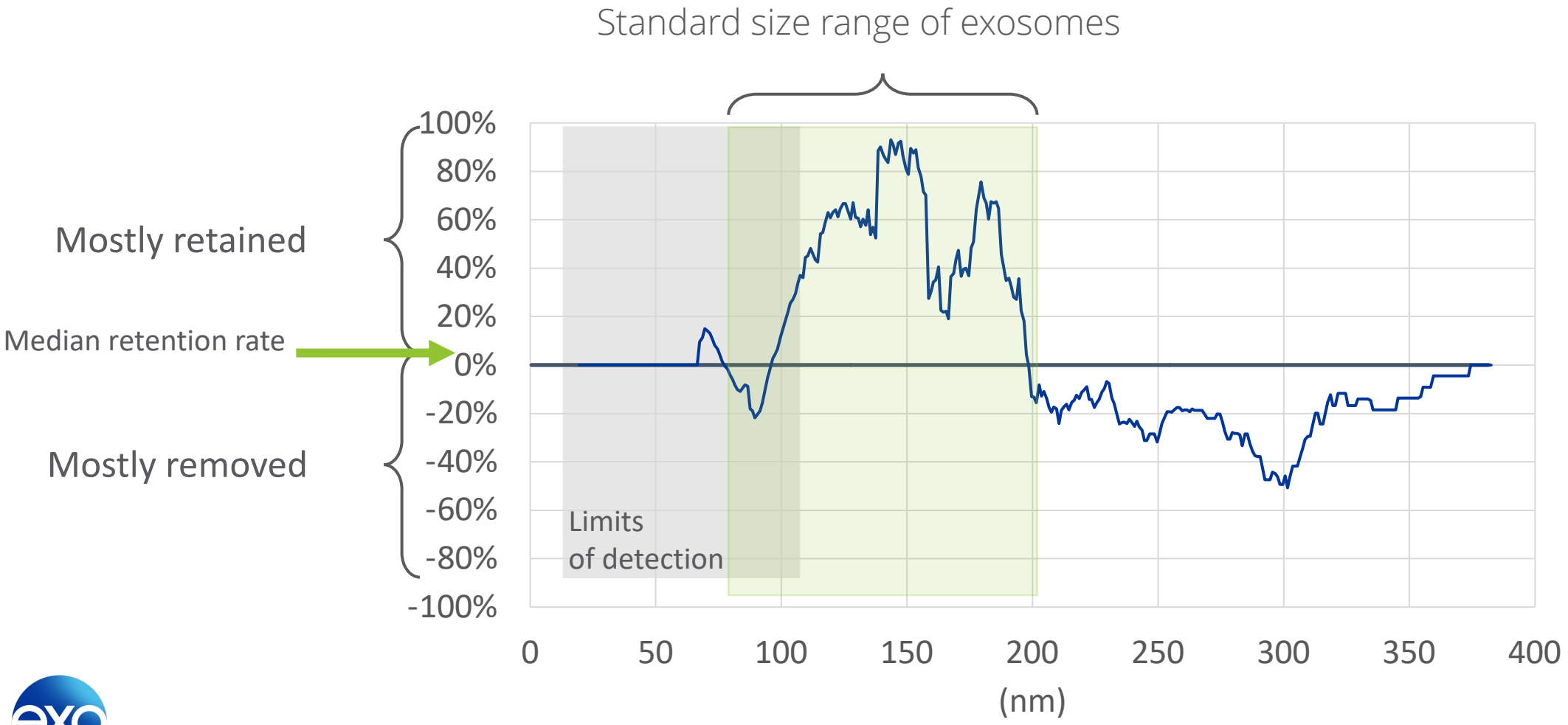
(22) Filed: **Jan. 12, 2021**

Exosomes (EVs) bind but not stick to the spaced functional charged 'R'-groups a bit like a ball sticks to Velcro ™



LEAP purification technology - performance

Relative retention as a function of size – purified v starting MSC conditioned media



LEAP purifies exosomes

LEAP purification technology – scalable in capacity

Commercial scalability to above 1000L scale using readily available larger equipment

AKTA*process*™

Commercial Manufacture

Scale-up, Clinical Trials

AKTA pure 25

Proof-of-Concept Scale

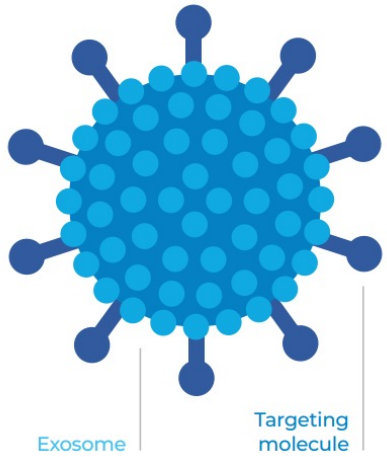
AKTA*ready*™

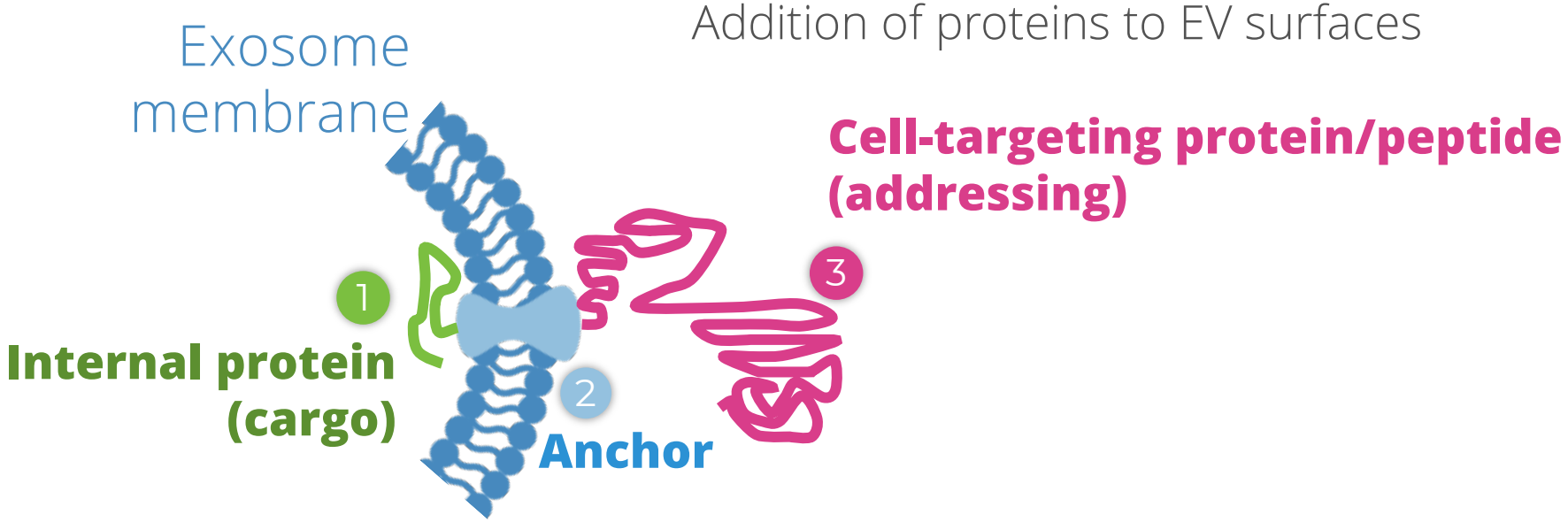
Research scale starting with 1-10ml cell conditioned media

Readily scalable exosome isolation and purification process.

- Uses standard industry equipment together with proprietary and patented LEAP ligand chemistry
- The process is scalable to beyond 1000L – industrial-scale

EVPS technology – engineering for targeted delivery





Exosome surface engineering for targeted delivery (tropism)

- Enables specific molecules to be attached to the surface of exosomes to guide them to target tissues or cell types
- Loaded drug can be delivered to recipient cell surface or cell interior
- Targeted delivery can improve efficacy and reduce off-target effects of the exosome's drug cargo

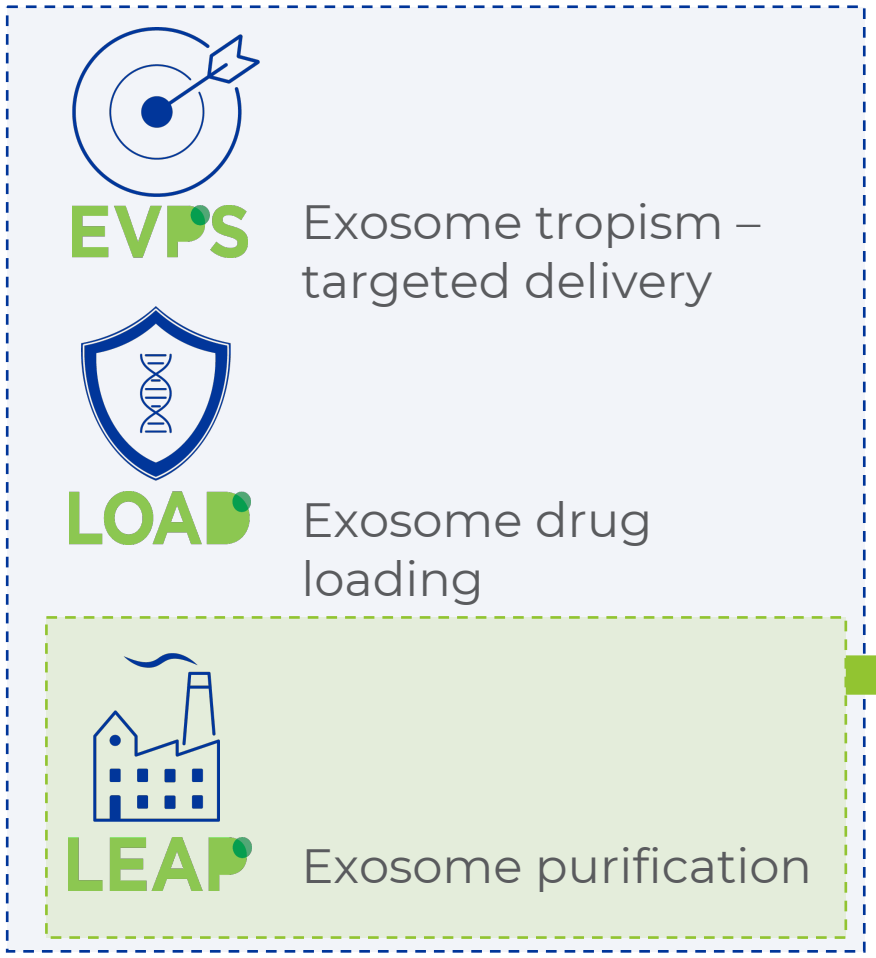
LOAD technology – API drug loading into exosomes

Exopharm has demonstrated loading of DNA, mRNA, siRNA and small molecule drug – data available

Loading of different drug cargo into exosomes

- Use LOAD to insert drug molecules into exosomes:
  - DNA
  - mRNA
  - Small molecule APIs
  - siRNA and other RNAs (e.g. miRNA)
  - Proteins (biologics)
- The exosomes protect the drug molecule from degradation as it is travels inside the body to the intended tissues
- Loading can occur pre- or post-purification

Technologies apply to Engineered and Naïve Exosome Products



Engineered exo-medicines

- Any combination of LEAP, EVPS with LOAD
- Precision-engineered medicines for select tissue targeting and optimized cargo delivery
- Genetic & other medicines

Naïve exo-medicines

- **LEAP** purification technology
- Harness the regenerative power of adult stem cells or donor blood material
- Cell-free product
- Regenerative medicine products
- Aesthetic products