Alnylam Pharmaceuticals is developing a novel therapy for the treatment of acute porphyria

Alnylam is a growing biotechnology company located in Cambridge, Massachusetts (USA). They are focused on developing a new class of medicines using a naturally occurring process in cells called RNA interference (RNAi). While DNA (deoxyribonucleic acid) is the chemical in cells that forms our genes and holds our genetic information, RNA is the chemical that cells use to produce proteins from the genes. Small interfering RNA (siRNA), the molecules that mediate RNAi, block the ability of RNA to make specific proteins, some of which cause diseases. While other classes of drugs, such as antibodies, are designed to inactivate proteins by directly binding to them, RNAi therapeutics act by preventing the production of disease-causing proteins. Thus, the RNAi approach can be thought of as trying to "turn off the tap" on disease-causing proteins; whereas other classes of medicines can be thought of as "mopping up the floor". RNAi therapies have been demonstrated to safely and effectively block the production of disease-causing proteins in animal models of human disease, as well as in humans in the early phases of clinical trials.

Alnylam is developing a new therapy, called ALN-AS1, to treat acute porphyria patients that have a defect in heme synthesis enzymes in the liver (acute hepatic porphyria). This therapy targets the first enzyme in heme synthesis in the liver, called aminolevulinic acid synthase (ALAS1). During acute attacks, ALAS1 protein levels increase, leading to overproduction of downstream heme intermediates, such as porphobilinogen (PBG) and aminolevulinic acid (ALA), that are thought to be the cause of attacks. By lowering the amount of ALAS1 proteins that can be made during an attack, this investigational RNAi therapy has the potential to reduce the levels of heme intermediates that trigger attacks.

Alnylam is starting the ***explore*** study – an observational study (no treatment is given) – this autumn, in patients with acute hepatic porphyria that have multiple yearly attacks (or are taking medication to prevent attacks). The study aims to better understand the disease course and treatment that these patients experience. Information obtained from this study may help increase healthcare providers' understanding of acute porphyria, as well as aid in the design of future clinical trials that test novel therapeutics, such as ALN-AS1. The ***explore*** study is enrolling in the UK at King's College Hospital, London and the University Hospital of Wales, Cardiff and is collaborating with the National Acute Porphyria Service (NAPS). If you would be

interested in taking part in this study, please contact the BPA on 0300 30 200 30 or helpline@porphyria.org.uk and we will send you more information.

In addition, Alnylam plans to initiate a phase 1 study with ALN-AS1 in late 2015. For more information on Alnylam and the status of the ALN-AS1 porphyria programme, please visit: *www.alnylam.com*.