Conference Call to Discuss FDA Approval of OXLUMO™ (lumasiran)

November 24, 2020

Alnylam® PHARMACEUTICALS

Agenda

Welcome

- Christine Lindenboom
  Senior Vice President, Investor Relations & Corporate Communications

Introduction

- John Maraganore, Ph.D.
  Chief Executive Officer

OXLUMO™ (lumasiran) Label & Data

- Akshay Vaishnaw, M.D., Ph.D.
  President of R&D

Commercialization Strategy

- Andy Orth
  Senior Vice President, Head of U.S. Business

Q&A Session

Alnylam Forward Looking Statements

This presentation contains forward-looking statements, within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. There are a number of important factors that could cause actual results to differ materially from the results anticipated by these forward-looking statements. These important factors include: 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 our products, or in patient enrollment in clinical trials, potential supply chain disruptions, and other potential impacts to our business, the effectiveness or timeliness of steps taken by us to mitigate the impact of the pandemic, and our ability to execute business continuity plans to address disruptions caused by the COVID-19 or any future pandemic; our ability to discover and develop novel drug candidates and delivery approaches and successfully demonstrate the efficacy and safety of our product candidates, pre-clinical and clinical results for our product candidates; actions or advice of regulatory agencies; delays, interruptions or failures in the manufacture and supply of our product candidates and our marketed products, including OXLUMO™ (lumasiran); intellectual property matters including potential patent litigation relating to our platform, products or product candidates; our and our partner's ability to obtain regulatory approval for our product candidates, including inclisiran, and our ability to maintain regulatory approval and obtain pricing and reimbursement for products, including ONPATTRO® (patisiran), GIVLAARI® (givosiran) and OXLUMO; our ability to successfully launch, market and sell our approved products globally, including ONPATTRO, GIVLAARI and OXLUMO, and achieve net product revenues for ONPATTRO within our further revised expected range during 2020; our ability to successfully expand the indication for ONPATTRO in the future; competition from others using similar technology and developing products for similar uses; our ability to manage our growth and operating expenses within the reduced ranges of guidance provided by us through implementation of further discipline in operations to moderate spend and our ability to achieve a self-sustainable financial profile in the future without the need for future equity financing; our ability to establish and maintain business alliances; our dependence on third parties, including Novartis, for the development, manufacture and commercialization of inclisiran, Regeneron, for development, manufacture and commercialization of certain products, including eye and CNS products such as ALN-APP 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; and the risk of government investigations; as well as those risks and other factors more fully discussed in our most recent annual, quarterly and current reports filed with the SEC. If one or more of these factors materialize, or if any underlying assumptions prove incorrect, our actual results, performance or achievements may vary materially from any future results, performance or achievements expressed or implied by these forward-looking statements. All forward-looking statements speak only as of the date of this presentation and, except as required by law, we undertake no obligation to update such statements.

John Maraganore, Ph.D.

Chief Executive Officer

Introduction

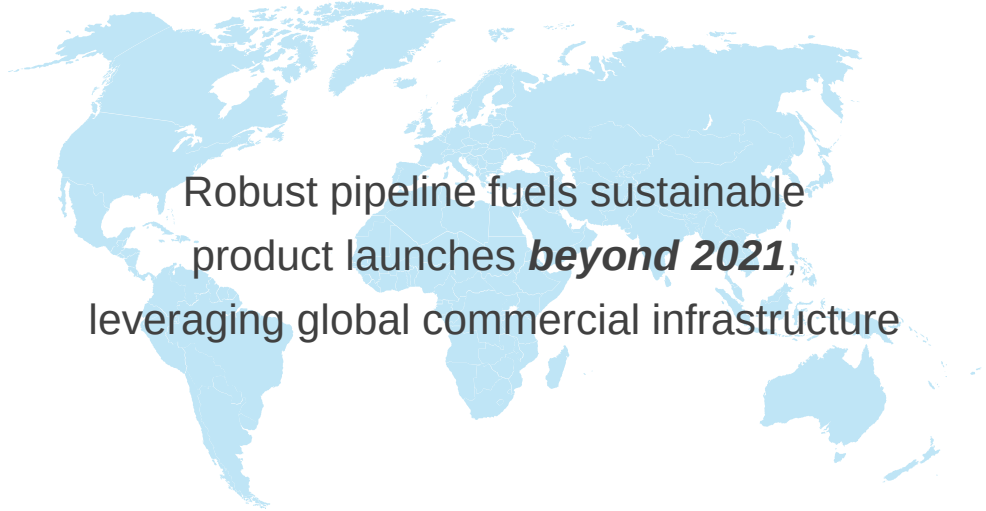
The third RNAi therapeutic is

NOW APPROVED IN THE U.S. & EU

OXLUMO™
(lumasiran) for injection
94.5 mg/0.5 mL

Additional Launches Planned Over Next 18 Months

2018	2019	2020	2020	2021-2022	
onpattro® (patisiran) lipid complex injection 10 mg/5 mL	GIVLAARI® (givosiran) injection for subcutaneous use 189 mg/mL	OXLUMO™ (lumasiran) for injection 94.5 mg/0.5 mL	**LEQVIO®***	**Vutrisiran**	**Fitusiran***
ONPATTRO is indicated in the U.S. for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults[1]	GIVLAARI is indicated in the U.S. for the treatment of adults with acute hepatic porphyria[2]	OXLUMO is indicated in the U.S. for the treatment of primary hyperoxaluria type 1 to lower urinary oxalate levels in pediatric and adult patients[3]	Hypercholesterolemia **Ph3** ✓	ATTR amyloidosis	Hemophilia
			NDA/MAA accepted Received positive CHMP opinion	*HELIOS-A Phase 3 topline results in early 2021*	*Two of three Phase 3 studies fully enrolled*



Robust pipeline fuels sustainable product launches ***beyond 2021***, leveraging global commercial infrastructure

* Novartis is leading and funding development of inclisiran and will commercialize inclisiran, assuming regulatory approvals; Sanofi Genzyme is leading and funding development of fitusiran and will commercialize fitusiran, if successful

[1] ONPATTRO is approved in the U.S. and Canada for the 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 polyneuropathy. For additional information on ONPATTRO, see Full Prescribing Information

[2] GIVLAARI is approved in the EU for the treatment of acute hepatic porphyria (AHP) in adults and adolescents over 12 years old, and in Brazil for the treatment of AHP in adults; Alnylam has filed or plans to file for marketing authorization for givosiran in Japan and other countries in 2020; For additional information on GIVLAARI, see Full Prescribing Information

[3] For additional information on OXLUMO, see Full Prescribing Information

Anticipated dates of launch based on current development timelines for investigational therapeutics and assuming positive pivotal study data and regulatory approval

Akshay Vaishnaw, M.D., Ph.D.

President of R&D

OXLUMO™ (lumasiran) Label & Data

Benson
Living with Primary Hyperoxaluria Type 1

Primary Hyperoxaluria Type 1

Lumasiran

Description

Rare autosomal recessive disorder of increased oxalate synthesis resulting in kidney stones and renal failure, with subsequent oxalate accumulation in extra-renal tissues

Onset generally

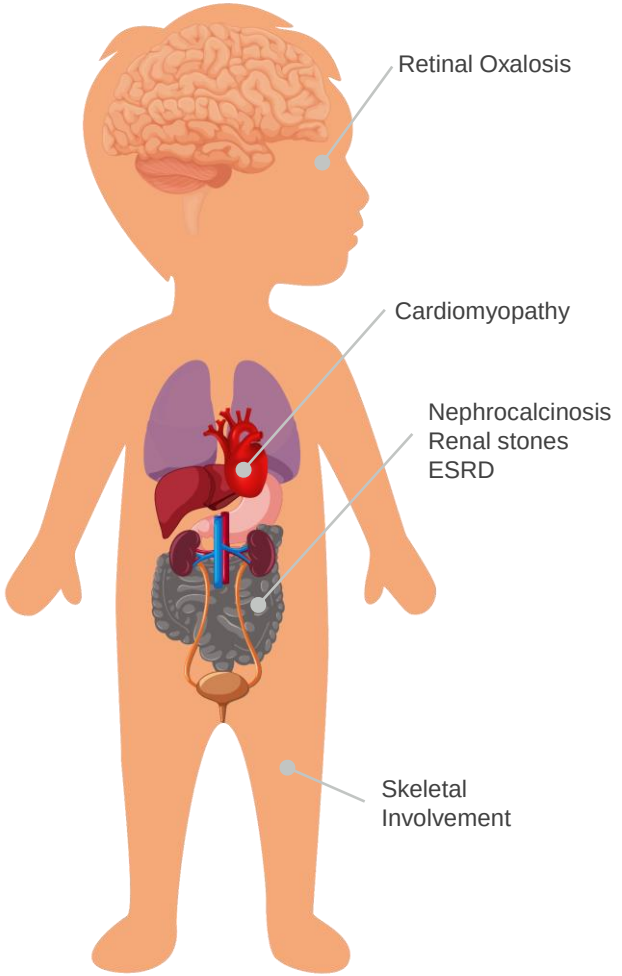
pediatric

very limited treatment options

Patient Population

~3,000

potentially symptomatic in U.S./EU[1]

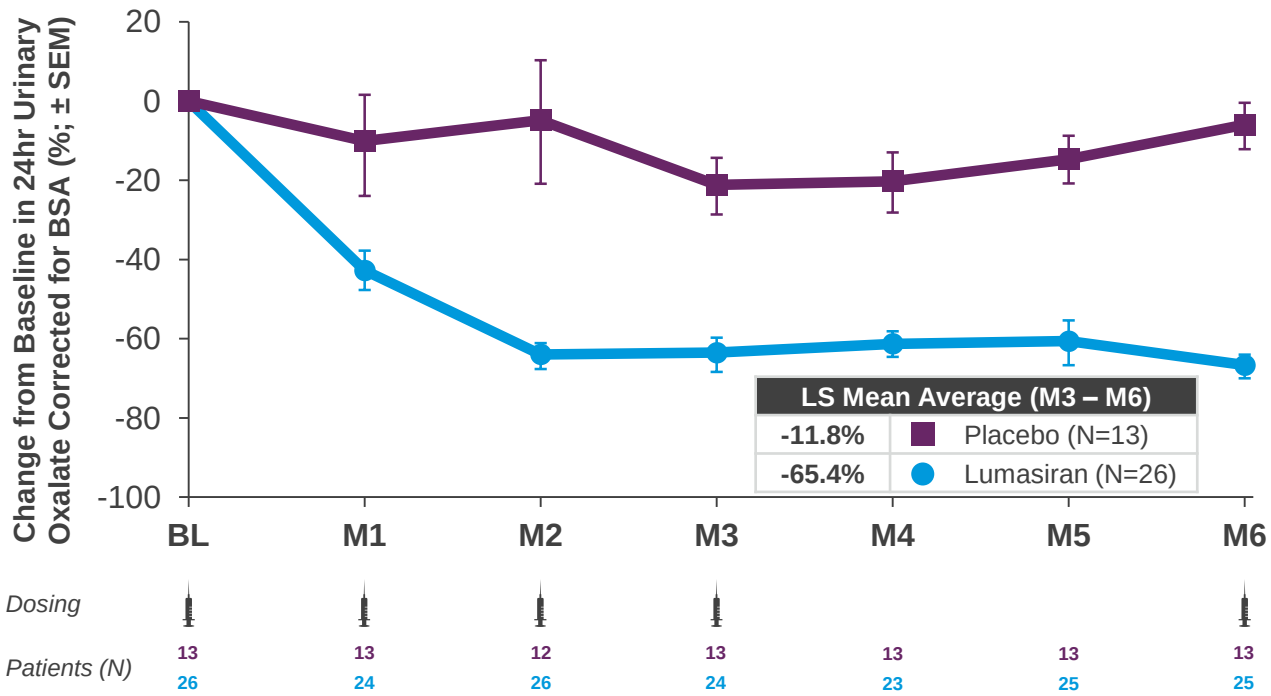


[1] Includes patients that are presymptomatic, subclinical, or symptomatic

Lumasiran ILLUMINATE•A Phase 3 Study

Met Primary and All Tested Secondary Endpoints with Encouraging Safety and Tolerability Profile

Rapid and sustained reduction in 24hr urinary oxalate levels from baseline to Month 6



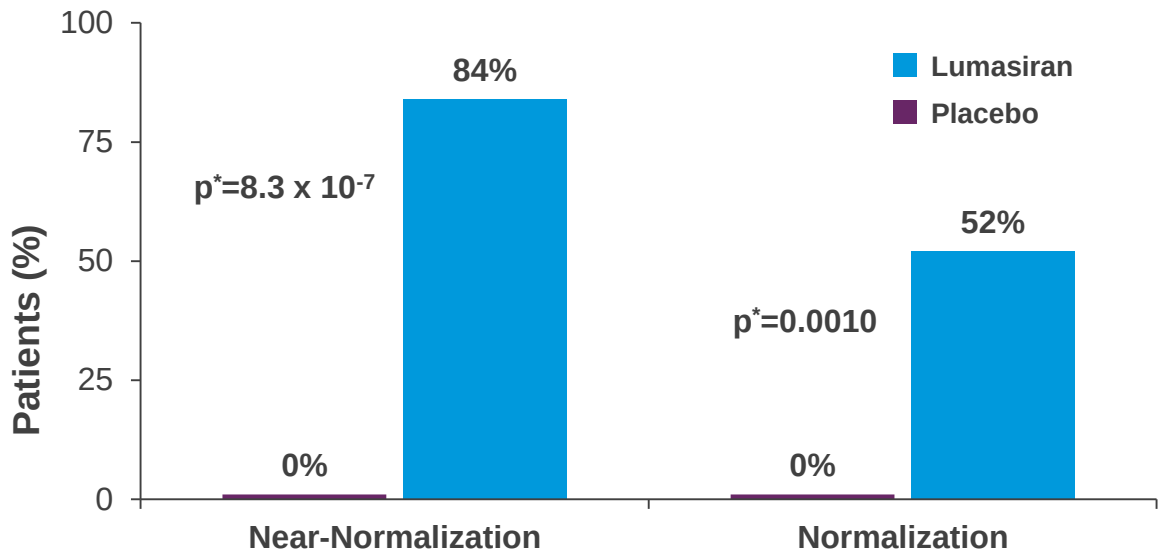
-53%

Difference in LS mean average M3-M6 (Lumasiran-Placebo) ($p=1.7 \times 10^{-14}$)

-76%

Mean maximal reduction

Majority of patients achieved near-normalization (≤1.5 x ULN) or normalization (≤ULN) in 24hr urinary oxalate levels at Month 6



Safety

- No deaths, severe, or serious AEs. All AEs mild or moderate
- Most common related AEs were injection-site reactions (N=10; 38%)
  - All generally mild; no discontinuation of treatment
  - Most common symptoms: erythema, pain, pruritus, and swelling
- No hepatic AEs reported in either group
- No clinically relevant changes in laboratory measures, vital signs, or electrocardiograms related to lumasiran observed

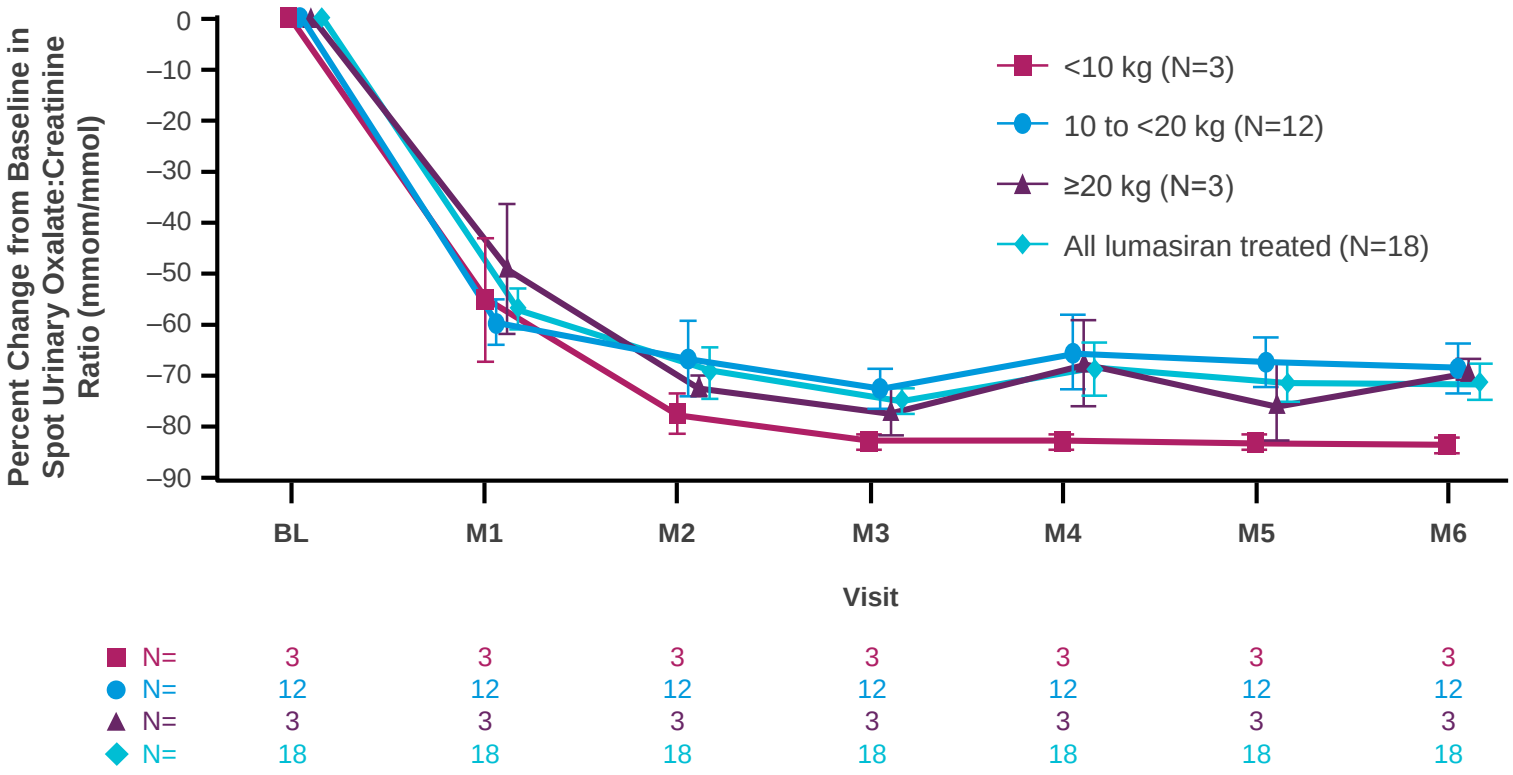
BL, baseline; BSA, body surface area; hr, hour; LS, least squares; M, month; ULN, upper limit of normal; AE, adverse event

* p-value is based on Cochran–Mantel–Haenszel test stratified by baseline 24 hr urinary oxalate corrected for BSA (≤1.70 vs >1.70 mmol/24 hr/1.73 m2)

Lumasiran ILLUMINATE-B Phase 3 Study

Efficacy Results and Safety Profile in Pediatric Patients Similar to Those Observed in ILLUMINATE-A

Rapid and sustained reduction in spot urinary oxalate:creatinine ratio across all weight groups



Primary Endpoint Result

-72%

LS mean reduction in spot urinary oxalate:creatinine ration from BL to M6 (average change of M3-M6)

Safety

- No deaths, discontinuations or withdrawals, or severe AEs
- One serious AE occurred, considered not related to lumasiran[1]
- Most common related AE was injection-site reactions
  - All mild and transient in severity
- No clinically relevant changes in laboratory measures, vital signs, or electrocardiograms related to lumasiran observed
- No hepatic events reported

Data in graph are presented as mean ± SEM of observed values
[1]Viral infection, considered not related to the study drug by the Investigator
BL, baseline; M, month; SEM, standard error of the mean; ULN, upper limit of normal; AE, adverse event; SAE, serious adverse event

OXLUMO™ (lumasiran) Label for U.S.

Indication

OXLUMO is indicated for the treatment of primary hyperoxaluria type 1 (PH1) to lower urinary oxalate levels in pediatric and adult patients

Dosing & Administration

The recommended dosing regimen of OXLUMO consists of loading doses followed by maintenance doses administered subcutaneously.
Dosing is based on actual body weight.

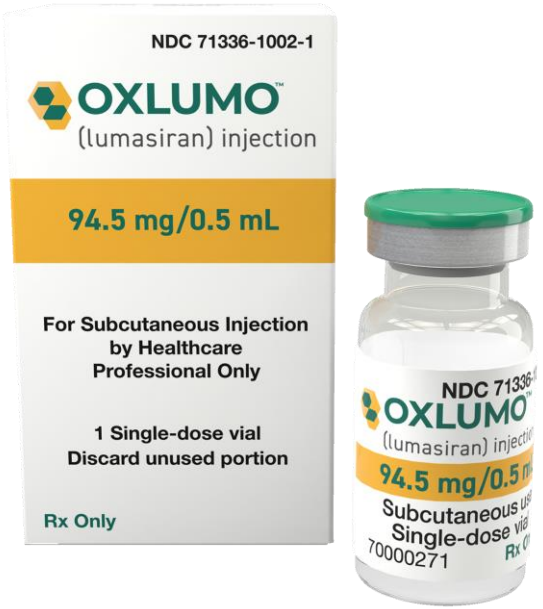
Safety

Contraindications

- None

Warnings and Precautions

- None
- For additional Important Safety Information on OXLUMO, see full Prescribing Information



Lumasiran Phase 3 Studies

Robust Registrational Program Evaluating Lumasiran Across all Ages and Full PH1 Disease Spectrum

ILLUMINATE

ILLUMINATE•A

Double-blind, placebo-controlled trial in PH1 patients at least 6 years old with preserved renal function

Full results presented
June 2020

ILLUMINATE•B

Single arm, open-label study in PH1 patients less than 6 years old with preserved renal function

Full results presented
October 2020

ILLUMINATE•C

Single arm, open-label study in PH1 patients with impaired renal function, including advanced disease

Topline results
expected in **2021**

Expanded Access Protocol (EAP) for PH1 patients initiated in U.S. and Europe

Andy Orth

Senior Vice President, Head of U.S. Business

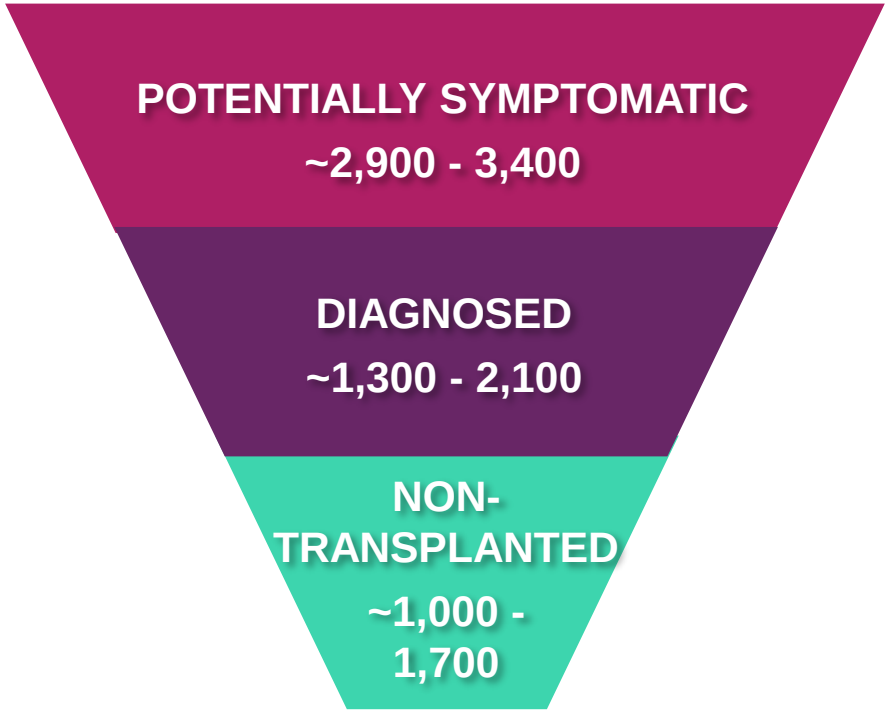
Commercialization Strategy

OXLUMO Market Opportunity

Estimated U.S./EU Prevalence and Addressable Population

MUTATION PREVALENCE[1]	POTENTIALLY SYMPTOMATIC PREVALENCE^	DIAGNOSED PREVALENCE[2-4]	DIAGNOSED & NON-TRANSPLANTED[5]
~4.3 per Million (U.S./EU)	~3.5 to 4.0 per Million (U.S./EU)	~1.5 to 2.5 per Million (U.S./EU)	~1.2 to 2.0 per Million (U.S./EU)

Patients in the U.S. / EU†



Opportunity for growth with increased awareness and diagnosis, as well as global commercial expansion

† US population=328MM, EU population (including UK) = 513MM

^ Includes patients that are presymptomatic, subclinical, or symptomatic

Sources: 1. Hopp K, et al. J Am Soc Nephrol. 2015 Feb 2; 2. Cochat et al. Nephrol Dial Transplant. 1995; 10: 3–7; 3. Kopp and Leumann. Nephrol Dial Transplant. 1995; 10: 2224–2227; 4. van Woerden, et al. Nephrol Dial Transplant. 2003; 18: 273–279; 5. Data on file. Alnylam chart review studies (US and EU) estimated 17% transplant rate, rounded up to 20%; 6. Cochat P, et al. N Engl J Med. 2013 Nov 28;369(22):2163; 7. Harambat J. Clin J Am Soc Nephrol. 2012 Mar;7(3):458-65; 8. Kamoun A. Pediatr Nephrol. 1996 Aug;10(4):479-82.

OXLUMO Market Opportunity

First-in-Class Product in Ultra-Rare Orphan Disease

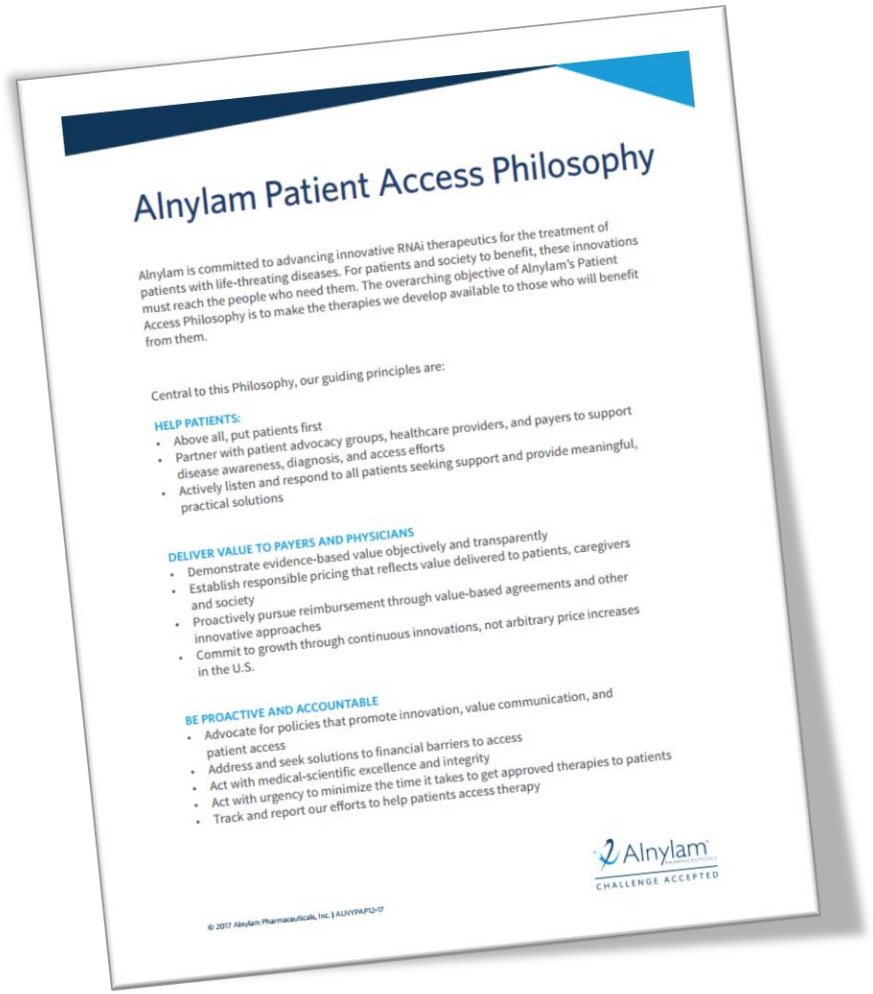
PREVALENCE	DIAGNOSIS	DISEASE BURDEN	COST BURDEN
~1,300–2,100	**~50%**	**30–65%**	**$1M+**
patients with a confirmed PH1 diagnosis in U.S./EU[1-3]	currently diagnosed[4]; mean time to diagnosis ~6 years[5]	reach end-stage renal disease before diagnosis[5]	average cost (transplant & lifelong immunosuppression)

LUMASIRAN | PRIMARY HYPEROXALURIA TYPE 1

>$500M potential market opportunity

1. Cochat et al. Nephrol Dial Transplant. 1995; 10: 3–7; 2. Kopp and Leumann. Nephrol Dial Transplant. 1995; 10: 2224–2227; 3. van Woerden, et al. Nephrol Dial Transplant. 2003; 18: 273–279; 4.Hopp R, et al. J Am Soc Nephrol. 2015;26:2559-2570; 5. Harambat J, et al. Kidney Int. 2010;77(5):443-449.

Alnylam's Patient Access Philosophy



Alnylam Patient Access Philosophy

Alnylam is committed to advancing innovative RNAi therapeutics for the treatment of patients with life-threating diseases. For patients and society to benefit, these innovations must reach the people who need them. The overarching objective of Alnylam's Patient Access Philosophy is to make the therapies we develop available to those who will benefit from them.

Central to this Philosophy, our guiding principles are:

HELP PATIENTS:
- Above all, put patients first
- Partner with patient advocacy groups, healthcare providers, and payers to support disease awareness, diagnosis, and access efforts
- Actively listen and respond to all patients seeking support and provide meaningful, practical solutions

DELIVER VALUE TO PAYERS AND PHYSICIANS
- Demonstrate evidence-based value objectively and transparently
- Establish responsible pricing that reflects value delivered to patients, caregivers and society
- Proactively pursue reimbursement through value-based agreements and other innovative approaches
- Commit to growth through continuous innovations, not arbitrary price increases in the U.S.

BE PROACTIVE AND ACCOUNTABLE
- Advocate for policies that promote innovation, value communication, and patient access
- Address and seek solutions to financial barriers to access
- Act with medical-scientific excellence and integrity
- Act with urgency to minimize the time it takes to get approved therapies to patients
- Track and report our efforts to help patients access therapy

Alnylam CHALLENGE ACCEPTED

Critical excerpts from Alnylam's Patient Access Philosophy

- Demonstrate evidence-based value objectively and transparently
- Establish responsible pricing that reflects value delivered to patients, caregivers and society
- Proactively pursue reimbursement through value-based agreements and other innovative approaches
- Commit to growth through continuous innovations, not arbitrary price increases in the U.S.

Help Patients | **Deliver Value** | **Be Proactive**

Pricing, Cost & Access Considerations

DEBILITATING DISEASE, CHILDHOOD ONSET

- Inherited disease typically presenting in childhood
- Oxalate overproduction causes painful, recurrent kidney stones leading to irreversible renal failure & multi-organ damage

RISKS OF RENAL FAILURE & TRANSPLANT WITH SoC

- Inevitable progression to renal failure can require 6-7 sessions of dialysis per week
- Some patients endure 10-12 hours of dialysis per day and night, until they can undergo a dual or sequential liver/kidney transplant

ULTRA-RARE POPULATION

- Estimated genetic prevalence in the range of 4 individuals per million in the US and EU
- OXLUMO may be a good option for ~1000-1700 of these patients with a confirmed PH1 diagnosis who have not received a transplant

FIRST THERAPY TO TREAT PH1

- 1st FDA-approved therapy to substantially reduce oxalate production in PH1
- 53% reduction in urinary oxalate (vs placebo)
- Safety profile understood in pediatric and adult patients

REDUCED BARRIERS TO ACCESS

- New value-based agreement (VBA) framework and innovative Patient Need Adjustment (PNA) seek to mitigate barriers to access
- Agreements aim to address payers' concerns on budget predictability:
    1) Administration across a broad age range of patients
    2) Unpredictable prevalence in rare and ultra-rare diseases

Average Annual WAC
$490,000 - before mandatory rebates to government institutions

Average Effective Net Price
$380,000

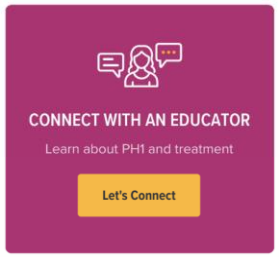
Price may vary per individual dosing, since OXLUMO is indicated for both pediatric and adult patients and is dosed according to body weight

Launching in a Pandemic

Execution Tailored to Meet Needs of Customers

Leading with Digital

New Engagement Models



Disease awareness being driven by digital and in-person education

- *Sales representatives*
- *Medical Science Liaisons*
- *Field Reimbursement Specialists*

AlnylamAct®

Broad Support Services

Alnylam ASSIST®

Comprehensive patient services program offering support to patients throughout treatment via wide range of personalized services:

- *In-house Case Managers*
- *Field-based Patient Education Liaisons*

Includes financial support for eligible patients

Proactive Payer Engagement

Value-Based Agreements tied to clinical experience

Price increase protection

Patient Need Adjustment to support patient access to therapy by providing budget predictability for payers

Prevalence-Based Adjustment to address uncertainty in plan patient prevalence

OXLUMO™ (lumasiran) FDA Approval

Q&A Session

Alnylam PHARMACEUTICALS