



# 2021 Alnylam Patient Access Philosophy Report

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## When I became CEO of Alnylam nearly 20 years ago,

I joined a team determined to translate the scientific possibility of Nobel prize-winning science into therapeutic reality for patients. After a decade and a half of tireless research and development, an entirely new class of medicines was born: RNAi therapeutics. More than a year before our first drug approval, we committed to our Patient Access Philosophy, a set of principles that guides how we think about pricing and access to our medicines. We believed that our efforts had the potential to improve the lives of patients worldwide. Yet at Alnylam, we know that scientific innovation is only worthwhile if people who can benefit have access.

As I write this letter, Alnylam remains steadfast in our beliefs. Though I'm preparing to embark on the next chapter in my career, I am humbled to reflect on our progress against these bold commitments in this annual report.

In 2021, with the Patient Access Philosophy as our guide, we supported maintenance of care during the pandemic for those on our therapies. And while in some markets, nearly 85 percent of rare disease patients experienced interrupted care<sup>1</sup>, most patients on Alnylam therapies had the ability to maintain treatment.

Alnylam has made strides this year serving more patients in more geographies. We have also reinforced our commitment to collaborate closely, early, and often with private and public payers.

For example, this year's report demonstrates how Alnylam has increased its presence in Canada, Europe, the Middle East, and Africa (CEMEA), where we have grown from 20 countries to more than 30 countries by providing broad market access to our first therapy, ONPATTRO® (patisiran). By securing access to ONPATTRO via direct contracts or distributor agreements in more than 50 countries, we are present in 65 percent of the CEMEA region.

One of the core components of the Patient Access Philosophy is our commitment to pursuing reimbursement through value-based agreements. We are proud to have maintained momentum in the United States, where we have now executed nearly 45 value-based agreements across our three commercially available products.

Serving more patients means we will encounter additional obstacles to access. In this year's report, we spotlight stories of innovation to overcome these obstacles, especially in markets where we are quickly growing such as Europe and Asia.

Importantly, across our portfolio, our therapies will never be subject to an arbitrary price increase, a commitment that we have unwaveringly held to since ONPATTRO received its first approval in 2018.

Throughout the past year with all its unusual challenges, Alnylam continued working to fulfill the promise of delivering RNAi therapeutics to more patients with rare and prevalent diseases. Alnylam's P<sup>5</sup>x25 strategy is focused on patients, products, pipeline, performance, and profitability, and is aimed towards becoming a top-tier biopharma company.

With my time as CEO coming to an end, I am proud to have led the company through our early commercial stages, marked by an important legacy of access and commercial innovation. I am optimistic as my colleague, Yvonne Greenstreet, leads Alnylam boldly into the next chapter. A physician by training, Yvonne knows firsthand the significance of patient access. Having served as a leader at Alnylam for five years, Yvonne also understands that access is integral to our growth as a company. I am excited to watch Yvonne and our growing team at Alnylam make real our belief that no patient should have to wait for hope.



**John Maraganore, PhD,**  
**Founding Chief Executive Officer,**  
**Alnylam Pharmaceuticals**

<sup>1</sup> EURORDIS-Rare Diseases Europe study (November 2020): <https://www.eurordis.org/content/people-living-rare-disease-were-severely-impacted-during-first-covid-19-wave-30-million-people-europe-must-not-be-forgot>

## Section 1: Expanding and diversifying patient access programs

Alnylam is committed to helping patients and partners by listening and responding to their challenges with meaningful, practical solutions. Patients have always been our North Star, so as society entered a second year of challenges posed by the pandemic, we were well-prepared to support with specialized patient-facing programs and assistance.

*Evelyn, diagnosed with acute hepatic porphyria (USA)*

“I love helping to provide hope to patients and their families by inspiring them to become advocates in their rare disease experience.”

*Rita, Patient Education Liaison for Alnylam in the U.S.*





## Key program descriptions



**Alnylam Assist®** offers personalized services throughout treatment with ONPATTRO® (patisiran), GIVLAARI® (givosiran), and OXLUMO® (lumasiran). Services include helping patients understand insurance coverage for therapy, informing them of options and eligibility for financial support, providing materials to start conversations with physicians and family members, and sharing information on patient advocacy organizations and other resources.



**Alnylam Act®** is a sponsored, no-charge, third-party genetic testing and counseling program for patients with a family history or suspected diagnosis of hereditary transthyretin-mediated (hATTR) amyloidosis, acute hepatic porphyria (AHP), or primary hyperoxaluria type 1 (PH1). The Alnylam Act program was developed to reduce barriers to genetic testing and counseling as a way of helping people make more informed decisions about their health.\*



**GeneAct™ (Europe):** A genetic testing and disease awareness program active in some countries across Europe that supports the diagnosis of patients with rare diseases. Alnylam currently has genetic testing programs in more than 11 countries in the region with ongoing discussions to expand into even more. These programs support physician education on the importance of early and correct diagnosis and have been shown to improve time to diagnosis.



**GENILAM™, DetecTTa, TRAMmoniTTR (Italy, Spain, Germany):** Genetic testing and disease awareness programs in Italy, Spain, and Germany that seek to spread knowledge about hATTR amyloidosis where there are limited resources.\*



**Patient Empowerment Group for Access and Sustainability (PEGASUS; Europe):** Supports patient advocacy groups' understanding of the access environment by ensuring partners are informed and empowered through the exchange of best practices and involvement in Health Technology Assessment processes.

**Regional disease education websites (Europe, U.S.):** Disease awareness sites for hATTR amyloidosis, AHP, and PH1 designed to help provide useful resources for patients or those at risk, and to help drive earlier, more accurate diagnosis.

## Helping patients from clinical development through commercialization



**More than 550 patients worldwide have received ONPATTRO, GIVLAARI, OXLUMO, and vutrisiran under compassionate use/early access**



### Home administration

- U.S.
  - ▷ ONPATTRO: 22% of U.S. patients
  - ▷ GIVLAARI: 28% of U.S. patients
  - ▷ OXLUMO: 65% of U.S. patients\*
- Europe
  - ▷ 366 patients over 11 countries
  - ▷ 36% of all patients, 43% of those in countries where homecare is available



### 921 U.S. patients enrolled in Alnylam Assist

- ONPATTRO: 640 patients
- GIVLAARI: 238 patients
- OXLUMO: 43 patients
- Connected with a Patient Education Liaison
  - ▷ ONPATTRO: 96%
  - ▷ GIVLAARI: 89%
  - ▷ OXLUMO: 97%\*
- Satisfaction score\*\*
  - ▷ ONPATTRO: 5/5
  - ▷ GIVLAARI: 5/5

“Primary Hyperoxaluria Type 1 (PH1) is a life-threatening, debilitating disease that affects children and adults, and only has one FDA-approved treatment, OXLUMO. Alnylam Assist is critical for helping patients, families, and providers who need access to high-quality care in a timely manner.”

*Kim Hollander, Executive Director, The Oxalosis and Hyperoxaluria Foundation, New Paltz, NY, USA*

\* Does not include a full year's worth of data as OXLUMO launched in Nov. 2020

\*\* Data pending for OXLUMO





### Longest duration treatment of ONPATTRO and GIVLAARI

- ONPATTRO: More than 8 years
- GIVLAARI: 4.5 years



### Total number of U.S. treatment sites for commercial products

- ONPATTRO: 324
- GIVLAARI: 120
- OXLUMO: 11\*

## Helping to address financial barriers



### U.S. patients with zero cost-share:

- ONPATTRO: 73%
- GIVLAARI: 84%
- OXLUMO: 92%\*



### U.S. patients enrolled in commercial copay program for ONPATTRO, GIVLAARI or OXLUMO in U.S.

- ONPATTRO: 166/30% enrolled in copay
- GIVLAARI: 79/54% enrolled in copay
- OXLUMO: 13/50% enrolled in copay\*

“Expanded access and compassionate use programs can fundamentally change lives for patients, caregivers, and advocates. We have the opportunity to impact these patients in a positive way by offering early access to our innovative medicines when no adequate treatments are available.”

*Karen Frascello, Director of Global Medical Affairs and Early Access at Alnylam Pharmaceuticals and author of The Global Guide to Compassionate Use Programs*

## Education and improving diagnosis



**39 patient education events hosted by Alnylam in 2021**



**EU PEGASUS advocacy education**

- PEGASUS has provided training for more than 50 patient advocates from 18 countries across TTR, AHP, and PH1, including representation from all four of the international groups in these disease areas.



**13 grants provided to patient organizations (TTR, AHP, PH1, and pipeline therapeutic areas) globally in 2021**



- 58,802 people genotyped through Alnylam Act or GeneAct\* (U.S., Canada, Brazil, Europe) since the program began.
- 3,331 positive test results for mutations related to hATTR amyloidosis, AHP, or PH1; 6%, 10% and 2% positive test rate respectively (U.S., Canada, Brazil, Europe) since the program began.
- 2,185 people participated in Alnylam-sponsored testing programs in Europe in 2021
  - ▷ 795 people participated in GENILAM in 2021 (Italy)
  - ▷ 373 people participated in DetecTTa in 2021 (Spain)
  - ▷ 732 people participated in TRAMmoniTTR in 2021 (Germany)

\*Alnylam does not receive patient identifiable information from the testing programs we support

“

We are proud to partner with Alnylam on our patient education and outreach materials, and we look forward to continuing our relationship as we work to fight kidney disease and help people live healthier lives.”

*LaVarne A. Burton, President and CEO of the American Kidney Fund, Rockville, MD, USA*

“

Particularly for patients with rare and ultra-rare diseases, financial and administrative barriers too often get in the way of crucial diagnoses. Alnylam Act is important because it allows patients to make a choice about genetic testing that isn't influenced by out-of-pocket cost concerns.”

*Elizabeth Fieg, MS, CGC, Senior Genetic Counselor, Brigham and Women's Hospital, Boston, MA, USA*



## Section 2: Collaborating with more partners worldwide to create value

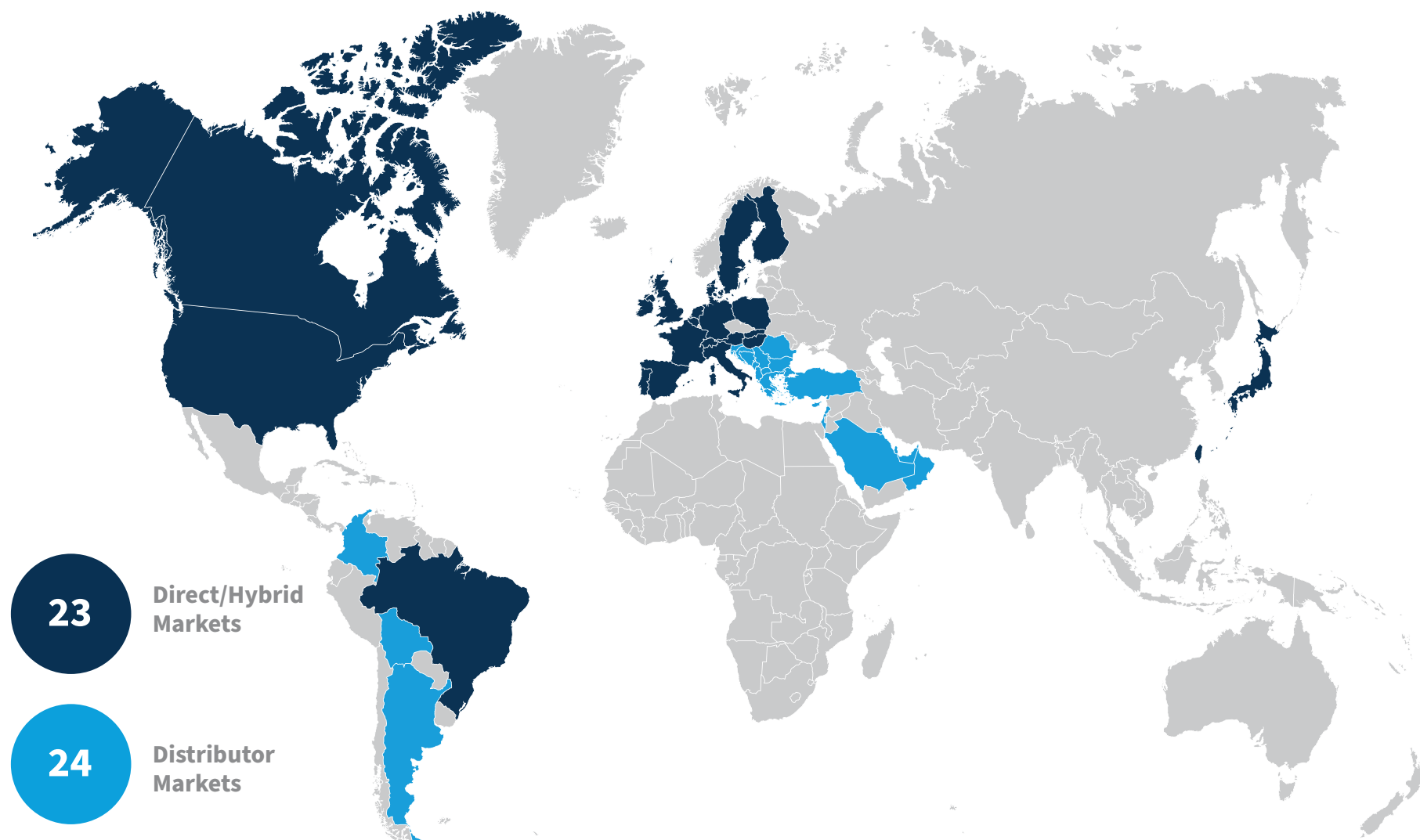
At Alnylam, our vision has established a revolutionary approach that promises rapid development of new therapies for patients who are waiting. As part of our P<sup>5</sup>x25 goals, we are working tirelessly to deliver RNAi therapeutics to patients by expanding our geographic footprint. With each new country and market that we enter comes new challenges and opportunities. Alnylam is committed to collaboration with payers, local governments, and industry leaders around value-based care and responsible pricing to support access to our medicines for patients who can benefit. This requires innovative solutions that remove barriers to access and respond to physician and payer concerns. Enclosed is our progress on expanding the reach of Alnylam therapies to people who need them.

“Being able to help problem solve with patients, and for them, by breaking it down, figuring out what next steps need to happen, who needs to be involved, and getting that end result is what inspires me to do what I do every day. I’m developing relationships with the patients and their caregivers. I get to know their families and hear about their lives and what they’ve really gone through since the time that they were diagnosed and even before.”

*Calleen, Case Manager for Alnylam Assist in the U.S.*



## Alnylam's Global Presence



### Alnylam delivers therapies in three ways:

**Direct:** Alnylam files regulatory submission and manages direct sales of approved RNAi therapeutics

**Hybrid markets:** Leverages distributor for regulatory submission where applicable; partner manages commercial distribution of approved RNAi therapeutics while Alnylam may drive promotional efforts

**Distributor:** Partner manages local regulatory submission and commercial distribution for faster market access of approved RNAi therapeutics



## Reaching patients worldwide



**Patients worldwide receiving commercial ONPATTRO, GIVLAARI, and OXLUMO**

- ONPATTRO > 1,875
- GIVLAARI > 300
- OXLUMO > 120

## U.S. market access



**% U.S. lives with confirmed access to ONPATTRO, GIVLAARI, or OXLUMO across commercial, Medicare, Medicaid, and other government payer categories**

- ONPATTRO: Commercial: 98%; overall: 98%
- GIVLAARI: Commercial: 85%; overall: 94%
- OXLUMO: Commercial: 98%; overall: 88%



**Zero U.S. price increases**



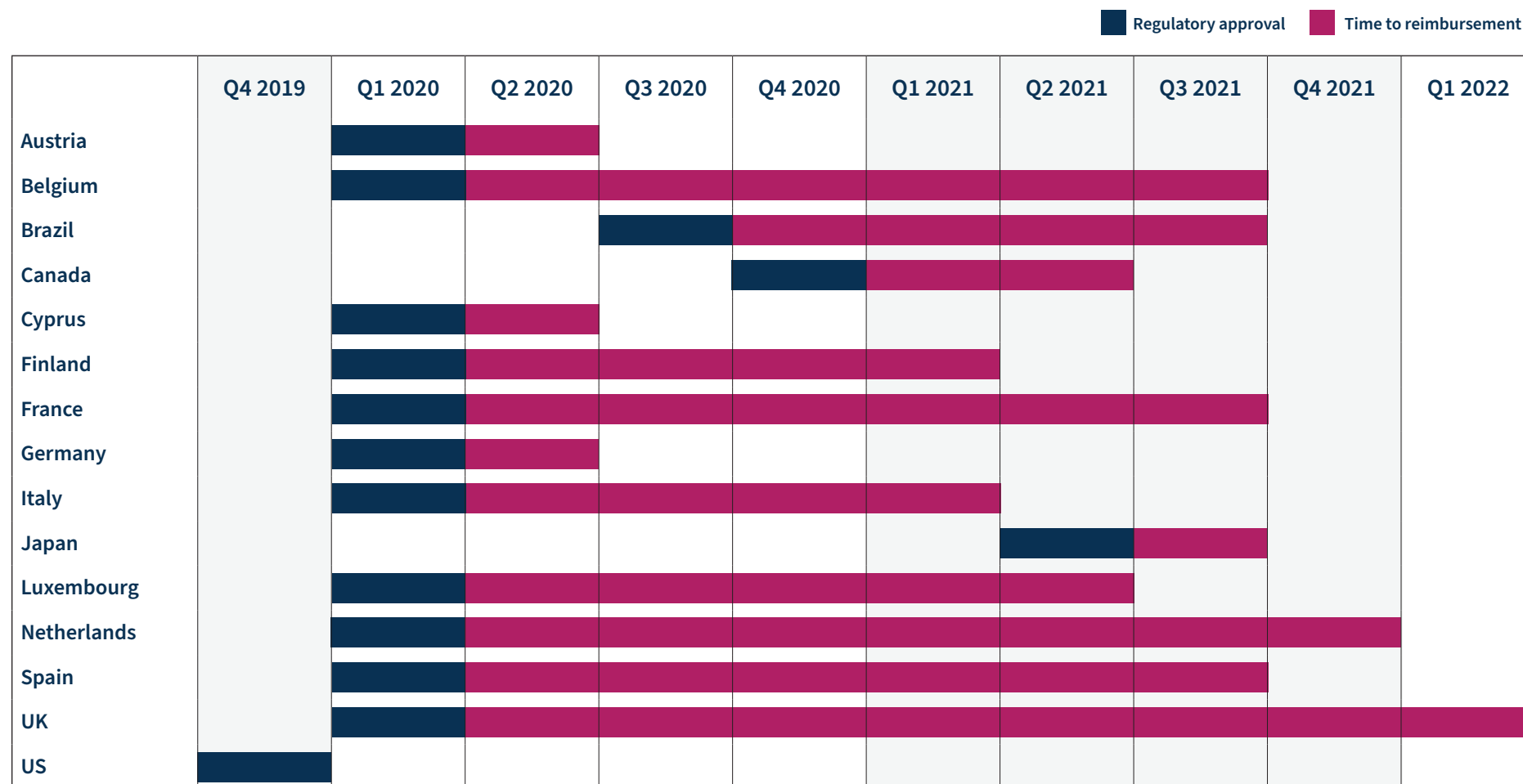
**43 U.S. VBAs for ONPATTRO, GIVLAARI, and OXLUMO**



*John, diagnosed with primary hyperoxaluria type 1 (USA)*

## GIVLAARI Commercial Access Timeline

Alnylam is committed to consistent and efficient delivery of our newest RNAi therapeutics to patients who need them. Last year, our report highlighted access and approval milestones for the first RNAi therapeutic, ONPATTRO. This year, we highlight the remarkable progress made with our second approved therapy, GIVLAARI.



## CEMEA market access

**Number of CEMEA countries where patients have broad access to ONPATTRO, GIVLAARI, or OXLUMO, if prescribed**

- 34 markets have access to ONPATTRO
- 24 markets have access to GIVLAARI
- 24 markets have access to OXLUMO

**% of CEMEA population where Alnylam has a presence and access is granted**

- 65% of the CEMEA population

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## Asia market access

**Countries where patients have access to Alnylam medicines:**

- Japan
- Singapore
- Taiwan

**Orphan drug designation:**

- ONPATTRO: Japan, Taiwan, Australia
- GIVLAARI: Japan, Taiwan

*Roland, diagnosed with hATTR amyloidosis, and his wife Nikki (Germany)*



## Section 3: Fulfilling our commitment to patients

Alnylam recognizes that no single solution can address every obstacle to patient access. In a year with so many challenges for patients, we've worked relentlessly to overcome barriers and minimize delay or disruption of treatment. We've acted with urgency to ensure patients have access to Alnylam therapies and we are proud to have secured innovative reimbursement contracts, developed new negotiation frameworks, and stayed in close contact with our patients throughout this year.

We have worked closely with our stakeholders around the world to support access to Alnylam therapies for patients who need them. These anecdotes illustrate our unique approach and the accomplishments we have made in fulfilling our commitment to patients.

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### Case Studies

#### **Improved time to reimbursement in Europe compared to other orphan drugs**

While on average only two out of three orphan drugs are reimbursed in the EU5 Markets, pricing and reimbursement (P&R) for both ONPATTRO and GIVLAARI has been achieved in the EU5 and other markets within 20 months of the European Commission's (EC) decision, which is faster than the average time to market for orphan drugs. For example, access to GIVLAARI in Spain was obtained within 17 months after EC decision, while the average time to market for orphan drugs in Spain is 32 months.

#### **Working with local governments in Asia to ensure access**

Alnylam's strategy to increase the accessibility of its treatments in Asia begins with close collaboration with local governments to obtain orphan drug status. Orphan drug status helps accelerate the commercial access and ensure treatments are obtainable and affordable to the patients who rely on them. With this designation, the government acknowledges the importance of treating these small patient populations with unmet needs as expeditiously as possible. Without this awareness, these patients would not be able to access life-changing therapies. Alnylam is proud to have achieved orphan drug status for our therapies in Japan, Taiwan, and Australia, with plans to expand access even further in the future.





## Case Studies (continued)

### Pioneering novel approaches to payer dialogue and negotiations in Europe with the value-based negotiation framework

We developed a new value-based negotiation framework (VBNF) to support better dialogue between companies and authorities to speed up time to reimbursement. This tool creates agreements that meet patient needs across diverse geographies while mitigating key concerns and enabling reimbursement of critical therapies that patients would otherwise not receive.

Our goal is to empower industry leaders and authorities to resolve unmet patient needs. To that end, we built a negotiation exercise to test the VBNF and have conducted it with payers and health economists in Belgium, the Netherlands, France, and at the EU level. The VBNF has also been presented in several congresses, notably The International Society For Pharmacoeconomics And Outcomes Research (ISPOR) congress.\*

These partnerships will expand access to treatment not only for patients on Alnylam medicines, but for any patient that requires innovative therapies that have yet to secure reimbursement.

### EU Biotech Social Pact

Our Founding CEO John Maraganore is co-leading the Biotech Social Pact, a community of industry CEOs and senior leaders from biotech and VCs united by an ambition to deliver breakthrough medical innovations that transform patients' lives. The group is committed to ensuring the sustainable development of, and access to, innovative therapies and technologies by agreeing to a set of principles.\*\* The Biotech Social Pact's objective is to build a platform for engaging with healthcare authorities and the broader life sciences community to identify common solutions to these challenges, grow biotech ecosystems, and deliver on the promise of the life sciences revolution for both patients and healthcare systems. Since the group was created in 2020, it has gathered 80 signatories including local chapters around Europe.



Value-based negotiating frameworks offer greater consistency and transparency, reducing conflict while forming agreements that serve public interests in cost control, health gain and wider socio-economic development.”

*David Taylor, Professor Emeritus of Pharmaceutical and Public Health Policy, University College London, UK*

“All people in the world deserve good medicine for reasonable prices. The good news is that many new medicines are being developed. Every day, the answer to how countries organize swift market access of new medicines becomes more urgent. I value initiatives like the value-based negotiation framework to address this issue. Let's hurry to get results. Patients benefit from this.”

*Bruno Bruins, Member of the Dutch State Council, Former Minister for Medical Care (2017–2020), The Hague, Netherlands*

\*<https://www.ispor.org/conferences-education/conferences/past-conferences/ispor-2021>

\*\*<https://biotechsociaspact.medium.com/a-new-european-biotech-social-pact-with-europe-and-patients-560fa38d360d>

## Case Studies (continued)

### Enabling patient access of ONPATTRO in Southeastern Europe

We understand that accessing innovative medicines in certain countries can be extremely challenging. Working with our partners in Southeastern Europe, we identified a large unmet need for patients with rare diseases in countries that lacked infrastructure to provide Alnylam therapies. This unmet medical need affected not only the patients, but also extended to their caregivers and family members. To alleviate this disease burden, we engaged Genesis Pharma to initiate early access programs in Bulgaria and Romania to enable patients with debilitating conditions to have access to medications at no cost.

Working together, we treated 12 patients who were suffering from hATTR amyloidosis in Bulgaria over a period of seven months, from December 2020 to July 2021. Additionally, in Romania, we provided care to four hATTR patients in urgent need of treatment over an eight-month period in 2021.

In parallel, Alnylam is committed to strengthening patient access in the region for other therapeutic areas including PH1 and AHP. By expanding early access programs in regions with a high unmet medical need and collaborating with payers and regulators, patients can access innovative therapies and medications for rare diseases.

### Medicaid value-based agreements (VBAs)

Even prior to the pandemic, U.S. Medicaid recipients have struggled with access to healthcare compared to those with private insurance. Value-based agreements (VBAs) offer payers greater certainty that they are paying for a drug that works for that patient. For years, Alnylam has urged states to adopt VBAs and encouraged federal agencies to expand options.

As responsible members of the industry, we recognized that states have had significant budget strain in their Medicaid programs, even prior to the pandemic. To support the sustainability of the healthcare system, we have entered into several Medicaid VBAs across the U.S. that ensure access for patients in Medicaid programs, while offering states greater budget certainty, addressing multiple risks where states have raised concerns.

Guided by our belief that price should be connected to the value a treatment delivers, we continue to work with states and Medicaid agencies to expand the use of Medicaid VBAs and apply new frameworks for value-based payment reform to serve the needs of patients in the U.S.

*Alnylam employee at the Norton  
Manufacturing Facility, USA*





# About Alnylam Pharmaceuticals

*Glauciene, diagnosed with acute  
hepatic porphyria (Brazil)*

## Our Science Is Changing the Way Medicine Treats Disease™

Alnylam has led the translation of RNAi (RNA interference) from Nobel Prize-winning discovery into an innovative, entirely new class of medicines. Founded in 2002 by a team of distinguished scientific leaders, Alnylam's vision is to harness the potential of RNAi therapeutics to transform the lives of people living with diseases for which there are limited or inadequate treatment options. Our pioneering work has delivered the world's first and only approved RNAi therapeutics – ONPATTRO® (patisiran) in 2018, GIVLAARI® (givosiran) in 2019, OXLUMO® (lumasiran) in 2020, and Leqvio® in 2020, with partner Novartis. We are advancing a deep pipeline of innovative RNAi-based medicines in four therapeutic areas: genetic medicines, cardio-metabolic diseases, infectious diseases, and central nervous system (CNS) and ocular diseases.



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