ASX Announcement

Melbourne, Australia, 12 October 2022

BUILDING MOMENTUM WITH IN-HOUSE PRODUCTS

- Company Presentation: Building Momentum with in-house Products

Genetic medicine and exosome-based drug-delivery company Exopharm Limited (ASX:EX1) releases additional information about its in-house Genetic Medicine programs.

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

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Building Momentum with in-house Products

October 2022

exopharm

ASX: EX1

Delivering transformative medicines

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2 Lead programs selected for in-house product pipeline

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

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

Existing data supporting product selection (see data slides in this presentation)

Potential of more than one product per program (e.g. different product formulations for skin and lungs)

Initial API-type
- ***mRNA as additive gene therapy***

Product formulations for localised delivery
- ***Lungs***
- ***Skin***

API = active pharmaceutical ingredient, ***CFTR*** = cystic fibrosis transmembrane conductance regulator

Development program outline

CY 2023

Exo product manufacture & validation studies:

- in vitro; and
- in animal models

Then . . .

Clinical trials of up to 4 products following POC validation:

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

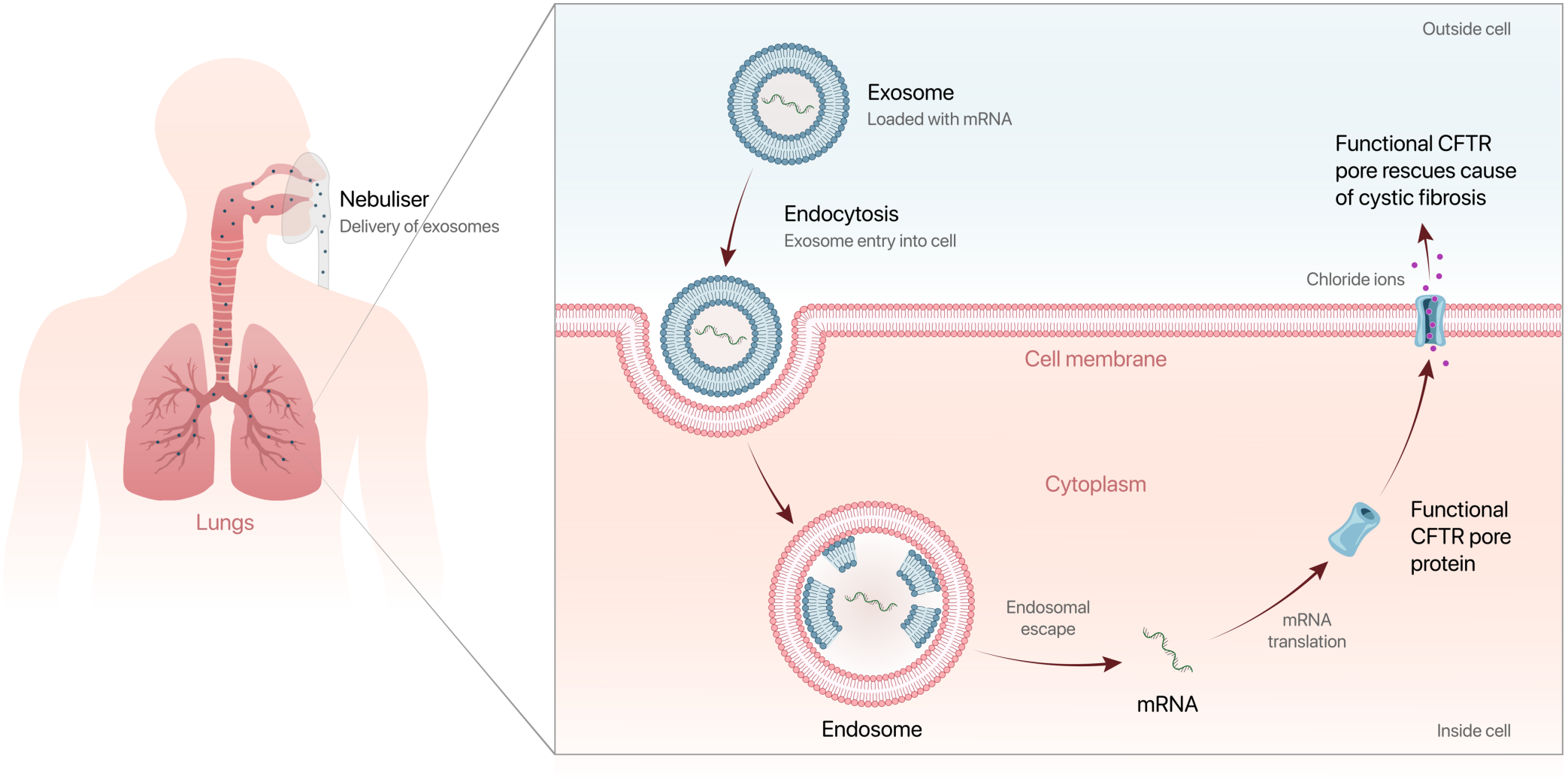
Final products will determine study designs, size of trials, trial costs and timing

Now

1	2	3	4	5	6
Gene selection and supportive ***in vitro*** data	Validation in vivo	Preclinical testing	**Clinical trials in humans P1, P2, P3**	**Marketing approval**	**Product sales**
Preclinical assets			**Clinical assets**		

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

EXO-RNA for Cystic Fibrosis



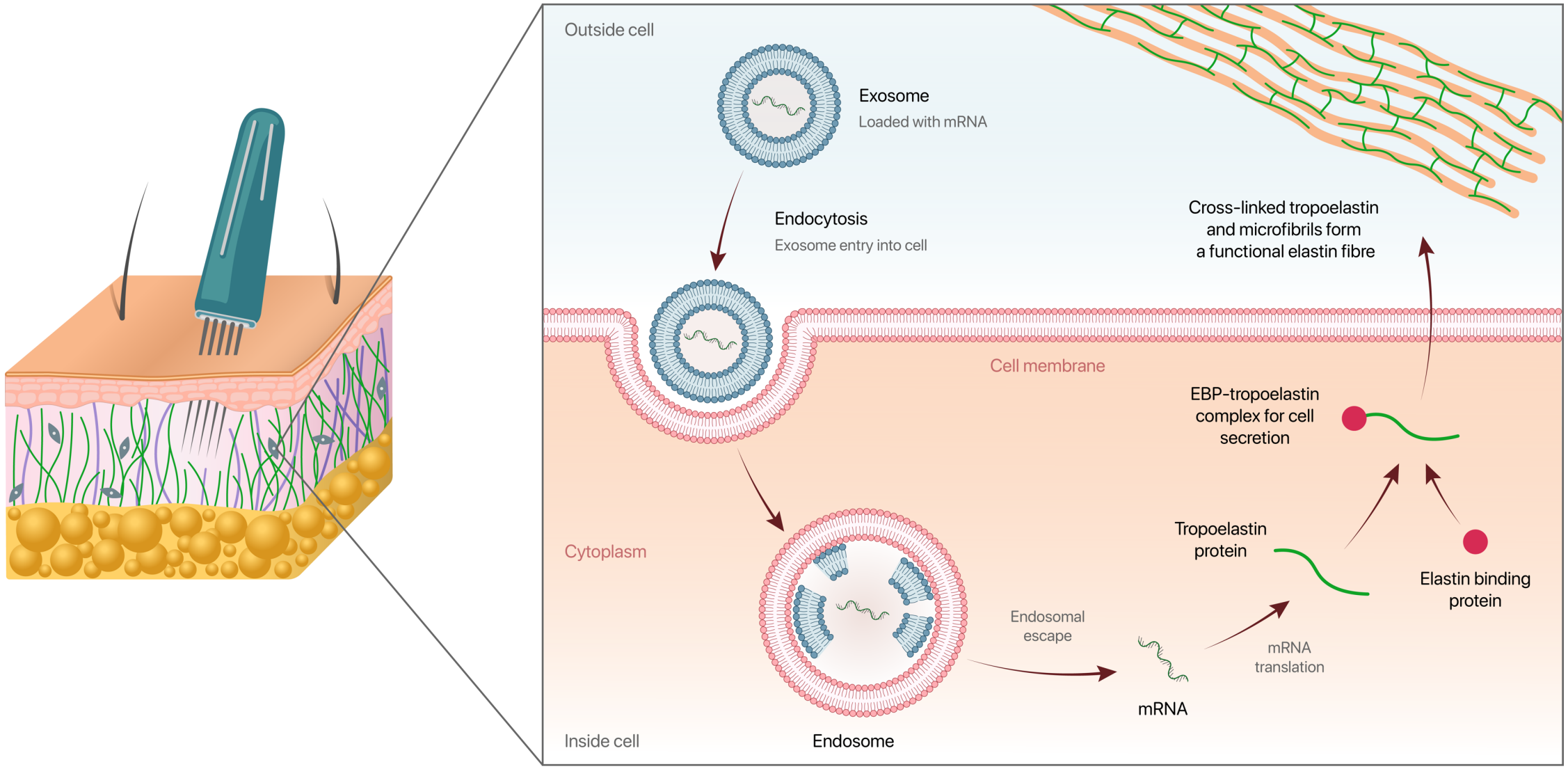
Product commercial opportunity outline – Exo-CFTR

Commercial outline and competition	Market metrics
Potential for FDA orphan drug designation, rare paediatric disease designation and priority review. Cystic Fibrosis (CF) is the most common autosomal recessive disease with >100,000 CF patients worldwide (around 40,000 in USA) and the median age of death is 32 years. Lung disorder is the main cause of morbidity and mortality There is no cure for cystic fibrosis, but treatment can ease symptoms, reduce complications and improve quality of life (QoL). Treatment options include antibiotics, anti-inflammatory medications, mucus-thinners, bronchodilators, oral pancreatic enzymes and CFTR modulators The launch of small molecule CFTR modulators was a significant advance from prior symptomatic therapies, however they: • correct the shape of some mutations of the CFTR molecule but do not repair gene malfunction • slow down but do not prevent continued disease progression • decrease but do not eliminate pulmonary exacerbation • are effective only in people with specific mutations; hence, do not address all classes of CF • require combination and triple-combination in order to provide an effective modulator treatment regimen in most patients • have high treatment cost (triple combination exceeding US$300,000 annually) • produce adverse effects such as hepatic dysfunction, upper respiratory tract infection, chest pain, increase in blood pressure, etc A relatively low level of CFTR correction has a high therapeutic potential (6–10% of normal CFTR activity is needed to restore the epithelial cells electrical properties[1] and 25% to restore mucociliary function[2])	The CF market is projected to reach US$31B by 2027 with 24% compound annual growth rate (CAGR), up from US$5B in 2019[1]. No direct competitors (exosome gene therapy) have been identified and the Exo-CFTR product would have clear mechanistic differentiation from: • the present established therapies (small molecule CFTR modulators); and • the limitations of the drug-delivery technologies used by others for experimental gene therapy (***and yet they get promising results, see slide 18***)

CFTR = cystic fibrosis transmembrane conductance regulator

[1] https://doi.org/10.1038/ng0992-21 [2] https://doi.org/10.1371/journal.pbio.1000155

EXO-RNA for Elastin deficiency



Product commercial opportunity outline – Exo-Elastin

Commercial outline and competition	Market metrics
Potential treatment for cardiopulmonary diseases, skin conditions and aesthetic dermatology. Four main product opportunities: ***Chronic obstructive pulmonary disease*** (COPD) including pulmonary emphysema and chronic bronchitis The global burden of COPD is growing. Destruction of elastin or abnormalities in elastic fibre assembly are major factors in emphysema and COPD. An estimated 3.1 million Americans have been diagnosed with emphysema and 11.2 million U.S. adults have been estimated to have COPD[6]. Tobacco use is the number one factor in the development and progression of COPD, exposure to air pollutants, genetic factors, and respiratory infections can also play a role in the disease. COPD is the third leading cause of death, after ischaemic heart disease and stroke and before cancers ***Arterial stiffness*** Hypertension and arterial stiffness are inversely related to elastin amounts. Relevant for cardiovascular disease (CVD) and hypertension (high blood pressure) treatments. Arterial stiffness increases with age, as well as in various pathological states, including obesity, diabetes mellitus, smoking, and dyslipidemia, and it has important consequences for cardiovascular health. Arterial stiffness is an attractive therapeutic target in terms of vascular aging. Also, opportunity as treatment for rare diseases (e.g. Williams-Beuren syndrome (WBS)) for accelerated approval / drug designations ***Scar prevention and treatment*** Elastin is inadequately expressed during wound healing, resulting in an absent intact elastic fibre network. Major scarring, such as from severe burns, remains a major rehabilitative challenge with serious impact on the patients' quality of life (itch, pain, restricted movement) or even delayed reintegration into society. There is a lack of effective scar prevention measures ***Photoaging, striae distensae alba (stretch marks) and aging skin*** In skin, overall half-life of elastin is similar to the human lifespan and therefore it is unlikely to be replaced. No established treatments that increase production of elastin. Product differentiation via clear mechanism of action compared to many other products. Opportunity for over-the-counter (OTC) products (at different price-points)	COPD market to reach US$19B in 2028[2] CVD market to reach US$231B by 2030[3]; Hypertension market to reach US$31.5B by 2028[4] Scar treatment market to reach US$16.7 billion by 2031[5] Medical dermal and aesthetic products have various market segments and access to a worldwide aging population

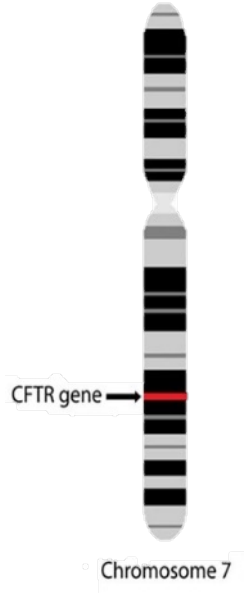
Further details

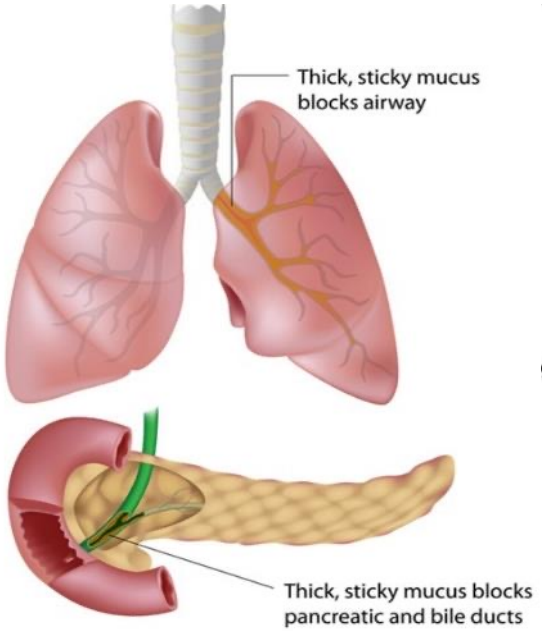
Cystic Fibrosis (CF)

Exo-mRNA CFTR

Cystic Fibrosis (CF) is a high-burden life-shortening genetic disease

- CF is caused by a mutation in the epithelial chloride channel—cystic fibrosis transmembrane conductance regulator (CFTR)
- CF leads to several chronic lung complications like thickened mucus, bacterial infection and inflammation, progressive loss of lung function, and ultimately, death





Most common autosomal recessive disease

> 100,000 CF patients worldwide

Median age of death **32**

Lung disease is the main cause of morbidity and mortality

CF market **US$31B by 2027 with 24% compound annual growth rate (CAGR), up from US$5B in 2019**

Sources: Fortune Business Insights ; Chen et al. Animal Model Exp Med. 2021; McBennett et al. Pediatr Pulmonol. 2022;

Cheaper, safer and more efficacious mutation-agnostic therapies are urgently needed

There is no cure for cystic fibrosis, but treatment can ease symptoms, reduce complications and improve QoL

More than 1,700 mutations of the CFTR gene have been identified in different patients

Treatment options include antibiotics, anti-inflammatory medications, mucus-thinners, bronchodilators, oral pancreatic enzymes and CFTR modulators

The launch of small molecule CFTR modulators was a significant advance from prior symptomatic therapies, however they:

- correct the shape of some mutations of the CFTR molecule but do not repair gene malfunction or mutation
- slow down but do not prevent continued disease progression
- decrease but do not eliminate pulmonary exacerbation
- are effective only in people with specific mutations; hence, do not address all classes of CF
- require combination and triple-combination in order to provide an effective modulator treatment regimen in most patients
- have high treatment cost (triple combination exceeding US$300,000 annually)
- have diverse negative effects such as hepatic dysfunction, upper respiratory tract infection, chest pain, increase in blood pressure, etc

Cheaper, safer and more efficacious mutation-agnostic therapies are urgently needed, especially for those who do not carry a modulator responsive mutation, or who cannot tolerate modulator therapy due to side effects

Sources : Almughem et al Pharmaceutics. 2020; Zaher et al Cureus. 2021

Additive gene therapy is a mutation agnostic approach with the potential to repair the defect in CFTR caused by genetic mutation

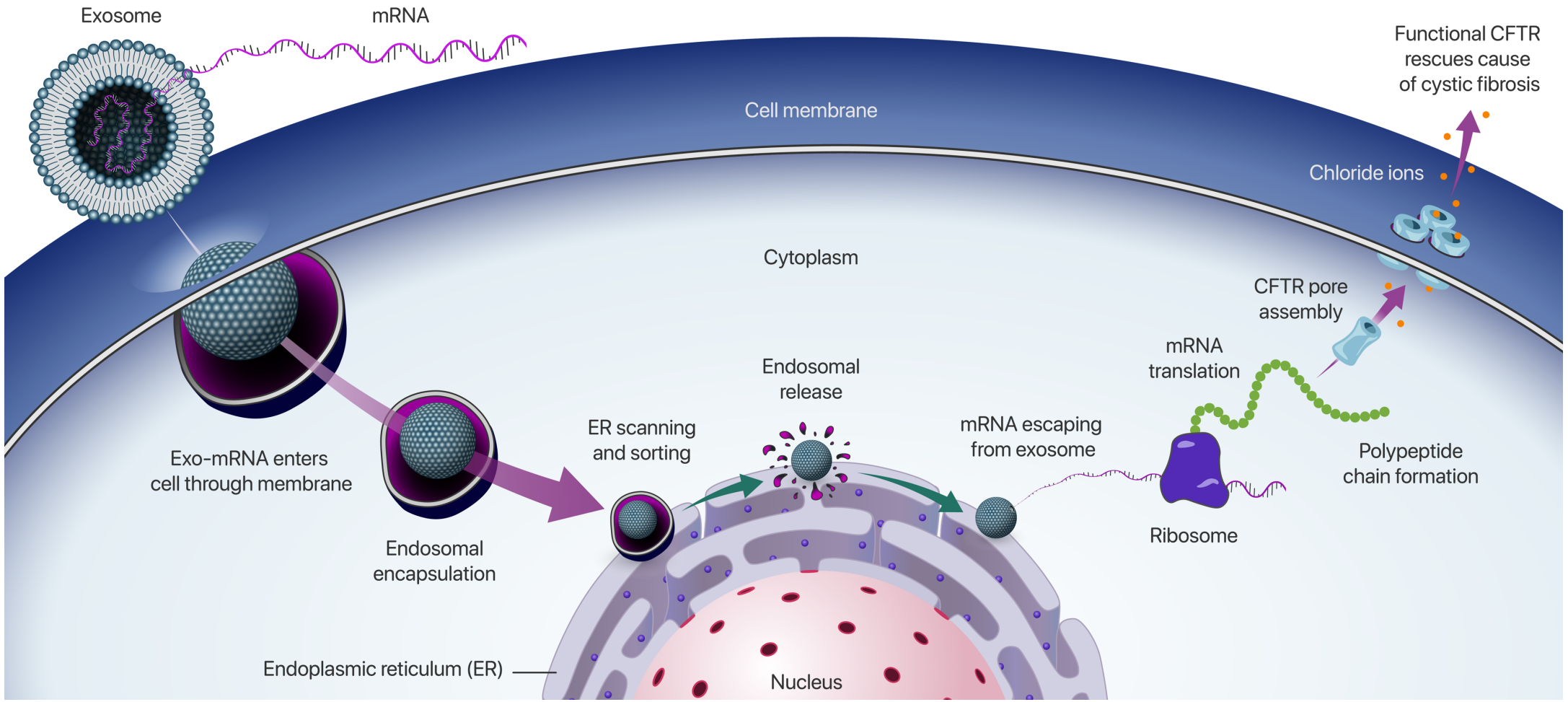
Additive gene therapy is ideal for CF compared to some other genetic diseases

- CF is caused by mutations in a single gene - so patients otherwise have good health
- Drug-delivery to the affected lung cells can be readily achieved through a pulmonary nebuliser
- A relatively low level of CFTR correction has a high therapeutic potential (6–10% of normal CFTR activity is needed to restore the epithelial cells electrical properties[1] and 25% to restore mucociliary function[2])
- Additive gene therapy causes functional 'wild-type' CFTR molecule to be produced – so restores CFTR-function
- The Exo-RNA approach has following advantages:
  - ❖ No need for translocation of the API into the nucleus
  - ❖ Avoids use of viral vectors such as AAVs
  - ❖ No risk of potential insertion into the host genome
- The Exo-CFTR mRNA product matches:
  - ❖ High turnover of lung cells makes mRNA more suitable
  - ❖ Nebuliser (inhaler) delivery allows regular dosing (daily or weekly)

API = active pharmaceutical ingredient, ***AAV*** = adeno-associated virus

Exo-mRNA CFTR – Product overview

Exo-mRNA CFTR – an additive gene therapy using exosomes loaded with the full CFTR mRNA for intracellular delivery, formulated to be administered via nebuliser (inhaler)



No direct competitors (exosome gene therapy) have been identified

Competitive landscape of current gene therapy programmes in development

Drug	Sponsor	Patient target	RoA	Delivery	Stage	References
pGM169/GL67A	Imperial College London	12 years or older	Inhalation	Liposome	Phase 2b	Publication
4D-710	4D Molecular Therapeutics	18 years and older	Inhalation	AAV	Phase 1/2	Press release
Eluforsen	ProQR Therapeutics	18 years and older with heterozygous F508del	Inhalation	ASO	Phase 1	Clinical trial
KB407	Krystal Biotech	18 years and older	Inhalation	HSV-1 vector	Phase 1	Clinical trial
SP-101	Spirovant (subsidiary of Sumitovant Biopharma)	n/a	Inhalation	AAV vector	Pre-clinical	spirovant.com
ARCT-032	Arcturus Therapeutics	n/a	Inhalation	LUNAR® LNP	Pre-clinical	Arcturus press release
Viral delivery of full length CFTR	Carbon Biosciences	n/a	Unknown	Parvovirus vector	Preclinical	https://www.carbonbio.com/
Gene therapy	Pioneering Medicine	n/a	Unknown	Unknown	Preclinical	Press release
mRNA delivery	ReCode Therapeutics	n/a	Inhalation	LNP	Preclinical	https://recodetx.com/pipeline/
Gene editing	SalioGen Therapeutics	n/a	Unknown	LNP	Preclinical	https://saliogen.com/our-programs/
MRT 5005	Translate Bio	-	Inhalation	LNP	Phase 1/2	Program ceased

SM = Small molecule, ***HSV*** = Herpes simplex virus, ***AAV*** **=** Adeno-associated virus, ***LNP*** = lipid nanoparticle, ***ASO*** = antisense oligonucleotide, ***ROA*** = route of administration

CFTR competitors that have been granted approval for sales or are in clinical trials

Drug	Company	RoA	Drug type	Stage	Comment
Ivacaftor (Kalydeco)	Vertex Pharma	Oral	SM	Approved	source
Lumacaftor/ivacaftor (Orkambi)	Vertex Pharma	Oral	SM	Approved	source
Tezacaftor/ivacaftor (Symdeko)	Vertex Pharma	Oral	SM	Approved	source
Elexacaftor, tezacaftor, and ivacaftor (Trikafta)	Vertex Pharma	Oral	SM	Approved	source
Eluforsen	ProQR Therapeutics	Inhalation	ASO	I	NCT02564354
KB407	Krystal Biotech	Inhalation	HSV-1 vector	I	NCT05095246
Ataluren	PTC Therapeutics	Oral	SM	II	NCT00234663
GLPG2222	Galapagos NV	Oral	SM	II	NCT03119649
4D-710	4D Molecular Therapeutics	Inhalation	AAV	I/II	NCT05248230
GLPG2737	Galapagos NV	Oral	SM	II	NCT04578548
GLPG1837	Galapagos NV	Oral	SM	II	NCT02707562
ELX-02	Eloxx Pharmaceuticals	Oral	SM	II	NCT04135495
Nesolicaftor	Proteostasis Therapeutics	Oral	SM	II	NCT03591094
pGM169/GL67A	Imperial College London	Inhalation	Liposome	IIb	source

SM **=** Small molecule, ***HSV*** **=** Herpes simplex virus, ***AAV*** = Adeno-associated virus, ***ASO*** = antisense oligonucleotide ***ROA*** = route of administration

Exosomes have advantages over current gene therapy programmes in development

Gene therapies are 'nucleic acid cargo' + delivery 'chassis' – ***nucleic acids cannot be administered 'naked' for therapeutic products***

From the previous slides, the gene therapy competitors are using the following delivery technologies:

- Liposomes
- Viral vectors
- LNPs

None are using exosomes – ***as Exopharm has unique exosome manufacturing technologies***

Delivery chassis	Comments
Liposomes	Liposomes are now outdated and replaced by LNPs
Viral vectors	Viral vectors generate immune responses that prevent repeated use - ***some also have toxicity and manufacturing challenges***
LNPs	LNPs are synthetic fat particles and are processed inside the cell very differently than exosomes – ***their delivery-efficiency is poor for therapeutic products***

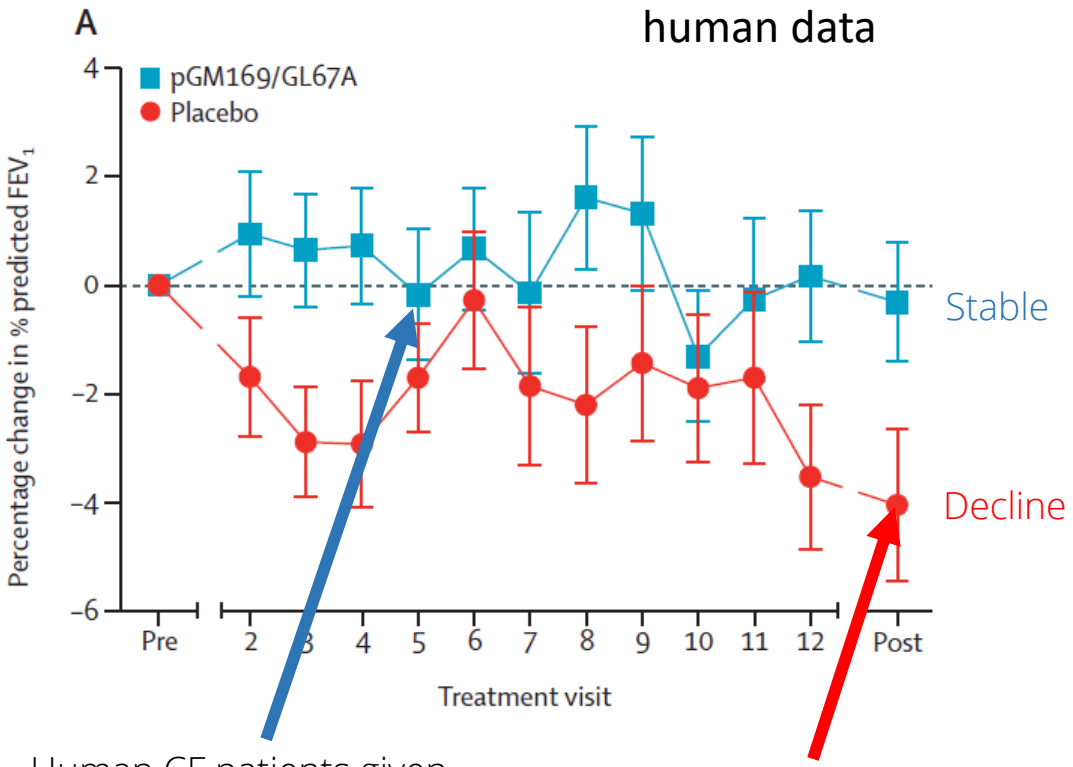
Refer to the Exopharm Investor presentation for more details and comparisons

LNP = lipid nanoparticle

CFTR Market opportunity summary

- CF market predicted to reach US$31B by 2027 with 24% compound annual growth rate (CAGR), up from US$5B in 2019
- Exo-CFTR has clear differentiation from current market key players (small molecule CFTR modulators)
  - ❖ Mutation-agnostic approach
  - ❖ No need for combination therapies
  - ❖ Potential to be more efficacious
  - ❖ Potential to be more cost-effective
- No direct competitors identified
- POC supported by successfully completed early clinical trials delivering CFTR plasmid via liposomes (***liposomes are an artificial LNP-like particle***)
- Potential for FDA orphan drug designation, rare paediatric disease designation and priority review

Additive CFTR gene therapy human data – showed improved lung function by forced expiratory volume (FEV) measure



Human CF patients given the monthly additive CFTR gene therapy over 12 months – shows stability in FEV at the end of the study period – patients in this group do not show decline and do show a treatment-benefit

Human CF patients placebo (nil gene therapy) over 12 months – shows decline in FEV at the end of the study period – patient's in this group are in decline

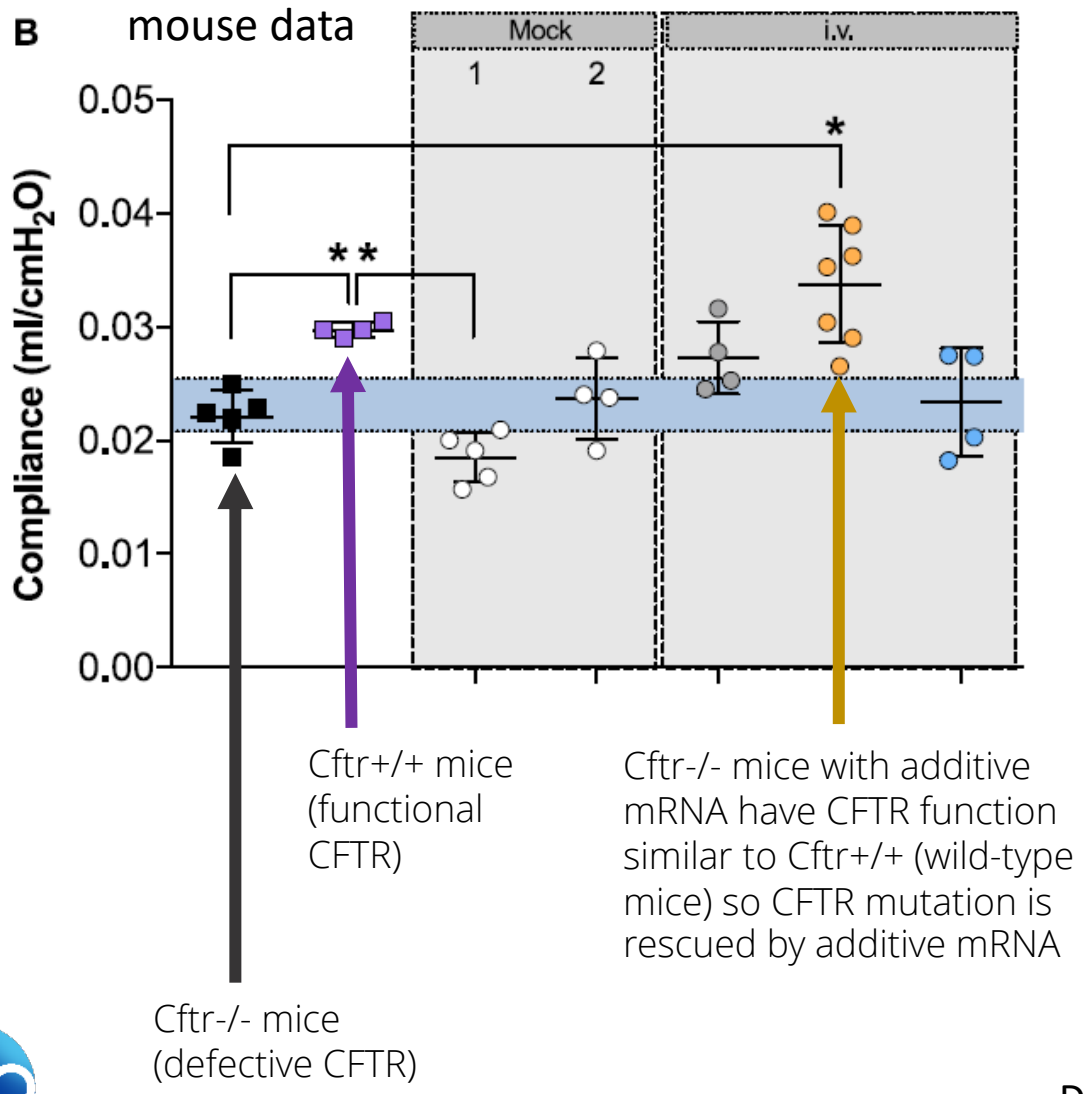
Alton et al (2015) 'We aimed to assess the efficacy of non-viral CFTR gene therapy in patients with cystic fibrosis'

Monthly application of the plasmid DNA gene therapy formulation (78 patients) gave a benefit in FEV1 compared with placebo (62 patients) at 12 months, ***showing stabilisation of lung function in the treatment group (blue) over the placebo (red)***

'***Our findings should encourage the rapid introduction of more potent gene transfer vectors into early phase trials, now that much of the groundwork has been established***'

Data from Alton et al 2015 http://dx.doi.org/10.1016/S2213-2600(15)00245-3

Additive CFTR mRNA in vivo data – improved lung function



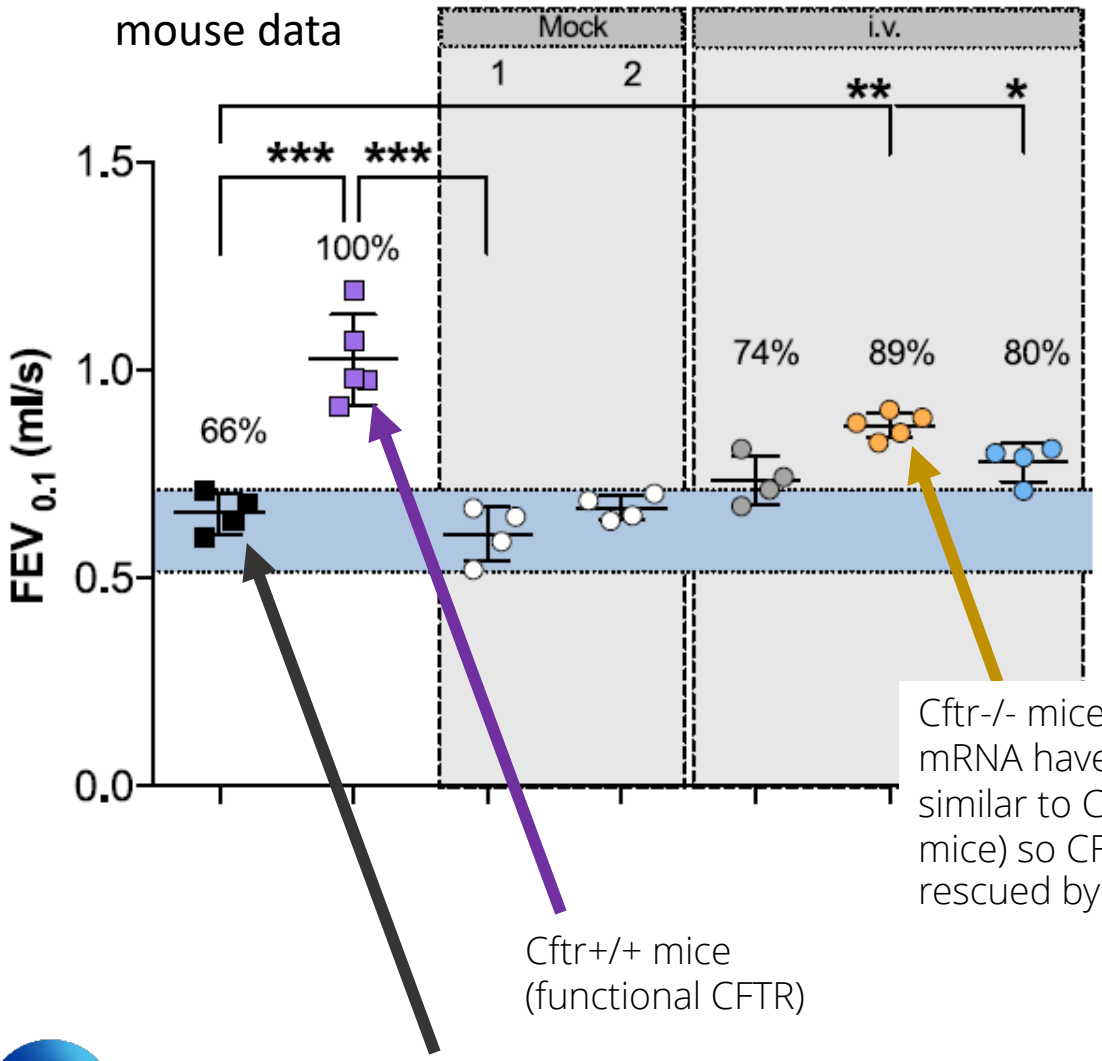
CFTR mRNA rescues expansion capacity of lungs (ml/cmH_2O) – a measure of lung function

in vivo data

i.v. administration of mRNA in nanoparticles rescued CFTR function in CFTR-mutant (Cftr-/-) mice
i.v. administration of mRNA CFTR in nanoparticles significantly increased the compliance from 0.02 ± 0.01 ml/cmH2O (Cftr−/− mice) to 0.03 ± 0.01 ml/cmH2O ($P \leq 0.05$), reaching equivalent values to those measured in Cftr+/+ mice

Data from Haque et al 2018 DOI:10.1038/s41598-018-34960-0

Additive CFTR mRNA in vivo data – improved lung function

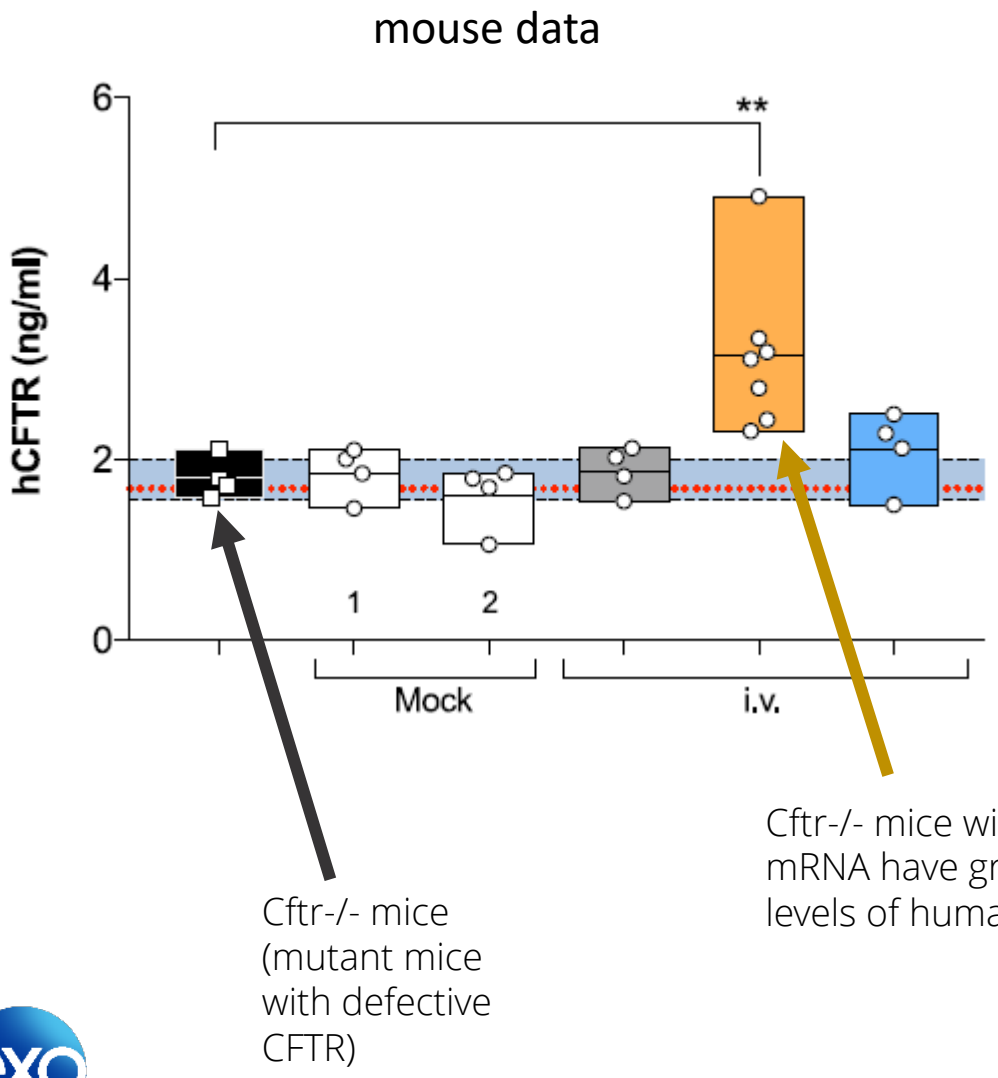


CFTR mRNA rescues forced expiratory volume (FEV) – a measure of lung function

in vivo data

Data from Haque et al 2018 DOI:10.1038/s41598-018-34960-0

Additive CFTR mRNA in vivo data – improved lung function



CFTR mRNA is converted into functional expression of human CFTR in cells

in vivo data

'Taken together, these results demonstrate significant lung function improvement in all relevant lung function parameters of Cftr−/− mice intravenously (i.v.) treated with mRNA human CFTR'

Data from Haque et al 2018 DOI:10.1038/s41598-018-34960-0

Further details

Cardiopulmonary diseases, dermatology & aesthetic medicines

Exo-mRNA ELN

Exo-mRNA ELN - Overview

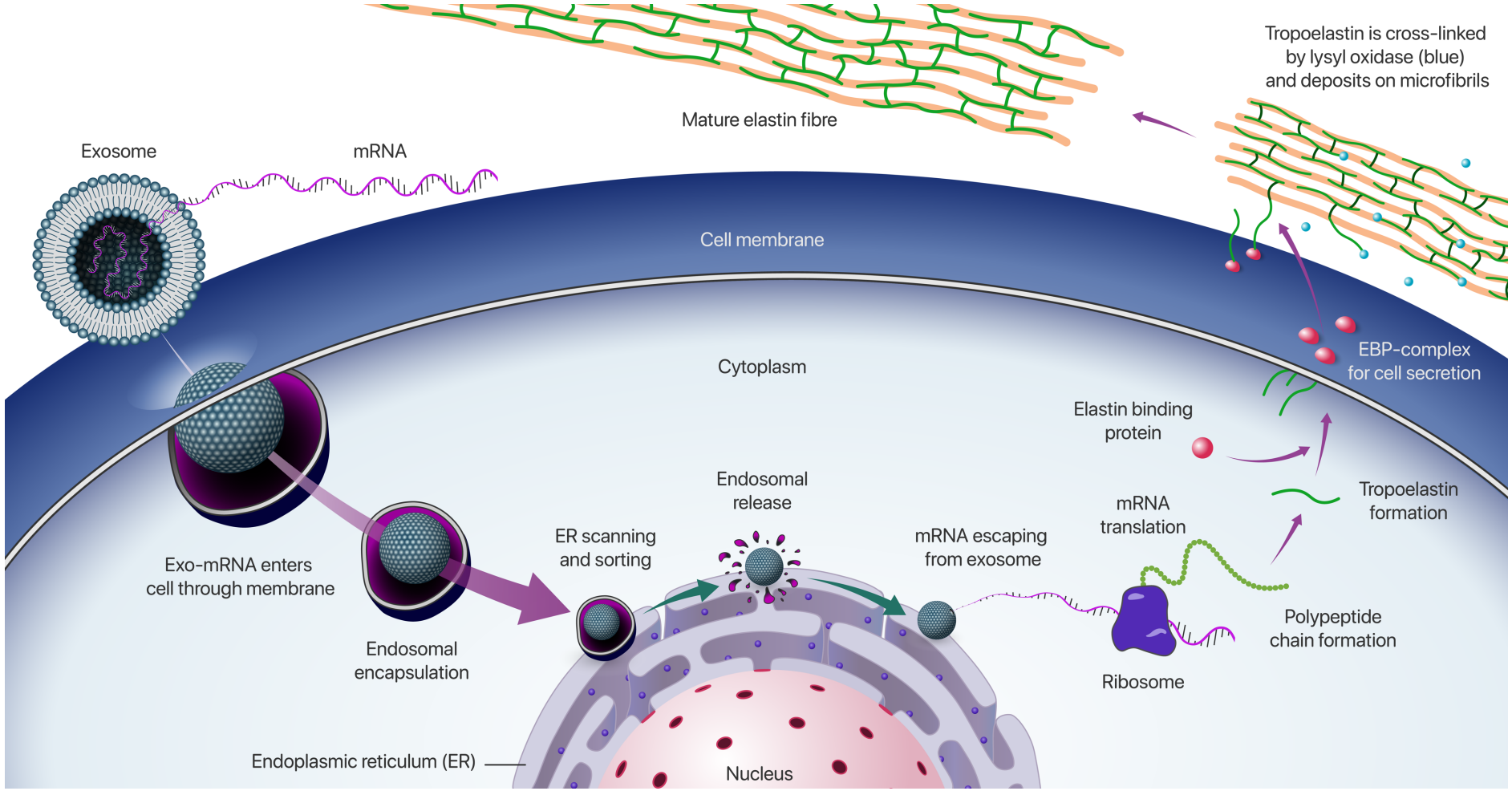
- Elastin is a critical natural endogenous protein made from the ELN gene and is a key component of the extracellular matrix
- Elastin imparts elasticity in various tissues such as skin, lungs, blood vessels and fascia
- With age and exposure to smoke, levels of elastin decrease and medical and aesthetic issues arise from that elastic deficiency
- Elastin is not taken from diet, but an additive gene therapy using ELN mRNA would produce additional Elastin in the body and could restore elastic structure of tissues back to normal

Exo-ELN product details

- Exo-mRNA ELN – an additive gene therapy of exosomes loaded with the full tropoelastin mRNA to cause cells to make elastin (***see next slide***)
- Formulation (route of administration) depending on target tissue

Exo-mRNA ELN – Product overview

Exo-mRNA ELN – An additive gene therapy using exosomes loaded with the full tropoelastin mRNA for intracellular delivery, formulated to be administered via topical application (for skin) or nebuliser (for lungs)



Elastin additive gene therapy offers a range of product options – each with significant market opportunities and needs

Medical condition to treat	COPD	Arterial stiffness	Scar prevention & treatment	Aging / photoaging / stretch marks
Relevance of Elastin (ELN)	Destruction of elastin or abnormalities in elastic fibre assembly are major factors in emphysema	Hypertension and arterial stiffness are inversely related to elastin amounts	Elastin is inadequately expressed during wound healing, resulting in an absent intact elastic fibre network	In skin, overall half-life of elastin is similar to the human lifespan and therefore unlikely to be replaced
Route of Administration	Inhalation	Systemic	Micro needling / topical / local	Topical / micro needling
Market metrics	COPD market to reach $19.3B in 2028 in top 7 world markets	CV market to reach US$231.7B by 2030; Hypertension market to reach 31.5B by 2028	Scar treatment market to reach US$16.7 billion by 2031	Anti-aging market worth $88.1B by 2028; Stretch marks treatment to reach USD4.17B by 2028,

Elastin Product market analysis

COPD

- The global burden of COPD is growing
- Significant unmet need (third leading cause of death)
- Differentiation through novel target/MoA
- Opportunity to leverage learnings from lung-delivery of Exo-CFTR product

Arterial stiffness

- Significant market size
- Attractive therapeutic target in terms of vascular aging
- Highly differentiated (novel MoA / directly targeting structural abnormalities)
- Opportunity for rare diseases (e.g. WBS) for accelerated approval / drug designations

Scar prevention & treatment

- Lack of effective scar prevention measures
- Significant market size
- No clinical candidates focused on delivering elastin / tropoelastin to the skin (excluding prefabricated matrix)
- Potential to improve QoL and reduce overall cost burden

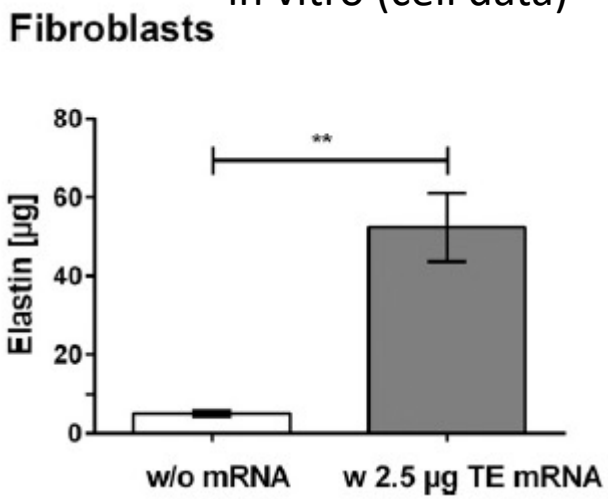
Aging / photoaging / stretch marks

- No established treatments that increase production of elastin
- Differentiation via clear MoA compared to many other 'anti-aging' products
- Significant market size
- Opportunity for OTC product (but at lower price points)
- Aesthetics medicines is a crowded and competitive market against some dubious products

COPD = chronic obstructive pulmonary disease, ***OTC*** = over the counter, ***MoA*** = mechanism of action, ***WBS*** = Williams-Beuren syndrome, ***QoL*** = quality of life

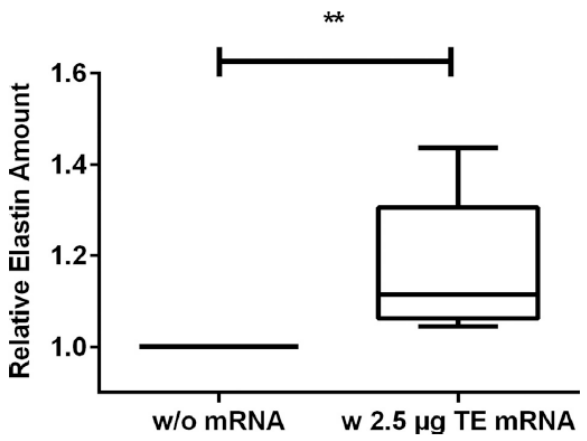
Additive Elastin mRNA in vitro and ex vivo skin data

in vitro (cell data)



Elastin levels increased using ELN mRNA delivered into human fibroblasts (cells)

ex vivo (pig skin)



Elastin levels increased using ELN mRNA microinjected into pig skin

'From a young age, elastin synthesis decreases and ceases in adults'

'this auspicious mRNA-based integration-free method has a huge potential in the field of regenerative medicine to induce de novo elastin synthesis, e.g., in skin, blood vessels'

Molecular Therapy Nucleic Acids
Original Article

AMERICAN SOCIETY of GENE & CELL THERAPY

De Novo Synthesis of Elastin by Exogenous Delivery of Synthetic Modified mRNA into Skin and Elastin-Deficient Cells

Data from Lescan et al 2018 https://doi.org/10.1016/j.omtn.2018.03.013

Exopharm Ltd (ASX:EX1)

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Founder and CEO

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Appendix

Exosomes can overcome current drug-delivery challenges

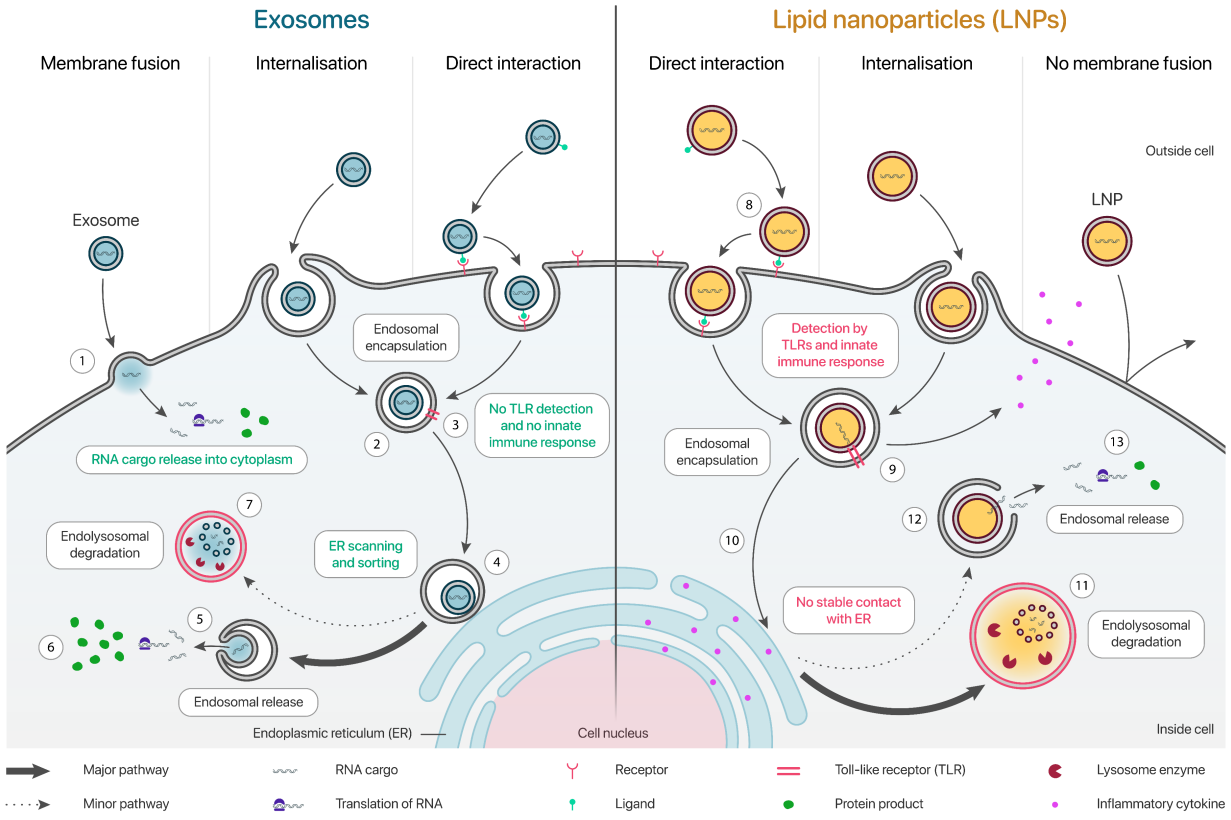
	Viral Delivery			Non-Viral Delivery	
Technology characteristic	AAVs	Herpesvirus (HSV)	Lentivirus (Lenti)	LNPs	Exosomes
Pre-existing immunity (none is good)	Yes	Yes	Yes	None	None
Suitable for repeat dosing without limit	No	No	No	Yes	Yes
Lacking toxicity of carrier	No	No	No	Potential for liver toxicity	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'

Exosomes compared with Lipid nanoparticles (LNPs)

1. Exosomes enter recipient cells via **three** main pathways. Unlike LNPs, exosomes are capable of fusing with the cell membrane to release RNA cargo directly into cell cytoplasm.
2. Some other exosomes become encapsulated by endosomes within the cell – and then undergo active transport inside the cell, trafficking to the endoplasmic reticulum (ER).
3. Endosomes containing exosomes form stable contact with the ER and undergo positive ER scanning and selection to induce endosomal release of exosome RNA cargo.
4. Since endosomal release of exosome-RNA occurs near the ER, the RNA is ideally located to become biologically active just like native RNA in the cells (e.g. protein binding to RNA, RNA post-translational modification, translation, DNA nuclear translocation).
5. Through this natural processing of exosomes, more of the delivered RNA becomes biologically active and the cell makes the therapeutic gene-product from the delivered RNA.
6. Exosomes do not trigger toll-like receptors (TLRs) and thereby avoid stimulating an innate immune response. Exosomes are seen as 'natural'.
7. Endosomes that fail the ER scanning step thereafter fuse with lysosomes, generating endolysosomes. Lysosomal enzymes break down and recycle contents of the endolysosome.



8. LNPs only enter the cell via **two** pathways and miss out on fusing with the cell membrane to release RNA cargo directly into cell cytoplasm.
9. LNPs become encapsulated by endosomes within the cell, which are actively trafficked to the ER. LNP-containing endosomes do not form stable contact with the ER, but rather remain unbound in the cytoplasm.
10. LNPs are not subject to positive ER scanning inside the cell the same way that exosomes are. Therefore, the majority of LNPs fail to escape their endosome, resulting in many endolysosomes forming and their LNPs being degraded and recycled (~70% of all LNPs that enter a cell are recycled, Patel et al. 2020).
11. Less than 2% of LNPs escape the endosome before degradation (Patel et al 2020), compared to up to 25% of exosomes escaping the endosome (Joshi et al 2020).
12. LNPs in endosomes are rapidly detected by TLRs, inducing an innate immune response. Synthetic LNPs are seen as non-natural.
13. LNP component materials also have toxicity issues.

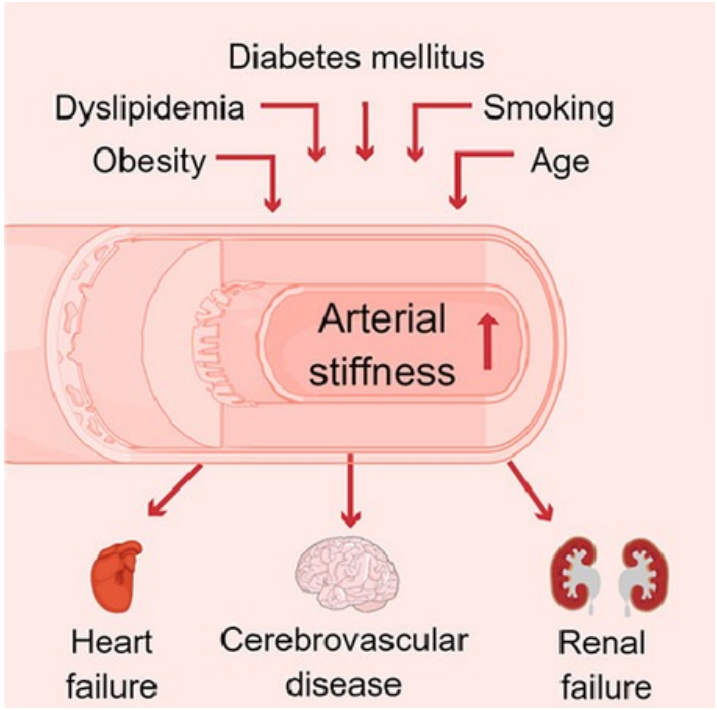
Whilst synthetic Lipid nanoparticles (LNPs) and exosomes share some features for delivery of therapeutic RNA - cells process LNPs and exosomes very differently – favouring exosomes for the delivery of therapeutic RNA as medicines

Major scarring remains a major rehabilitative challenge

- Major scarring, such as from severe burns, remains a major rehabilitative challenge with serious impact on the patients' quality of life (itch, pain, restricted movement) or even delayed reintegration into society
- Scar management ranges from massages, moisturising, wearing pressure garment, using silicone gels, sun protection, laser treatment, to surgery
- Scarring can take up to 2 years and sometimes beyond to mature so treatment may continue for this long
- The repeated treatments can increase costs significantly, especially for laser therapy and surgery
- Health insurance might not cover cost of aesthetic treatments
- There is a lack of effective scar prevention measures

Arterial stiffness represents an unmet therapeutic target to reduce the global burden of cardiovascular events and vascular aging

- Arterial stiffness increases with age, as well as in various pathological states, including obesity, diabetes mellitus, smoking, and dyslipidaemia, and it has important consequences for cardiovascular health
- Current treatments aim to reduce risk factors (comorbidities control)
  - ❖ Antihypertensive medications (e.g. ARBs)
  - ❖ Lipid-lowering medications
  - ❖ Anti-diabetic medications
  - ❖ Body-weight loss
- Although providing some usefulness, these agents have not solved the problem, and there remains a serious lack of effective therapies that directly target the structural abnormalities and changes in vascular signalling that underlie stiffening
- Arterial stiffness is an attractive therapeutic target in terms of vascular aging



www.journal-of-cardiology.com/article/S0914-5087(21)00194-5/fulltext

Emphysema/COPD is a major global health problem

- Emphysema is a lung condition that causes shortness of breath due to reduced surface area of the lungs
- Emphysema and chronic bronchitis are two conditions that make up chronic obstructive pulmonary disease (COPD)
- An estimated 3.1 million Americans have been diagnosed with emphysema and 11.2 million U.S. adults have been estimated to have COPD.
- Tobacco use is the number one factor in the development and progression of COPD, exposure to air pollutants, genetic factors, and respiratory infections can also play a role in the disease
- COPD is the third leading cause of death, after ischaemic heart disease and stroke and before cancers
- The goal of therapy for emphysema is to provide relief of symptoms, prevent complications and slow the progression of the disease
  - ❖ Bronchodilator Medications
  - ❖ Steroids
  - ❖ Antibiotics
  - ❖ Oxygen therapy