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**Alnylam Announces Innovative Value-Based Agreement Framework for OXLUMO™ (lumasiran) to Accelerate Access for Patients with Primary Hyperoxaluria Type 1 and Deliver Ultra-Rare Orphan Disease Pricing Solutions to U.S. Payers**

*– Expedited Access to OXLUMO Aims to Support Children and Adults Living with PH1 who Face Inevitable Disease Progression and Irreversible Kidney Damage in the Absence of New Treatment Options –*

*– New Value-Based Agreement Framework Includes an Innovative Patient Need Adjustment that Offers Payers Increased Cost Predictability Across the Entire Spectrum of PH1 Patient Ages, from Infant to Adult –*

*– Express Scripts, Harvard Pilgrim, and Highmark are Among Leading Payers Pursuing Agreements in Principle –*

CAMBRIDGE, Mass.--[BUSINESS WIRE]— November 24, 2020 - [Alnylam Pharmaceuticals, Inc.](#) (Nasdaq: ALNY), the leading RNAi therapeutics company, announced today a new framework for value-based agreements (VBAs) designed to help people with primary hyperoxaluria type 1 (PH1) gain access to OXLUMO™ (lumasiran). Now [approved](#) by the U.S. Food and Drug Administration (FDA) for the treatment of PH1 to lower urinary oxalate levels in pediatric and adult patients, OXLUMO is the first-ever approved targeted therapeutic that substantially curbs oxalate production in patients living with PH1, an ultra-rare genetic disease characterized by oxalate overproduction.

Alnylam is in active discussions with leading payers and has reached an agreement in principle with Express Scripts, Harvard Pilgrim, and Highmark to pursue VBAs for OXLUMO.

Oxalate overproduction in PH1 results in elevated urinary oxalate and the deposition of calcium oxalate crystals in the kidneys and urinary tract. People with PH1 typically endure intensive management of debilitating, painful and recurrent kidney stones. With limited treatment options previously available, the disease would inevitably progress to kidney failure, nephrocalcinosis (calcification of the kidneys), and multi-organ dysfunction as a consequence of systemic oxalosis (the spread of oxalate to organs and tissues outside of the kidneys).<sup>1</sup> People with PH1 often present with kidney failure at the time of diagnosis.<sup>2</sup> PH1 patients with renal failure undergo dialysis

almost daily, for up to 10-12 hours per day and night.<sup>2</sup> A dual or sequential liver/kidney transplant is then typically performed to resolve the underlying metabolic defect in the liver and restore kidney function,<sup>2</sup> but these interventions are associated with life-long immunosuppression and a high risk of morbidity and mortality. Until now, there have been no FDA-approved pharmaceutical therapies for PH1. There are approximately one to three individuals per million across the U.S. and Europe with a confirmed PH1 diagnosis, of those it is estimated that 1,000 - 1,700 individuals have not yet received a liver transplant, making them potentially eligible for treatment.<sup>3</sup>

### **VBA Framework for OXLUMO**

Building on the Alnylam Patient Access Philosophy and Alnylam's ongoing commitment to deliver fair value to payers and providers, the Company has worked with payers on a new and enhanced VBA framework. Since OXLUMO is indicated for both pediatric and adult patients, and is dosed by weight, related costs can vary relative to each patient and use over time. As such, Alnylam has structured a new VBA component that specifically addresses many payers' concerns for budget predictability and value, particularly for ultra-rare orphan disease therapies that are administered across a wide spectrum of ages from infants to adults.

The new VBA component, called a Patient Need Adjustment (PNA), is now being added to Alnylam's overall VBA offering for OXLUMO. Participating payers will qualify for the PNA rebate if the average number of vials utilized by a plan member exceeds an established threshold, providing payers with greater short-term and long-term predictability. The PNA was designed to mitigate the risk of escalating or varying costs associated with dosing requirements, thereby accelerating access for people diagnosed with PH1.

To further address budget predictability, Alnylam is also making available its Prevalence Based Adjustment (PBA) component, which was first introduced last year for Alnylam's second-approved therapy, GIVLAARI<sup>®</sup> (givosiran). There are often uncertainties in diagnosis rates and disease prevalence estimates in ultra-rare, poorly diagnosed orphan diseases, making it challenging for payers to predict the number of patients who will be covered within their plans. This feature triggers a rebate to participating payers if the number of diagnosed patients they cover exceeds current epidemiologic estimates for PH1.

“Value-based agreements for OXLUMO focus on three critical priorities for Alnylam in PH1: first, do everything possible to speed covered access to OXLUMO to begin reducing oxalate overproduction in patients; second, link OXLUMO price to actual value delivered; and, third, remove the cost variability to payers associated with medicines administered across a broad age range, while also addressing budget unpredictability concerns arising from uncertain prevalence estimates in ultra-rare diseases,” said Andy Orth, Senior Vice President, Head of U.S. Region at Alnylam. “Our new Patient Need Adjustment component was born out of direct feedback from our payer partners, and experience with our first two approved therapies. We've listened to the needs of payers covering PH1 patients and have responded with what we believe is an attractive solution. At Alnylam, we will continue to pursue commercial innovation that offers good value and straightforward pricing for potentially transformative RNAi therapies like OXLUMO, the first-ever approved medicine for PH1.”

“We’re pleased to expand on our legacy of innovative contracting with Alnylam and support access to a transformative therapy for patients with primary hyperoxaluria type 1. The Patient Need Adjustment is an innovative component of the OXLUMO value-based agreement intended to provide budget predictability,” said Michael Sherman, M.D., M.B.A., Chief Medical Officer of Harvard Pilgrim Health Care.

“With an expanding number of medicines being approved for rare and ultra-rare diseases, payers and plans face the increasingly difficult task of predicting costs for therapies while establishing coverage for patients in need. The Patient Need Adjustment is a responsible and very welcome model to address certain payer challenges, creating a solution that mitigates cost risks associated with ultra-rare medicines administered across a broad range of patient age groups,” said Steve Miller, M.D., Chief Medical Officer, CIGNA, Express Scripts.

“Highmark is focused on ensuring that our members have access to effective therapies, including increasingly available rare and ultra-rare disease therapies, while addressing costs,” said Sean Quinn, PharmD., Pharmaceutical Manufacturer Relations Director for Highmark Inc. “We have emerged as a leader in the value-based agreements space for therapies that address a number of chronic, high-cost health conditions. VBAs can help speed access to new medicines by tying outcomes to clinical trial performance, but payers are seeking other barometers for predicting need, which can be complex for therapies indicated across a spectrum of patient ages. We have collaborated with Alnylam to tackle new and evolving problems in rare and ultra-rare disease drug coverage, and are proud to work on this innovative Patient Need Adjustment to help people seeking treatment with OXLUMO.”

### **Alnylam’s Patient Access Philosophy**

The innovative agreements announced today further reinforce Alnylam’s [Patient Access Philosophy](#), which was created three years ago to seek solutions for patients, deliver value to payers and physicians, and remove barriers to access. This Philosophy commits that Alnylam will not increase the price of OXLUMO by more than the consumer price index for urban consumers (CPI-U), a measure of inflation, unless it is approved for new conditions by the U.S. FDA. Patients with private (commercial) insurance are expected to have little-to-no out-of-pocket copayments for OXLUMO. To see Alnylam’s progress, visit <https://www.alnylam.com/about-alnylam/patient-access-philosophy/>.

### **Alnylam Assist<sup>®</sup> and Alnylam Act<sup>®</sup>**

Alnylam offers multiple programs to support patients. A comprehensive patient support services program, Alnylam Assist<sup>®</sup>, will help patients gain access to OXLUMO. Alnylam Assist<sup>®</sup> will offer an in-house team of Case Managers to assist patients with verification of insurance benefits and financial assistance for those who qualify. Patients will also be eligible to receive support from Patient Education Liaisons, who can answer questions about disease and treatment. Physicians and patients can learn more about Alnylam’s comprehensive patient services by visiting [AlnylamAssist.com](http://AlnylamAssist.com) or calling 1-833-256-2748. Alnylam also continues to offer its third-party genetic testing service in the U.S., Canada, and Brazil, called Alnylam Act<sup>®</sup>. The program is provided at no charge to patients and their physicians and aims to reduce the time to accurate diagnoses for genetic diseases, such as PH1.

Visit OXLUMO.com for more information, including full [Prescribing Information](#).

## **IMPORTANT SAFETY INFORMATION**

### **Adverse Reactions**

The most common adverse reaction that occurred in patients treated with OXLUMO was injection site reaction (38%). Symptoms included erythema, pain, pruritus, and swelling.

### **Pregnancy and Lactation**

No data are available on the use of OXLUMO in pregnant women. No data are available on the presence of OXLUMO in human milk or its effects on breastfed infants or milk production. Consider the developmental and health benefits of breastfeeding along with the mother's clinical need for OXLUMO and any potential adverse effects on the breastfed child from OXLUMO or the underlying maternal condition.

For additional information about OXLUMO, please see the full [Prescribing Information](#).

### **About OXLUMO™ (lumasiran)**

OXLUMO is an RNAi therapeutic targeting hydroxyacid oxidase 1 (HAO1) for the treatment of primary hyperoxaluria type 1 (PH1) to lower urinary oxalate levels in pediatric and adult patients. HAO1 encodes glycolate oxidase (GO), an enzyme upstream of the disease-causing defect in PH1. OXLUMO works by degrading HAO1 messenger RNA and reducing the synthesis of GO, which inhibits hepatic production of oxalate – the toxic metabolite responsible for the clinical manifestations of PH1. In the pivotal ILLUMINATE-A study, OXLUMO was shown to significantly reduce levels of urinary oxalate relative to placebo, with the majority of patients reaching normal or near-normal levels. Injection site reactions (ISRs) were the most common drug-related adverse reaction. In the ILLUMINATE-B pediatric Phase 3 study, OXLUMO demonstrated an efficacy and safety profile consistent to that observed in ILLUMINATE-A. OXLUMO utilizes Alnylam's Enhanced Stabilization Chemistry (ESC)-GalNAc conjugate technology designed to increase potency and durability. OXLUMO is administered via subcutaneous injection once monthly for three months, then once quarterly thereafter at a dose based on actual body weight. For patients who weigh less than 10 kg, ongoing dosing remains monthly. OXLUMO should be administered by a healthcare professional. For more information about OXLUMO, visit OXLUMO.com.

### **About Primary Hyperoxaluria Type 1 (PH1)**

PH1 is an ultra-rare genetic disease that affects an estimated one to three individuals per million in the United States and Europe. PH1 is characterized by oxalate overproduction in the liver. The excess oxalate results in the deposition of calcium oxalate crystals in the kidneys and urinary tract and can lead to the formation of painful and recurrent kidney stones and nephrocalcinosis. Renal damage is caused by a combination of tubular toxicity from oxalate, calcium oxalate deposition in

the kidneys, and urinary obstruction by calcium oxalate stones. PH1 is associated with a progressive decline in kidney function, which exacerbates the disease as the excess oxalate can no longer be effectively excreted, resulting in subsequent accumulation and deposition of oxalate in bones, eyes, skin, and heart, leading to severe illness and death. Management options to date were limited to hyperhydration, crystallization inhibitors and, in a minority of patients with a specific genotype, pyridoxine (vitamin B6). These measures do not adequately address oxalate overproduction and are intended to delay inevitable progression to kidney failure and the need for intensive dialysis as a bridge to a dual or sequential liver/kidney transplant. Liver transplantation is the only intervention that addresses the underlying metabolic defect, but is associated with high morbidity and mortality, and life-long immunosuppression. Until today, there were no approved pharmaceutical therapies for PH1.

### **About RNAi**

RNAi (RNA interference) is a natural cellular process of gene silencing that represents one of the most promising and rapidly advancing frontiers in biology and drug development today. Its discovery has been heralded as "a major scientific breakthrough that happens once every decade or so," and was recognized with the award of the 2006 Nobel Prize for Physiology or Medicine. By harnessing the natural biological process of RNAi occurring in our cells, a new class of medicines, known as RNAi therapeutics, is now a reality. Small interfering RNA (siRNA), the molecules that mediate RNAi and comprise Alnylam's RNAi therapeutic platform, function upstream of today's medicines by potently silencing messenger RNA (mRNA) – the genetic precursors – that encode for disease-causing or disease pathway proteins, thus preventing them from being made. This is a revolutionary approach with the potential to transform the care of patients with genetic and other diseases.

### **About Alnylam Pharmaceuticals**

Alnylam (Nasdaq: ALNY) is leading the translation of RNA interference (RNAi) into a whole new class of innovative medicines with the potential to transform the lives of people afflicted with rare genetic, cardio-metabolic, hepatic infectious, and central nervous system (CNS)/ocular diseases. Based on Nobel Prize-winning science, RNAi therapeutics represent a powerful, clinically validated approach for the treatment of a wide range of severe and debilitating diseases. Founded in 2002, Alnylam is delivering on a bold vision to turn scientific possibility into reality, with a robust RNAi therapeutics platform. Alnylam's commercial RNAi therapeutic products are ONPATTRO® (patisiran), GIVLAARI® (givosiran), and OXLUMO™ (lumasiran). Alnylam has a deep pipeline of investigational medicines, including six product candidates that are in late-stage development. Alnylam is executing on its "Alnylam 2020" strategy of building a multi-product, commercial-stage biopharmaceutical company with a sustainable pipeline of RNAi-based medicines to address the needs of patients who have limited or inadequate treatment options. Alnylam is headquartered in Cambridge, MA. For more information about our people, science and pipeline, please visit [www.alnylam.com](http://www.alnylam.com) and engage with us on Twitter at [@Alnylam](https://twitter.com/Alnylam) or on [LinkedIn](https://www.linkedin.com/company/alnylam).

## **Alnylam Forward Looking Statements**

Various statements in this release concerning Alnylam's future expectations, plans and prospects, including, without limitation, Alnylam's views with respect to the safety and efficacy of OXLUMO as demonstrated in the ILLUMINATE-A and ILLUMINATE-B Phase 3 studies and the potential for OXLUMO to address the underlying pathophysiology of PH1 in adults, children and infants, the potential for OXLUMO to substantially curb or reduce oxalate production in pediatric and adult patients with PH1, expectations regarding Alnylam's new framework for VBAs designed to help people with PH1 gain covered access to OXLUMO, link OXLUMO price to actual value delivered, remove the cost variability to payers associated with medicines administered across a broad age range, and address budget unpredictability concerns arising from uncertain estimated prevalence of ultra-rare diseases such as PH1, expectations regarding the attractiveness of Alnylam's new VBA component to payers, expectations regarding the entry into definitive VBA agreements for OXLUMO with leading payers, including Express Scripts, Harvard Pilgrim, and Highmark, among others, and expectations regarding the potential for Alnylam to meet or exceed its "Alnylam 2020" guidance for the advancement and commercialization of RNAi therapeutics, constitute forward-looking statements for the purposes of the safe harbor provisions under The Private Securities Litigation Reform Act of 1995. Actual results and future plans may differ materially from those indicated by these forward-looking statements as a result of various important risks, uncertainties and other factors, including, without limitation: the direct or indirect impact of the COVID-19 global pandemic or any future pandemic, such as the scope and duration of the outbreak, government actions and restrictive measures implemented in response, material delays in diagnoses of rare diseases, initiation or continuation of treatment for diseases addressed by Alnylam products, or in patient enrollment in clinical trials, potential supply chain disruptions, and other potential impacts to Alnylam's business, the effectiveness or timeliness of steps taken by Alnylam to mitigate the impact of the pandemic, and Alnylam's ability to execute business continuity plans to address disruptions caused by the COVID-19 or any future pandemic; Alnylam's ability to discover and develop novel drug candidates and delivery approaches and successfully demonstrate the efficacy and safety of its product candidates; the pre-clinical and clinical results for its product candidates, which may not be replicated or continue to occur in other subjects or in additional studies or otherwise support further development of product candidates for a specified indication or at all; actions or advice of regulatory agencies, which may affect the design, initiation, timing, continuation and/or progress of clinical trials or result in the need for additional pre-clinical and/or clinical testing; delays, interruptions or failures in the manufacture and supply of its product candidates or its other marketed products, including OXLUMO; obtaining, maintaining and protecting intellectual property; intellectual property matters including potential patent litigation relating to its platform, products or product candidates; obtaining regulatory approval for its product candidates, and maintaining regulatory approval and obtaining pricing and reimbursement for its products, including ONPATTRO, GIVLAARI and OXLUMO; progress in continuing to establish an ex-United States infrastructure; successfully launching, marketing and selling its approved products globally, including ONPATTRO, GIVLAARI and OXLUMO, and achieving net product revenues for ONPATTRO within its revised expected range during 2020; Alnylam's ability to successfully expand the indication for ONPATTRO in the future; competition from others using technology

similar to Alnylam's and others developing products for similar uses; Alnylam's ability to manage its growth and operating expenses within the ranges of guidance provided by Alnylam through the implementation of further discipline in operations to moderate spend and its ability to achieve a self-sustainable financial profile in the future without the need for future equity financing; Alnylam's ability to establish and maintain strategic business alliances and new business initiatives; Alnylam's dependence on third parties, including Regeneron, for development, manufacture and distribution of certain products, including eye and CNS products, and Vir for the development of ALN-COV and other potential RNAi therapeutics targeting SARS-CoV-2 and host factors for SARS-CoV-2; the outcome of litigation; the risk of government investigations; and unexpected expenditures; as well as those risks more fully discussed in the "Risk Factors" filed with Alnylam's most recent Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) and in other filings that Alnylam makes with the SEC. In addition, any forward-looking statements represent Alnylam's views only as of today and should not be relied upon as representing its views as of any subsequent date. Alnylam explicitly disclaims any obligation, except to the extent required by law, to update any forward-looking statements.

<sup>1</sup>Lorenzo V, Torres A, Salido E. Primary hyperoxaluria. *Nefrologia*. 2014 May 21;34(3):398-412. English, Spanish. doi: 10.3265/Nefrologia.pre2014.Jan.12335. Epub 2014 Apr 30. PMID: 24798559.

<sup>2</sup>Cochat P, et al. Primary hyperoxaluria Type 1: indications for screening and guidance for diagnosis and treatment. *Nephrol Dial Transplant*. 2012 May;27(5):1729-36. doi: 10.1093/ndt/gfs078. PMID: 22547750.

<sup>3</sup>Lumasiran, in Development for the Treatment of Primary Hyperoxaluria Type I. Alnylam RNAi Roundtable 2020; (August 10, 2020). Available at: [https://event.webcasts.com/viewer/event.jsp?ei=1351579&tp\\_key=7522004032](https://event.webcasts.com/viewer/event.jsp?ei=1351579&tp_key=7522004032)