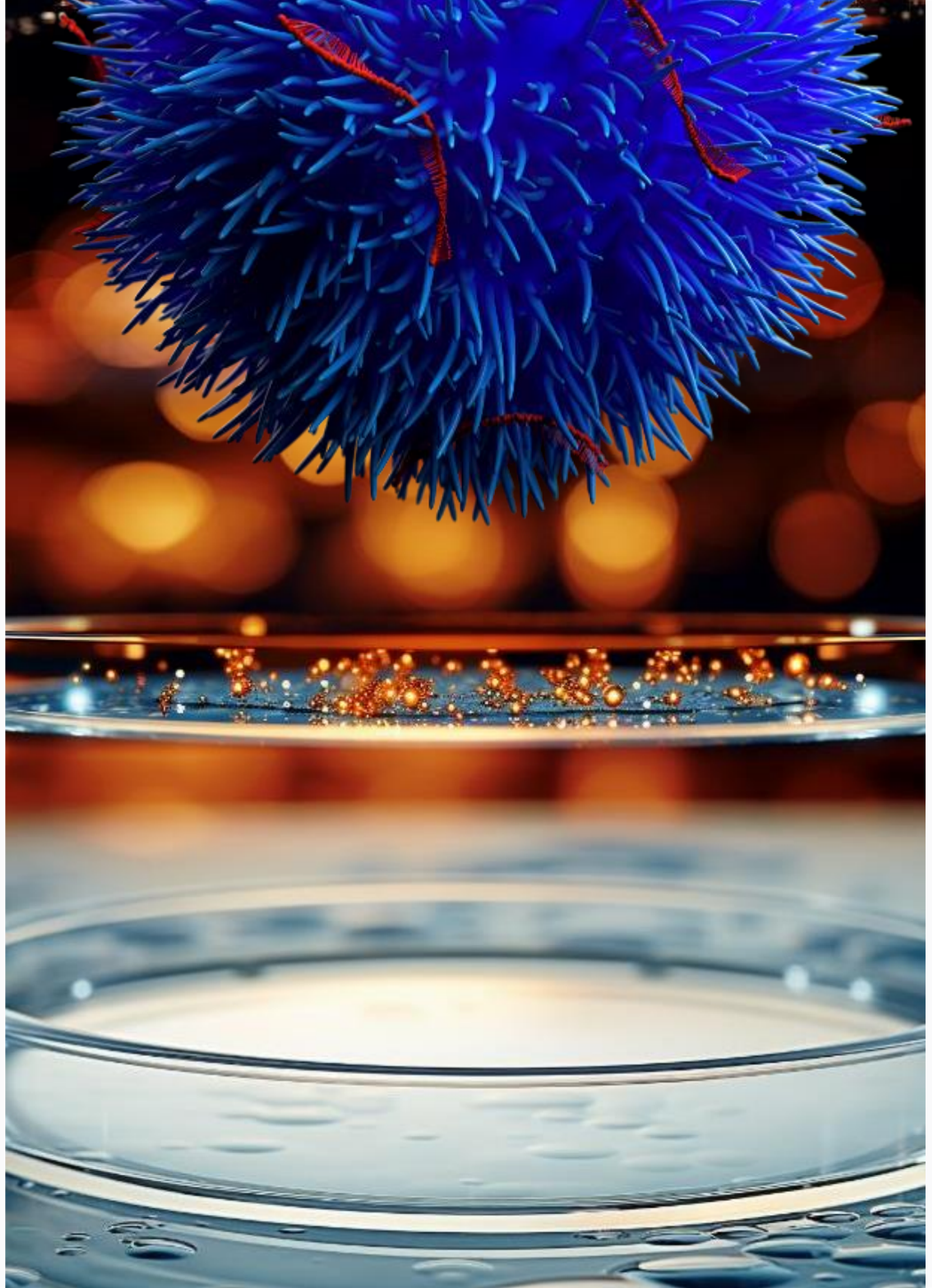
N4 PHARMA

Corporate presentation

October 2024



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Introduction to N4 Pharma plc

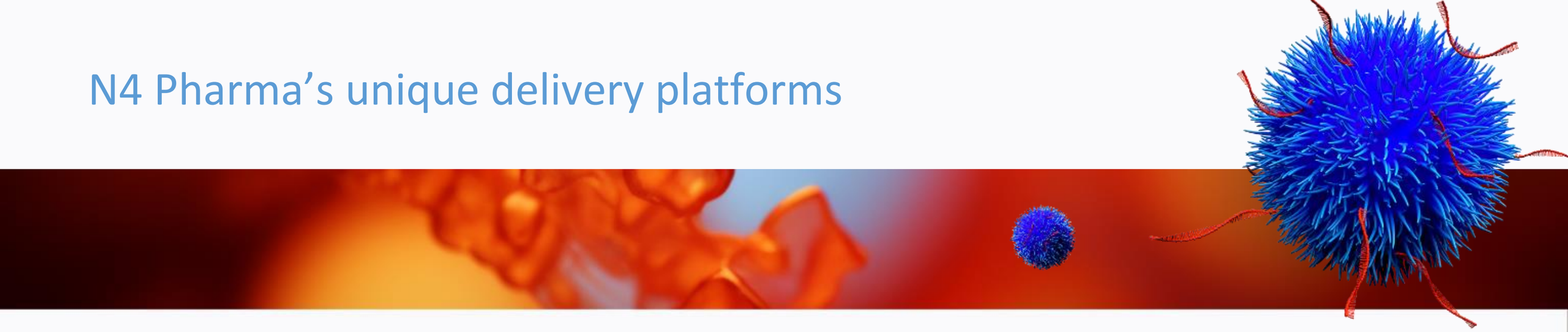
- Exciting investment opportunity in highly undervalued Biotech company
  - Potential 20-50 x multiples once milestones hit, exit via trade sale or US specialty investment
- Established in 2014, N4 Pharma saw an unmet need for targeted and effective delivery of nucleic acids as therapeutics
  - Next big biotech development but larger than traditional molecules so need delivery systems
  - Borne out by Covid 19 vaccines
  - Many existing systems cause unwanted side effects and target the liver
- Nucleic acid therapeutics market $5bn in 2023 growing to over $15bn by 2033
- N4 has two proprietary delivery systems with strong pre-clinical data suitable for scale-up and clinical development
- N4 is able to leverage its proprietary delivery platforms to create superior nucleic acid therapies

N4 PHARMA

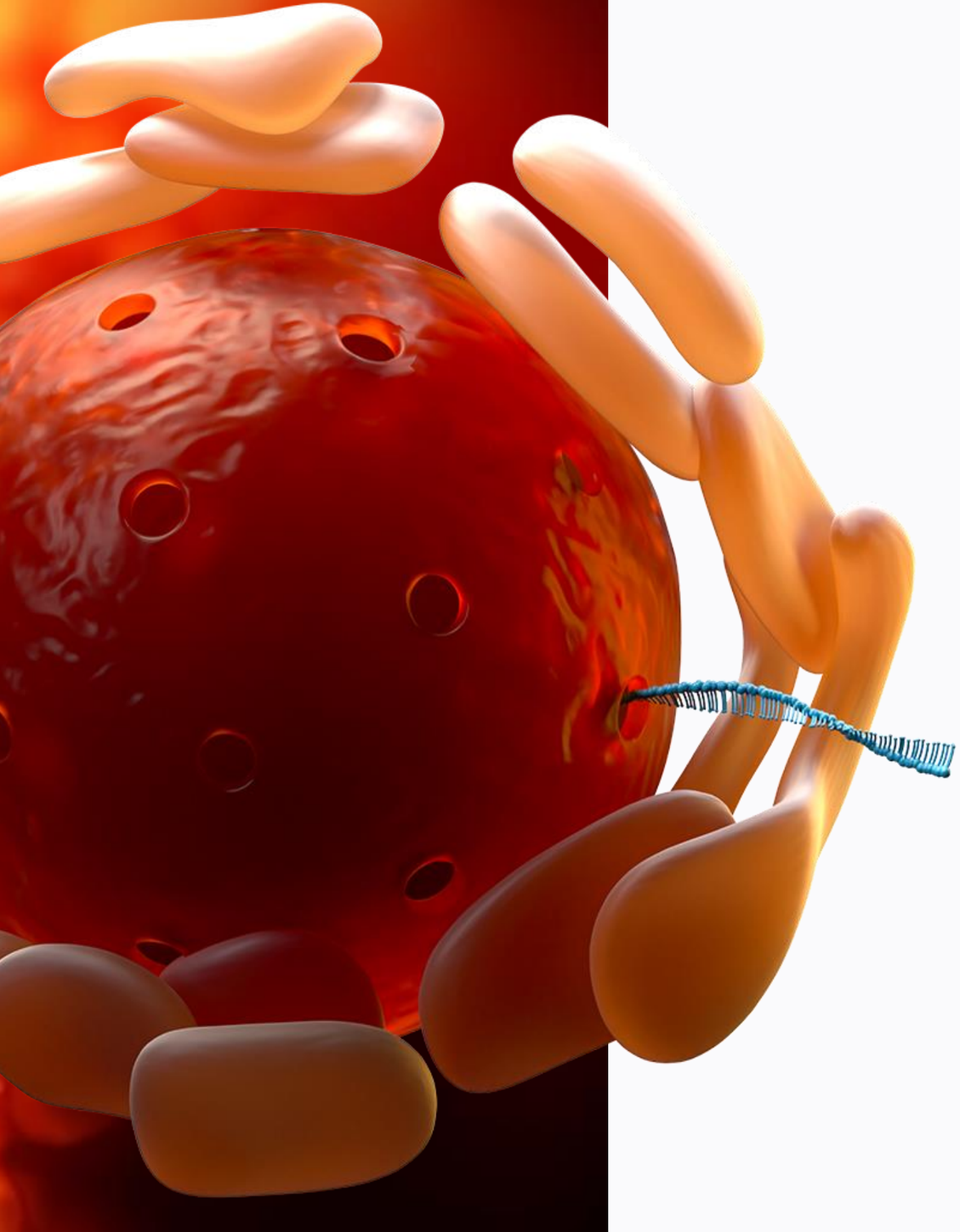
Introduction to N4 Pharma plc

- Preclinical stage biotech company with two lead programmes designed to address unmet clinical needs
  - N4 101 is an orally delivered inflammation inhibitor for Irritable Bowel Disease (IBD) using Nuvec®
  - ECP 105 is for prevention of scarring post glaucoma surgery, using LipTide™
- Programmes take advantage of N4 Pharma's two patented nanoparticle delivery systems (Nuvec® and LipTide™)
- Both programmes in pre-clinical development with anticipated CTA/IND filings in 2026
- License to partner to take first product into phase 1 clinical
- Funds then to take 2nd and subsequent products into phase 1 ourselves
- Phase 1 license allows multiple future product developments

N4 Pharma’s unique delivery platforms



Key Benefits	Nuvec®	LipTide™	Viral vectors	Lipids
Interchangeable payload	✓	✓	✓	✓
Interchangeable targeting	✓	✓		
Cytotoxic			✓	✓
Multiple Payloads	✓			
Non-viral	✓	✓		✓
IP-protected	✓	Specific lipids		Legal fights
Validated in early preclinical studies	✓	✓	Approved	Approved
Oral delivery	✓			



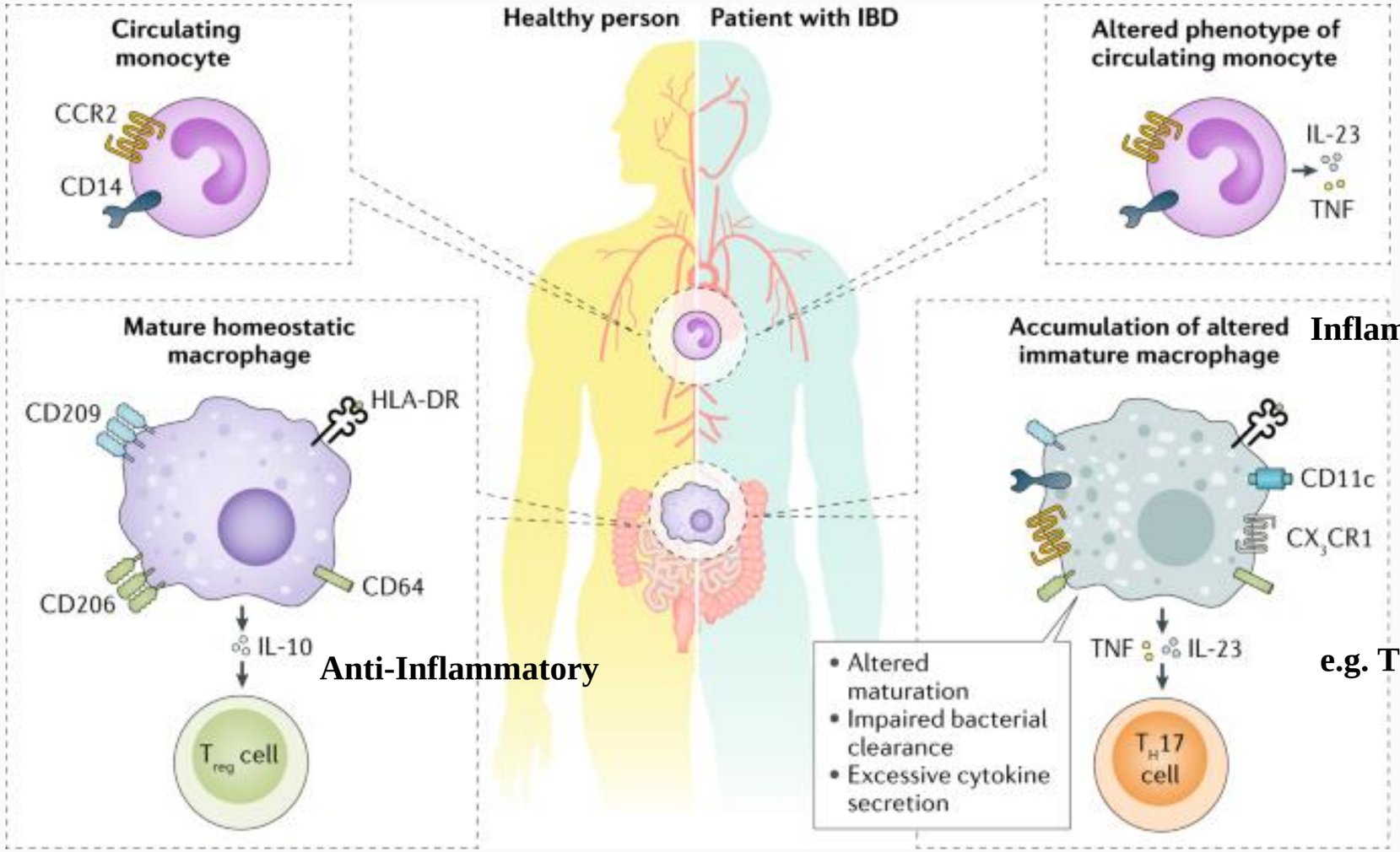
N4 101: Oral IBD treatment

Oral RNA treatment for IBD to replace regular injections

- Oral capsule containing dual loaded nucleic acids delivered to the GI tract
- Uses Nuvec® proprietary non-lipid, non-viral silica nanoparticle
- Local delivery in gut and targeted uptake by macrophages involved in inflammation

Dual action simultaneously reduces excessive TNF-alpha production and promotes the body's own anti-inflammatory response

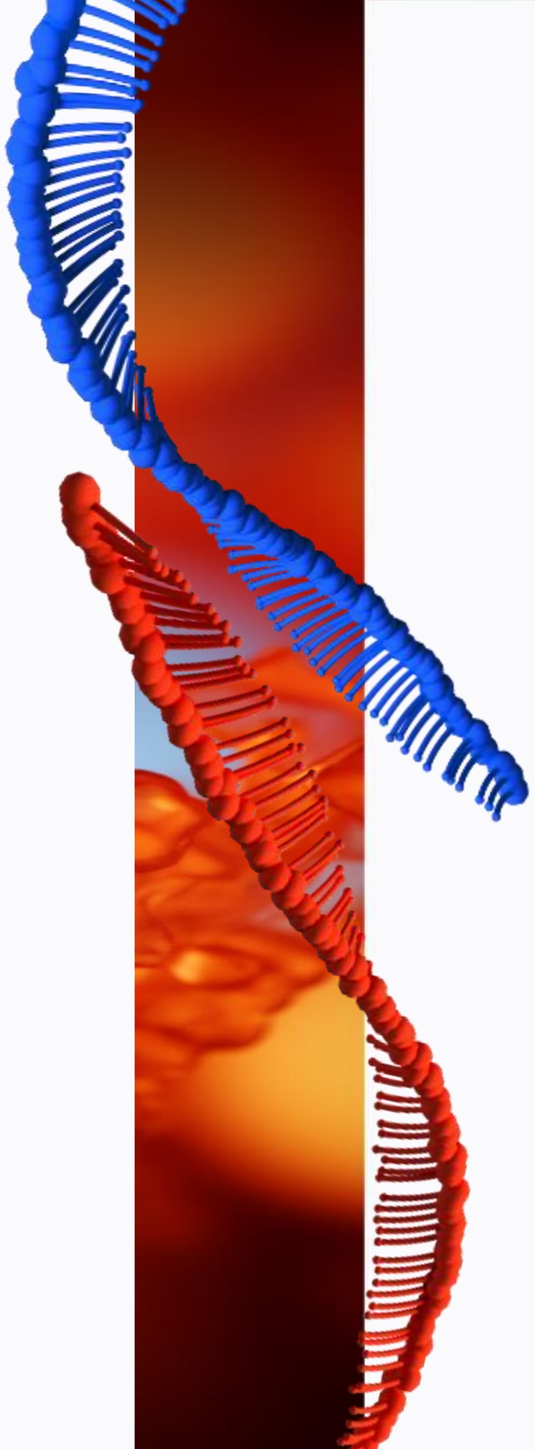
IBD patients have altered macrophage cells



Anti-Inflammatory

Inflammatory

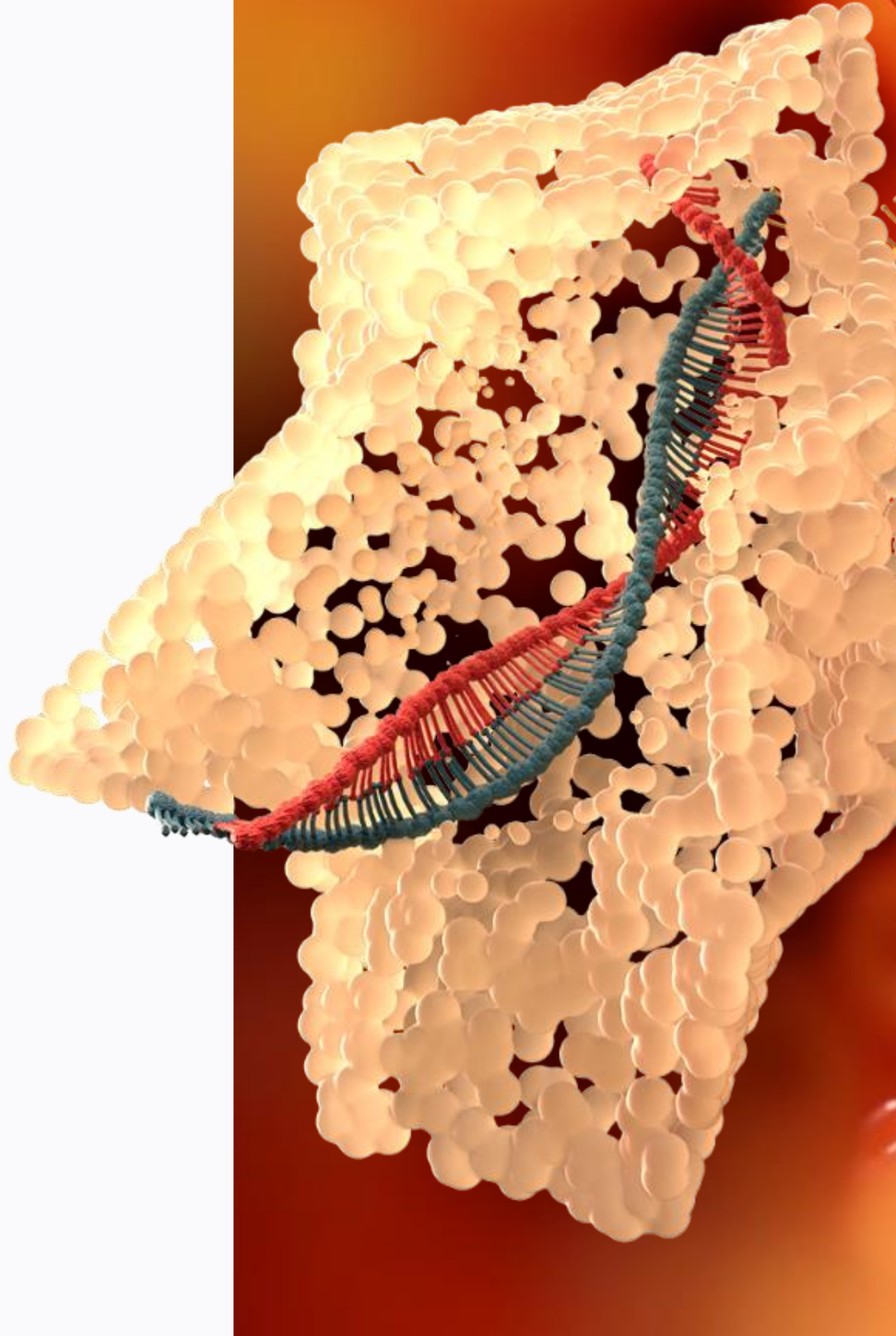
e.g. TNF-α



Oral IBD treatment market opportunity

Current IBD treatments

- Current therapies for IBD TNF-alpha inhibition effective but come with issues
  - tolerance, non responders and immune sensitivity
- Antibody therapeutics, known as TNF-alpha inhibitors, offer best treatment today and represent 78% of the market in 2022.
  - Side effects and regular inconvenient injections result in reduced patient compliance.
- Treatment audience size: 5 million sufferers globally of the two main types of IBD (Crohn's disease and ulcerative colitis).
- IBD treatment market globally is worth $20.4bn in 2023 and expected to grow by a CAGR of 3.9% to over $27.6nn by 2030[1].



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Oral IBD treatment market opportunity

- Trend is towards oral treatment – Janus Kinase inhibitors (JAKs)
- Lack of tissue selectivity causes JAKs to have toxicity issues in other organs
- Potential market size: By 2030 the oral segment is expected to be worth $7bn[1]
- N4 101 oral TNF-alpha inhibitor will replace inconvenient injections with systemic effects and replace need for oral kinase inhibitors

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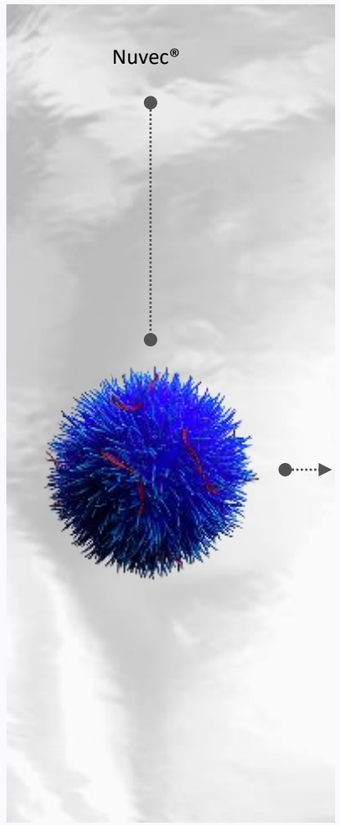
N4 101 Mechanism of Action | siRNA knockdown

1



Nuvec® protects siRNA until it attaches to the target cell.

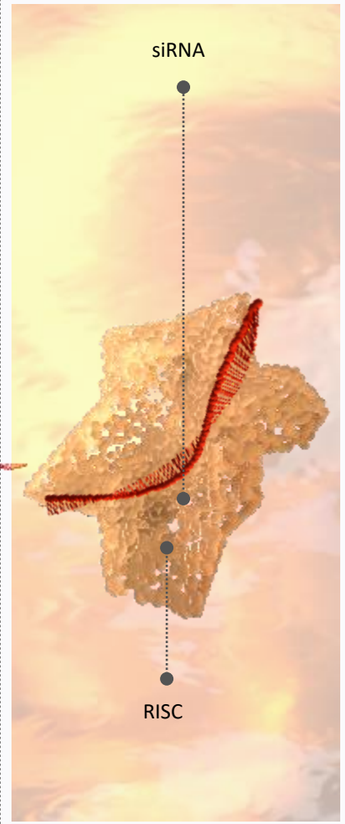
2

Cellular uptake is general and dynamic dependent endocytosis.

3

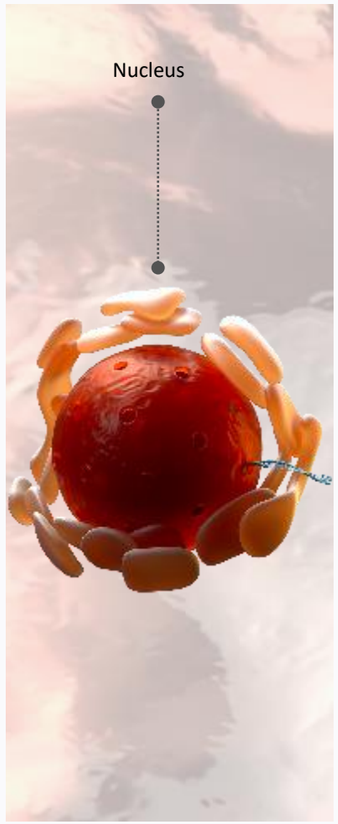
Endosome escape, siRNA is Released into the cytoplasm facilitated by PEI loaded on Nuvec®.

4



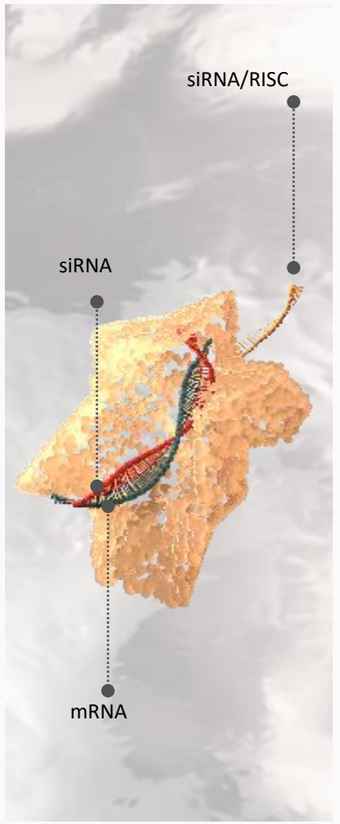
siRNA released into the cytoplasm and binds to RNA-induced silencing complex (RISC).

5



In the nucleus, DNA is transcribed to RNA and then mRNA to be transported for
Further processing into the cytoplasm.

6



One siRNA/RISC complex binds to a specific mRNA and
Leads to degradation - no translation into functional protein.

7

Another siRNA/RISC complex Binds to yet another specific mRNA and leads to degradation - no translation into functional protein.

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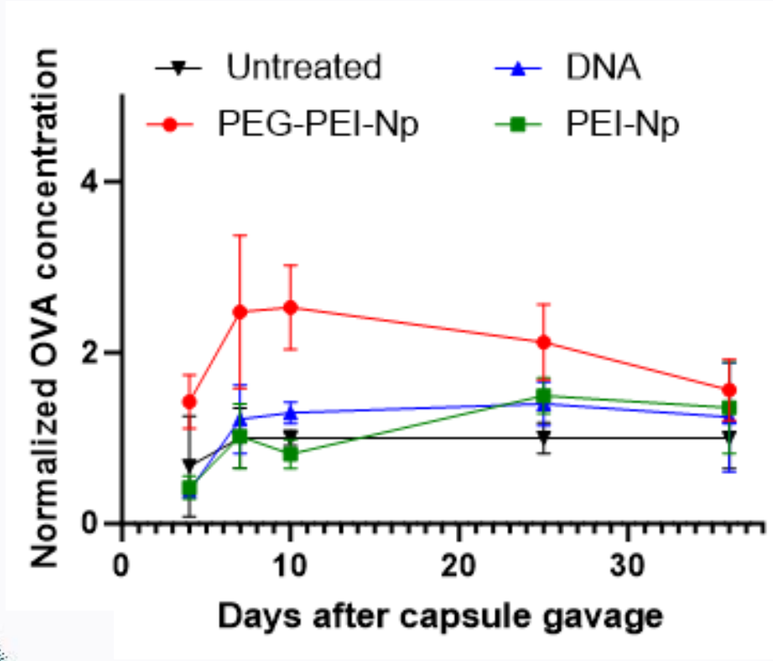
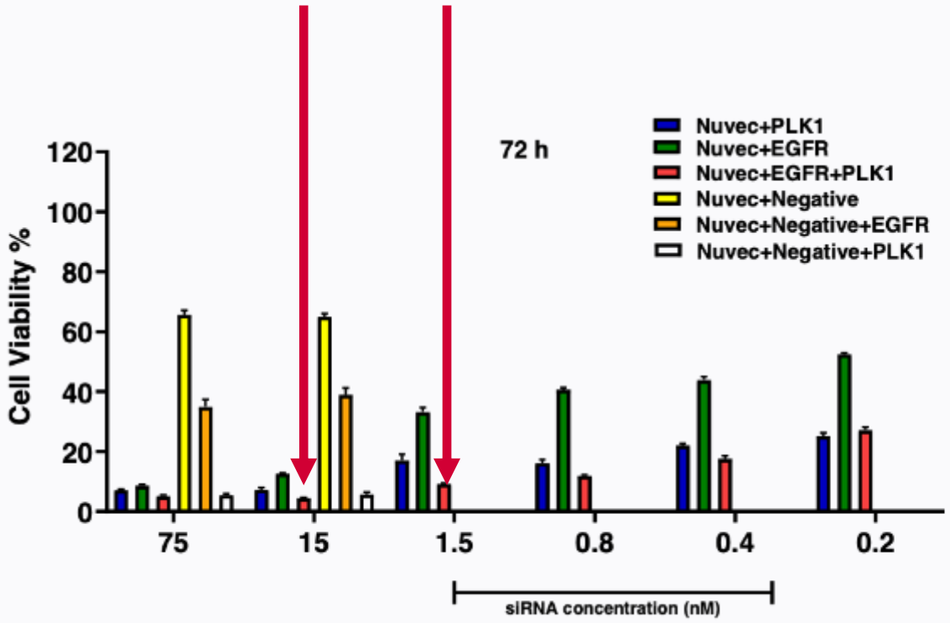
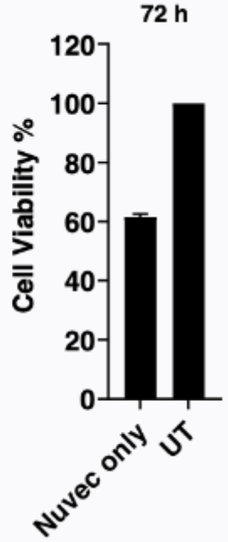
N4 101 current progress

Demonstrated with DNA localised delivery in the gut

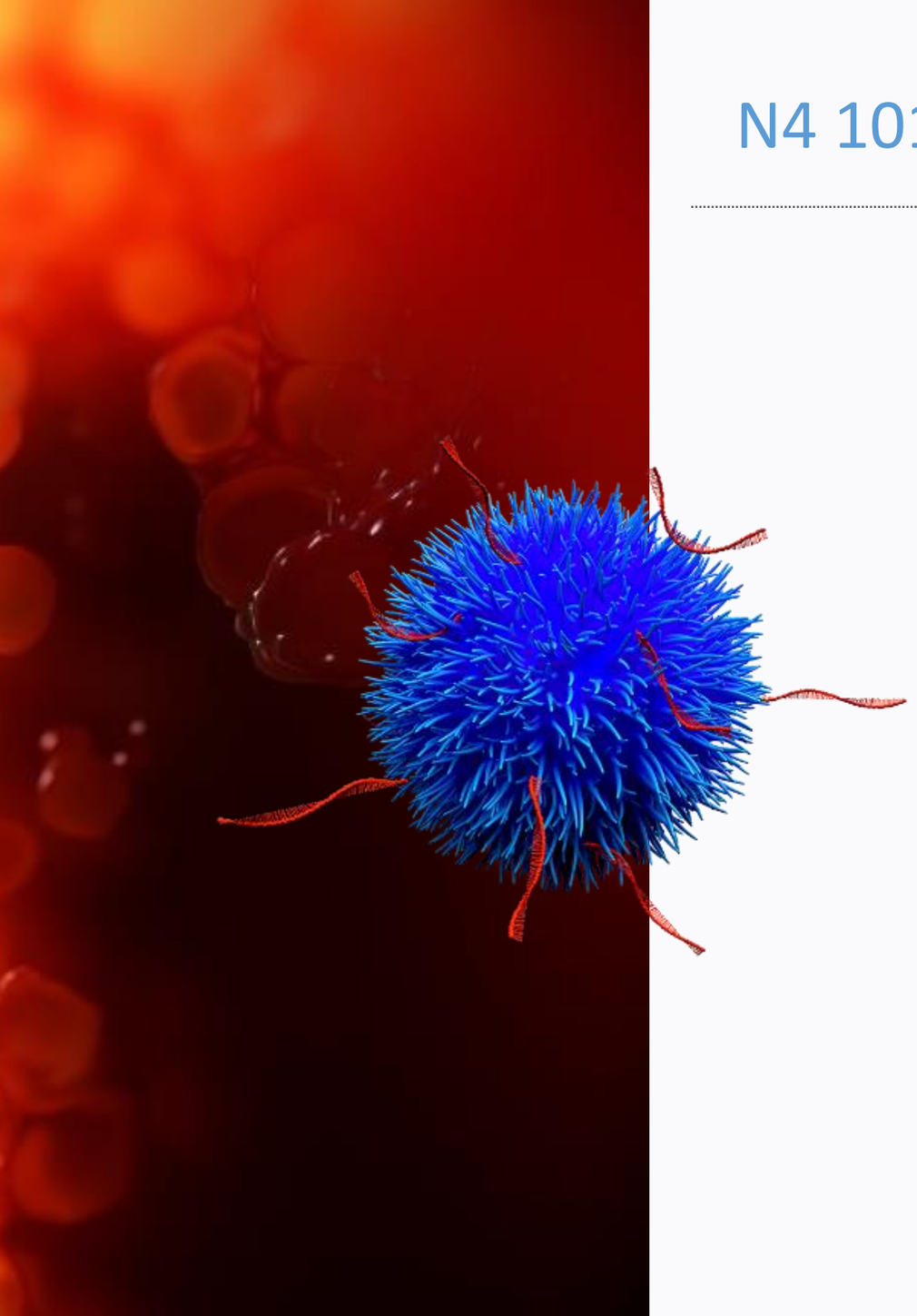


Double loaded Nuvec (red) showed greater reduction in cell viability than compared to single loaded showing an additive effect





N4 101 pre-clinical program



- In vitro testing of reduction in TNF-alpha activity and increase in anti-inflammatory actions to optimise ratio of dual activities
- In vivo testing of oral capsule to demonstrate release in large intestine and reduced inflammation in mouse model
- Key In vivo results in animal model of IBD by mid 2025 via University of Queensland to extrapolate dosage and regime for clinical evaluation

ECP105: Prevention of ocular scarring

Post-glaucoma surgery fibrosis

- Trabeculectomy is the current ‘gold standard’ glaucoma filtration surgical treatment to lower intraocular pressure when pharmaceutical management is unsuccessful.
- However, fibrosis following the surgery means that failure rates can be as high as 50% after 5 years.
- Current treatments to prevent fibrosis – e.g. mitomycin C (MMC) – are unlicensed and risk severe side effects

ECP 105 addresses this unmet need by providing a simple and effective anti-fibrotic therapy to maximise surgical success in glaucoma by reducing post-surgical scarring, without exposing patients to the risk of cytotoxic medication.

Prevention of fibrosis market opportunity

Treatment audience size:

Glaucoma currently affects 80 million people worldwide, estimated to rise to nearly 112 million by 2040. Estimated 300,000 Glaucoma Filtration Surgeries (trabeculectomy) worldwide and growing. Other procedures also lead to scarring

Potential market size:

Treatment cost estimate $6,500 per surgery – use of ECP105 between $600 and $1,000 per use gives market size of $180 - $300mn per annum*

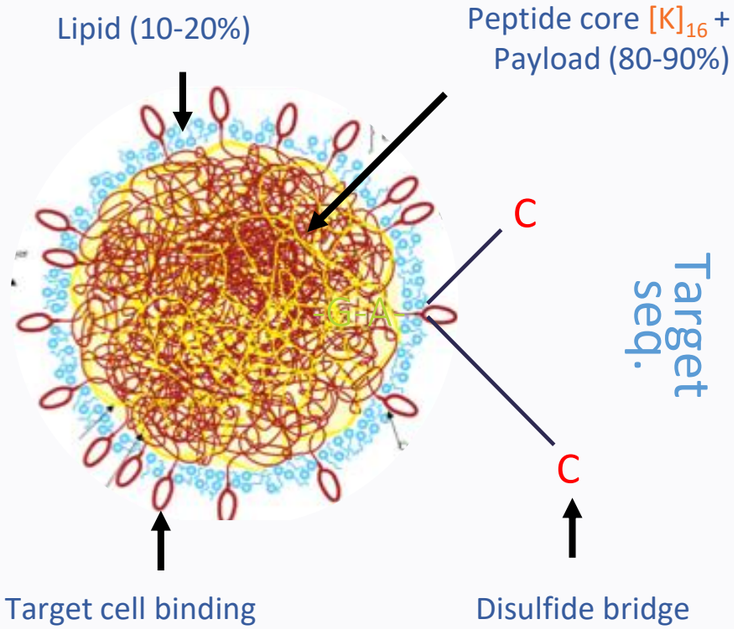
ECP105 will replace use of off label Mytomycin-C to achieve a minimum of same efficacy but without the toxic side effects and be used again if any repeat surgery

*current estimates

ECP105 – targeted RNA therapy for fibrosis

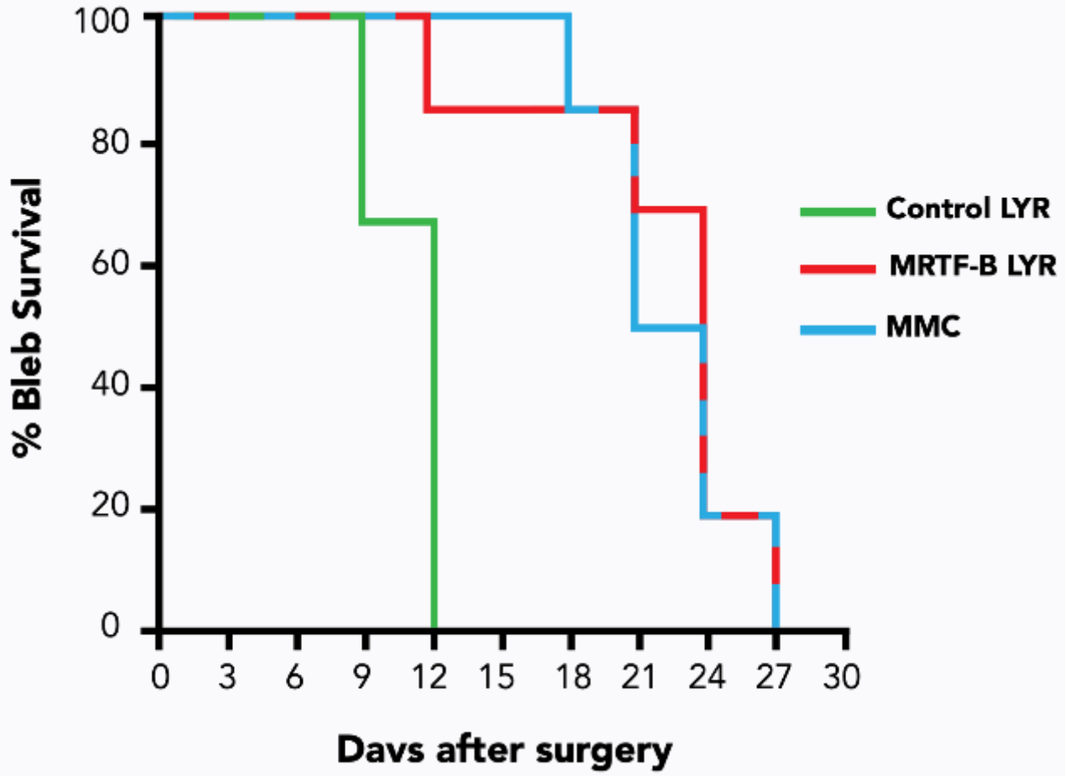
- N4 acquisition of controlling stake in Nanogenics
- Nanogenics has used the LipTide platform to deliver a siRNA specific against the specific MRTF-B gene responsible for fibrosis
- Knockdown of MRTF-B prevents activation of fibroblasts responsible for scarring
- This siRNA was delivered to the eye by a single subconjunctival injection in a rabbit model of glaucoma filtration surgery.
- This treatment led to a doubling in bleb survival and matched the current gold-standard MMC treatment. Crucially, no adverse side effects were observed.

LipTide™ mechanism of action



ECP105 proof of concept study in rabbits

- Following a single subconjunctival administration of LipTide containing a MRTF-B siRNA;
  - MRTF mRNA expression reduced by 30%
  - ICH revealed less scarring
  - Bleb survival increased from 11 days to 22 days
  - A single dose of LipTide with 25ug MRTF siRNA had the same effect in this in vivo model of glaucoma fibrosis as the current standard treatment mitomycin C
  - No local or systemic toxicity observed with LipTide



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Key players in IBD market

- AbbVie Inc
- Amgen Inc.
- Biogen
- CELLTRION INC
- Ferring B.V.
- Johnson & Johnson
- Lilly
- Novartis AG
- Pfizer Inc
- Takeda
- UCB Group

Key players in Glaucoma market

- AbbVie Inc
- Amgen Inc.
- Atsena
- Astellas
- Boehringer
- Innovent
- Merck
- Novartis AG
- Santen

SRI / N4 collaboration

SRI Biosciences
A DIVISION OF SRI INTERNATIONAL

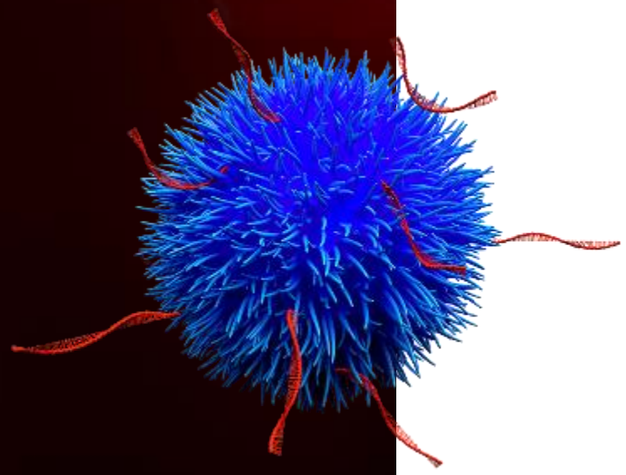
N4 PHARMA

- Combined SRI's Fox 3 MGS targeting peptide to Nuvec® nanoparticle
- Confirmed combined particle only taken up into target cells
- Strong specific cellular knockdown of target gene
- Data being presented to major pharma players for joint development and licensing

SRI / N4 business model options

Actively seeking partners for current assets/programmes as well as new Discovery/Development programmes

A flexible modified biotech model to discover, develop and transition products to commercial partners



Research Collaboration Agreement

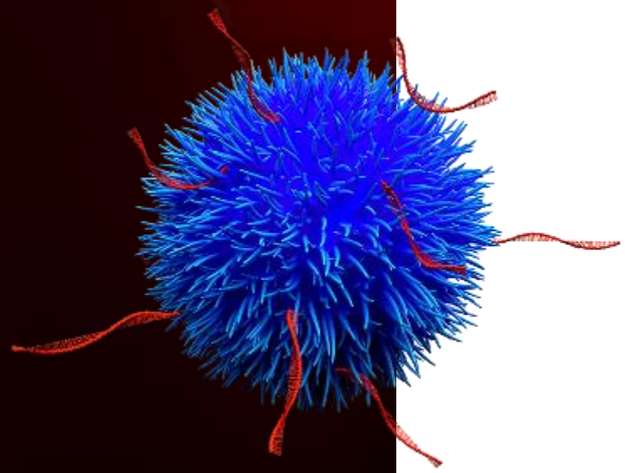
- Define initial project scope
- Milestone based fee structure
- Option for staged projects
- Multiple stage options to transition to License/Option agreement (in-vitro/in-vivo stages)

License/Option Agreement

- Phase and Milestone based (Discovery through Preclinical)
- Executed at partner's choice of milestones
- Development Milestones and Commercial royalties –following standard biotech terms

SRI / N4 intellectual property strategy

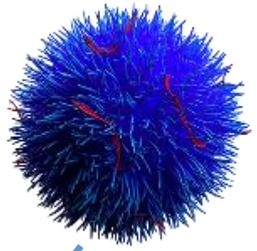
- IP strategy is designed to allow for the longest patent life
- Generates new composition of matter patents with new MGS-cargo combinations
- The partner has commercialisation rights



SRI's Background IP

Composition of Matter IP- MGS as a solo entity

N4 Background IP



Composition of Matter IP- spiky silica nanoparticle

SRI MGS customised and optimised for the cargo type and bound to Nuvec
+
the partner's cargo

Partner's therapeutic cargo

New composition of matter IP

New IP –the new combined product will be co-owned by All Parties with the commercial partner having exclusive rights to commercialise

Anticipated value inflection points

H2 2024	H1 2025	H2 2025	2026	2027
N4 1000		12-15 months N4 Pharma completes current pre-clinical POC programme and obtains pre-IND approval on oral IBD product		3 years Possible IND filing on oral IBD product
ECP105	6 months N4 Pharma completes current pre-clinical POC programme and obtains pre-IND approval on ECP105		24 months Possible IND filing on ECP105	
SRI		Initial Pharma collaboration		

Commercial strategy

- Licensing (pre-clinical or clinical stage) of lead programmes – deal value driven by data
  - Potential partners for N4101
  - Potential partners for ECP105
- Licensed products will be taken through clinical trials by partner
- N4 aims to take at least one programme into the clinic – clinical stage assets strongly drive shareholder value via acquisition or licensing
- Expansion of the development portfolio when resources permit will provide a pipeline of licensable assets
- Platform proof of concept via N4101/ECP 105 allows N4 to seek platform deals with non-competitive nucleic acid therapy companies.

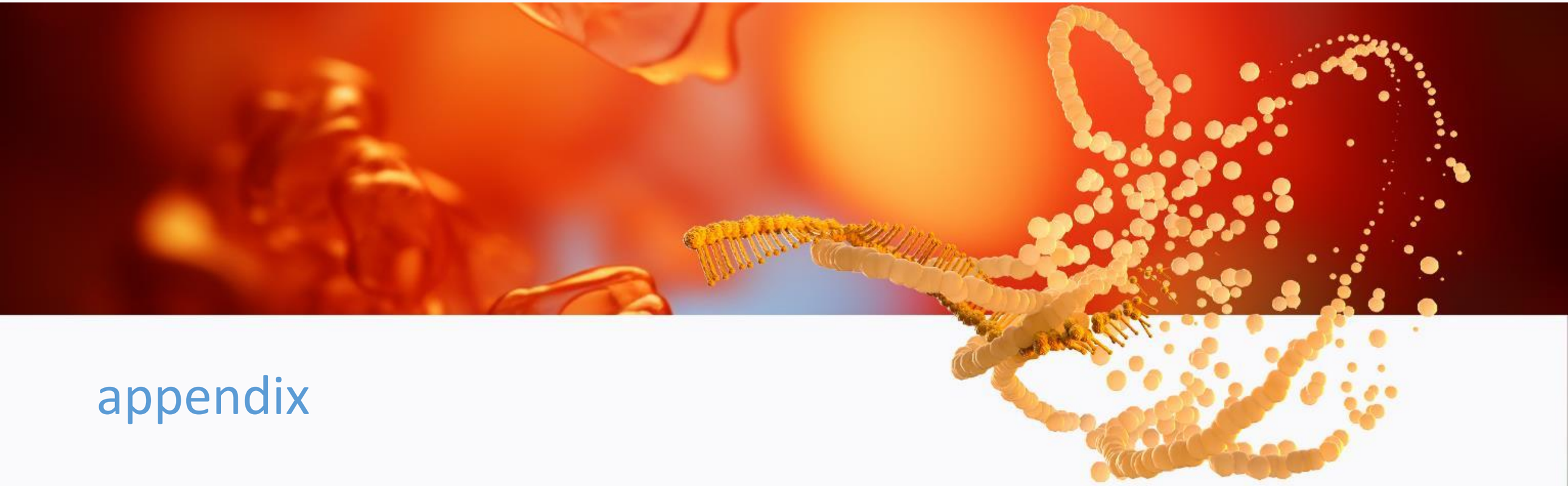
Proven business model for platform companies

Transition from technology platform to product company:

- Aro Biotherapeutics.
  - Protein platform, raised $41.5m at $400m valuation – 3 early stage products
- Arrowhead Pharmaceuticals
  - 4 products phase 1-3. targeted siRNA platform to specific tissues – mkt cap $3.3bn
- Dicerna Pharmaceuticals
  - Galnac platform. Acquired by Novo Nordisk for £3.3bn with 2 products in phase 2
- DTx Pharma
  - Ligandised fatty acids, acquired by Novartis $500m upfront rising to £1bn – on back of orphan designation for rare genetic disorder
- Wave Lifesciences
  - Galnac-siRNA platform. Pre-clinical Weight loss product, deal with GSK for hepatology – mkt cap $793m

Summary

- N4 Pharma is a targeted nucleic acid medicine company
- N4 Pharma is developing two lead products designed to address unmet clinical needs with substantial commercial value
- Leveraging N4 Pharma's proprietary delivery technologies, Nuvec® and LipTide™, provide us with competitive advantages to deliver superior medicines.
- Pre-clinical data package being completed for both products – aiming for IND filings in 2025 and 2026
- Commercial strategy includes pre-clinical and clinical licensing opportunities as well as potential platform deals in non-competitive indications.
- Proprietary cell targeting platforms available to third parties for own development

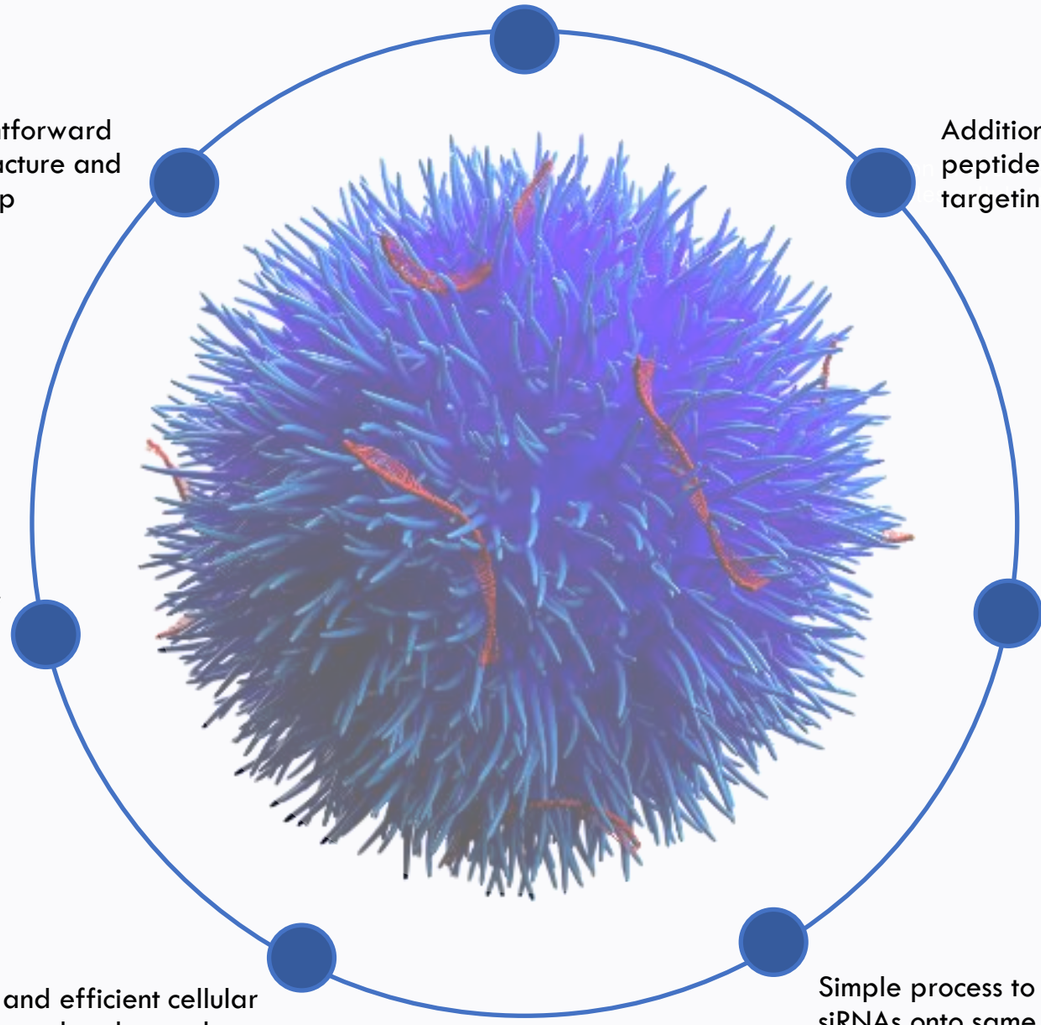


appendix

Nuvec®

Non-lipid, non-viral, silica-based nanoparticle with targeting capability and payload protection

Technology benefits:



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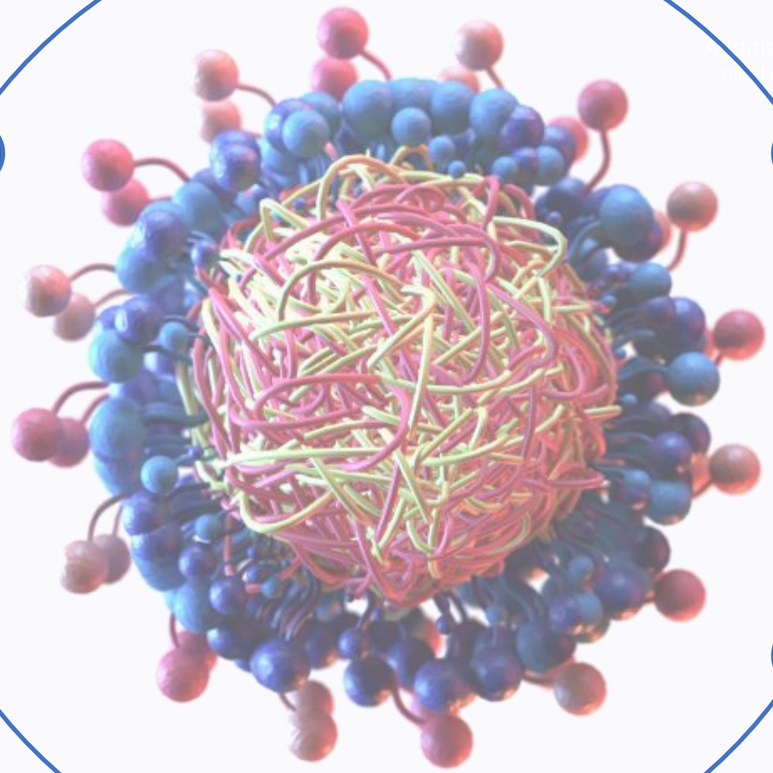
LipTide™

Non-viral, peptide-based nanoparticle with targeting capability and payload protection

Technology benefits:

The lipid element encapsulates the payload to protect it



The peptide element allows efficient take up by the target cell

Like a virus, LipTide can bind to specific cell surface proteins to gain entry into the cell. Unlike a virus, these can be easily changed

Improved safety profile compared to viral vectors

High tolerability, making it suitable for regular, repeat dosing

Higher delivery rates and specificity than traditional liposomal vectors

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ECP105 development plan

Pre-Clinical Activities	Phase 1	Phase 2	Phase 3	Market Authorisation
Efficacy Studies	Dose escalation in Glaucoma patients	Randomised blinded study compared with Standard of Care	2 x Phase 3 trials (US and European)	UK, EU and US initially
CMC – GMP Manufacturing and stability	Safety and Tolerability; determination of single dose level	Demonstrate positive Patient outcome in disease state; confirms safety	Superiority to Standard of Care; longer follow up period (2 years)	Orphan status enables 7 years exclusivity in US; 10 years in EU
Toxicology	Regulatory application for EU Orphan Status	Proposes patient groups and hypothesis for Phase 3	Establishes label claims for MAA	
18 months	12 months	24 months	48 months	12 months

N4101 development plan

Pre-Clinical Activities	Phase 1	Phase 2	Phase 3	Market Authorisation
Efficacy Studies POC, in-vitro & in-vivo	PK/PD Multiple vs single dose study	Randomised blinded study compared with Standard of Care	2 x Phase 3 trials (US and European)	UK, EU and US initially
CMC – pre clin GMP Manufacturing and stability	Safety and Tolerability	Demonstrate positive Patient outcome in disease state; confirms safety	Superiority to Standard of Care; longer follow up period (2 years)	
Toxicology	GMP Manufacturing and stability	Proposes patient groups and hypothesis for Phase 3	Establishes label claims for MAA	
18 months	12-15 months	24 months	48 months	12 months

Intellectual property

Patent	USA	Europe	China	Others
Nuvec silica particle matter of composition & manufacture	Granted expiry 2036	Granted expiry 2036	Granted expiry 2036	Granted India, Japan, Australia, Canada
Use of Nuvec with viral vectors	National phase examination	National phase examination	Filed awaiting response	Filed India, Japan, Australia, Canada
Liptide use of Peptide	Granted expiry 2028			
Liptide use of tri-chain lipids	Granted expiry 2037	Granted expiry 2037, UK, FR,DE, ES, IT	Granted expiry 2037	Granted Hong Kong, Japan, S Korea, Mexico
Liptide use of anionic lipids	Granted expiry 2039	Granted expiry 2039, UK, FR, DE, ES, IT		

Examples of broader applications of our platform technologies

- **Dual siRNA in cancer resistance:**
  - Combination therapy is the main means of preventing drug resistance in cancer therapy (e.g. antibodies or small molecules)
  - siRNAs could knock down two targets on one pathway, or two different pathways
  - Nuvec® has ability to deliver more than one siRNA to same cell
  - Dual or multiple siRNA loading on one particle, offering the potential to reduce relapse during cancer treatments
  - Further in-vitro and in-vivo work in progress.
- **Viral vector enhancement**
  - For in vivo gene therapy, the Adenovirus (AV) and Adeno-Associated virus (AAV) are acknowledged as the most used delivery vehicles, but relatively high amounts are needed to be clinically efficient and this appears directly correlated with adverse events in patients.
  - Nuvec® can deliver increased transduction efficacy, when complexed with Adeno-Associated virus 8 ("AAV8").
  - Nuvec® has the potential to reduce the amount of AV and AAV needed and thus decrease both the cost of goods and immunogenicity associated with using these viral vectors.
  - Early-stage in vitro work in collaboration with Brunel University.
- **Further Fibrosis treatments for MRTF-B gene**

N4 PHARMA