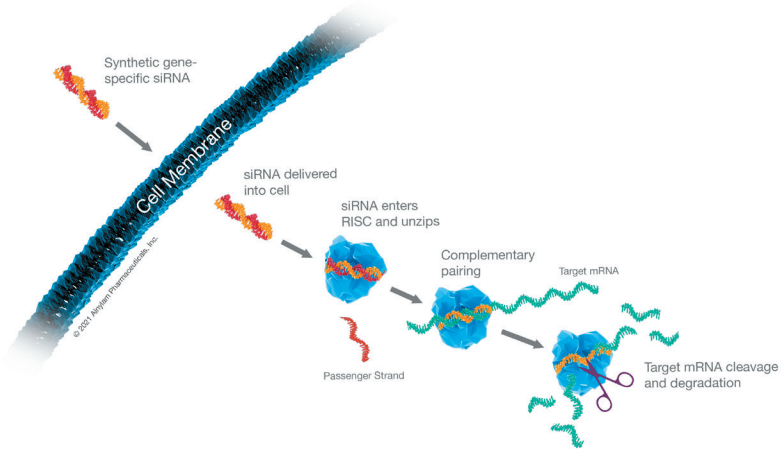
Alnylam Pharmaceuticals

Focused on Developing RNAi Therapeutics

Alnylam is a biopharmaceutical company leading the development of RNA interference (RNAi) therapeutics. The discovery of RNAi has been heralded as a major scientific breakthrough, and represents one of the most promising and rapidly advancing frontiers in biology and drug discovery today.

RNAi is a natural mechanism of gene silencing that occurs in organisms ranging from plants to mammals. RNAi therapeutics in development have the potential to treat diverse disease states and help patients in a fundamentally new way.



Investigational RNAi Therapeutics

Active Product Pipeline and Experience to Date

RNAi therapeutics in development by Alnylam are engineered to enable a consistent level of target knockdown. Alnylam's pipeline of investigational RNAi therapeutics is focused in four Strategic Therapeutic Areas (STArs): **Genetic Medicines, Cardio-Metabolic Diseases, Infectious Disease**, and **CNS/Ocular Diseases**. These STArs represent a range of diseases from rarest to most common globally.

PROGRAMS CURRENTLY IN CLINICAL DEVELOPMENT*
11

PEER-REVIEWED PAPERS*
>250

CLINICAL STUDIES TO DATE*
>40

LONGEST DURATION OF EXPOSURE*
>8 yrs

** As of January 2023 across all active programs. Numbers are approximate as many studies are ongoing and several are blinded.*

To learn more about Alnylam and our pipeline advancements, please visit Alnylam.com

Alnylam®

Our Pipeline

Focused in 4 Strategic Therapeutic Areas (STARs):

Genetic Medicines | Cardio-Metabolic Diseases | Infectious Diseases | CNS/Ocular Diseases

		HUMAN POC[1]	BREAKTHROUGH DESIGNATION	EARLY/MID STAGE *(IND or CTA Filed-Phase 2)*	LATE STAGE *(Phase 2-Phase 3)*	REGISTRATION/ COMMERCIAL[2] *(OLE/Phase 4/IIS/registries)*	COMMERCIAL RIGHTS
ONPATTRO® (patisiran)[3]	*hATTR Amyloidosis-PN*	✓	✓			●	Global
GIVLAARI® (givosiran)[4]	*Acute Hepatic Porphyria*	✓	✓			●	Global
OXLUMO® (lumasiran)[5]	*Primary Hyperoxaluria Type 1*	✓	✓			●	Global
Leqvio® (inclisiran)[6]	*Hypercholesterolemia*	✓				●	Milestones & up to 20% Royalties[7]
AMVUTTRA® (vutrisiran)[8]	*hATTR Amyloidosis-PN*	✓				●	Global
Patisiran	*ATTR Amyloidosis-CM Label Expansion*	✓				●	Global
Vutrisiran	*ATTR Amyloidosis-CM*	✓			●		Global
ALN-TTRsc04	*ATTR Amyloidosis*	✓		●			Global
Fitusiran	*Hemophilia*	✓			●		15-30% Royalties
Cemdisiran (+/- Pozelimab)[9]	*Complement-Mediated Diseases*	✓			●		Global Milestone/Royalty
Belcesiran[10]	*Alpha-1 Liver Disease*	✓		●			Ex-U.S. option post-Phase 3
ALN-HBV02[11] (VIR-2218)	*Hepatitis B Virus Infection*	✓		●			50-50 option post-Phase 2
Zilebesiran (ALN-AGT)	*Hypertension*	✓		●			Global
ALN-HSD	*NASH*	✓		●			Royalty
ALN-APP	*Alzheimer's Disease; Cerebral Amyloid Angiopathy*			●			50-50
ALN-PNP	*NASH*			●			50-50
ALN-KHK	*Type 2 Diabetes*			●			Global

[1] POC, proof of concept – defined as having demonstrated target gene knockdown and/or additional evidence of activity in clinical studies
[2] Includes marketing application submissions
[3] Approved in the U.S. and Canada for the polyneuropathy (PN) of hATTR amyloidosis in adults, and in the EU, Japan and other countries for the treatment of hATTR amyloidosis in adults with stage 1 or stage 2 PN
[4] Approved in the U.S., Brazil and Canada for the treatment of adults with acute hepatic porphyria (AHP), and in the EU and Japan for the treatment of AHP in adults and adolescents aged 12 years and older
[5] Approved in the U.S. for the treatment of primary hyperoxaluria type 1 to lower urinary and plasma oxalate levels in children and adults, and in the EU and Brazil for the treatment of primary hyperoxaluria type 1 in all age groups
[6] Novartis has obtained global rights to develop, manufacture and commercialize inclisiran
[7] 50% of inclisiran royalty revenue from Novartis will be payable to Blackstone by Alnylam
[8] Approved in the U.S. for the polyneuropathy (PN) of hATTR amyloidosis in adults, and in the EU and Japan for the treatment of hATTR amyloidosis with stage 1 or 2 polyneuropathy
[9] Alnylam and Regeneron are evaluating potential combinations of the investigational therapeutics cemdisiran and pozelimab
[10] Dicerna is leading and funding development of Belcesiran
[11] Vir is leading and funding development of ALN-HBV02

As of December 2022