N4 Pharma plc

N4 Pharma has successfully raised £0.63m through an equity placing and subscription ('the Placing') priced at 0.5p/share. Completed using authorities granted at the Group's 23 May 2024 AGM and seen providing it with roughly a 12-months forward runway, this new funding is expected to support delivery of a number of key valuation inflection points across its two novel complementary non-viral delivery technologies. Accretive newsflow expected to be generated over this period includes progress with the recently announced collaborative research agreement with Silicon Valley-based SRI International ('SRI'), potentially advancing preclinical work sufficiently to commence early partnership negotiations with third parties. Elsewhere, preclinical validation of Nuvec®'s novel oral siRNA Irritable Bowel Disease ('IBD') product offers potential to become a new development drug with important licensing opportunities, while (75%-owned) Nanogenics' lead-development, ECP105, is expected to secure Orphan Drug Designation ('ODD') through the FDA's regulatory fast track, ahead of a pre-IND meeting in 2025. Along with its continuing research into adeno-associated virus ('AAV') vector enhancement, the Group's unique portfolio now offers multiple, near-term opportunities to secure value-creating, possibly even transformative, trade sale(s)/licencing agreements. Admission of the Placing shares is expected to become effective and dealings commence on or around 13 June 2024.

Use of placing funds

The Placing proceeds will be used to advance N4P's three primary work streams, whilst also providing working capital into 2025. More specifically:

- Based on the excellent data obtained on the use of Nuvec® for multiple delivery of siRNA and its oral work the Group will commence a program of work with the University of Queensland ('UoQ') to establish proof of concept for a product to treat IBD. The program will seek to demonstrate through *in vitro* and *in vivo* studies that dual loaded Nuvec® in an oral capsule can reduce inflammation associated with IBD;
- Subject to data as it arises from the ongoing work with SRI, continue to support further development work with SRI's MGS technology along with the co-marketing of any resulting data to collaborators and commercial partners;
- The increased funds will provide flexibility to further support Nanogenics in obtaining Pre-IND Approval for ECP105, whilst *in viv*o work concludes and it awaits the result of its application for orphan designation status for ECP105 which, if granted, would give seven years exclusivity in the USA on the product post authorisation;
- In addition to the core work outlined above, all of which are expected to provide steady newsflow for the rest of the year, efforts will continue in the background to identify a distribution partner(s) to supply Nuvec® to AAV vector companies.
- The Board will also look to potentially add additional director(s) with proven track records or contacts in the commercialisation and/or sale of products and IP in the pharmaceutical and biotech space.

Funding expected to be sufficient for coming 12 or so months

N4P is a highly efficient, specialist biotech company. It oversees continuing development of two unique, patented nanoparticle delivery systems for the reformulation and development of cancer treatments, gene therapy and

Stock Data

Share Price	0.53p
Market Capitalisation	£2.07m*
Shares in issue:	394.78m*
52 week high/low	2.10p/0.50p

**Post Placing Numbers*

Company Profile

Sector:	Pharmaceuticals
Ticker:	N4P
Exchange:	AIM

Activities

N4 Pharma plc ('N4 Pharma', 'N4P' or 'the Group') is a specialist pharmaceutical company nanoparticle and try developing a novel silica nanoparticle delivery system for vaccines and therapeutics for licensing to pharmaceutical and biotech partners.

www.n4pharma.com

5-year share price performance

Source: LSE

Past performance and forecasts are not a reliable indicator of future results.

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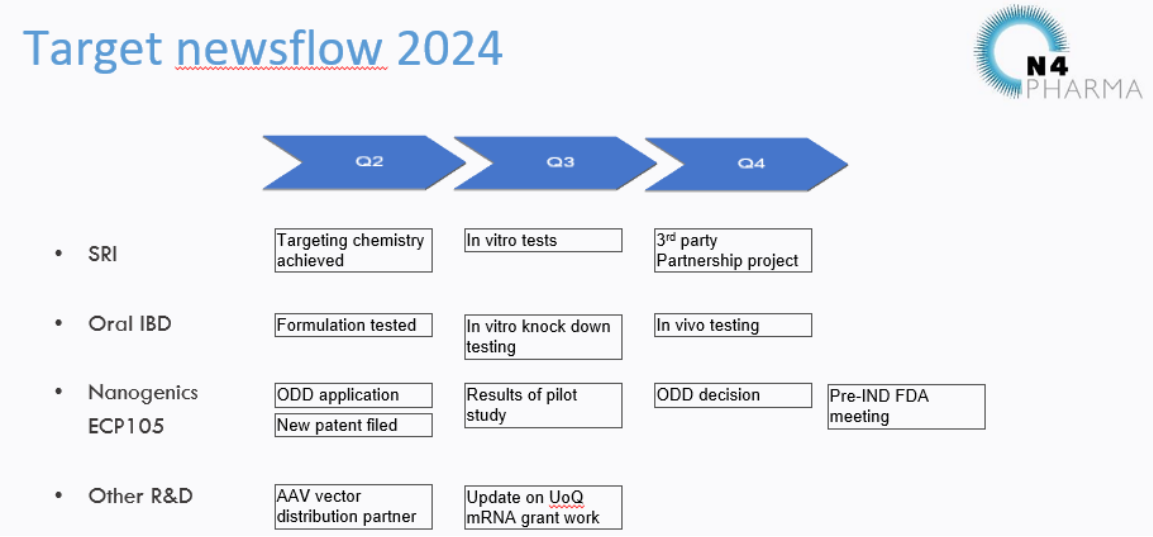
vaccines using RNA/DNA, while progressing a lead product that utilises the Liptide® platform in combination with a proprietary siRNA sequence for prevention of fibrosis post Glaucoma surgery. Despite this ongoing workload, last year's operational burn of c.£0.1m/month (net of R&D tax credit) is expected to remain roughly stable during the current period. An estimated existing cash balance of c.£0.5m plus today's net new funding is expected to be sufficient to support planned operations through to around mid- 2025.

Based on the above projected expenditure, N4P expects to reach (amongst other things) a number of key valuation inflexion points during this period. Each of these are expected to progress it toward prospective trade sale/licensing opportunities, including the following:

- SRI International collaboration targeting first 3rd party partnership
- Proof of concept for novel oral siRNA IBD product
- EPC105 achieves ODD and pre-IND FDA meeting approval

N4P's target news flow for 2024

N4P's two novel and complementary non-viral delivery technologies, Nuvec® and LipTide®, are expected to deliver preclinical and clinical validation over the coming 18 or so months. This is expected to significantly raise their profile which, against a background of significant demand in the gene therapy space following the success of COVID vaccines, opens various opportunities to commence third-party licensing negotiations. Research also remains ongoing for advancement of the Group's lead opportunity, ECP105, which targets prevention of fibrosis post Glaucoma surgery, along with work on combining Nuvec® with Adeno-associated virus/Adenovirus ('AAV'/'AV'), in order to enhance performance in terms of both immunogenicity associated with the use of such vectors for gene therapy and a substantial reduction in cost of goods. Targeted news flow that N4P expects to deliver this year and early in 2025 is detailed below:



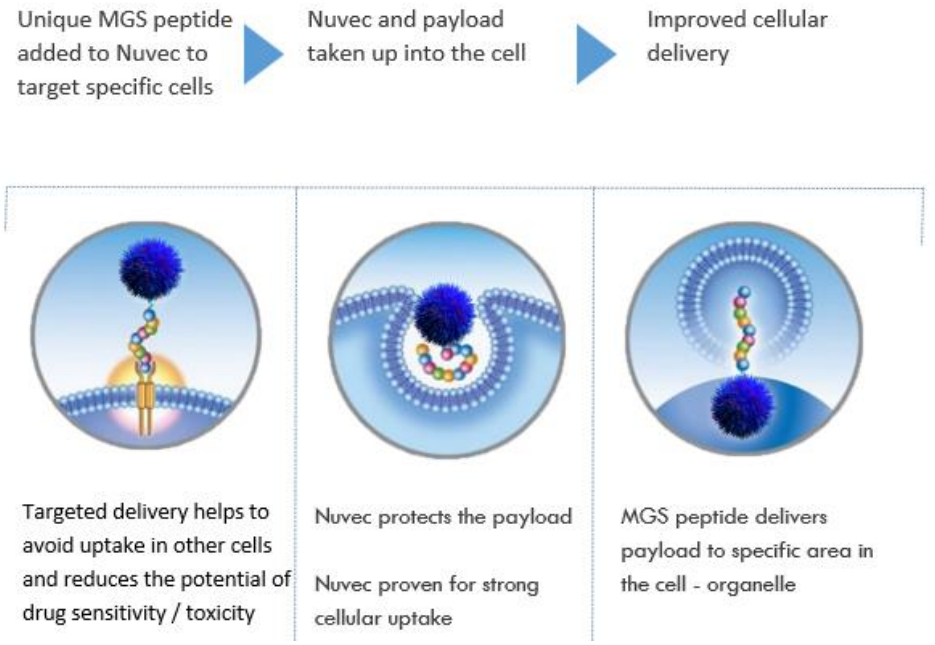
Source: N4P, Investor Presentation, May 2024

Co-marketing with SRI Fox 3 Molecular Guidance System

Nuvec®'s mechanism of action ('MOA') as a delivery system is highly complementary to SRI's FOX Three Molecular Guidance System ('MGS'), which operates proprietary procedures to identify unique peptide delivery agents. Their joint research agreement ('the Agreement') aims for co-discovery of MGSs that recognise target cells/intracellular locations for uptake of Nuvec® carrying nucleic acid payloads defined by N4P.

The collaboration is intended to pave a route toward highly targeted treatments, with ambition for the combined technologies to ultimately realise the full potential of 'next generation' precision healthcare. N4P and SRI will have joint ownership of any novel IP developed as a result of the Agreement, with separate license deals to be negotiated with prospective commercial partners for which, under the terms of the Agreement, N4P retains an exclusivity option.

Unique MGS Peptide Added to Nuvec® to Target Specific Cells



Source: N4P, Investor Presentation, May 2024

The role that each company plays in this collaboration is clear. For example, one of the key properties of the Nuvec® nanoparticle includes its ability to prevent enzymatic breakdown of nucleotides, along with a large 'spikey' surface area coupled with polyethyleneimine ('PEI'), that permits it to be heavily loaded with siRNA/DNA/mRNA (or a wide range of plasmids including TNFalpha, IL12, IL2) via a simple mixing process. It protects and delivers each compound/molecule to the same cell and generates the desired antigen protein expression, protein silencing or other required outcome, while featuring strong binding, localised transfection efficiency and tumour growth suppression.

Nuvec® nanoparticles are highly scalable with stable formulation. Utilising Nuvec® alongside the targeting abilities provided by MGS, offers potential to significantly enhance the use of nucleotides as they travel to and internalise within target cells via general and dynamin endocytosis. Once internalised, the PEI is seen to alter its charge and begins to disassociate, releasing the payload into the cytoplasm followed by transfection to produce the desired biological effect.

The coming 3 to 4 months are expected to see completion of POC studies for targeting chemistry with siRNA, followed by *in vitro* testing to demonstrate selectivity (i.e., only permitting uptake within cells that specifically express the unique peptide). Subject to a satisfactory outcome, promotion and marketing exercises could then commence with a view to identify potential third-party partnership projects.

While utilising its proprietary FOX Three MGS platform with a view to advancing development of N4P's nucleic acid-based therapies, SRI Biosciences will also provide collaborative marketing and 'door opening' opportunities across its extensive client/contacts lists. These range from small and virtual biotechnology companies to top 10 pharmaceutical companies and other leading industry partners with whom it has developed novel platforms and programs in a variety of therapeutic areas targeting high unmet medical needs.

Collaborations established by SRI since the 1950s have enabled advancement of more than 200 drugs to clinical trials, of which 25 have commercialised. Upon successfully entering a third-party partnership project, N4P and SRI would be expected to independently negotiate milestone payments followed by licence fees upon successful commercialisation. A first joint profile-raising exercise was undertaken at the recent San Diego BIO 2024 conference (3rd to 6th June 2024).

Nuvec® - A potential oral delivery system for oligonucleotides

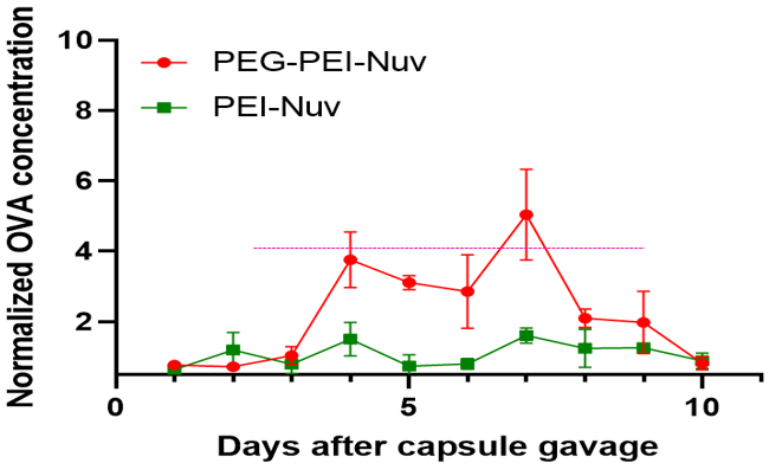
IBD is a term used primarily for two medical conditions (Crohn's disease and ulcerative colitis) that are characterised by chronic inflammation of the gastrointestinal ('GI') tract. Estimated numbers of global suffers vary with, for example, the European Federation of Crohn's & Ulcerative Colitis Associations ('EFCCA') suggesting there are as many as 10 million people worldwide living with it.

Inflammatory macrophages in the lining of the gut wall are considered the major driver of the disease. These release multiple cytokines, such as Tumour Necrosis Factor alpha ('TNF'), locally and result in a variety of clinical responses, such as persistent diarrhoea, as well as blood or mucus in the stool plus unexplained weight loss and fatigue. Anti-TNF antibody biologics (such as infliximab, golimumab etc.) have been already developed but often come with numerous, sometimes disabling, limitations and side effects, while requiring frequent painful injections that negatively affects patient compliance.

The solution being proposed by N4P and supported through a partially grant-funded research programme at the UoQ, is based on Nuvec® acting as an oral delivery system for oligonucleotides, whereby administration of a novel capsule containing dual loaded siRNA and mRNA can be delivered to the GI tract. *In vivo* studies have demonstrated that an enterically-coated capsule containing Nuvec® loaded with DNA encoding ovalbumin is able to pass through the lining of the stomach to successfully transfect the upper intestine.

Using a single dose, ovalbumin expression was observed after 3 days. In a second study, a further PEGylated capsule was administered on day three and a much higher sustained level of expression was observed on days four to seven. Additional testing completed on 18 April 2024 indicated that further staged administration over a period of 21 days, can maintain the protein expression for even longer and produce antibodies. This demonstrates protection of the DNA payload during transit through the stomach. Once in the upper GI tract, control of the pH permits payload release, with acidity being modified to produce different colonic conditions.

Ovalbumin Concentration Following Administration of PEGylated Nuvec®



Source: N4P, Investor Presentation, May 2024

Upon successful transfection, the siRNA induces knockdown TNF concentration and delivers anti-inflammatory Interleukin 10 ('IL10') mRNA to infected tissue. As well as hindering host response to microbial pathogenesis and preventing resolution of associated tissue damage/hemodynamic disturbances, a significantly improved patient experience is also anticipated. Beyond this, N4P also recognises future potential for specific macrophage targeting using MGS peptides. Altogether, this suggests Nuvec® offers significant potential for use as an oral delivery system across a number of applications, including as a product for GI disorders, a vaccine or to treat colon cancer amongst various different possibilities.

Work currently planned for the remaining quarters of 2024 and into 2025 is expected to complete rigorous POC

testing, starting with formulation assessment and *in vitro* examination of TNF knockdown/IL10 expression. Subject to a positive outcome, a further phase of *in vivo* work using oral capsules will commence, seeking to demonstrate reduced localised concentration of TNF/increased IL10, along with histological proof of disease modification. With multiple potential collaborators having recognised the need for a more satisfactory patient outcome than is presently available using antibody-based products, success at the preclinical stage is expected to result in detailed assessment of clinical potential, possibly opening the door for creation of the Group's second development drug and licensing negotiations for a Phase 1 trial in 2025.

Nanogenics' lead opportunity, ECP105, for prevention of fibrosis post Glaucoma surgery

N4P acquired a 75% stake in Nanogenics Limited in October 2023. This introduced a new, proprietary delivery technology, LipTide®, along with a lead product, ECP105, which is designed to enhance glaucoma outcomes post-surgery without toxic side effects. The intention is to avoid any need for progressive tissue remodelling and/or formation of a fibrotic scar, leading to reduced prevalence of Glaucoma-related vision loss.

LipTide® is a peptide and lipid-based delivery system for nucleic acids. Its MOA is to utilise peptides to bind payload and target specific cells, with lipids then permitting efficient endosomal release into target cells. ECP105 offers a targeted approach designed to prevent fibrosis scaring post Glaucoma surgery, utilising the LipTide® platform to deliver a Nanogenics-developed proprietary siRNA sequence.

In vitro POC has already demonstrated siRNA inhibition of proteins related to fibrosis and ophthalmic indications. Positive preliminary data for delivery has already been reported along with efficacy *in vivo* for prevention of glaucoma surgery failure. A pilot rabbit study using a new formulation is expected to deliver results during Q3 2024, ahead of which the drug has Orphan status precedence set for regulatory fast track through FDA, with a decision expected as early as September 2024. An additional patent has already been filed for lifecycle extensions with the intention to also generate new novel IP related to (rabbit/human) siRNA sequences.

Following a further *in vivo* GLP-toxicity regulatory study, ECP105 could move toward First-in-Human studies. Advice will be sought from the FDA ahead of a pre-IND meeting targeted for 2025, covering formulation methodology/final product formulation/intended use of ECP105 and proposed trial designs. Funding for subsequent clinical trials will ideally be sourced through partnership with an existing ophthalmology products company or perhaps a larger pharmaceutical business that undertakes such joint ventures.

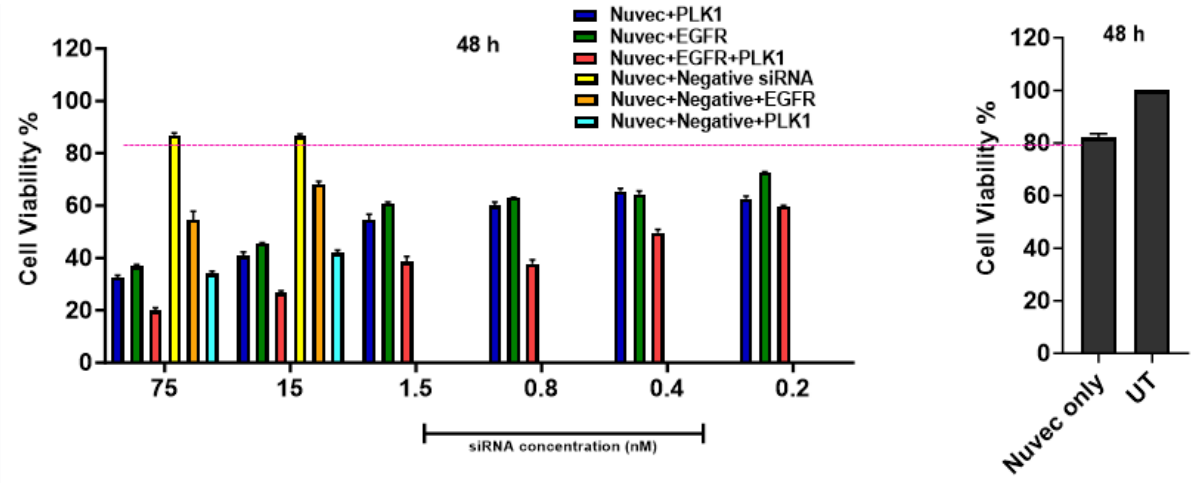
Process to clinic will initially involve the transfer of manufacturing and source components to GMP, preparation of an Investigator's Brochure ('IB') followed by compilation of an Investigational Medicinal Product Dossier ('IMPD') in anticipation of seeking Clinical Trial Authorisation ('CTA'). With patient recruitment expected to be relatively quick, the trial itself would likely involve a 6-month dosing period, with as much as a year of follow-up assessment.

Subject to a successful outcome, Nanogenics also recognises potential to create additional IP for other fibrosis conditions. The global fibrotic diseases treatment market has been estimated to grow from US$3.6bn in 2023 at a CAGR of 5.5% to US$5.56bn by 20231, according to Data Bridge Market Research.

Ongoing R&D programmes: Dual loading of Nuvec®, AAV vector enhancement

In vitro results for Nuvec® loaded with two different clinically relevant siRNA, EGFR and BCL-2, show comparable cellular apoptosis to two commercially available products. More recent work has also demonstrated it can bind not only single, but dual siRNAs aimed at simultaneously targeting pathways responsible for cancer progression, from which a heightened reduction in cell viability after 48 hours has been demonstrated. *In vivo* testing of preferred formulations using a cancer model are now underway, subject to which, dual loading of Nuvec® offers potential to become an important tool for combination therapy treatments.

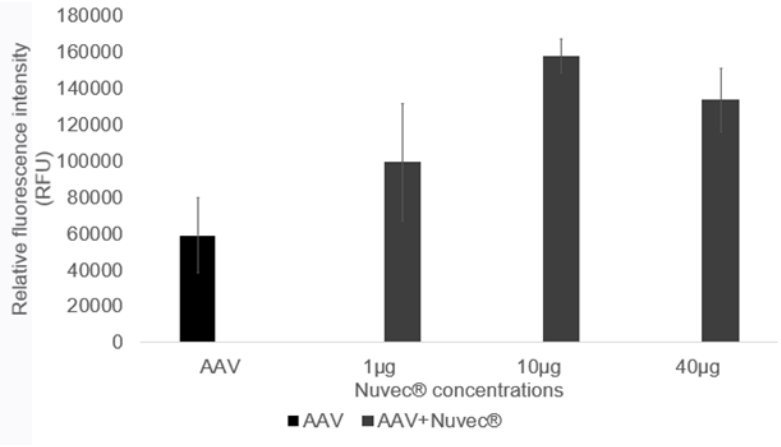
Test Results from Single and Dual Loading of Nuvec® with Clinically Relevant Cancer Models



Source: N4P, Investor Presentation, May 2024

Although viral vectors presently remain the preferred delivery vehicle for use in gene therapy, they come with a number complications, including their cost of production (for the volumes required) and side effects (due to their inflammatory nature) that deteriorate patient experience.

Viral Vector AAV8 Complexed with Nuvec®



Source: N4P, Investor Presentation, May 2024

N4P has taken a novel approach to how Nuvec® might be used to improve the overall outcome in this area. Early stage *in vitro* work in conjunction with Brunel University has demonstrated its combination with a viral vector produces a significant improvement in efficiency; as can be seen above, a Nuvec® AAV8 viral vector complex can, for example, increase the transfection efficacy of the viral vector twofold This suggests that products formulated with viral vectors could deliver the desired therapeutic effect, despite consuming a substantially reduced volumes (therein reducing the cost of goods) while also potentially diminishing unwanted side effects (such as joint/muscle pain, nausea, fatigue etc.)

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