

**Stock Data**

Share Price	2.15p
Market Capitalisation	£4.97m*
Shares in issue:	231.08m*
52 week high/low	8.69p/1.50p

\*Post-Placing numbers

**Company Profile**

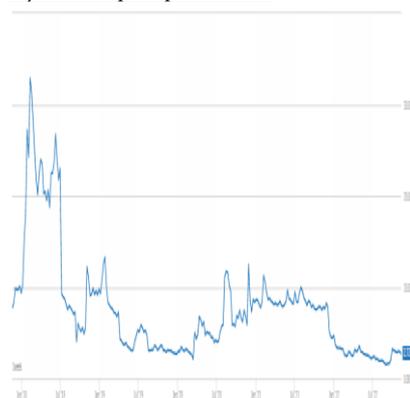
Sector:	Pharmaceuticals
Ticker:	N4P
Exchange:	AIM

**Activities**

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

[www.n4pharma.com/](http://www.n4pharma.com/)

**5-year share price performance**



Source: [LSE](https://www.lse.com)

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

**Turner Pope contact details**

Tel: 0203 657 0050  
Email: [info@turnerpope.com](mailto:info@turnerpope.com)  
Web: [www.turnerpope.com](http://www.turnerpope.com)

Andrew Thacker  
Corporate Broking & Sales

Barry Gibb  
Research Analyst

Turner Pope acts as joint broker to N4 Pharma plc.

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# N4 Pharma plc

N4 Pharma has successfully raised £1.0 million (gross) new funding through an equity placing ('the Placing') priced at 2.0p/share. As agent for the Group, TPI has now also launched a broker offer ('Broker Offer') under which it invites subscriptions for additional new ordinary shares from qualifying shareholders for an initial expected value of £0.25 million, which may be extended with N4P's express agreement to £1.0 million in the event the Broker Offer is oversubscribed. This fundraising follows the Group's 4 October 2022 announcement that highlighted successful *in vitro* testing of Nuvec® loaded with two small interfering RNA ('siRNA') probes which achieved significant silencing of their respective genes. In accordance with its strategic update of 14 September 2022, this provides sufficient validation to commence further work covering both epidermal growth factor receptor ('EGFR') and B-cell lymphoma 2 ('BCL-2') in a PC9 lung cancer model. Although management tightly controlled H1 2022 expenditure, leaving it with cash of £1.58m at 30 June 2022 (31 December 2021: £1.78m), this newly proposed 15-month testing programme comes on top of an already scheduled marketing outreach programme plus further required development work on oral delivery/viral vector improvement etc., thereby creating a near-term funding gap that needed to be plugged. Focused on generating sufficient proof of concept ('PoC') data to attract large pharma and biotech partners into collaborations to explore Nuvec® as their chosen delivery system to get products into clinic, positive results expected from this siRNA work could significantly speed its route to commercialisation.

To subscribe for Broker Offer shares, existing shareholders or other interested parties who are qualified investors and wish to register their interest in participating in the Broker Offer should click on the following link: [N4 Pharma Broker Offer](#)

## Use of net proceeds

Directed Funding	Amount (£)
Double siRNA testing using EGFRm, BCL-2 siRNA compounds - 15-month program including associated internal costs	£1.0m
Exploring acquisition opportunities	

Source: N4 Pharma, [RNS of 18 November 2022](#)

The Placing was conducted utilising the Group's existing share authorities. Trading in the Placing shares is expected to commence at 8.00 a.m. on or around 24 November 2022 and, for the Broker Offer shares, 8:00 a.m. on or around 25 November 2022.

## Broker Offer

In order to provide shareholders and other investors who did not initially participate in the Placing with the opportunity to invest in the Group under the Placing agreement, TPI has launched a Broker Offer under which it is now, as N4P's agent, inviting subscriptions for additional new ordinary shares that has an initial expected value of £0.25 million but may be extended, with N4P's express agreement, to £1.0 million in the event the Broker Offer is oversubscribed. The Broker Offer opened immediately following today's RNS announcement and will close at 4.30 p.m. on 21 November 2022.

As far as is practical, participation in the Broker Offer will be prioritised for qualifying shareholders (direct or indirect) on the register at the close of business on 17 November 2022. If the expected initial subscription under the Broker Offer is taken up, it will raise an additional £0.25 million before expenses for the Group. Any net proceeds from the Broker Offer are expected to be directed toward its working capital requirements.

A further announcement will be made following the end of the period during which the Broker Offer is open that, amongst other things, will detail the prospective Admission to trading of the Broker Offer shares. If the Broker Offer is not fully subscribed by 4.30 p.m. on 21 November 2022, orders from eligible investors will be satisfied in full and the balance shall lapse.

### Successful development work on multiple loaded siRNA on Nuvec®

On 14 September 2022, N4P provided an operational update on its development plans for commercialising Nuvec®, the Group’s unique silica nanoparticle delivery system for reformulations and development of cancer treatments and vaccines. Having uncovered a unique ability to concurrently load multiple siRNA compounds onto Nuvec®, enabling both to be concurrently taken up into the same cell, initial testing was undertaken using two generic siRNA probes, GFP (‘Green Fluorescent protein’) and EHMT-2 (‘Euchromatic Histone Lysine Methyltransferase 2’).

Following successful completion of this work, the Board undertook a strategic review to consider where it was likely to achieve the greatest and most rapid commercial traction, in addition to the ongoing Material Transfer Agreement (‘MTA’) work it already has in place. Given Nuvec®’s preclinical status, it concluded that development efforts should focus on loading more than one siRNA sequence onto the same nanoparticle. The ambition here being to silence complimentary pathways, in turn leading to an increased therapeutic response while establishing a significant differential in this marketplace. Accordingly, the next step was to test *in vitro* whether Nuvec® loaded with both forms of siRNA is able to silence both targets, which has already been demonstrated with singular loading.

### Results of Initial *in vitro* Testing of Nuvec® Loaded with Two Generic siRNA Probes

#### Silencing both GFP and EHMT with 2x loaded Nuvec

- Nuvec loaded with both GFP and EHMT2 siRNA 50/50 mix
- Double loaded particles were then tested on both targets
- Both targets significantly knocked down

**GFP**

**EHMT2**

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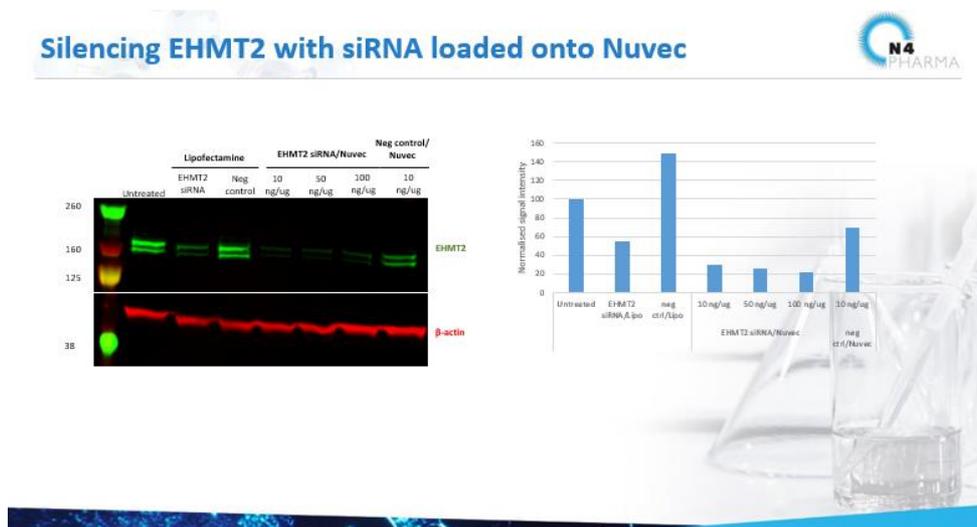
#### Silencing GFP with siRNA loaded onto Nuvec

IC<sub>50</sub>: 0.415 nM of siRNA (with 70 ug/ml of Nuvec)

- Cells carrying the GFP gene were transfected with Nuvec loaded with silencing siRNA and compared to
  - Untreated
  - GFP siRNA/lipofectamine
  - Non relevant siRNA/lipofectamine (neg) or Nuvec (neg)
- The cells transfected with siRNA GFP loaded onto Nuvec showed strongest silencing effects on the cells
- A clear dose response was seen that was comparable and even outperformed lipofectamine transfection with GFP siRNA

Source: N4 Pharma, Investor Presentation, October 2022

By 4 October 2022 this work had been completed. Allocated in equal amounts at a concentration previously shown to be active, testing demonstrated that both were able to significantly silence their respective targets. This provides sufficient validation for N4P to begin the further testing, starting with *in vitro* EGFR and BCL-2 studies in a PC9 lung cancer model followed by *in vivo* studies in xenograft tumours. The results are expected to further support the commercial outreach discussions that commenced following initial successful siRNA testing.



Source: N4 Pharma, Investor Presentation, October 2022

**Successful completion could provide strong clinical validation for using Nuvec®**

Because N4P cannot take relevant generic vaccines into the clinic itself without significantly increased expenditure, it decided to focus its development work on oncology and siRNA delivery as these sectors have proven clinical models the Group can access. Furthermore, Nuvec® can be used to work with generic siRNA and plasmids capable of being used in phase 1 clinical trials, which are increasingly found in development as therapeutics, particularly in oncology and gene therapy. At present, delivery of multiple siRNAs would require multiple carriers, thereby decreasing the probability of transfecting the same cell with more than one siRNA, while hitting multiple aspects of a cellular pathway is also less likely. Delivery of two SiRNA acting on two complimentary pathways in the same cell, therefore has the potential to provide an improved clinical response with lower adverse events compared to conventional chemotherapy.

There are said to be over 300 companies presently working in this space, with 106 clinical trials already in place using siRNA. The Group’s new strategic focus therefore provides two clear advantages in that: (i) It is able to identify a wider target audience and; (ii) The number of compounds it can use to collaborate with provide the opportunity to get into the clinic much more rapidly than if it were to concentrate purely on vaccines.

**The Nuvec® Solution**

The Nuvec® delivery system provides significant advantages to existing solutions:

- Unique spiky structure to allow binding of siRNA
- Simple process to load multiple siRNAs onto same nanoparticle
- Protects siRNA from enzymatic digestion and pH exposure after injection.
- Thermostability – Nuvec® can be dried, stored at room temperature, and reconstituted without degradation
- Easy manufacture and chemical modification to allow cellular targeting

Source: N4 Pharma, Investor Presentation, October 2022

## Commercialisation Strategy - Focusing on strong commercial point of difference

N4P has refined its immediate commercial strategy to focus on and highlight Nuvec® specific point of difference as a carrier of multiple siRNS compounds that has been uncovered by its research and development. The ability to deliver multiple siRNA into the same cell provides a unique solution for combination therapy treatments. Given that many drug development companies are presently undertaking early-phase pre-clinical/clinical testing/trials, they are generally more open to new, novel solutions than those at more advanced stages.

Based on feedback from the patent examiner and further work the Group has already completed, it has been demonstrated that combining Nuvec® with adenoviral vectors (in addition to its earlier work on lentiviral vectors) can lead to an improvement in vector performance and a reduction in the amount of the viral vector required. Accordingly, it is presently pursuing patent applications in Europe (including UK); USA; Japan; India and Canada (and intends to file similar applications in Australia and China in due course) which, if granted, would be in addition to those exclusively licensed from the University of Queensland ('UQ') in an effort to further strengthen the commercial protection of the nanoparticle delivery system.

N4P is also exploring next generation uses in oral delivery. Positive preliminary results from ongoing studies undertaken at UQ demonstrate orally delivered Nuvec® is capable of transfecting cells in the small intestine. The next step in this work is for UQ to repeat the success of this through an *in vivo* study, which management understands will be undertaken soon.

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