RNAi Medication Discovery Helps Improve Quality Of Life In Rare Disease Patients

Max Planck Society (MPG)

The research of Thomas Tuschl has enabled an entirely new class of therapeutics which is harnessing the potential of RNA interference (RNAi). As a researcher at the Max Planck Institute for Biophysical Chemistry, located in Goettingen, Germany, Tuschl was able to prove that the known RNAi mechanism is effective in mammals and, consequently, in humans.

His patented research findings were exclusively licensed in 2002, to Alnylam Pharmaceuticals, a leading RNAi therapeutics company, and in 2018 they received the first-ever FDA approval of an RNAi Therapeutic, ONPATTRO® (patisiran). ONPATTRO® (patisiran) is approved for the treatment of the polyneuropathy of hereditary transthyretin-mediated (hATTR) amyloidosis in adults. hATTR is a rare, adult-onset disease that can be life-threatening and lead to dysfunction of various organs and tissues, including the heart and kidneys. In the largest controlled study of hATTR amyloidosis, ONPATTRO was shown to improve polyneuropathy – with significant benefit on the neurological

components of the disease in many patients – and to improve a composite quality of life measure, reduce autonomic symptoms, and improve activities of daily living.

Amy, a hATTR patient, started with a clinical trial, and in the four-plus years she's used ONPATTRO, she's regained some strength and endurance, and is able to eat regular food.

> *"After a few months, I began to have an appetite, and I was soon able to eat real food more and more, and use the feeding tube less and less. Eventually, I was able to stop using the feeding tube completely. I was so grateful I was given the chance to try something other than liver transplant surgery."*

In a testimonial, ONPATTRO user Mike said, "I am happy to report that my symptoms have improved since I started on ONPATTRO. I no longer have pains in my hands and feet, and the numbness and tingling only happen at night in my hands, where it used to happen all over, all the time. [...] Above all, I'm so thankful to be able to concentrate on the good things in my life: spending time with my wife, and being a loving dad to my kids."

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The natural cellular process of gene silencing makes it possible to "switch off" individual genes by introducing synthetically produced short strands of RNA into the cell, destroying the relevant mRNA and deactivating a single gene. Max Planck Innovation, the tech transfer office of the Max Planck Society, saw the enormous potential for future medical applications especially for hereditary diseases and campaigned for the patenting and marketing of the technology.

In 2019, Alnylam received FDA approval for its drug GIVLAARI®(givosiran), also based on Tuschl's RNAi research. The newly approved active agent givosiran is used in the treatment of acute hepatic porphyria (AHP), an extremely rare genetic disease. With Oxlumo® (Lumasiran) a third RNAi drug using Tuschl's research has been approved in 2020 by the authorities in the USA and Europe. The very rare genetic disease "primary hyperoxaluria type 1" can be treated with the new drug. Alnylam employs more than 2,000 people at 19 locations worldwide, with a market value of around $15 billion. They have a further 12 drugs currently in clinical development.

Max Planck Innovation took the lead in filing the patent application for the so-called Tuschl I and II patents and was actively involved in the granting of the patents. The RNAi medications of Alnylam are based on the Tuschl patents. The Tuschl I patented technology is based on joint research by the Max Planck Society, the Whitehead Institute for Biomedical Research at the Massachusetts Institute of Technology, and University of Massachusetts. The Tuschl II patent is based on the research of the Max Plank Society alone, where it was discovered that RNAi works in mammalians, including humans.

Max Planck Innovation pooled these technologies and took the lead in licensing. In addition, Max Planck Innovation promoted and supported the establishment Alnylam, and later the merger with Ribopharma. The license revenues for Max Planck Society alone from the RNAi patents (therapeutics and research tools) are over $30 million to date.

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