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N4 Pharma PLC
14 September 2022

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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 an operational update on its development plans for commercialising Nuvec®.

On 13 June 2022 and 15 July 2022, the Company provided updates that *in vivo* investigations of Nuvec® loaded with various doses of TNF alpha had showed clear tumour suppression and that the Company had successfully loaded Nuvec® with siRNA and shown a good *in-vitro* knockdown response.

The Company has now completed initial testing on loading Nuvec® with two generic siRNA probes, GFP (Green Fluorescent protein) and EHMT-2 (Euchromatic Histone Lysine Methyltransferase 2) at the same time. The Company's next step will be 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.

Following this work, the Company has undertaken a review of where it believes it will likely get greatest traction to allow a commercial license deal to be agreed, in addition to the ongoing MTA work it already has in place.

After the development of successful mRNA vaccines, major companies in this space appear to be focusing future development on gene therapy treatments in particular using siRNA to silence identified pathways involved in cancer. Given the pre-clinical status of Nuvec®, the Company believes that focusing its work on loading more than one siRNA sequence onto the same nanoparticle will result in silencing of complimentary pathways leading to an increased therapeutic response and establish a significant differential in this marketplace.

Having established the capability of Nuvec® to carry two siRNA species and provide a functional response, the Company is now undertaking a series of experiments over the coming months using two siRNA sequences directed against known, and clinically validated, oncology targets. Specifically, the targets are the EGFR signalling pathway, which regulates cell cycle progression and BCl-2, which regulates apoptosis, a form of programmed cell death. Silencing of the EGFR pathway is expected to inhibit cell division while silencing BCl-2 will promote apoptosis and the potential for additive or synergistic effects will be explored. Initial studies will be conducted *in vitro* using a lung cancer cell line. This will be followed by *in vivo* studies in mice.

Further updates will be provided as this programme of work progresses.

Nigel Theobald, Chief Executive Officer of the Company, commented:

"The world of vaccines and cancer therapy development is a fast changing one and the wide applicability of Nuvec® as a delivery system leaves us well placed to adapt to this ever-changing climate.

"We have now identified a very strong commercial point of difference for Nuvec® in that it can be successfully loaded with at least two siRNA genes and maintain a monodisperse formulation. The area of combination cancer treatments is attracting a lot of interest and investment and siRNA is an exciting and growing area for clinical development. Our research has shown over 300 companies active in the RNA gene therapy space with 106 clinical trials using siRNA already underway and likely many more to follow.

"Vaccine developers are looking to use their existing tried and tested systems in late-stage clinical work but companies working with siRNA are much more open to using novel delivery systems with a strong point of difference and are mainly focused in early-stage clinical work making this an ideal space for Nuvec®. Our vaccine work is reliant on finding a partner to take Nuvec® into clinical development, however using the siRNA genes EGFR and BCl-2 allows us to demonstrate the efficacy of using Nuvec® ourselves in a proven clinical model, without major investment.

"We remain well funded to complete the next phases of our siRNA work and present this data to Companies working in this space with a view to licensing Nuvec®."

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.

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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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