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 (STAr(s): Genetic Medicines, Cardio-Metabolic Diseases, Infectious Disease, and CNS/Ocular Diseases. These STAr(s) represent a range of diseases from rarest to most common globally.

*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
## Our Pipeline

Focused in 4 Strategic Therapeutic Areas (STArS):

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<th>Genetic Medicines</th>
<th>Cardio-Metabolic Diseases</th>
<th>Infectious Diseases</th>
<th>CNS/Ocular Diseases</th>
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<td><strong>EARLY/MID STAGE</strong></td>
<td><strong>LATE STAGE</strong></td>
<td><strong>REGISTRATION/COMMERCIAL</strong></td>
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<td>(Mid to Late-Phase 2)</td>
<td>(Phase 2-Phase 3)</td>
<td>(Ole/Phase 4/Phase 4-IIS/registries)</td>
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- **ONPATTRO®** *(patisiran)*
  - hATTR Amyloidosis-PN
  - Global

- **AMVUTTRA®** *(vutrisiran)*
  - hATTR Amyloidosis-PN
  - Global

- **GIVLAARI®** *(givosiran)*
  - Acute Hepatic Porphyria
  - Global

- **OXLUMO®** *(lumasiran)*
  - Primary Hyperoxaluria Type 1
  - Global

- **Leqvio®** *(inclisiran)*
  - Hypercholesterolemia
  - Milestones & up to 20% Royalties

- **Patisiran**
  - ATTR Amyloidosis-CM Label Expansion
  - Global

- **Vutrisiran**
  - ATTR Amyloidosis-CM
  - Global

- **Fitusiran**
  - Hemophilia
  - 15-30% Royalties

- **Cemdisiran (+/- Pozelimab)**
  - Complement-Mediated Diseases
  - Global Milestone/Royalty

- **ALN-TTRsc04**
  - ATTR Amyloidosis
  - Global

- **Belcesiran**
  - Alpha-1 Liver Disease
  - Ex-U.S. option post-Phase 3

- **ALN-HBV02 (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

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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. 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
5. 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
6. 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
7. Novartis has obtained global rights to develop, manufacture and commercialize inclisiran
8. 50% of inclisiran royalty revenue from Novartis will be payable to Blackstone by Alnylam
9. Alnylam and Regeneron are evaluating potential combinations of the investigational therapeutics cemdisiran and pozelimab
10. Novo Nordisk is leading and funding development of Belcesiran
11. Vir is leading and funding development of ALN-HBV02
12. Regeneron is leading and funding development of ALN-HSD

As of May 2023

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