RNAi FACT SHEET

# Alnylam is Leading the RNAi Revolution™

## Alnylam has pioneered RNA interference (RNAi) therapeutics, an innovative class of medicines that's disrupting disease.

Alnylam was founded in 2002 to harness the breakthrough discovery of RNAi to treat disease in a different way and transform the lives of patients who have no or inadequate treatment options.

Performing the earliest research to leverage the naturally occurring RNAi process to silence genes that cause disease, Alnylam pioneered the first phase of the RNAi Revolution. Through sustained research and development efforts over more than 15 years, Alnylam's work yielded the critical breakthroughs and innovations that made the field of RNAi therapeutics possible.

In 2018, the world's first RNAi therapeutic—and Alnylam's first commercial medicine—was approved. Since then, Alnylam has brought forward multiple medicines, with a robust and rapidly expanding pipeline of investigational therapies across disease areas. Our approved RNAi therapeutics are currently available in more than 60 countries.

### What Are RNAi Therapeutics?

**RNAi therapeutics are a type of gene-silencing medicine.**

They represent an innovative, clinically-validated approach to treating rare and common diseases.

### How Do RNAi Therapeutics Work?

**RNAi therapeutics silence the genes that cause or contribute to disease.**

Many genes contain the instructions for making proteins. Proteins are the "workers" in the biochemistry of life and are responsible for almost all cellular and body functions.

Sometimes a mutation in a gene results in a faulty protein that causes disease, or other times, a normal gene produces a protein that contributes to disease. RNAi therapeutics can treat disease in both scenarios by interfering with the production of these unwanted proteins.

They use specially designed small interfering RNA (siRNA) to target messenger RNA (mRNA) that genes use to tell the body how to make the unwanted proteins. The mRNA molecules are degraded before they can pass the message.

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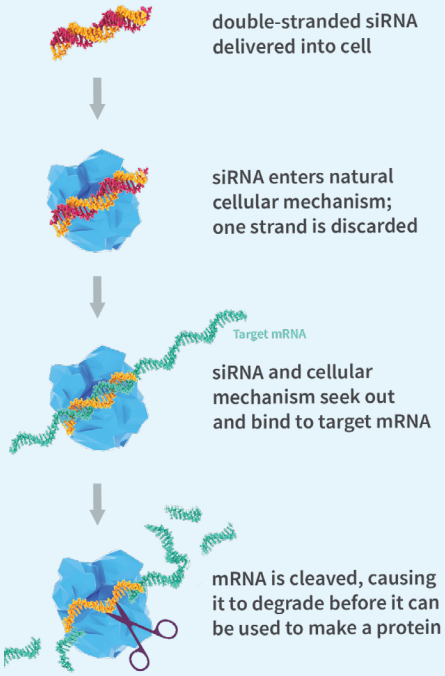
## Our Expanding Pipeline –

We are rapidly expanding our pipeline, working across rare and common diseases—including cardiometabolic and neurologic disorders—to bring RNAi therapeutics to many additional patients.

## Nobel Prize Winning –

The discovery of RNAi was awarded the 2006 Nobel Prize in Physiology or Medicine.

## The Process of RNAi Therapeutics –



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## How Do RNAi Therapeutics Differ From Conventional Medicines?

### They act before proteins are made.

Most conventional pills, injections and infusions work by directly targeting proteins involved in disease after they are already made. In contrast, RNAi therapeutics disrupt the production of unwanted proteins, acting **before** they are made. If a disease is compared to a leaking tap, then RNAi provides a new way of fixing the leak, rather than mopping up the floor after the leak has occurred.

### They are long-lasting.

Many conventional medicines must be taken daily to be effective. In contrast, a single dose of an RNAi therapeutic can reduce the levels of a protein for months, which means that it can be administered infrequently—every three or six months, for example. Patients can be prescribed and administered an RNAi therapeutic to optimally treat their disease without worrying about having to take a daily dose.

## How Does RNAi Differ from Other Genetic Medicines?

### RNAi therapeutics are a class of medicines within the broader category of genetic medicines that employ DNA and/or RNA to treat disease but they differ in an important way.

Unlike some genetic medicines such as CRISPR-based treatments, RNAi therapeutics don't permanently alter the genes (DNA) within cells. This is a key safety feature of the RNAi approach to treating disease.

## From Rare to Common Diseases—Challenge Accepted!

### Rare diseases validated the concept and proved to be just the beginning for RNAi therapeutics.

We continue to pursue treatments for devastating rare diseases, but we've also expanded to common diseases, which generally have more complex causes.

With one Alnylam-discovered medicine already approved to treat a common disease, and multiple programs in development to treat diseases like hypertension, Alzheimer's disease and type 2 diabetes mellitus, Alnylam is working to bring the therapeutic benefits of RNAi to millions of people around the world.

Learn more at alnylam.com

"RNAi therapeutics are now a proven class of innovative medicines, and with our strong track record of clinical success, we're scaling to bring our transformative technology to many additional patients living with both rare and common diseases, disrupting the way that diseases are treated."

Dr. Pushkal Garg
CHIEF MEDICAL OFFICER AND EVP, DEVELOPMENT & MEDICAL AFFAIRS

"Founded in 2002, the year after RNAi was first observed in mammals, Alnylam has followed the science for more than two decades, challenging medical wisdom and overcoming obstacles to pioneer a new class of medicines, with the single-minded goal of helping patients."

Dr. Kevin Fitzgerald
CHIEF SCIENTIFIC OFFICER AND EVP, RESEARCH & EARLY DEVELOPMENT