ASX ANNOUNCEMENT

Science Webinar – Overcoming the Nucleic Acid Delivery Challenge

26 August 2021, Melbourne, Australia: Exosome medicine company Exopharm Limited (ASX: EX1) is pleased to advise that it will host a webinar on Thursday, 26 August 2021 at 10:30AM AEST. It is open to all, with no advanced registration required.

The webinar will provide insights into the emerging class of therapeutics known as nucleic acid-based medicines and will explore technologies that are being developed to overcome the challenge of delivering these exciting new therapies within the body.

Pharmaceutical industry veteran Dr Jennifer King and nanomedicine expert Dr Anna Cifuentes Rius will present the attached slide deck. Following their presentations, they will respond to questions in a Q&A session hosted by Dr Chris Baldwin, Deputy CEO and Chief Commercial Officer at Exopharm. Dr Ian Dixon, CEO at Exopharm, will join for a business Q&A section following the main presentation.

To join the webinar, simply copy and paste the following link into your internet browser: https://exo.ph/WebinarAugust2021.

By the Board - this announcement has been authorised for release by the board.

Company and Media Enquiries:

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ABOUT EXOPHARM

Exopharm (ASX:EX1) is a clinical-stage biopharmaceutical company using exosomes to deliver a new class of transformative medicines and generate revenue from multiple partnership deals.

Exosomes are seen by the Biopharma industry as a highly differentiated platform with the potential to enhance tissue delivery for a variety of payloads like mRNA and proteins – part of the global market for drug delivery systems which is growing at a compound annual growth rate (CAGR) of 5% and valued at around US$170 billion in 2021.

For some medicines, exosomes are an alternative and superior means for delivery inside the body, alongside technologies such as lipid nanoparticles (LNP), cell penetrating peptides, viral vectors and liposomes.

Exopharm's LEAP technology solves the challenge of purifying clinical-grade exosomes at large scale and low cost.

Exopharm also has two exclusive proprietary technologies that allow advanced customisation of exosomes – the LOAD technology improves loading of nucleic medicines into exosomes and the EVPS technology allows exosomes to be directed towards selected cell types.

Exopharm uses variations and combinations of LOAD and EVPS to enable its Biopharma partners to improve delivery of their drug candidates and help them design and test new exosome medicines aimed at treating a wide scope of medical problems including neurological disease, infectious disease, cancer, and fibrosis.

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.

exopharm

Webinar:

Overcoming the Delivery Challenge for Nucleic Acid Drugs

26 August 2021
10:30am AEST

Presenters

Dr Jennifer King
King BioConsulting

RNA Medicines and Delivery: The Importance for the Future of Medicine

Dr Anna Cifuentes-Rius
Monash University

Delivery by LNPs and Exosomes: When They Are Useful and Why

Novel and Emerging Pharmaceutical Therapeutics

August 2021

Jennifer King, PhD, MBA

Novel Nucleic Acid Based Therapies Are Making the News and Earning Revenue

mRNA Vaccines

AAV Gene Therapies

zolgensma®
(onasemnogene abeparvovec-xioi)

RNA-Based Therapies

onpattro®
(patisiran) lipid complex injection 10 mg/5 mL

EXONDYS 51
(eteplirsen) Injection

waylivra®
(volanesorsen) injection 285 mg/1.5 mL

Tegsedi®
(inotersen) injection 284 mg/1.5 mL

GIVLAARI®
(givosiran) injection for subcutaneous use 189 mg/mL

AMONDYS 45
(casimersen) Injection

VYONDYS 53
(golodirsen) Injection

KYNAMRO®
(mipomersen sodium) injection 200mg/ml

OXLUMO™
(lumasiran) for injection 94.5 mg/0.5 mL

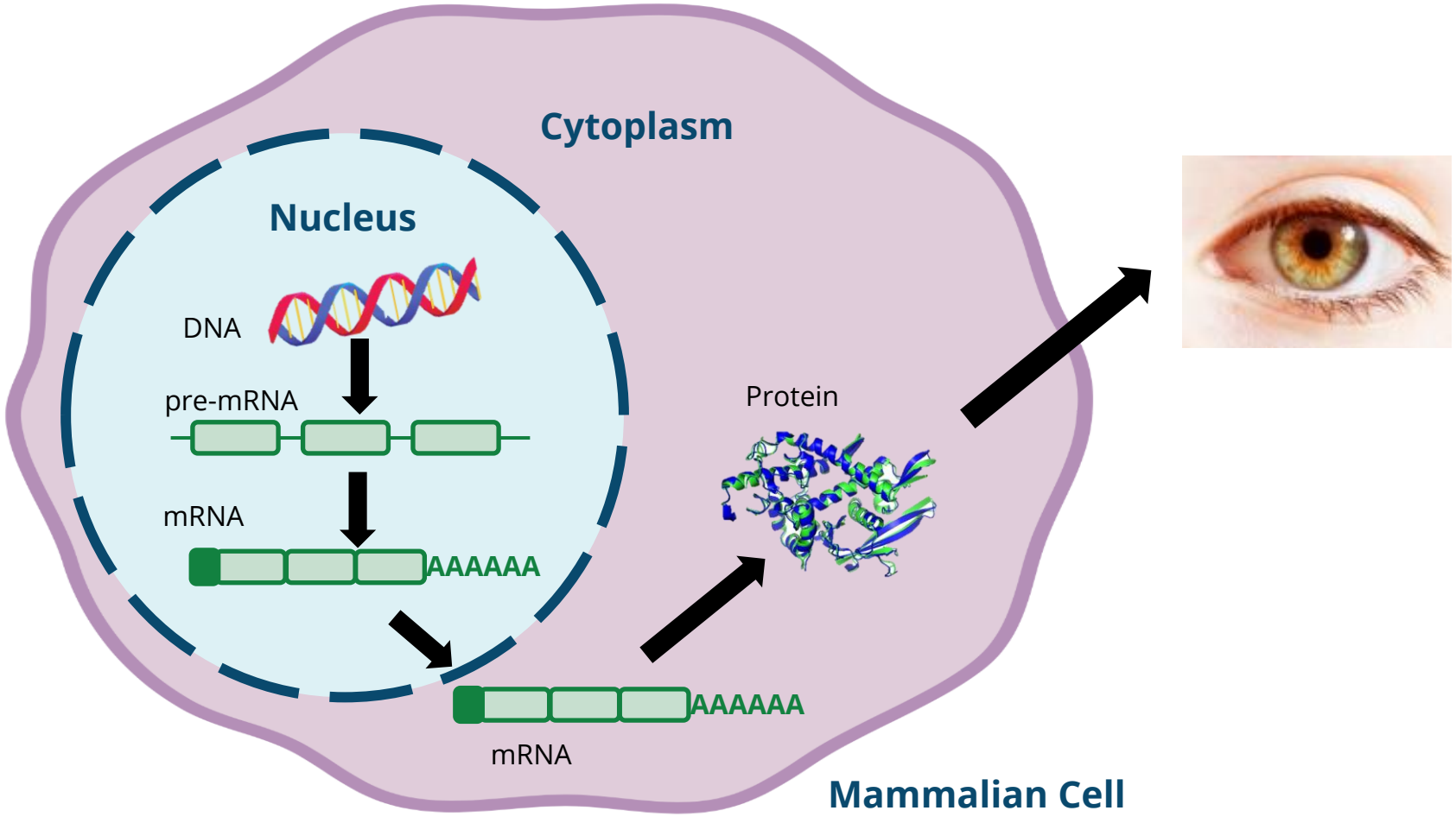
Viltepso®
(viltolarsen) injection

SPINRAZA®
(nusinersen) injection 12 mg/5 mL

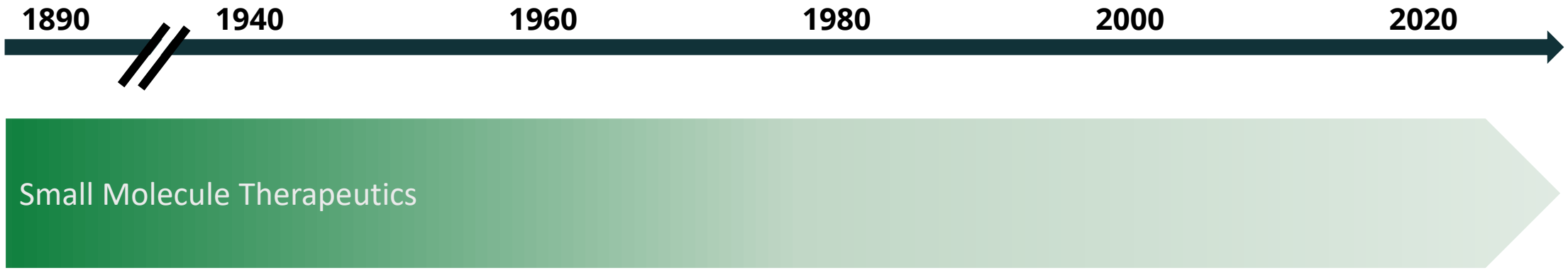
Logos sourced from company websites.

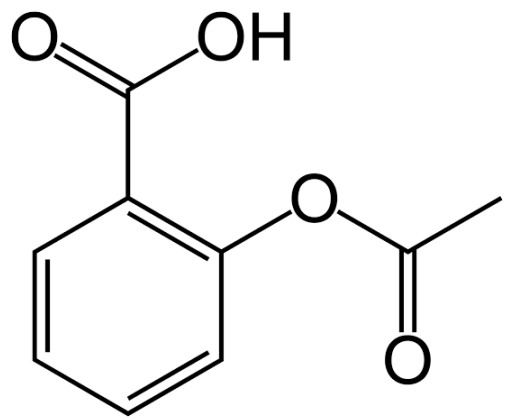
The Central Dogma of Molecular Biology

DNA → RNA → Protein → Trait



Evolution of Pharmaceutical Therapies: Chemistry to Gene Therapy

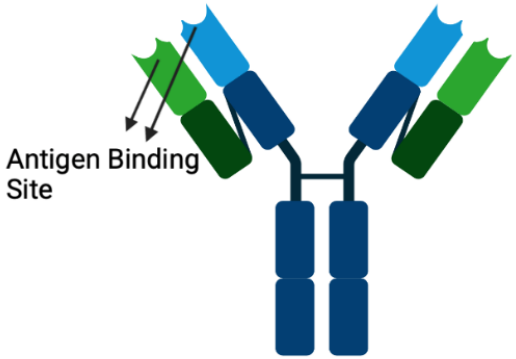


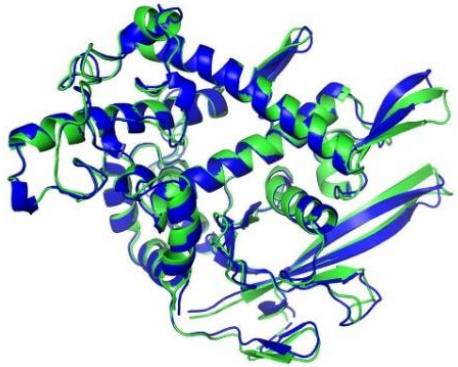


Evolution of Pharmaceutical Therapies: Chemistry to Gene Therapy

1890 1940 1960 1980 2000 2020

Small Molecule Therapeutics

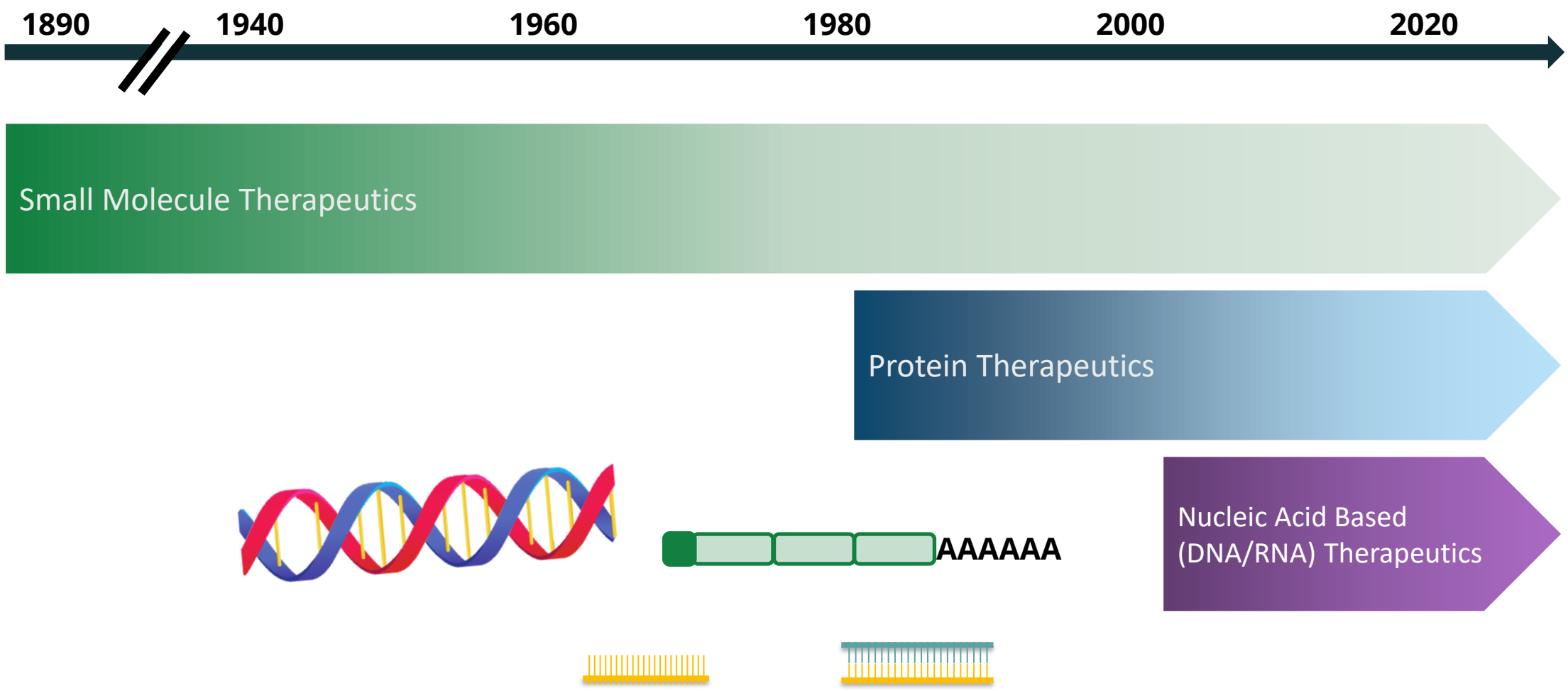




Protein Therapeutics

Created in BioRender.com

Evolution of Pharmaceutical Therapies: Chemistry to Gene Therapy



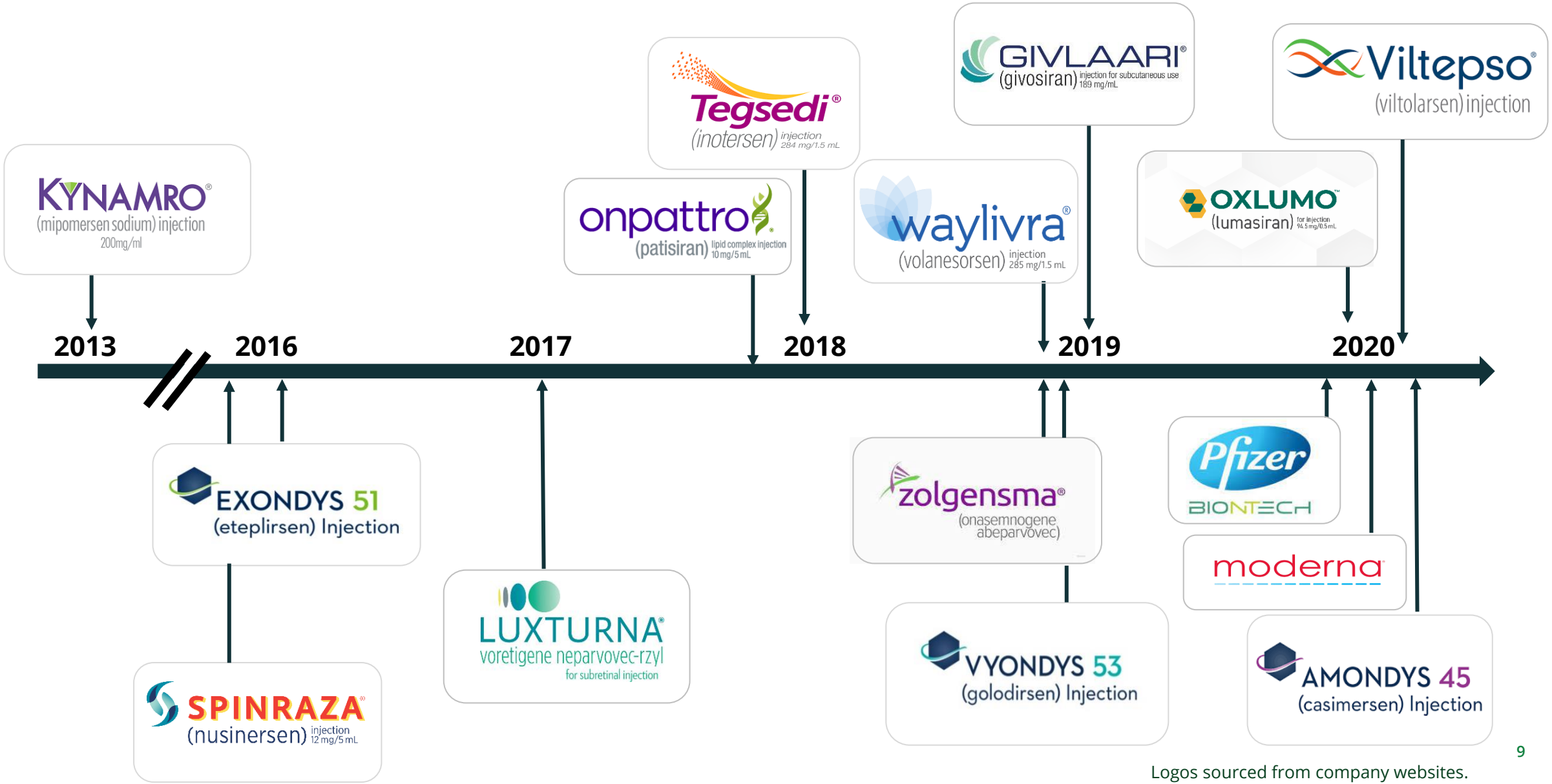
Created in BioRender.com

The Promise of Nucleic Acid Therapies

- **Gene therapy is a potentially curative therapy for Genetic Disease**

- **“Undruggable” targets can be addressed using RNA**
  - Current estimates are only about 20% of all proteins can be targeted by small molecules

Regulatory Approvals of Nucleic Acid Therapies Have Accelerated in the Last 5 Years



Logos sourced from company websites.

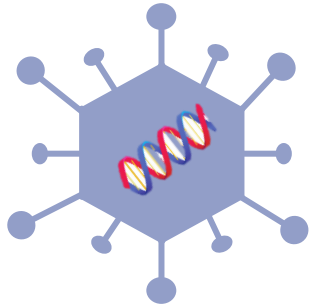
Top 5 Grossing Pharmaceuticals in 2020

Logos sourced from company websites.

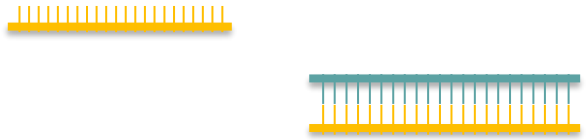
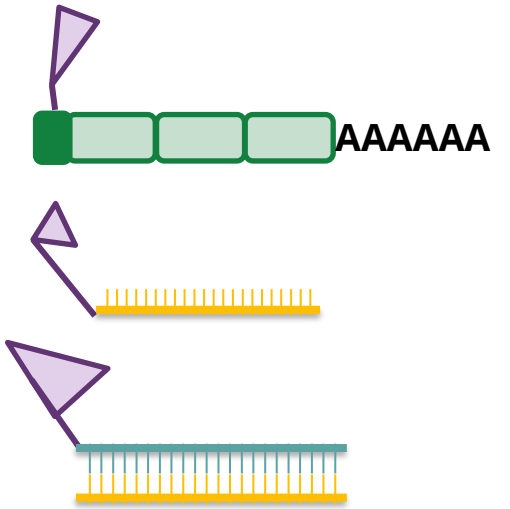
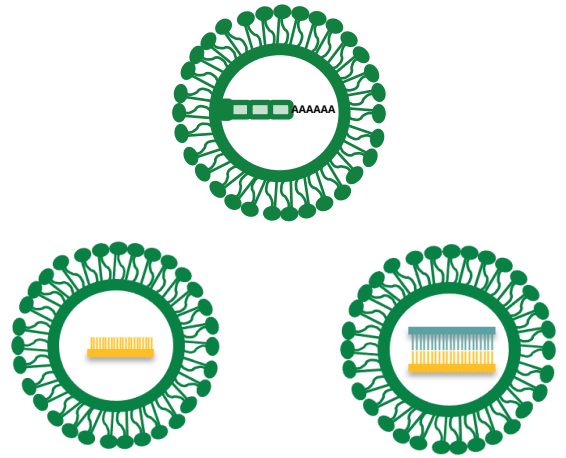
Delivery is a Major Challenge of Nucleic Acid Therapeutics

DNA Delivery

Viral Vector



RNA Delivery

No Vehicle	Directly Conjugated	Lipid Nanoparticle
		

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Delivery is a Major Challenge of Nucleic Acid Therapeutics

DNA Delivery

Viral Vector
LUXTURNA® voretigene neparvovec-rzyl for subretinal injection zolgensma® (onasemnogene abeparvovec)

RNA Delivery

No Vehicle	Directly Conjugated	Lipid Nanoparticle
KYNAMRO® (mipomersen sodium) injection 200mg/ml EXONDYS 51 (eteplirsen) Injection SPINRAZA® (nusinersen) injection 12 mg/5 mL VYONDYS 53 (golodirsen) Injection Viltepso® (viltolarsen) injection AMONDYS 45 (casimersen) Injection	GIVLAARI® (givosiran) injection for subcutaneous use 189 mg/mL OXLUMO™ (lumasiran) for injection 94.5 mg/0.5 mL	onpattro® (patisiran) lipid complex injection 10 mg/5 mL Pfizer BIONTECH moderna

Logos sourced from company websites.

MONASH University

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PHARMACEUTICAL
SCIENCES

Delivery by lipid nanoparticles and exosomes: when they are useful and why

Dr Anna Cifuentes-Rius

Medicines Manufacturing Innovation Centre
Monash Institute of Pharmaceutical Sciences

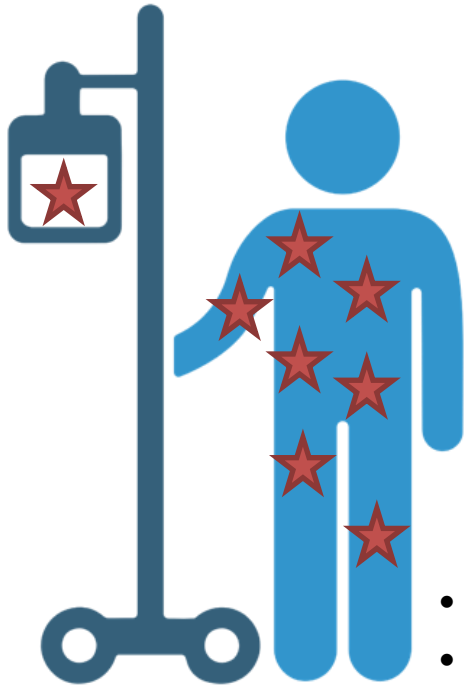
GROUP OF EIGHT AUSTRALIA

@AnnaCifuR

A fascinating journey

Barriers to efficient and safe delivery of therapeutics

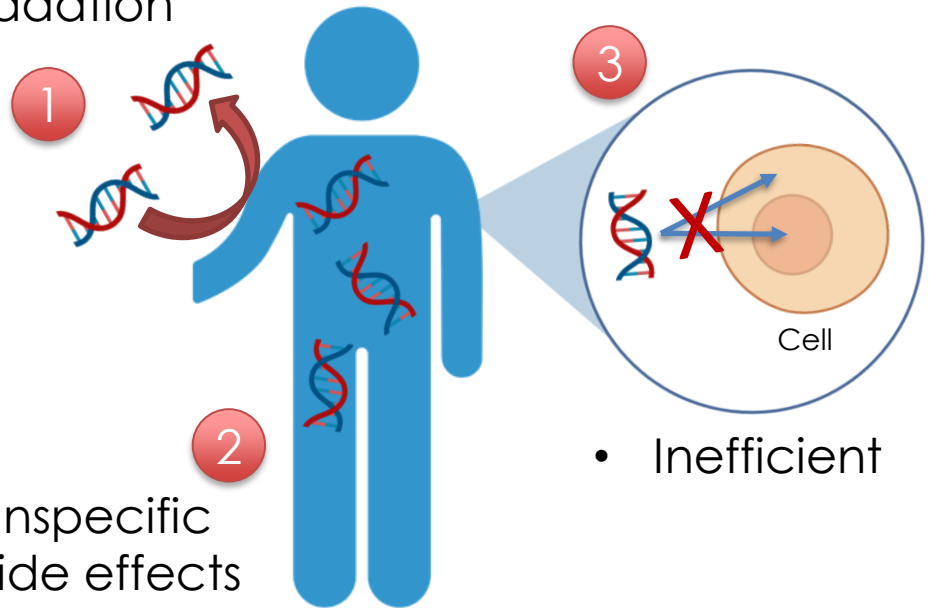
Traditional therapy
(e.g. chemotherapy)



- Unspecific
- Severe adverse effects

Gene therapy – using nucleic acids (RNA, DNA)

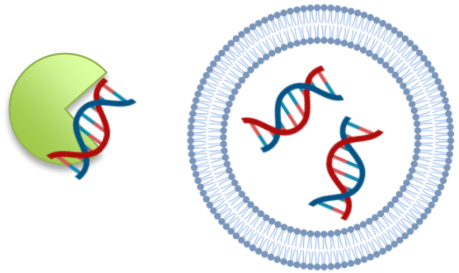
- Fast clearance
- Degradation



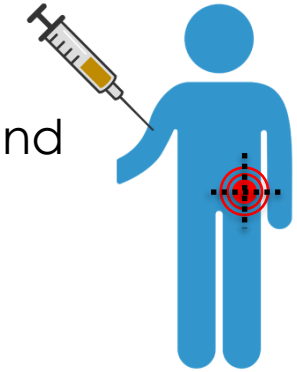
- Unspecific
- Side effects
- Inefficient

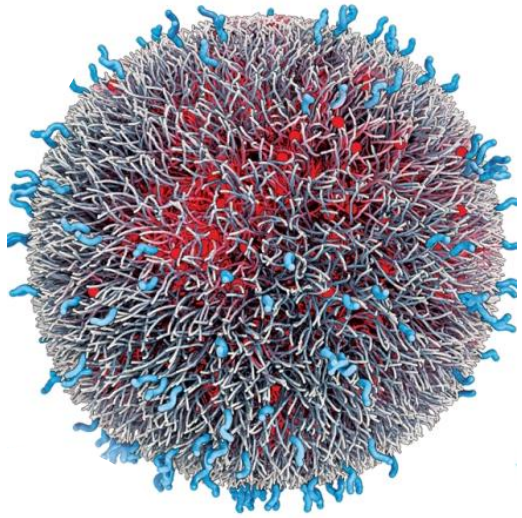
Overcoming barriers – the birth of nanomedicine

1 Protect the cargo



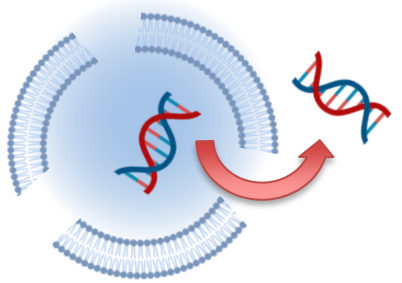
3 Minimise adverse effects and target specific organs



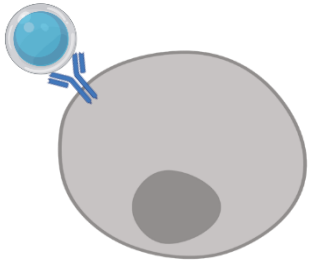


Nanomedicine

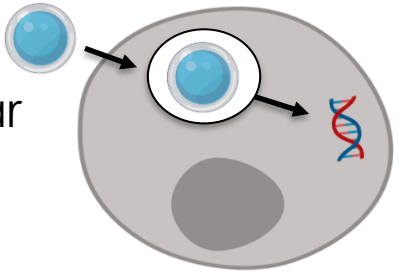
2 Control release of cargo



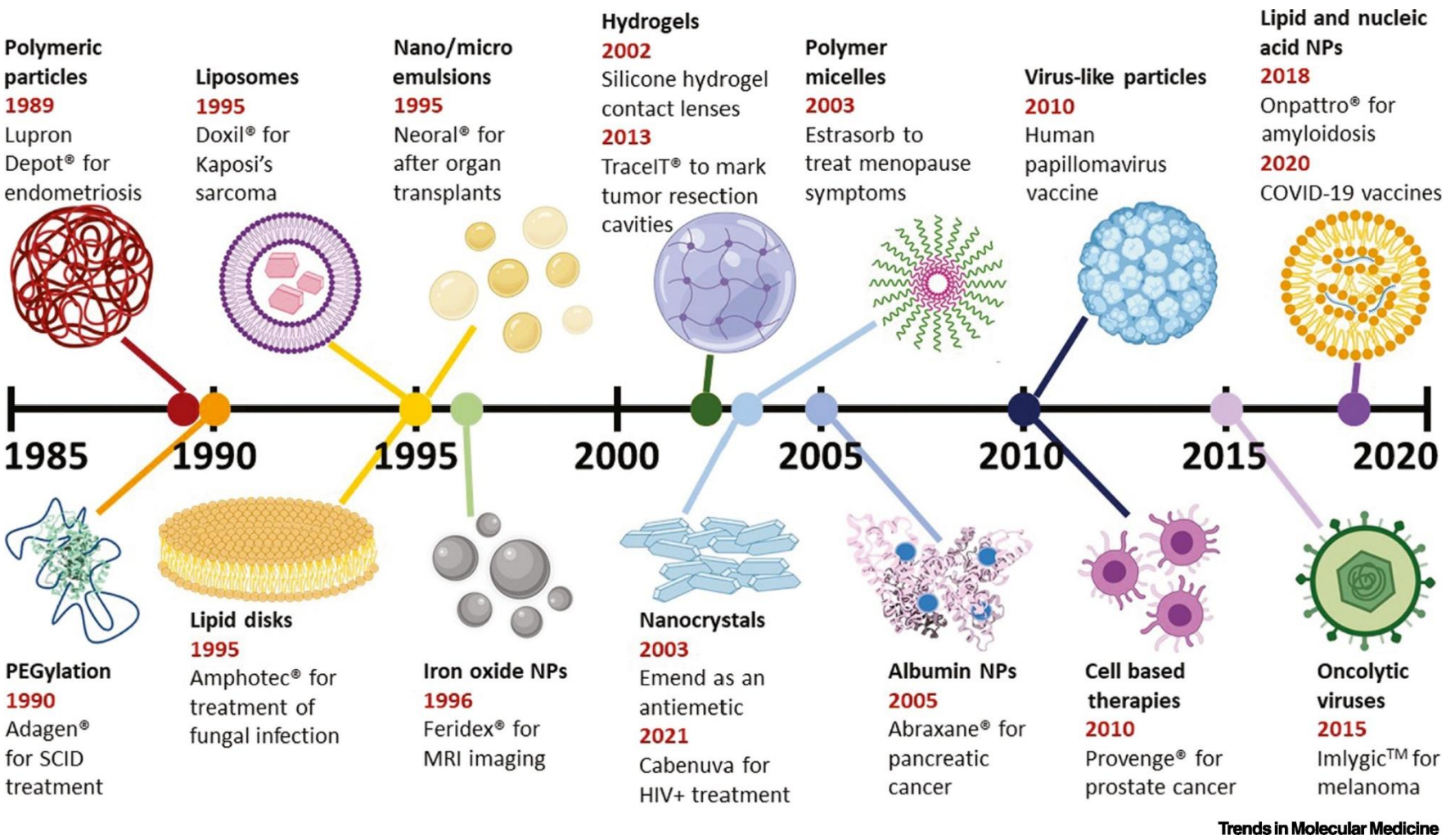
4 Target specific cell populations



5 Optimise intracellular delivery

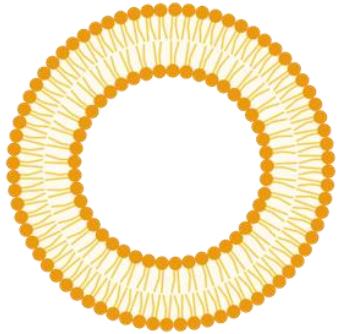


Timeline of FDA-approved nano-enabled therapeutics

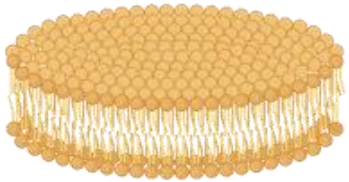


Batty *et al.* Trends in Molecular Medicine 2021

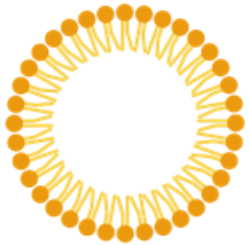
Lipid-based nanoparticles



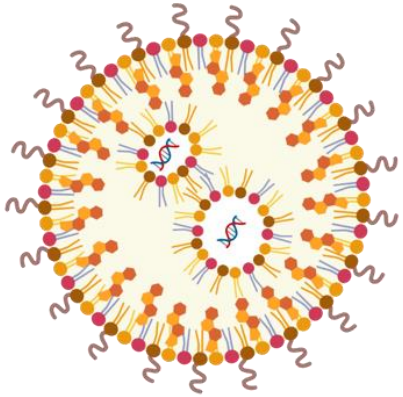
Liposomes



Lipid disks



Lipid micelles



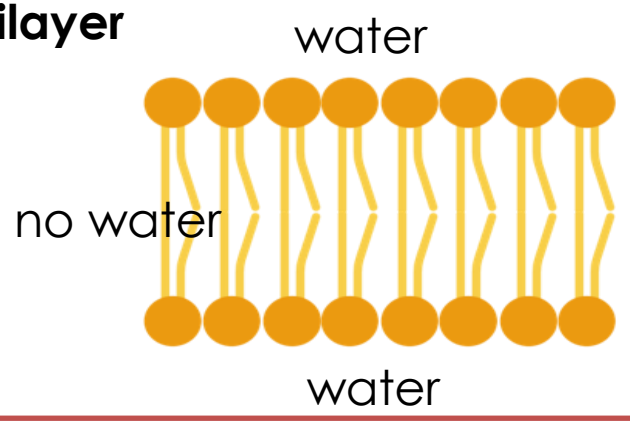
Solid lipid nanoparticles (LNPs)

Phospholipid

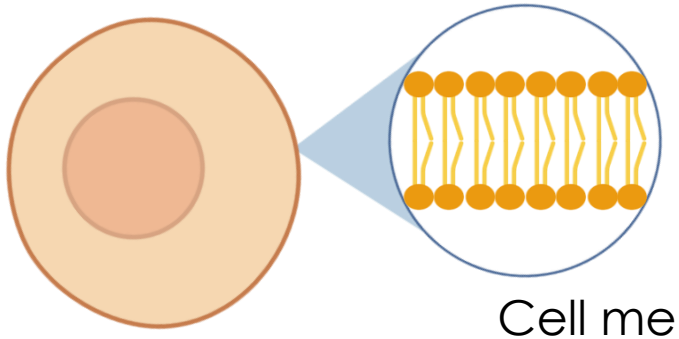
Head

Tail

Lipid bilayer

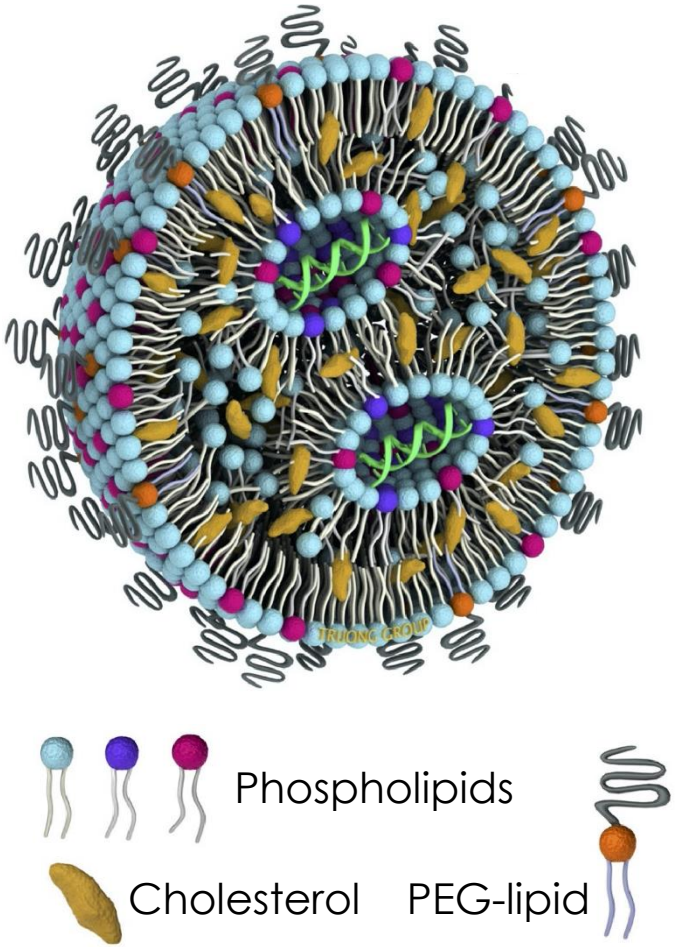


Present in all our cells



Cell membrane

Lipid nanoparticles (LNPs)



Key characteristics:

- The most advanced non-viral delivery system
- High nucleic acid encapsulation and transfection efficiency
- Enhanced penetration into tissues
- Low cytotoxicity and immunogenicity compared to viral particles

Challenges:

- Fine balance of lipid ratios for a specific property (e.g. cargo encapsulation and release *vs.* stability, loading siRNA *vs.* mRNA)
- Large scale manufacturing

Pilkington *et al.* Acta Biomaterialia 2021

Lipid nanoparticles: when successful and why

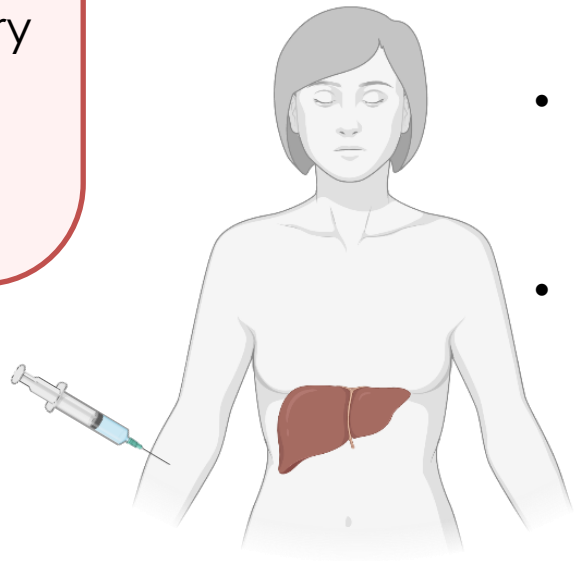
COVID Vaccines – mRNA delivery

- Localised delivery into the muscle tissue (intramuscular administration)
- Immune activation

Limitations:

- Difficulty in targeting other organs
- Low encapsulation and cytosol delivery (2 doses, long infusion times)
- Immune responses

Onpattro® – siRNA delivery



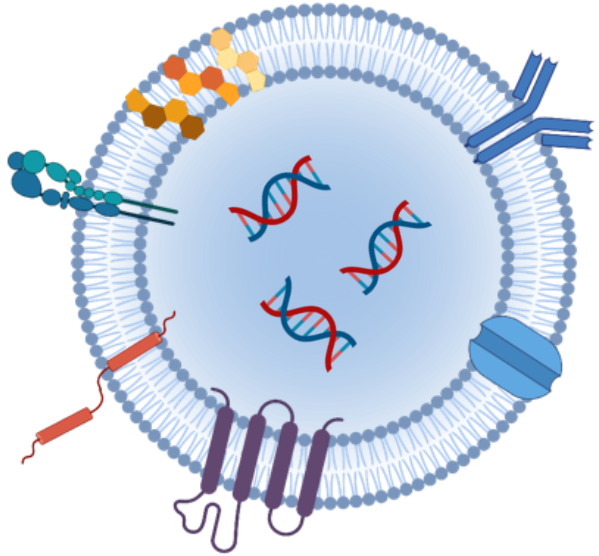
- Blood infusion (intravenous administration)
- Liver accumulation (hepatocytes)

Pilkington *et al.* Acta Biomaterialia 2021
Huang *et al*. Current Opinion in Colloid & Interface Science 2021
Aknic *et al.* Nature Nanotechnology 2019

Exosomes: emergent nanomedicines

Key characteristics:

- Endogenous nanoparticles from biological origin
- Biocompatible
- Intrinsically expressing proteins on the surface
- Naturally carrying nucleic acids



Exosome

How exosomes can overcome some of LNP limitations?

- Increased cargo encapsulation
- Enhanced cytosol delivery
- Ability to target specific organs
- Low immunogenicity

Reshke *et al.* Nature Biomedical Engineering 2020
Wiklander *et al*. Science Translational Medicine 2019
Kamerkar, et al. Nature 2017

Question Time

exopharm