

13 December 2021

N4 Pharma Plc

("N4 Pharma" or the "Company")

Operational Update

N4 Pharma Plc (AIM: N4P), the specialist pharmaceutical company developing Nuvec®, a novel delivery system for cancer treatments and vaccines, is pleased to provide a strategic update following data from its proof-of-concept programmes and ongoing activities.

As announced previously, the Company has spent the last few months conducting various *in vivo* studies both in oncology and vaccine delivery. In parallel, work has continued with third party collaborators under Material Transfer Agreements ("MTAs").

Oncology programme

The Company has successfully completed an *in vivo* confirmatory oncology study which reinforces the results from an earlier pilot study. The initial pilot study was designed to test the ability to use a monodispersed Nuvec® formulation in an *intra venous* ("i.v") route of administration using a DNA plasmid (pDNA) encoding TNF alpha to assess the tolerance of different doses and to look at tumour regression.

The confirmatory study incorporated the following control and test groups: TNF alpha pDNA alone, unloaded Nuvec®, Nuvec® loaded with 50ug of the TNF alpha pDNA and Nuvec® loaded with 20ug of TNF alpha pDNA. The study was conducted in untreated tumour-bearing mouse models with dosing for each cohort completed intravenously.

The results showed a clear inhibition of tumour progression for the groups where Nuvec® was loaded with TNF alpha pDNA when compared to the other three groups. In addition, the use of Nuvec® was shown to improve animal survival rates in the life of the study.

These excellent findings show that injection of a TNF alpha plasmid loaded onto Nuvec® into tumour bearing mice successfully leads to the transfection and release of TNF alpha which results in the suppression of tumour growth and increased survival rates.

The results from the successful oncology study are an exciting finding and opens up the field of gene therapy and *in vivo* protein production as a key opportunity for Nuvec®. This will become an important area of focus moving forward. This advancement is the result of the ongoing optimisation work to produce a consistently monodispersed product, presenting potentially huge market opportunities for Nuvec®.

In vivo studies for vaccine delivery

The preliminary results from mouse immunogenicity studies carried out by Evotec using Covid-19 plasmid DNAs and other controls have not shown meaningful immunological response despite good *in vitro* antigen expression. Lack of immunological response in positive control animals brings into question the validity of the whole study. Nevertheless these results again highlight that a number of variables such as dose, route of administration, timing of injection and formulation require extensive optimisation for each plasmid loaded onto Nuvec®. Likewise, the Company's initial mRNA OVA *in vivo* immunogenicity study showed sub optimal responses. As a result, the Company has taken the decision to concentrate future vaccine work through its MTAs with a focus on specific products linked to proprietary DNA or mRNA sequences.

This strategy is validated by the fact that the Company is in advanced discussions with another company focussing on mRNA delivery with a view to scoping the work to be undertaken under a new MTA. This is in addition to the two ongoing MTAs signed looking at Nuvec® with proprietary Covid 19 DNA plasmids and gene therapy.

Aside from the *in vivo* work, The Medicines Catapult has recently assessed, *in vitro*, Nuvec® loaded with DNA that had been stored at room temperature for six months. Cell transfection was successful demonstrating the stability of the Nuvec® loaded with DNA and the potential storage advantages of Nuvec. Thus, it has been shown that both mRNA and DNA loaded on Nuvec® are conferred a high level of stability which may be an important feature in the MTA related studies.

Next Steps

Taking into account the recent data and very positive oncology work, the Company has strategically decided to focus its resources on advancing its work in gene therapy whilst continuing its vaccine delivery efforts in conjunction with partners working with specific, proprietary products. Once the full analysis is complete on the oncology study, the Company will scope out the next study in this area to commence early in the new year with a view to demonstrating a clinically relevant therapeutic effect with a targeted end point that will enable the Company to enter commercial discussions in this area.

Nigel Theobald, Chief Executive Officer of the Company, commented: "We are delighted with the results from our more expansive oncology study repeating and validating the earlier results from our pilot. Having successfully formulated a monodispersed version of Nuvec®, this has allowed the Company to determine the most attractive way for it to commercialise Nuvec®.

"Whilst the results on the vaccine work from Evotec were unexpected, the proof-of-concept data, that we have collated to date, has been sufficient to allow the Company to sign MTAs with potential vaccine collaborators. We expect other collaborations will follow, so it makes sense to continue the vaccine platform optimisation with collaborators who own their own DNA plasmids and mRNA compounds. This will allow us to focus internal efforts on developing commercial products in the gene therapy space.

"The Company remains well funded to complete the next phase of its gene therapy product development which we believe will give it the greatest chance to negotiate partnerships in this space with a range of different companies.

"I believe this evolved strategy gives us the best opportunity to grow the Company into a successful and sustainable life sciences business."

The information contained within this announcement is deemed by the Company to constitute inside information as stipulated under the Market Abuse Regulations (EU) No. 596/2014 which

has been incorporated into UK law by the European Union (Withdrawal) Act 2018. Upon the publication of this announcement via Regulatory Information Service, this inside information is now considered to be in the public domain.

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About N4 Pharma

N4 Pharma is a specialist pharmaceutical company developing a novel delivery system for cancer and vaccine treatments using its unique silica nanoparticle delivery system called Nuvec®.

N4 Pharma's business model is to partner with companies developing novel antigens for cancer and vaccine treatments to use Nuvec® as the delivery vehicle to get their antigen into cells to express the protein needed for the required immunity. As these products progress through pre clinical and clinical programs, N4 Pharma will seek to receive up front payments, milestone payments and ultimately royalty payments once products reach the market.

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