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N4 Pharma Plc
("**N4 Pharma**" or the "**Company**")

siRNA 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 further update on its ongoing *in vitro* siRNA research work.

BCL-2 assay has been established

Further to the announcement on 18 April 2023, the Company has now completed work on establishing assays to measure how Nuvec® loaded with BCL-2 siRNA can silence expression of the BCL-2 protein. BCL-2 is a form of protein that regulates cell death in healthy cells however aberrant expression can facilitate tumour development and resistance to cancer therapy.

Testing underway to generate dose response curve for BCL-2 studies

This means that the Company can now proceed to generate a dose response curve for knockdown of BCL-2 expression to compliment the one already generated for EGFR (epidermal growth factor receptor). EGFR is found on the surface of some normal cells and is involved in cell growth. It may also be found at high levels on some types of cancer cells, which causes these cells to grow and divide.

In vitro studies indicate similar inhibition profile to two commercial therapies

Further *in vitro* studies have demonstrated that the maximum inhibition of cell growth by SiRNA to either EGFR or BCL-2 loaded on Nuvec® was comparable to that produced by two commercially available small molecule drugs, Gefitinib for EGFR and Venetoclax for BCL-2.

Gefitinib: (sold in Europe and Asia) is a type of targeted small molecule cancer drug called a tyrosine kinase inhibitor (TKI). Tyrosine kinases are proteins that send signals telling cancer cells to grow. Gefitinib blocks these signals. For Gefitinib to work the cancer cells need to have receptors for EGFR.

Venetoclax: sold under the brand names Venclexta and Venclyxto, is a type of targeted therapy drug called a BCL-2 inhibitor (blocker)used to treat adults with chronic lymphocytic leukaemia, small lymphocytic lymphoma, or acute myeloid leukaemia. Some leukaemia or cancer cells make too much of the BCL-2 protein.

Next steps

Further work is planned to assess the minimal loading of siRNA on Nuvec® to achieve comparable inhibition to the two commercially available drugs. The next step in the *in vitro research work* is to undertake a full dose response curve study for siRNA loaded Nuvec® and compare to the dose response curve for Gefitinib and Venetoclax.

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

"We are very pleased with these *in vitro* results for Nuvec® loaded with EGFR and BCL-2, which show that the first investigated dose produces comparable cellular apoptosis to two commercially available products.

"We also now have the assay established to complete the dose response expression work for BCL-2, but we already know that BCL-2 must be expressed, as the cell apoptosis work has shown that it knocks down the gene to produce cell death."

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Glossary

siRNA: silencing RNA / short interfering RNA

Nucleotides: organic molecules composed of a nitrogenous base, a pentose sugar and a phosphate.

EGFR: epidermal growth factor receptor, is found on the surface of some normal cells and is involved in cell growth. It may also be found at high levels on some types of cancer cells, which causes these cells to grow and divide.

BCL-2: (B-cell lymphoma 2), encoded in humans by the BCL-2 gene, is the founding member of the BCL-2 family of regulator proteins that regulate cell death.

Cell apoptosis: the process of programmed cell death.

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 upfront payments, milestone payments and ultimately royalty payments once products reach the market.

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