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N4 Pharma plc
("N4 Pharma" or the "Company")

N4 101 *in vitro* Results

Latest data demonstrate key benefits of the Nuvec® delivery platform

N4 Pharma Plc (AIM: N4P),the UK biotech developing Nuvec® its proprietary gene delivery system to enable advanced therapies for cancer and other diseases, is pleased to provide a progress update on the *in vitro* pre-clinical development of its lead Nuvec® proof-of-concept programme, N4 101, an oral anti-inflammatory product for the treatment of Inflammatory Bowel Disease (IBD).

The size of the global RNA therapeutics market was $13.7 billion in 2023 and is expected to reach $18.0 billion by 2028[1]. Challenges associated with the manufacturing and delivery of RNA therapeutics are known to impact this market growth - challenges which N4 Pharma is addressing with its Nuvec® technology, aiming to become an industry leading delivery platform used by multiple pharmaceutical partners.

N4 Pharma's oral IBD product, N4 101, is designed to showcase the key benefits of the Nuvec® delivery technology where other approaches struggle: i) it can straightforwardly load multiple RNA therapeutics onto the same particle, ii) it protects the payload from enzyme degradation to allow oral delivery to the gut and iii) it can be functionalised to target specific cells.

The Company has completed a series of *in vitro* experiments (see Methodology below for details) which clearly demonstrate these competitive advantages.

Key Highlights:

- The efficiency of delivery and efficacy of an siRNA and an mRNA therapeutic used to treat IBD are demonstrably enhanced when delivered by targeted Nuvec® particles compared with untargeted delivery;
- A Nuvec® formulation dual loaded with both therapeutics at the same time shows equivalent efficacy to the separate treatments;
- A patent has been filed reflecting the clear advantages of Nuvec® for targeting and dual loading; and,
- The Company is awaiting ethics committee approval to build on these excellent *in vitro* data and begin an *in vivo* study in an appropriate animal model early in 2025 at the University of Queensland.

Find more information and an additional video by Nigel Theobald, CEO and submit any questions via the N4 Pharma investor hub:*https://investors.n4pharma.com/link/4PK87y*.

[1]Marketsandmarkets: RNA Therapeutics Market size and share sep 2024

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

"RNA therapeutics are set to impact the treatment of a wide range of diseases and the ability to deliver multiple therapies in a targeted fashion is going to be central to the success of these new treatments.

"The data we have generated using our IBD proof-of-concept programme, N4 101, clearly demonstrates the dual loading capability of Nuvec® and the ability to target Nuvec® to specific cells, both of which are difficult to achieve in a controlled way with other delivery approaches such as lipid nanoparticles.

"Targeting two RNA therapies simultaneously means they act on different pathways in the same cell and the data we have released today show that a dual loaded Nuvec® treatment results in a decrease in pro-inflammatory TNF-alpha together with an increase in anti-inflammatory IL-10 in this in vitro cell-based assay.

"These data represent further excellent validation of our Nuvec® platform and for the potential of N4 101 to make a difference in the future to patients with IBD.

"We will continue to strengthen our pre-clinical data and work towards first-in-human clinical data for Nuvec® with the aim of securing multiple commercial partnerships for the platform."

Methodology

The objective of RNA therapeutics is to deliver RNA into specific cells to stimulate a reduction or an increase in the production of certain proteins depending on the disease that is being treated.

In the recent *In vitro* experiments, mouse macrophage cells were used to establish the ability of Nuvec® delivered RNA to:

1. to reduce the production of TNF-alpha which is a chemical produced by the immune systems that causes inflammation, and
2. to increase the expression of IL-10 which is a molecule that has an anti-inflammatory role.

In the treatment of an inflammatory condition such as IBD a reduction in TNF-alpha production and an increase in IL-10 is desirable.

Cells were exposed to Nuvec® with and without functionalisation with mannose that binds to the CD206 mannose receptor, which is expressed on the surface of macrophages, the cells that are believed to cause the problems associated with IBD. Functionalisation with mannose has the effect of targeting the Nuvec® particles to the macrophages.

Cells were treated separately in one experiment with Nuvec® loaded with an siRNA designed to reduce TNF-alpha production and in a separate experiment with Nuvec® loaded with an mRNA designed to increase IL-10 production. The mannose receptor-targeted Nuvec® siRNA treatment significantly reduced the production of TNF-alpha, and showed faster and greater reduction compared to non-targeted Nuvec®. Targeted particles carrying the mRNA showed a faster and greater increase in IL-10 expression than non-targeted particles. These data demonstrate the ability to target active RNA therapeutics to a specific cell type using Nuvec®.

In a separate experiment both the siRNA and mRNA were loaded on the same mannose-targeting Nuvec® particle in a controlled ratio. A qualitatively similar reduction in TNF-alpha and increase in IL-10 was observed to the single loaded versions, showing that Nuvec® can be dual loaded and deliver active RNA therapies to the same cell simultaneously.

For more information please contact:

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Via N4 Pharma Investor Hub

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Glossary

RNA: Ribonucleic acid, present in all living cells

mRNA: messenger RNA, whose role is to carry protein information from the DNA in a cell's nucleus to the cells cytoplasm to produce a particular protein.

siRNA: small interfering RNA, a short double-stranded RNA, one of whose strands can complement and inactivate a sequence mRNA to stop protein production.

IBD: Inflammatory Bowel Disease (Crohns disease & ulcerative colitis)

Macrophages: A type of white blood cell that surrounds and kills microorganisms, removes dead cells, and stimulates the action of other immune system cells, in IBD the stimulation of

inflammation aspect is key.

TNF alpha: Tumour Necrosis Factor alpha (TNF alpha), is an inflammatory cytokine produced by macrophages/monocytes during acute inflammation.

Mannose: a sugar important in human metabolism, especially in the glycosylation of certain proteins.

Glycosylation: is the process by which a carbohydrate is covalently attached to a target macromolecule, typically proteins and lipids but in this case Nuvec®

Ligand: A molecule that binds to another molecule, used especially to refer to a small molecule that binds specifically to a larger molecule

IL10: Interleukin 10, also known as human cytokine synthesis inhibitory factor (CSIF), is an anti-inflammatory cytokine.

Cytokine: A type of protein that is made by certain immune and non-immune cells and has an effect on the immune system. Some cytokines stimulate the immune system and others slow it down.

About N4 Pharma

N4 Pharma is a pre-clinical biotech company developing Nuvec®,its proprietary gene delivery system, to enable advanced therapies for cancer and other diseases.

RNA therapeutics are set to impact the treatment of a wide range of diseases and Nuvec® has several key advantages for RNA gene delivery including the ability to deliver multiple RNA therapies in a single particle, ease of manufacturing,protection of the RNA payload to allow for oral delivery, no unwanted immune response and excellent stability and storage.

N4 Pharma is building out its preclinical data set, and working towards first-in-human clinical data, to support significant licensing deals for its Nuvec® platform with gene therapy partners.

N4 Pharma lead programme, N4 101, is an oral anti-inflammatory product for IBD which serves as a proof-of-concept programme showcasing all the benefits of the Nuvec® platform.

For further information on the Company visitwww.n4pharma.comor sign up athttps://investors.n4pharma.com/auth/signup.

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