SP ANGEL

Non-Independent Research

MiFID II Exempt

** SP Angel acts as Nomad and Joint Broker to N4 Pharma, and therefore this information should be viewed as a Marketing Communication.*

## 15 July 2021

### Stock Data

| | |
|---|---|
| Ticker | N4P.L |
| Share Price: | 8.5p |
| Market Cap: | £16.1m |

*Source: Bloomberg (prior trading day's close)*

### Company Description

Biotechnology business focused on the development of Nuvec®, the Group's silica nanoparticle-based system for the delivery of nucleic acid-based vaccines and therapies.

### Share Price Chart (p)


*Source: Bloomberg*


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# Update Note

# N4 Pharma*

## AIM: N4P

## MTAs demonstrate commercial interest

### Key points

- **Material Transfer Agreements (MTAs) in place with two biopharma companies:** Although early-stage, the MTAs demonstrate industry interest in Nuvec® across two different treatment modalities and could lead to more formal commercial agreements.
- **Encouraging formulation data from an *in vivo* pilot study:** N4 Pharma demonstrated that an optimised version of Nuvec® requires fivefold less dosage compared to prior versions. This could significantly reduce material and manufacturing costs.
- **Proof of concept study results expected in Q3-21:** Given the recent results from the formulation work, the Group is reviewing its ongoing *in vivo* proof of concept work to ensure the study protocols are aligned. Results are now expected in Q3-21.
- **Healthy cash position:** With a FY20 year-end cash position of £3.6m, the Group is well capitalised to progress preclinical development of Nuvec®.

Whilst N4 Pharma ('the Group', 'the Company) continues preclinical work on Nuvec®, its novel delivery system for nucleic acid-based therapies, the Group is shifting its focus towards the commercialisation of the platform. The Company recently announced MTAs with two different biopharma companies which are evaluating Nuvec® integrated with plasmid DNA encoding a COVID-19 vaccine and a gene therapy. These agreements provide N4 Pharma with a valuable opportunity to demonstrate how Nuvec® may improve the partners' therapies. The successful completion of one or both of these MTA programmes would put the Group in a strong position to sign a more formal collaboration, such as a licensing agreement. N4 Pharma is continuing discussions with other parties with a view to strike further agreements.

Whilst the Group will continue to develop the Nuvec® particle, the formal optimisation programme that has been ongoing for the past 18 months is nearing completion. The programme has been a success with a number of features developed which we expect to be attractive to potential commercial partners. A recent study indicated that optimised Nuvec® required fivefold less dosage for a similar immune response compared to a prior version of Nuvec®. A lower dose requirement would be of significant interest to partners as it could substantially reduce material and manufacturing costs. These results follow *in vitro* work demonstrating that optimised Nuvec® showed no significant drop in transfection capability after being freeze-dried and stored for 14 days at ambient temperatures.

N4 Pharma is currently reviewing its proof-of-concept programme. These studies are designed to generate *in vivo* data on Nuvec® surrounding key areas of interest to partners. The review period is in place to ensure these studies incorporate recent findings from the optimisation programmes, such as the reduced dose requirement. Given the improvements these features can offer, the inclusion of these findings in the studies provides an opportunity to generate valuable supporting data. Results from these studies are expected in Q3-21 and the data should form a valuable cornerstone for discussions with prospective partners looking to license Nuvec® to support development of their own nucleic acid-based products.

| Year-end Dec | 2017A | 2018A | 2019A | 2020A |
|---|---|---|---|---|
| Revenue (£m) | 0.11 | 0.07 | - | - |
| Pre-tax Profit (£m) | (1.93) | (1.39) | (0.95) | (1.57) |
| Net Cash/(Debt) (£m) | 1.33 | 0.79 | 0.97 | 3.56 |
| Basic EPS (GBp) | (2.84) | (1.32) | (0.87) | (0.96) |
| Diluted EPS (GBp) | (2.84) | (1.32) | (0.87) | (0.94) |

*Source: Company reports; SP Angel forecasts*

## MTA agreements mark commercial progress

In May 2021, N4 Pharma announced that it had entered into two Material Transfer Agreements (MTAs) relating to Nuvec®. Whilst MTAs represent an early form of collaboration, they highlight the industry interest in the Group's technology. In both cases, the partner remains unnamed due to confidentiality clauses.

The first MTA is with a major international company working in the gene therapy space. Nuvec® is well suited to this modality as gene therapies typically involve the introduction of DNA or RNA into certain cells. The second agreement is with a pharmaceutical company developing a DNA-based COVID-19 vaccine. Given N4 Pharma's work within COVID-19, it is good to see the Group strike an agreement within this area.

### Potential for a commercial agreement

The MTAs aim to assess how well Nuvec® can bind and be optimised for transfection using the proprietary plasmids developed by the partners. N4 Pharma is working with the partners to develop Nuvec® particles which are integrated with the desired genetic material. Once the integration is complete, the particles are then transferred to the partners for testing via their internal laboratory assays. Should the MTA programmes demonstrate positive results, we expect the Group to strike more formal collaborations with the partners, such as a licencing agreement.

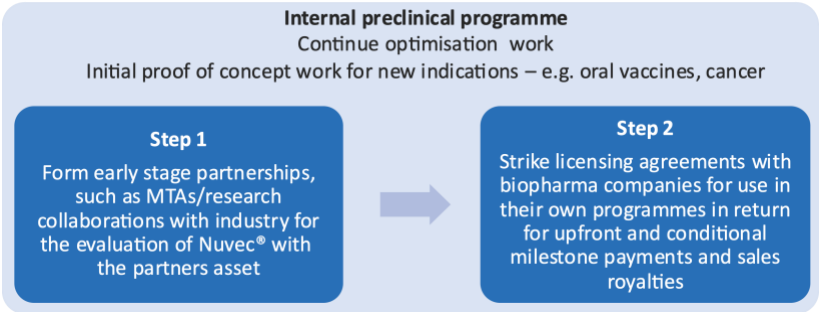
### MTA programmes provides third-party validation

Alongside the current MTAs, the Company is progressing discussions with multiple other parties with a view to strike additional agreements regarding the use of Nuvec®. Positive results from the current MTA programmes would provide external validation regarding the use of Nuvec® in enhancing nucleic acid delivery and should support discussions with other potential partners.

### Platform nature of Nuvec® can enhance income generation

The MTAs demonstrate the potential to use Nuvec® as a delivery system for multiple treatment markets, such as gene therapy and vaccines. Management remains focused on striking licensing agreements for the use of Nuvec® in a particular indication. By focusing on licencing agreements related to the use of the platform in a specific therapy area, the Group retains the freedom to strike licencing deals with other developers for different indications. This offers scope to achieve multiple licencing agreements and increase income generation from the platform.

*Company business model*




*Source: N4 Pharma*

## Optimisation programme continues to deliver

N4 Pharma is conducting studies to further understand the activity of the Nuvec® platform and optimise the particle to improve nucleic acid delivery and transfection. A significant focus of this work has been the development of an optimised formulation of Nuvec® which produces a monodisperse suspension. Previous versions of Nuvec® were observed to agglomerate after DNA was loaded onto the particles. A more monodisperse formulation of Nuvec® is expected to improve transfection efficiency and lead to more consistent results.

### Pilot study by Nanomerics indicates lower dosage requirements

In May 2021, N4 Pharma announced encouraging results regarding the use of an optimised, monodisperse, version of Nuvec®. The *in vivo* pilot study was completed by Nanomerics, a nanoparticle specialist, who is conducting the optimisation programme. The study compared optimised Nuvec® loaded with 10ug of pDNA encoding for Ovalbumin (a test antigen) against 50ug of Ovalbumin pDNA dose bound to a Nuvec® formulation used in previous *in vivo* studies. Despite the lower dose, the optimised Nuvec® was shown to generate an improved immune response compared to the earlier version of Nuvec®.

### Follow up study planned to validate the dosage findings

A shift from a 50ug dose to a 10ug dose would dramatically reduce material and manufacturing costs. Nanomerics intends to conduct a larger follow-on study to replicate the results of the pilot study. The study would follow a similar protocol to the pilot study but would involve an increased number of test subjects. Results from this study would provide valuable supporting data regarding the use of a lower dose and would be of significant interest to potential partners.

### Results follow encouraging storage data

The dosage results follow positive data regarding the ability of Nuvec® to be stored at ambient temperatures. Last year, N4 Pharma demonstrated that Nuvec®, which has been freeze-dried and stored for 14 days at room temperature, showed no significant drop in *in vitro* transfection capability compared to fresh formulations. An issue with nucleic acid-based therapies is the requirement to be stored at a cold temperature. BioNTech and Moderna's RNA-based COVID-19 vaccines require storage at -80°C and -20°C, respectively. Therefore, the use of Nuvec® to enable the storage of nucleic acid therapies at ambient temperatures is an attractive feature to developers.

## *in vivo* study results for Nuvec® expected in Q3-21

N4 Pharma has outlined a series of *in vivo* proof-of-concept studies using Nuvec® generated from the optimisation programme. The purpose of these studies is to confirm that the properties of optimised Nuvec® which have been observed *in vitro* can also be seen *in vivo*. The studies aim to evaluate Nuvec® integrated with COVID-19 pDNA and a pDNA encoding for Ovalbumin (a commonly used test antigen). Study areas include:

- Determining antibody production following dosing with optimised Nuvec®.
- Exploring the dose-response relationship to determine the minimum and maximum plasmid dose required for effect.
- Confirming that activity is retained after freeze drying and reconstitution at different intervals.
- Assessing the improvements against the results of *in vivo* studies using unoptimised Nuvec®.

The studies have been designed to ensure that data generated covers the key areas of interest from commercial partners. Positive results should increase the likelihood of the Group striking future agreements and reduce the need for additional studies.

### Programme under review to include recent optimisation data

N4 Pharma is currently reviewing the proof-of-concept programme to ensure that the studies follow the approach undertaken in the Nanomerics *in vivo* pilot study. Whilst the review may slightly delay the studies (results now expected in Q3-21; previously expected H1-21), it provides an opportunity to incorporate recent findings from the optimisation programme into these study protocols. We view this as an appropriate strategy given the expected interest of prospective partners regarding the potential cost savings of the reduced dose requirement.

### Potential to use a commercial COVID-19 pDNA for *in vivo* work

N4 Pharma has been using a COVID-19 plasmid generated by the US National Institute of Health (NIH) to conduct its proof-of-concept work. This plasmid was generated at the start of the pandemic. As our understanding of the virus has improved, there are now a number of alternative COVID-19 plasmids available. As a result, the Group is assessing the need to complete the proof-of-concept work using the NIH COVID-19 plasmid. This is appropriate given the results of a pilot *in vivo* study using the NIH plasmid. No measurable quantity of SARS-CoV-2 Spike protein was observed across the experiment. This was surprising given that a positive control is used to generate a known response and the Group expects this may be due to the plasmid having a low expression profile.

N4 Pharma now has an MTA in place regarding a DNA-based COVID-19 vaccine. We expect the workstreams for the MTA, and any potential further work, to be similar to the Group's proof-of-concept programme. This provides an opportunity to use a commercial plasmid, rather than a research-focused 'off the shelf' plasmid to generate the data required from the proof-of-concept studies. Furthermore, positive results from the MTA would provide valuable third-party validation regarding the ability of Nuvec® to improve a COVID-19 vaccine candidate.

## Other work programmes

### Manufacturing scale-up

N4 Pharma is working with Ardena, a Dutch-based contract development and manufacturing organisation, to complete technology transfer and manufacturing scale-up activities for Nuvec®. Work with Ardena has started well and the group is currently establishing an understanding of the current manufacturing process for Nuvec®. Once N4 Pharma has completed the proof-of-concept work and established a final formulation of Nuvec®, Ardena can support the manufacturing process to ensure the development of a consistent and reliable end-product as well as GMP certification.

### Oral vaccine programme

The Group is exploring the use of Nuvec® in other applications and has initiated a programme to establish the viability of Nuvec® as an oral delivery system. Feasibility work regarding this programme is ongoing, with a focus on assessing the ability of Nuvec® to transfect epithelial cells in the gut.

### Cancer therapeutics programme

The Group is also evaluating the use of Nuvec® as a delivery system for cancer therapies and has appointed Nanomerics to complete a preclinical proof of concept study. Initial work has commenced, however, at this time, Nanomerics is primarily focused on the completion of the optimisation work.

## IP Update

N4 Pharma continues to build a robust IP estate surrounding the use of Nuvec®. In February 2021, N4 Pharma noted that the University of Queensland received notification from the European Patent Office (EPO) of its intention to grant a patent in relation to Nuvec®. This patent has now been granted by the EPO. N4 Pharma has a licence for the exclusive worldwide rights to Nuvec® from the University of Queensland. It is important that the Group continues to expand its IP estate as a potential industry partner would want to see adequate patent protection surrounding the use of the platform.

## Peer group analysis

We have updated our peer group of London-listed drug developers from our initiation note (published in November 2020). We compare N4 Pharma to a number of London-listed, early-stage drug development companies. N4 Pharma's £16.1m market capitalisation is still well below the £80.5m median market capitalisation for the group, and we maintain that the wide applicability of Nuvec® and the progress made to date is not fully captured by its current valuation.

*Peer-group analysis of AIM or LSE Standard-listed companies*

| Name | Ticker | Mkt Cap (£m) |
|---|---|---|
| **Median** | **x** | **80.5** |
| **Average** | **x** | **102.7** |
| **N4 Pharma** | **N4P LN** | **16.1** |
| Hemogenyx Pharmaceuticals | HEMO LN | 20.3 |
| C4x Discovery Holdings | C4XD LN | 80.5 |
| Sareum Holdings | SAR LN | 230.0 |
| E-Therapeutics | ETX LN | 111.7 |
| Okyo Pharma | OKYO LN | 57.3 |
| Redx Pharma | REDX LN | 158.0 |
| Scancell Holdings | SCLP LN | 181.4 |
| Midatech Pharma | MTPH LN | 28.1 |
| 4basebio | 4BB LN | 57.2 |

*Source: Bloomberg*



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# Financials

## Income Statement

| Profit and Loss (£) | 2017A | 2018A | 2019A | 2020A |
|---|---|---|---|---|
| Fiscal period end-date | 31/12/2017 | 31/12/2018 | 31/12/2019 | 31/12/2020 |
| **Government Grant Income** | **109,913** | **72,832** | **-** | **-** |
| **Total revenue** | **109,913** | **72,832** | **-** | **-** |
| Costs of goods sold | - | - | - | - |
| **Gross profit** | **109,913** | **72,832** | **-** | **-** |
| *Gross Margin (%)* | *100%* | *100%* | *NA* | *NA* |
| R&D expenses | (409,808) | (846,176) | (216,948) | (900,410) |
| General & Admin. (incl exceptionals) | (316,632) | (643,745) | (730,392) | (664,011) |
| Share based payments | (281,298) | - | - | - |
| Depreciation & Amortisation | - | - | - | - |
| **TOTAL OVERHEAD EXPENSE** | **(1,007,738)** | **(1,489,921)** | **(947,340)** | **(1,564,421)** |
| **Operating profit (loss)** | **(897,825)** | **(1,417,089)** | **(947,340)** | **(1,564,421)** |
| **Finance Income** | - | - | - | - |
| **Finance Expense** | (1,029,033) | (981) | (1,385) | (1,963) |
| **Gain on sale of investment** | | 27,693 | | |
| **Profit before tax (loss)** | **(1,926,858)** | **(1,390,377)** | **(948,725)** | **(1,566,384)** |
| *tax (%)* | *19* | *19* | *19* | *19* |
| **tax** | 89,874 | 205,534 | 72,352 | 261,541 |
| **Profit after tax (loss)** | **(1,836,984)** | **(1,184,843)** | **(876,373)** | **(1,304,843)** |
| Ordinary Shares in issue (basic) | 64,783,082 | 89,440,373 | 100,168,016 | 136,303,141 |
| Ordinary Shares in issue (diluted) | 64,783,082 | 89,440,373 | 100,168,016 | 139,432,226 |
| **EPS (GBp)** | **(2.84)** | **(1.32)** | **(0.87)** | **(0.96)** |
| **EPS diluted (GBp)** | **(2.84)** | **(1.32)** | **(0.87)** | **(0.94)** |

*Source: Company announcements, SP Angel forecasts*



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## Cash Flow (GBP)

| Fiscal period end-date | 2017A 31/12/2017 | 2018A 31/12/2018 | 2019A 31/12/2019 | 2020A 31/12/2020 |
|---|---|---|---|---|
| **Profit/(Loss) before tax** | **(1,926,858)** | **(1,390,377)** | **(948,725)** | **(1,566,384)** |
| Finance expenditure | 5,299 | 981 | 1,385 | 1,963 |
| Deemed cost of acquisition | 1,023,734 | - | - | - |
| Share based payments to employees | - | 629 | 5,713 | 3,977 |
| Gain on sale of investments | - | (27,693) | - | - |
| **Operating gain/(loss) before changes in working capital** | **(897,825)** | **(1,416,460)** | **(941,627)** | **(1,560,444)** |
| | | | | |
| Movements in working capital | | | | |
| Trade and other receivables | (109,513) | (9,266) | 29,441 | (30,534) |
| Trade and other payables | 56,538 | 10,905 | (112,440) | 91,399 |
| Taxations | - | 70,574 | 220,568 | 120,507 |
| **Cash used in operations** | **(950,800)** | **(1,344,247)** | **(804,058)** | **(1,379,072)** |
| | | | | |
| **Net cash flows used in operating activities** | **(950,800)** | **(1,344,247)** | **(804,058)** | **(1,379,072)** |
| | | | | |
| **Investing activities** | | | | |
| Cash acquired on reverse acquisition | 402,990 | - | - | - |
| Sale of investments | - | 27,693 | - | - |
| **Net cash flows from investing activities** | **402,990** | **27,693** | **-** | **-** |
| | | | | |
| **Financing activities** | | | | |
| Finance expenditure | (5,299) | (981) | (1,385) | (1,963) |
| Net proceeds of ordinary share issue | 1,988,970 | 784,404 | 978,054 | 3,970,862 |
| Cost of share issue | (129,340) | - | - | - |
| **Net cash flow from financing activities** | **1,854,331** | **783,423** | **976,669** | **3,968,899** |
| | | | | |
| Net increase/(decrease) in cash and cash equivalents | 1,306,521 | (533,131) | 172,611 | 2,589,827 |
| Cash and cash equivalents at the beginning of the year | 19,751 | 1,326,272 | 793,141 | 965,752 |
| **Cash and cash equivalents at the end of the year** | **1,326,272** | **793,141** | **965,752** | **3,555,579** |

*Source: Company announcements, SP Angel forecasts*



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## Balance Sheet (GBP)

| Fiscal period end-date | 2017A 31/12/2017 | 2018 A 31/12/2018 | 2019A 31/12/2019 | 2020A 31/12/2020 |
|---|---|---|---|---|
| **Total non-current assets** | - | - | - | - |
| Trade and other receivables | 132,700 | 276,926 | 99,269 | 270,837 |
| Inventory | - | - | - | - |
| Cash and cash equivalents | 1,326,272 | 793,141 | 965,752 | 3,555,579 |
| **Total current assets** | **1,458,972** | **1,070,067** | **1,065,021** | **3,826,416** |
| **TOTAL ASSETS** | **1,458,972** | **1,070,067** | **1,065,021** | **3,826,416** |
| Trade and other payables | (143,788) | (159,666) | (51,547) | (142,484) |
| Accruals and deferred income | (35,430) | (30,457) | (26,136) | (26,598) |
| Borrowings and loans | - | - | - | - |
| **Total current liabilities** | **(179,218)** | **(190,123)** | **(77,683)** | **(169,082)** |
| **Total non-current liabilities** | - | - | - | - |
| **TOTAL LIABILITIES** | **(179,218)** | **(190,123)** | **(77,683)** | **(169,081)** |
| Share capital | 8,579,396 | 8,634,675 | 8,676,675 | 8,995,146 |
| Share premium | 8,513,670 | 9,328,848 | 10,327,258 | 13,945,602 |
| Share option reserve | 147,635 | 81,909 | 25,266 | 63,290 |
| Reverse Acquisition reserve | (14,138,244) | (14,138,244) | (14,138,244) | (14,138,244) |
| Merger Reserve | 299,045 | 279,347 | 279,347 | 279,347 |
| Retained Earnings | (2,121,748) | (3,306,591) | (4,182,964) | (5,487,807) |
| **TOTAL EQUITY** | **1,279,754** | **879,944** | **987,338** | **3,657,334** |

*Source: Company announcements, SP Angel forecasts*



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Buy - Expected return >15%

Hold - Expected return range -15% to +15%

Sell - Expected return < 15%