Glaucienne
Diagnosed with AHP (Brazil)

Third Quarter 2021 Financial Results

October 28, 2021

Alnylam® PHARMACEUTICALS

Agenda

Welcome

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

Overview

- John Maraganore, Ph.D.
  Chief Executive Officer

Leadership Transition

- Yvonne Greenstreet, MBChB, MBA
  President and Chief Operating Officer

Commercial Highlights

- Tolga Tanguler
  Chief Commercial Officer

Alnylam Pipeline

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

Financial Summary and Upcoming Milestones

- Jeff Poulton
  Chief Financial Officer

Q&A Session

Alnylam Forward Looking Statements & Non-GAAP Financial Measures

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, including expectations regarding our aspiration to become a leading biotech company and the planned achievement of our "Alnylam P^{5}x25" strategy, the CEO leadership transition planned for year end, plans for additional global regulatory filings and the continuing product launches of our approved products, the achievement of additional pipeline milestones and data, including relating to ongoing clinical studies of patisiran, vutrisiran, lumasiran, zilebesiran, fitusiran, and ALN-HSD, the initiation of additional clinical studies for zilebesiran, lumasiran and the combination of cemdisiran and pozelimab, the expected timing for filing a CTA for each of ALN-APP and ALN-XDH, a JNDA for vutrisiran for the treatment of hATTR amyloidosis with polyneuropathy and supplemental regulatory filings with the FDA and EMA for lumasiran, the expected range of net product revenues and net revenues from collaborations and royalties for 2021, and the expected range of aggregate annual GAAP and non-GAAP R&D and SG&A expenses for 2021. 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 on our business, results of operations and financial condition and the effectiveness or timeliness of our efforts to mitigate the impact of the pandemic; the potential impact of the planned leadership transition at year end on our ability to attract and retain talent and to successfully execute on our "Alnylam P^{5}x25" strategy; our ability to discover and develop novel drug candidates and delivery approaches, including using our IKARIA platform, and successfully demonstrate the efficacy and safety of our product candidates; the pre-clinical and clinical results for our product candidates; actions or advice of regulatory agencies and our ability to obtain and maintain regulatory approval for our product candidates, including vutrisiran, as well as favorable pricing and reimbursement; successfully launching, marketing and selling our approved products globally; delays, interruptions or failures in the manufacture and supply of our product candidates or our marketed products; obtaining, maintaining and protecting intellectual property; our ability to successfully expand the indication for ONPATTRO (and potentially vutrisiran) in the future; our ability to manage our growth and operating expenses through disciplined investment in operations and our ability to achieve a self-sustainable financial profile in the future without the need for future equity financing; our ability to maintain strategic business collaborations; our dependence on third parties for the development and commercialization of certain products, including Novartis, Sanofi, Regeneron and Vir; the outcome of litigation; the potential impact of current and the risk of future government investigations; and unexpected expenditures; as well as those risks more fully discussed in the "Risk Factors" filed with our most recent Quarterly Report on Form 10-Q filed with the SEC and in our other SEC filings. If one or more of these factors materialize, or if any underlying assumptions prove incorrect, our actual results, performance, timelines 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.

This presentation references non-GAAP financial measures. These measures are not in accordance with, or an alternative to, GAAP, and may be different from non-GAAP financial measures used by other companies. The items included in GAAP presentations but excluded for purposes of determining non-GAAP financial measures for the periods referenced herein are stock-based compensation expenses, unrealized (gains) losses on marketable equity securities, costs associated with our strategic financing collaboration, upfront payment on license and collaboration agreement, change in estimate of contingent liabilities and loss on contractual settlement. We have excluded the impact of stock-based compensation expense, which may fluctuate from period to period based on factors including the variability associated with performance-based grants for stock options and restricted stock units and changes in our stock price, which impacts the fair value of these awards. We have excluded the impact of the unrealized (gains) losses on marketable equity securities because we do not believe these adjustments accurately reflect the performance of our ongoing operations for the period in which such gains or losses are reported, as their sole purpose is to adjust amounts on the balance sheet. We have excluded the impact of the costs associated with our strategic financing collaboration, upfront payment on license and collaboration agreement, change in estimate of contingent liabilities and loss on contractual settlement because we believe these items are non-recurring transactions outside the ordinary course of our business.

John Maraganore, Ph.D.

Chief Executive Officer

Overview

TRANSFORMATIONAL MEDICINES

ROBUST & HIGH-YIELD R&D PIPELINE

ORGANIC PRODUCT ENGINE

John Maraganore
Chief Executive Officer

Yvonne Greenstreet
President & Chief Operating Officer

Yvonne Greenstreet, MBChB, MBA

President and Chief Operating Officer

Leadership Transition

Our New 5-Year Strategy

Patients: Over 0.5 million on Alnylam RNAi therapeutics globally

Products: 6+ marketed products in rare and prevalent diseases

Pipeline: Over 20 clinical programs, with 10+ in late stages and 4+ INDs per year

Performance: ≥40% revenue CAGR through YE 2025

Profitability: Achieve sustainable non-GAAP profitability within period

Please join us for

Alnylam® R&D Day

November 19, 2021

A VIRTUAL EVENT

Registration information coming soon.

Tolga Tanguler

Chief Commercial Officer

Commercial Highlights

ONPATTRO® (patisiran) Launch Update: Q3 2021

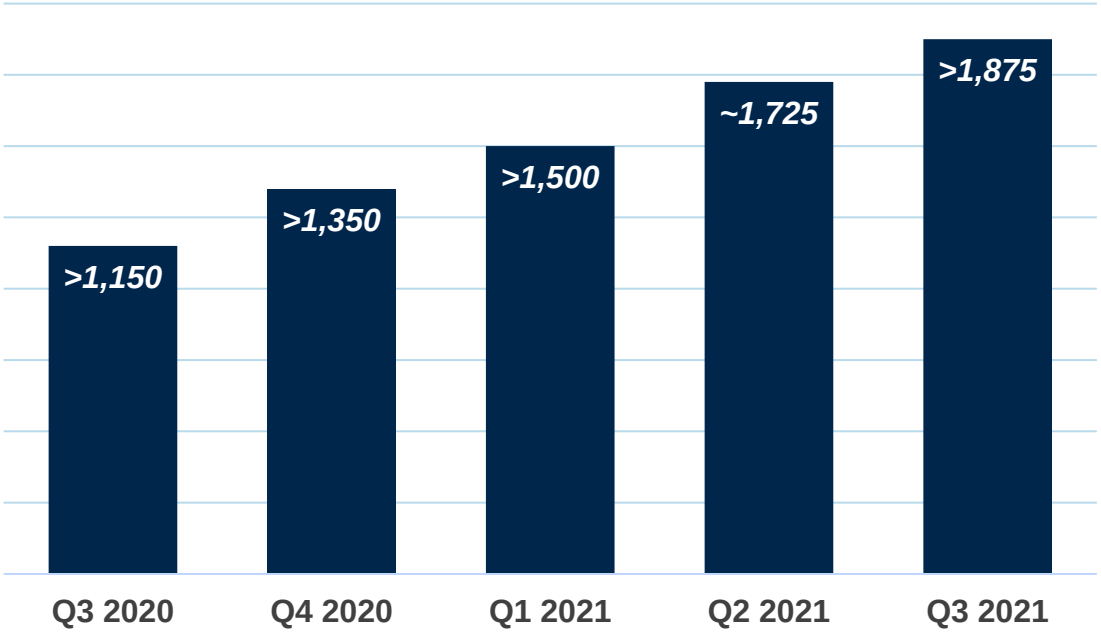
Steady and Continued Growth

$120M

ONPATTRO Global Q3 2021 Net Product Revenues

>1,875

Patients Worldwide on Commercial ONPATTRO at end of Q3 2021



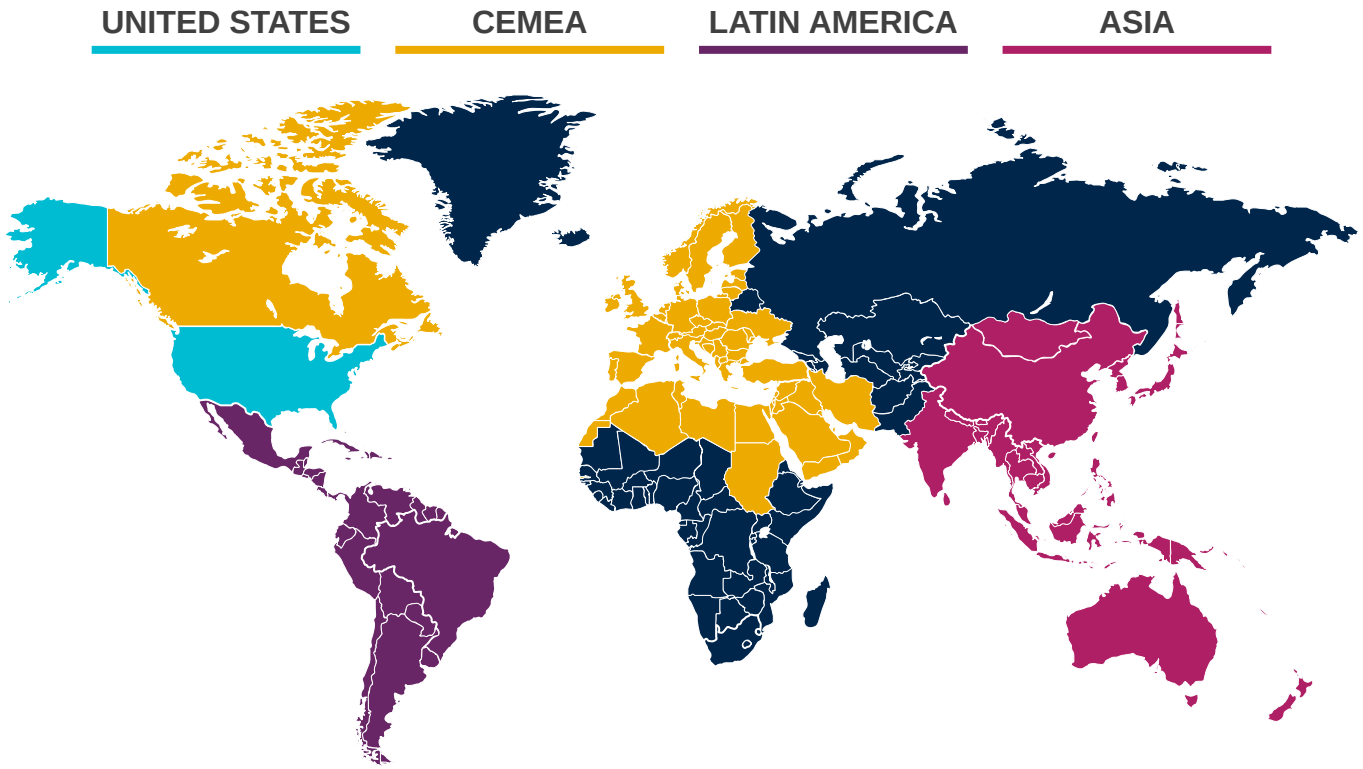
Q3 U.S. Highlights

- Steady, continuous patient growth; notable growth in demand and new prescribers
- Increase driven by addition of new patients on therapy and continuation of >90% patient treatment compliance; second highest number of Start Forms since launch

ONPATTRO Global Commercialization

Increasing Access and Value Recognition

- Progress with global ONPATTRO availability
  - Over 30 countries now selling ONPATTRO through direct reimbursement, named patient sales, or reimbursed expanded access
  - Pricing and reimbursement achieved in Ireland
  - Balanced use in both first-line treatment in hATTR patients with PN and switching from other products, including stabilizers



onpattro® (patisiran) lipid complex injection 10 mg/5 mL

CEMEA: Canada, Europe, Middle East, North Africa

GIVLAARI® (givosiran) Launch Update: Q3 2021

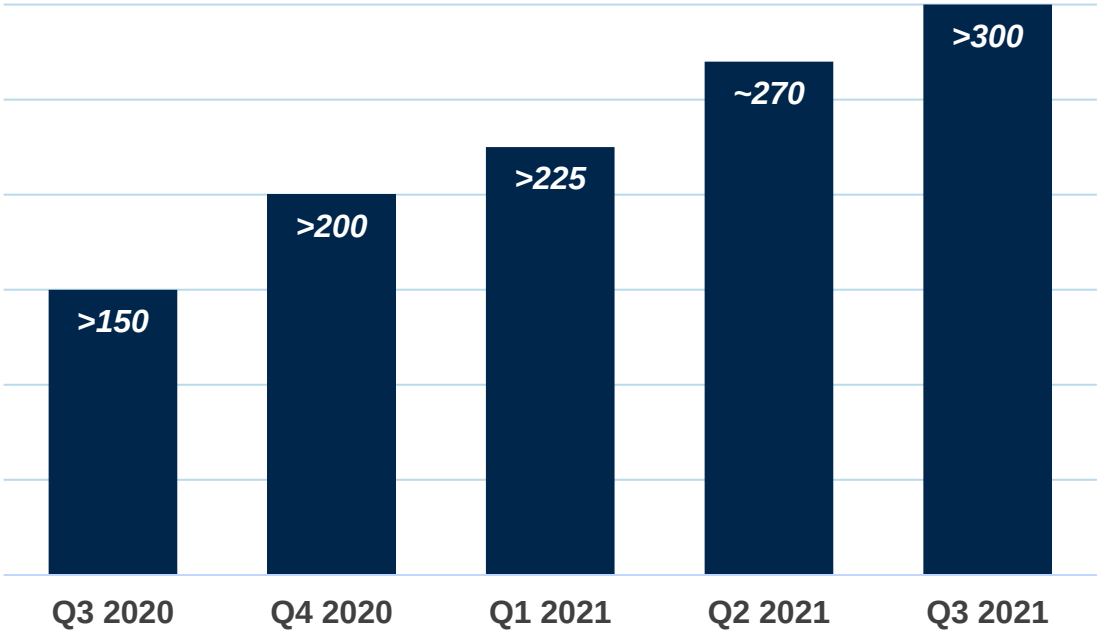
Continued Progress with Uptake and Access

$32M

GIVLAARI Global Q3 2021 Net Product Revenues

>300

Patients Worldwide on Commercial GIVLAARI at end of Q3 2021



Q3 U.S. Highlights

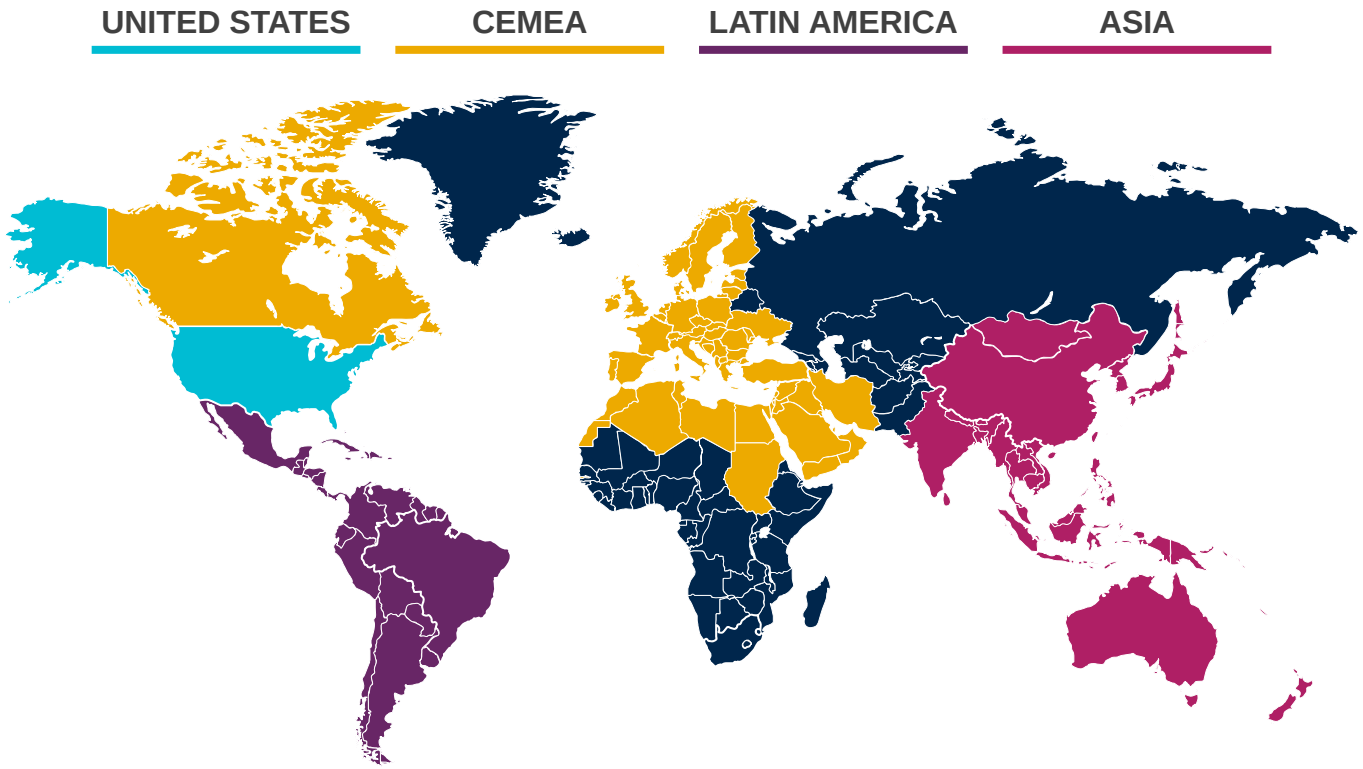
>10 Value-Based Agreements (VBAs) finalized

>94% covered U.S. lives with confirmed access to GIVLAARI, if prescribed

GIVLAARI Global Commercialization

Ensuring GIVLAARI Availability Around the World

- Progress with global GIVLAARI availability
  - Recent launches in Japan and Spain
  - Pricing and reimbursement achieved in UK and France



GIVLAARI® (givosiran) injection for subcutaneous use 189 mg/mL

CEMEA: Canada, Europe, Middle East, North Africa

OXLUMO® (lumasiran) Launch Update: Q3 2021

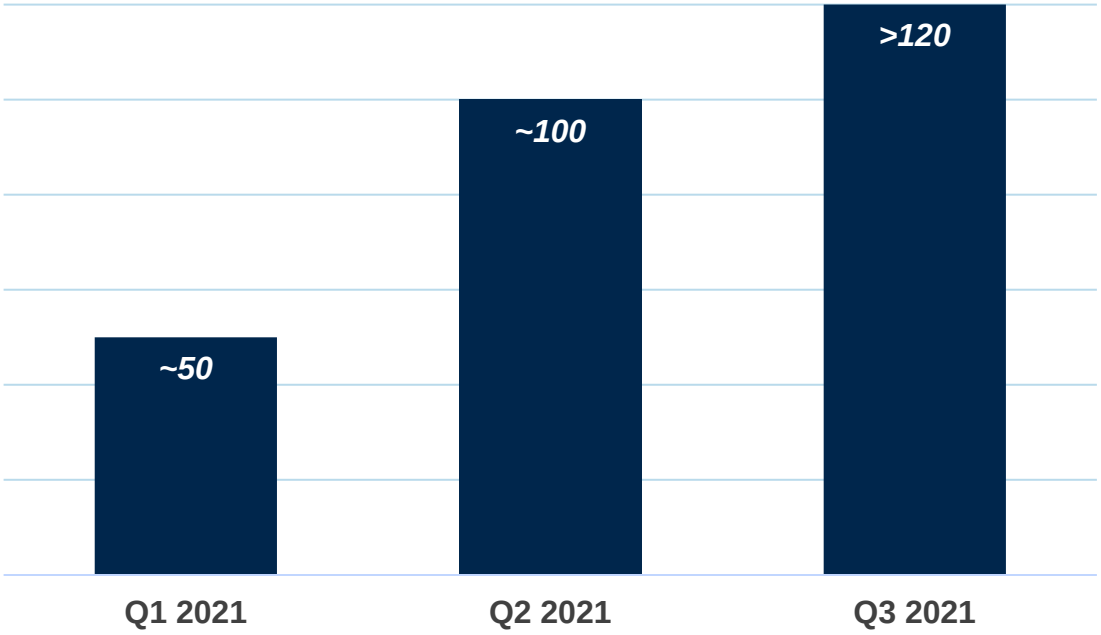
Continuous Launch Execution

$15M

OXLUMO Global Q3 2021 Net Product Revenues

>120

Patients Worldwide on Commercial OXLUMO at end of Q3 2021



Q3 U.S. Highlights

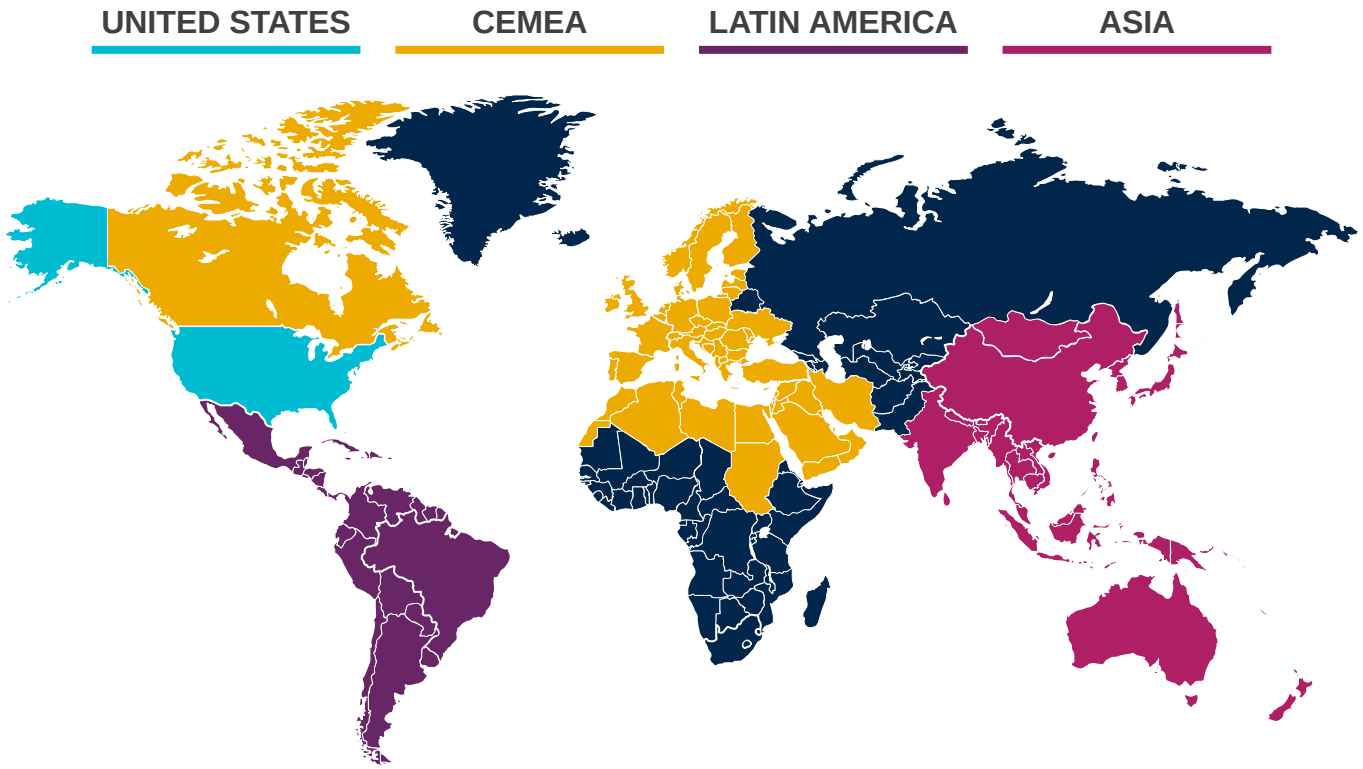
Net growth in new patients; revenues reflect transition of initial bolus of commercial patients from monthly loading dose to quarterly maintenance dose

>10 Value-Based Agreements (VBAs) finalized; **>85%** covered U.S. lives with confirmed access to OXLUMO, if prescribed

OXLUMO Global Commercialization

Ensuring OXLUMO Availability Around the World

- Progress with global OXLUMO availability
  - Launches underway in Germany and France
  - Timely transitions from Expanded Access Program
  - Broad utilization across age groups and EGFR categories



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

CEMEA: Canada, Europe, Middle East, North Africa

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

President of R&D

Alnylam Pipeline

Patisiran APOLLO-B Phase 3 Study

Randomized, Double-Blind, Placebo-Controlled Study in ATTR Amyloidosis Patients with Cardiomyopathy

N ~ 300
Patient Population

- ATTR amyloidosis; wild-type or any TTR mutation
  - TTR stabilizer naïve and/or TTR stabilizer progressor
- Confirmed cardiomyopathy and medical history of symptomatic heart failure
- NYHA ≤III; minimum walk and NT-proBNP limits at baseline

1:1 RANDOMIZATION

Patisiran
IV q3w†
0.3 mg/kg

or

Placebo
IV q3w†

Primary Endpoint

- Change in 6-MWT at 12 months

Key Secondary Endpoints

- Cardiomyopathy symptoms and health status
- Death and hospitalization outcomes
- Cardiac biomarkers

12-Month Treatment Extension

ClinicalTrials.gov Identifier: NCT03997383

APOLLO-B

Enrollment **complete**

Topline results expected **mid-2022**

Concomitant use of local standard of care allowed during study, including TTR stabilizer

† To reduce likelihood of infusion-related reactions, patients receive following premedication or equivalent at least 60 min. before each study drug infusion: 10 mg (low dose) dexamethasone; oral acetaminophen; H1 and H2 blockers

NYHA: New York Heart Association; NT-proBNP: N-terminal pro b-type natriuretic peptide; 6-MWT: 6-Minute Walk Test

Vutrisiran HELIOS·A Phase 3 Study

Randomized, Open-Label Study in Hereditary ATTR Amyloidosis Patients with Polyneuropathy

N ~ 164
Patient Population

- hATTR amyloidosis; any TTR mutation
- Neuropathy Impairment Score (NIS) of 5-130
- Prior tetramer stabilizer use permitted

3:1 RANDOMIZATION

Vutrisiran
SC q3M
25 mg

or

Reference Comparator
(patisiran)

9-Month Efficacy

- Assessment vs. APOLLO placebo arm

18-Month Efficacy

- Assessment vs. APOLLO placebo arm

Open-Label Extension

ClinicalTrials.gov Identifier: NCT03759379

HELIOS·A

Efficacy Assessments vs. APOLLO placebo arm

Primary Endpoint at 9M^

- Change in mNIS+7 from baseline

Secondary Endpoints at 9M

- Change in Norfolk QOL-DN from baseline
- 10-meter walk test (10MWT)

Secondary Endpoints at 18M Include:

- Change in mNIS+7 from baseline, change in Norfolk QOL-DN from baseline, 10MWT, mBMI, R-ODS

Exploratory Endpoints Include

- NT-proBNP
- Echo parameters
- Technetium (select sites only, change from baseline)

Positive results presented at **AAN (April 2021)**

PDUFA date
April 2022

^ Primary endpoint for the study is at 9 months; in the Helios A statistical analysis plan for U.S. submissions, change in Norfolk QOL-DN from baseline will be treated as a co-primary endpoint
Vutrisiran has not been approved for any indication and conclusions regarding the safety or efficacy of the drug have not been established

HELIOS-A 18-Month Topline Results: Efficacy

Sustained Treatment Benefit with Vutrisiran Through 18 Months

Positive results for all Month 18 secondary efficacy endpoints, relative to external APOLLO placebo

Month 18 Secondary Endpoint	P-value
mNIS+7	6.5E-20
Norfolk QoL-DN total score	1.8E-10
10-MWT	1.2E-07
mBMI	4.2E-15
R-ODS	3.5E-15

Confirmed non-inferiority of vutrisiran relative to within-study patisiran, as expected

Encouraging results on exploratory cardiac endpoints at 18 months

- Favorable changes in NT-proBNP and certain echocardiographic parameters, relative to external APOLLO placebo
- Favorable change in cardiac technetium uptake relative to baseline in majority of cohort patients, suggesting potential evidence for reduced cardiac amyloid burden

HELIOS-A 18-Month Topline Results: Safety

Continued signs of encouraging safety and tolerability profile during 18-month treatment period

- No drug-related discontinuations or deaths
- Three discontinuations due to adverse events in vutrisiran arm during 18-month treatment period (none considered related to study drug)
  - Two fatal events (previously reported at month 9); one due to COVID-19, one due to iliac artery occlusion during hospitalization for pneumonia in patient with CHF
  - Single event of cardiac failure leading to discontinuation
- Two SAEs deemed drug-related: dyslipidemia, urinary tract infection
- Treatment emergent adverse events occurring in ≥10% of patients receiving vutrisiran included fall, pain in extremity, diarrhea, peripheral edema, urinary tract infection, arthralgia, and dizziness
  - With exception of pain in extremity and arthralgia, each event occurred at similar or lower rate as compared with external placebo
- Injection site reactions (ISRs) reported in five patients (4.1%); all mild and transient
- No hepatic safety concerns

Vutrisiran HELIOS·B Phase 3 Study

Randomized, Double-Blind Outcomes Study in ATTR Amyloidosis Patients with Cardiomyopathy

N ~ 600
Patient Population

- ATTR amyloidosis; wild-type or any TTR mutation
  - ≤ 30% tafamidis use at baseline
- Confirmed cardiomyopathy and medical history of symptomatic heart failure
- NYHA ≤ III; minimum walk and NT-proBNP limits at baseline

1:1 RANDOMIZATION

Vutrisiran
SC q3M
25 mg

or

Placebo
SC q3M

Primary Endpoint

- Composite outcome of all-cause mortality and recurrent CV events (when last patient reaches Month 30)

Select Secondary Endpoints

- 6-MWT distance
- Kansas City Cardiomyopathy Questionnaire (KCCQ OS) score
- Echocardiographic parameters
- All-cause mortality and recurrent all-cause hospitalizations and HF events
- All-cause mortality
- Recurrent CV events
- NT-proBNP

ClinicalTrials.gov Identifier: NCT04153149

HELIOS·B

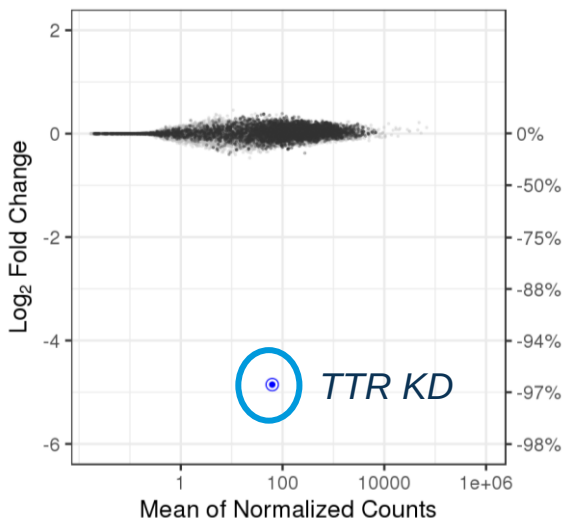
Enrollment **complete**

Study includes optional interim analysis

IKARIA™ Platform: Proprietary siRNA Design with Novel Chemistry

Super-specific siRNAs May Enable Higher Doses to Achieve Annual Dosing

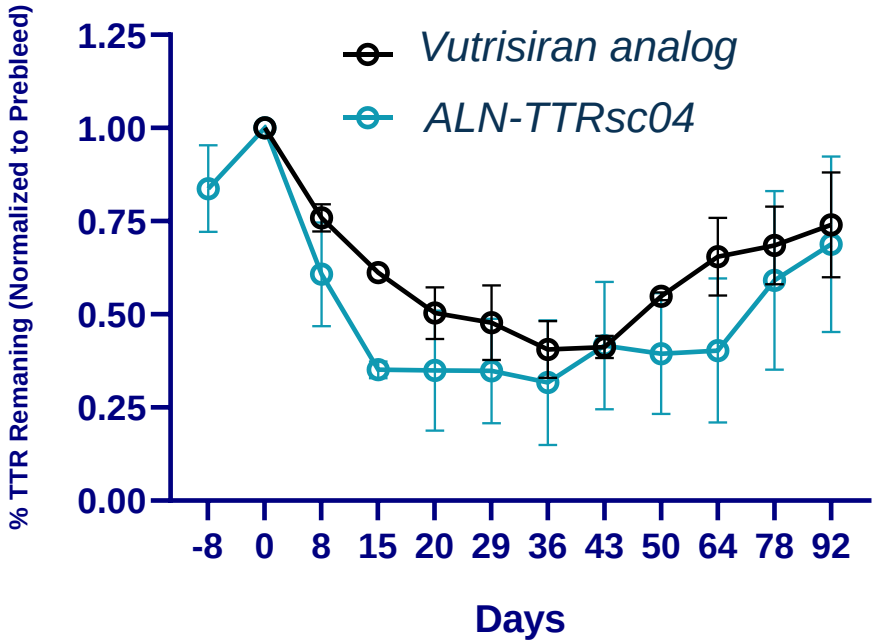
Exquisite specificity



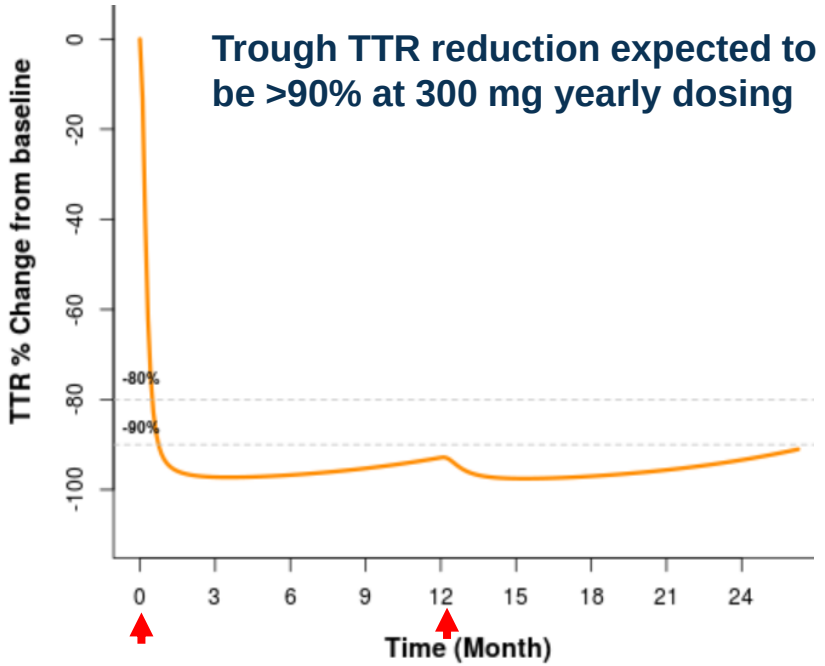
RNAseq analysis

High potency in NHP

0.5 mg/kg single sc dose



Human dose projection



Trough TTR reduction expected to be >90% at 300 mg yearly dosing

Modeling predicts potential for once-a-year dosing in humans with greater than 90% TTR reduction

ILLUMINATE-C Phase 3 Results

Single Arm, Open-Label Study in PH1 Patients with Impaired Renal Function, Including Advanced Disease (N=21)

Lumasiran achieved substantial reductions in plasma oxalate relative to baseline

- Both in dialysis-independent and -dependent patients

Lumasiran demonstrated an encouraging safety and tolerability profile

- No deaths or drug-related SAEs
- Most common AEs were ISRs in 5 patients (23.8%), all of which were mild
- Two discontinuations due to AEs, both occurring during extension period and neither related to study drug

Full results to be presented at American Society of Nephrology Kidney Week, November 2-7

Supplemental regulatory filings expected to be submitted to FDA and EMA in late 2021

ILLUMINATE•C

Alnylam Clinical Development Pipeline

Focused in 4 Strategic Therapeutic Areas (STArs):

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

		EARLY/MID-STAGE *(IND/CTA Filed-Phase 2)*	LATE STAGE *(Phase 2-Phase 3)*	REGISTRATION/ COMMERCIAL[1] (OLE/Phase 4/IIS/registries)	COMMERCIAL RIGHTS
onpattro (patisiran)	*hATTR Amyloidosis-PN*[2]			●	Global
GIVLAARI (givosiran)	*Acute Hepatic Porphyria*[3]			●	Global
OXLUMO (lumasiran)	*Primary Hyperoxaluria Type 1*[4]			●	Global
Leqvio® (inclisiran)	*Hypercholesterolemia*			●	Milestones & up to 20% Royalties[5]
Vutrisiran*	*hATTR Amyloidosis-PN*			●	Global
Patisiran	*ATTR Amyloidosis*		●		Global
Vutrisiran*	*ATTR Amyloidosis*		●		Global
Fitusiran*	*Hemophilia*		●		15-30% Royalties
Lumasiran	*Severe PH1* *Recurrent Renal Stones*	●	●		Global
Cemdisiran (+/- Pozelimab)[6]*	*Complement-Mediated Diseases*	●			50-50; Milestone/Royalty
Belcesiran[7]*	*Alpha-1 Liver Disease*	●			Ex-U.S. option post-Phase 3
ALN-HBV02 (VIR-2218)[8]*	*Hepatitis B Virus Infection*	●			50-50 option post-Phase 2
Zilebesiran (ALN-AGT)*	*Hypertension*	●			Global
ALN-HSD*	*NASH*	●			50-50
ALN-APP*	*Alzheimer's Disease;* *Cerebral Amyloid Angiopathy*	○			50-50
ALN-XDH*	*Gout*	○			Global

[1] Includes marketing application submissions; [2] 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; [3] 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; [4] Approved in the U.S., EU and Brazil for the treatment of primary hyperoxaluria type 1 in all age groups; [5] Novartis has obtained global rights to develop, manufacture and commercialize inclisiran; 50% of inclisiran royalty revenue from Novartis will be payable to Blackstone by Alnylam; [6] Cemdisiran and pozelimab are each currently in Phase 2 development; Alnylam and Regeneron are evaluating potential combinations of these two investigational therapeutics; [7] Dicerna is leading and funding development of Belcesiran; [8] Vir is leading and funding development of ALN-HBV02; * Not approved for any indication and conclusions regarding the safety or efficacy of the drug have not been established.

As of October 2021

Alnylam Clinical Development Pipeline

Focused in 4 Strategic Therapeutic Areas (STARs):

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

		EARLY/MID-STAGE *(IND/CTA Filed-Phase 2)*	LATE STAGE *(Phase 2-Phase 3)*	REGISTRATION/ COMMERCIAL[1] (OLE/Phase 4/IIS/registries)	COMMERCIAL RIGHTS
onpattro (patisiran)	*hATTR Amyloidosis-PN*[2]			●	Global
GIVLAARI (givosiran)	*Acute Hepatic Porphyria*[3]			●	Global
OXLUMO (lumasiran)	*Primary Hyperoxaluria Type 1*[4]			●	Global
Leqvio® (inclisiran)	*Hypercholesterolemia*			●	Milestones & up to 20% Royalties[5]
Vutrisiran*	*hATTR Amyloidosis-PN*			●	Global
Patisiran	*ATTR Amyloidosis*		●		Global
Vutrisiran*	*ATTR Amyloidosis*		●		Global
Fitusiran*	*Hemophilia*		●		15-30% Royalties
Lumasiran	*Severe PH1 Recurrent Renal Stones*	●	●		Global
Cemdisiran (+/- Pozelimab)[6]*	*Complement-Mediated Diseases*	●			50-50; Milestone/Royalty
Belcesiran[7]*	*Alpha-1 Liver Disease*	●			Ex-U.S. option post-Phase 3
ALN-HBV02 (VIR-2218)[8]*	*Hepatitis B Virus Infection*	●			50-50 option post-Phase 2
Zilebesiran (ALN-AGT)*	*Hypertension*	●			Global
ALN-HSD*	*NASH*	●			50-50
ALN-APP*	*Alzheimer's Disease; Cerebral Amyloid Angiopathy*	○			50-50
ALN-XDH*	*Gout*	○			Global

[1] Includes marketing application submissions; [2] 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; [3] 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; [4] Approved in the U.S., EU and Brazil for the treatment of primary hyperoxaluria type 1 in all age groups; [5] Novartis has obtained global rights to develop, manufacture and commercialize inclisiran; 50% of inclisiran royalty revenue from Novartis will be payable to Blackstone by Alnylam; [6] Cemdisiran and pozelimab are each currently in Phase 2 development; Alnylam and Regeneron are evaluating potential combinations of these two investigational therapeutics; [7] Dicerna is leading and funding development of Belcesiran; [8] Vir is leading and funding development of ALN-HBV02; * Not approved for any indication and conclusions regarding the safety or efficacy of the drug have not been established.

As of October 2021

Zilebesiran Phase 2 Clinical Development Plan

KARDIA$_1$

Monotherapy Phase 2 Study (N ~375)

- IND opened May 2021
- Evaluate efficacy and safety of zilebesiran as a monotherapy in patients with mild-to-moderate hypertension
- Exploring both quarterly and biannual dosing regimens
- Study initiated **June 2021**

KARDIA$_2$

Add-On Phase 2 Study (N ~800)

- Evaluate efficacy and safety of zilebesiran as add-on therapy in patients with hypertension despite treatment with a potent RAAS inhibitor, a calcium channel blocker, or a diuretic
- Targeting study initiation in **late 2021**

Alnylam Clinical Development Pipeline

Focused in 4 Strategic Therapeutic Areas (STArs):

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

		EARLY/MID-STAGE *(IND/CTA Filed-Phase 2)*	LATE STAGE *(Phase 2-Phase 3)*	REGISTRATION/ COMMERCIAL[1] (OLE/Phase 4/IIS/registries)	COMMERCIAL RIGHTS
onpattro (patisiran)	*hATTR Amyloidosis-PN*[2]			●	Global
GIVLAARI (givosiran)	*Acute Hepatic Porphyria*[3]			●	Global
OXLUMO (lumasiran)	*Primary Hyperoxaluria Type 1*[4]			●	Global
Leqvio® (inclisiran)	*Hypercholesterolemia*			●	Milestones & up to 20% Royalties[5]
Vutrisiran*	*hATTR Amyloidosis-PN*			●	Global
Patisiran	*ATTR Amyloidosis*		●		Global
Vutrisiran*	*ATTR Amyloidosis*		●		Global
Fitusiran*	*Hemophilia*		●		15-30% Royalties
Lumasiran	*Severe PH1* *Recurrent Renal Stones*	●	●		Global
Cemdisiran (+/- Pozelimab)[6]*	*Complement-Mediated Diseases*	●			50-50; Milestone/Royalty
Belcesiran[7]*	*Alpha-1 Liver Disease*	●			Ex-U.S. option post-Phase 3
ALN-HBV02 (VIR-2218)[8]*	*Hepatitis B Virus Infection*	●			50-50 option post-Phase 2
Zilebesiran (ALN-AGT)*	*Hypertension*	●			Global
ALN-HSD*	*NASH*	●			50-50
ALN-APP*	*Alzheimer's Disease;* *Cerebral Amyloid Angiopathy*	○			50-50
ALN-XDH*	*Gout*	○			Global

[1] Includes marketing application submissions; [2] 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; [3] 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; [4] Approved in the U.S., EU and Brazil for the treatment of primary hyperoxaluria type 1 in all age groups; [5] Novartis has obtained global rights to develop, manufacture and commercialize inclisiran; 50% of inclisiran royalty revenue from Novartis will be payable to Blackstone by Alnylam; [6] Cemdisiran and pozelimab are each currently in Phase 2 development; Alnylam and Regeneron are evaluating potential combinations of these two investigational therapeutics; [7] Dicerna is leading and funding development of Belcesiran; [8] Vir is leading and funding development of ALN-HBV02; * Not approved for any indication and conclusions regarding the safety or efficacy of the drug have not been established.

As of October 2021

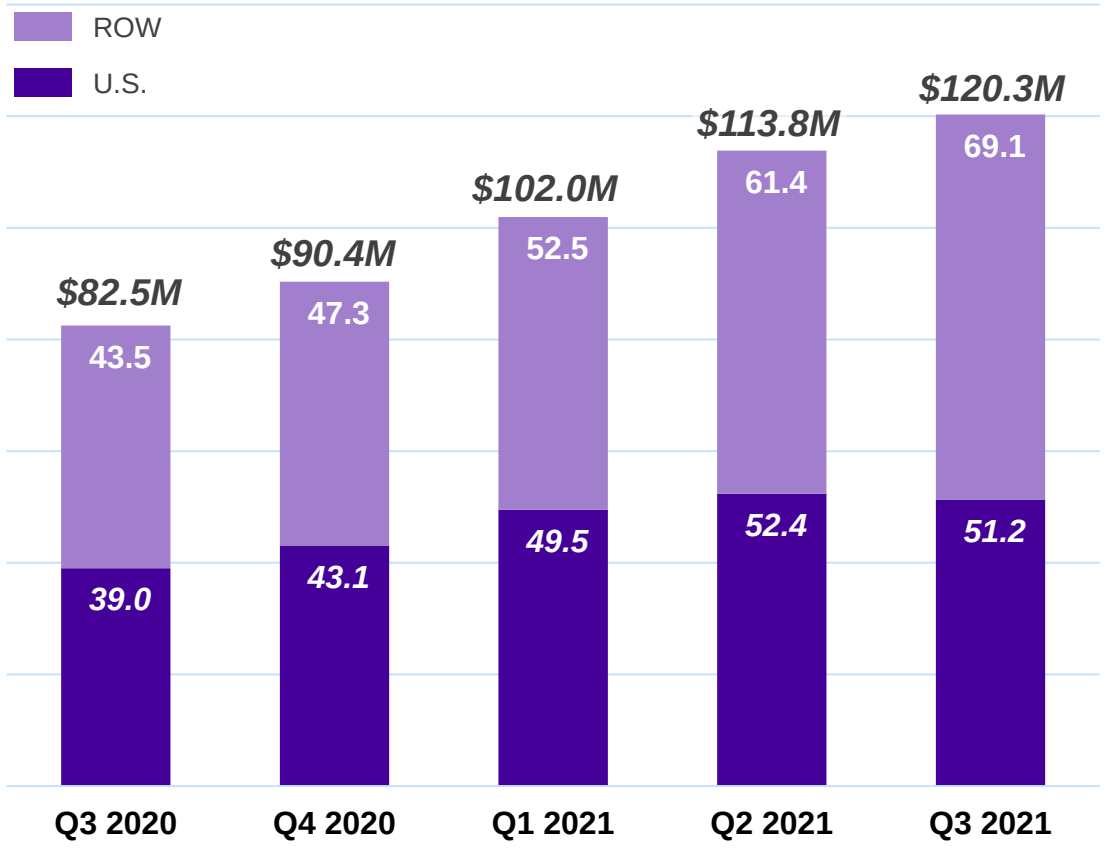
Jeff Poulton

Chief Financial Officer

Financial Summary and Upcoming Milestones

Global ONPATTRO Q3 2021 Performance

Revenue ($M)



Q3 Highlights

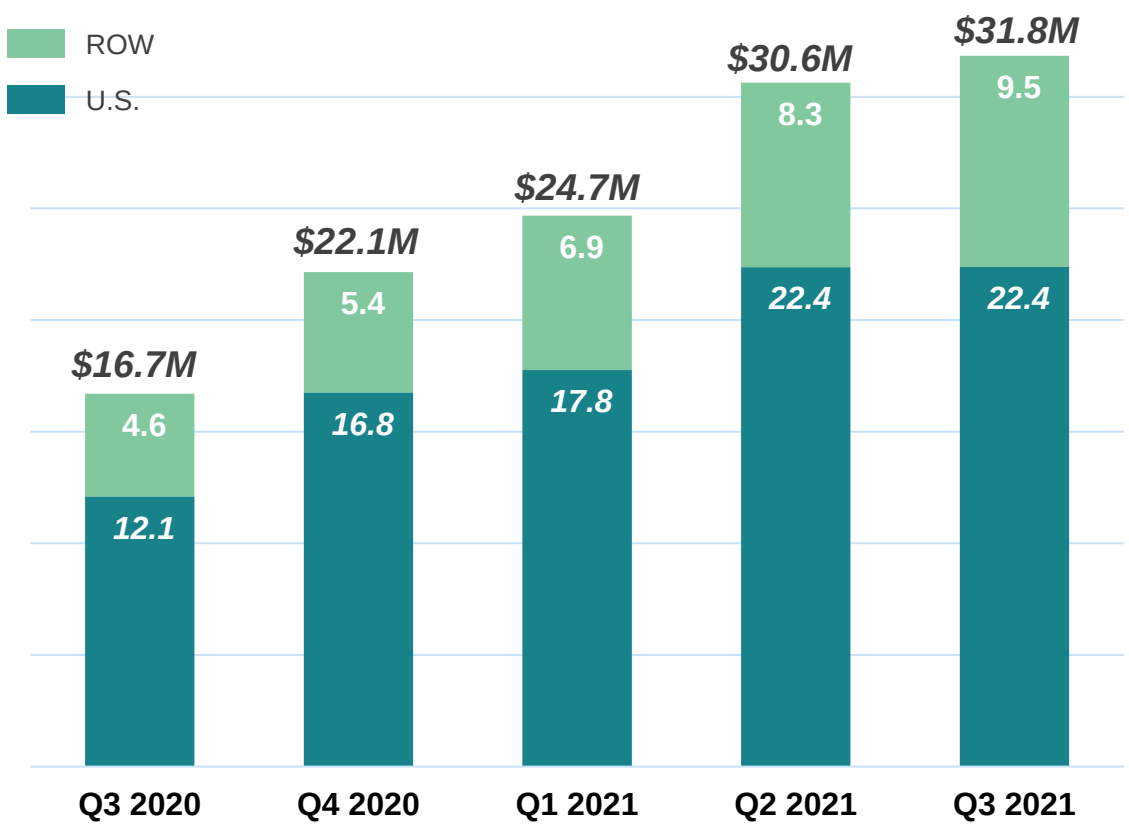
	YoY % Growth	QoQ % Growth
U.S.	31%	-2%
ROW	59%	12%
Global	46%	6%

- Steady and continuous patient growth continues across key markets (>1,875 commercial patients at end of Q3)
- U.S. QoQ demand growth +12% primarily due to an increase in patients on therapy and >90% patient treatment compliance
- U.S. QoQ demand growth offset by inventory destocking (~-10%) and higher gross to net deductions (~-3%)
- ROW growth driven broadly by contributions from Europe, Canada, and Japan

onpattro® (patisiran) lipid complex injection 10 mg/5 mL

Global GIVLAARI Q3 2021 Performance

Revenue ($M)



Q3 Highlights

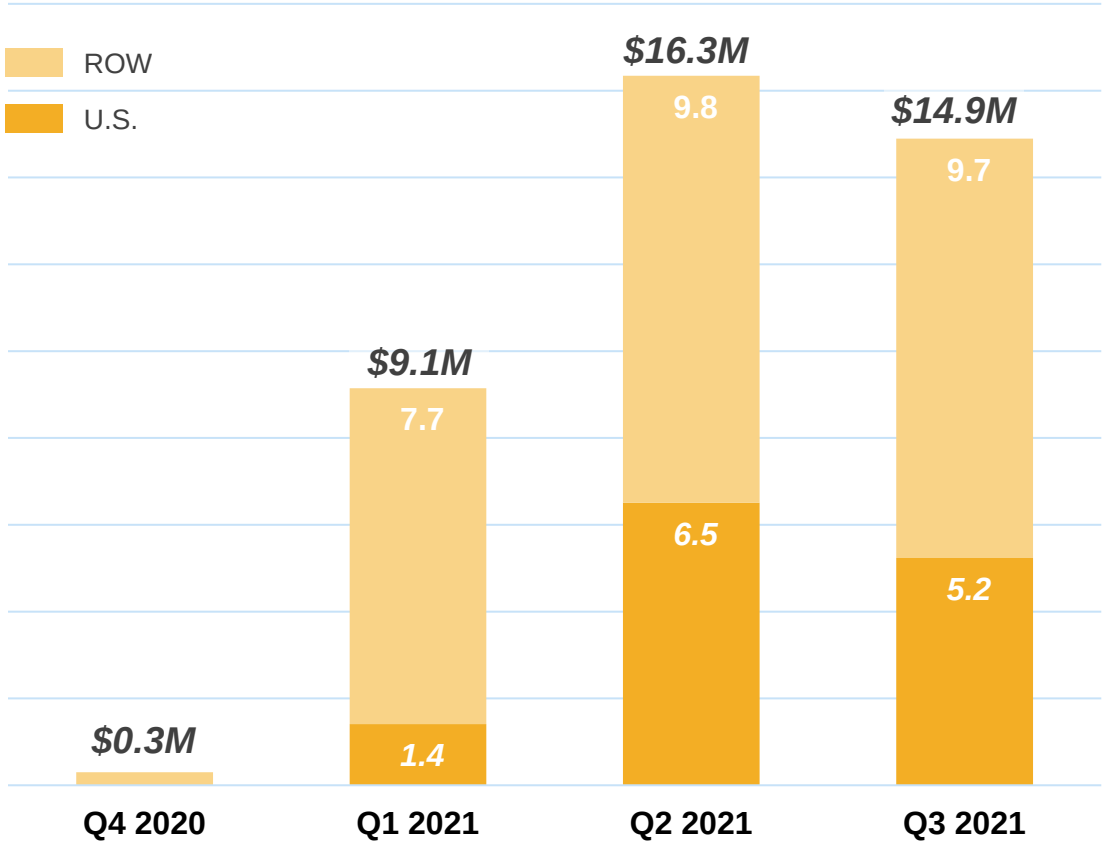
	YoY % Growth	QoQ % Growth
U.S.	85%	0%
ROW	106%	15%
Global	91%	4%

- >300 global patients on therapy since launch
- U.S. QoQ demand growth +9% primarily due to an increase in patients on therapy and >90% patient treatment compliance
- U.S. QoQ demand growth offset primarily by inventory destocking (~-8%)
- Generated initial sales in Japan and Spain in Q3

GIVLAARI® (givosiran) injection for subcutaneous use 189 mg/mL

Global OXLUMO Q3 2021 Performance

Revenue ($M)



Q3 Highlights

	QoQ % Growth
U.S.	-20%
ROW	-2%
Global	-9%

- >120 patients on commercial treatment in U.S. and Europe since launch
- QoQ sales decreased in both U.S. and ROW, despite growth in patients on therapy, due to the transition of initial bolus of commercial patients from monthly loading dose to quarterly maintenance dose regimens
- Progressing pricing and reimbursement discussions in many European countries

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

Q3 2021 Financial Summary

Financial Results ($ millions)	Q3 2021	Q3 2020	YoY % Change
Net Product Revenues	$167.0	$99.2	68%
Net Revenues from Collaborations	$20.1	$26.6	(24%)
Royalty Revenues	$0.5	-	-
Total Revenues	$187.6	$125.9	49%
Cost of Goods Sold and Cost of Collaborations and Royalties	$32.7	$21.8	50%
Gross Margin	$155.0	$104.1	49%
GM as % of Total Revenues[1]	*82.6%*	*82.7%*	-
Non-GAAP R&D Expenses[2]	$172.2	$148.1	16%
Non-GAAP SG&A Expenses[2]	$121.1	$114.5	6%
Non-GAAP Operating Loss [2]	($138.3)	($158.5)	(13%)

Financial Results ($ millions)	Sep 30, 2021	Dec 31, 2020
Cash & Investments[3]	$2,327.9	$1,874.4

[1] GM as a % of Total Net Product Revenues for Q3 2021 is 83.2% and Q3 2020 is 79.0% (Q3 2021 and 2020 exclude $4.6M and $1.0M Cost of Collaborations and Royalties associated with Net Revenues from Collaborations, respectively).
[2] Non-GAAP R&D expenses, non-GAAP SG&A expenses and non-GAAP operating loss primarily exclude costs related to stock-based compensation expense and a change in estimate of contingent liabilities.
[3] Cash, cash equivalents and marketable securities
See Appendix for a reconciliation between GAAP and non-GAAP measures

2021 Full Year Guidance Reiterated

	FY 2021 Guidance[1]
Net Product Revenue (ONPATTRO, GIVLAARI, OXLUMO)	$640M - $665M
Net Revenue from Collaborations & Royalties	$150M - $200M
Non-GAAP Combined R&D and SG&A Expenses[2]	$1,175M - $1,275M

[1] As of August 3, 2021

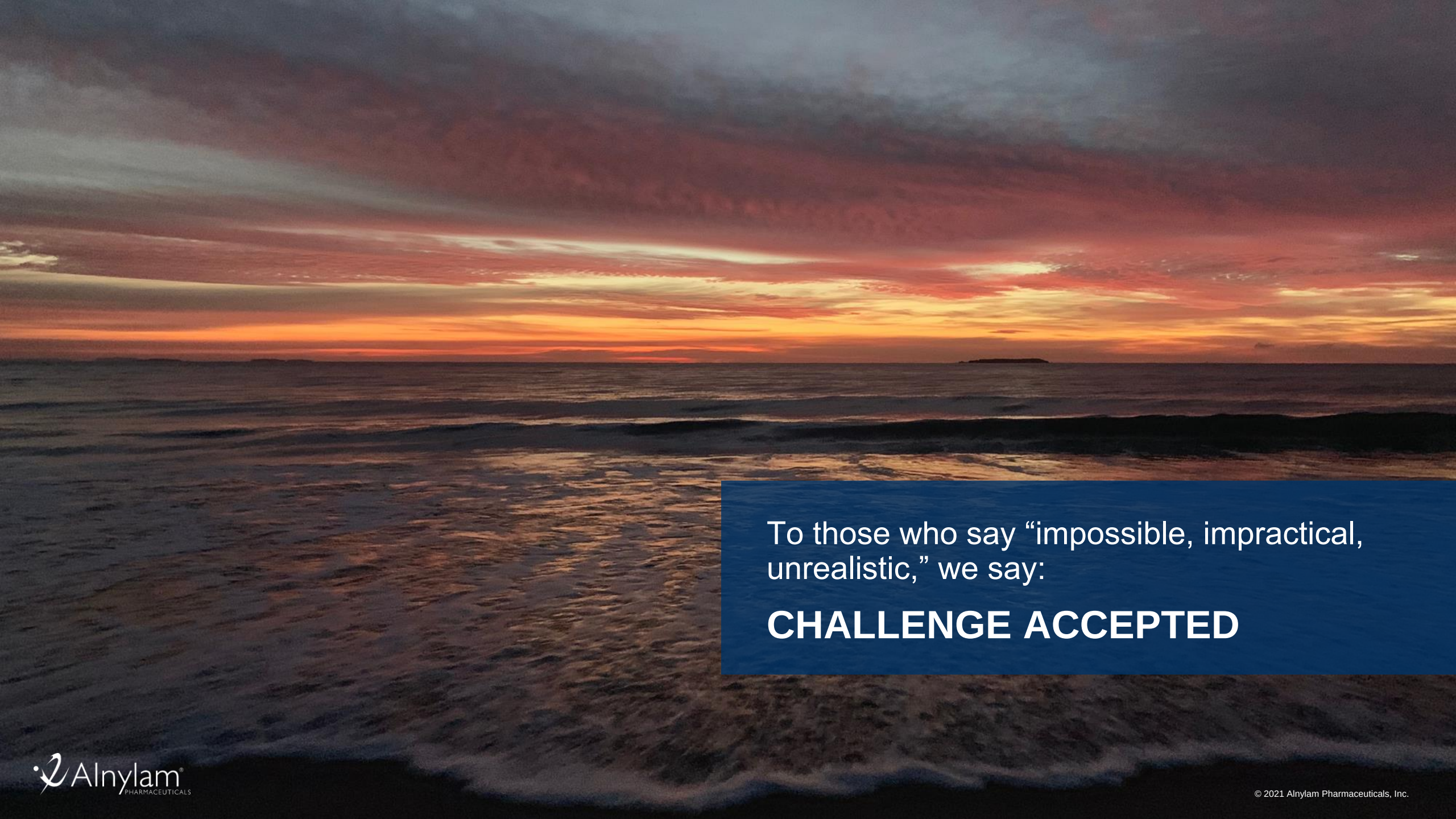
[2] 2021 Non-GAAP Combined R&D and SG&A Expenses guidance primarily excludes stock-based compensation expense estimated at $160M - $180M

Upcoming Milestones in Late 2021

Program	Upcoming Milestones
Vutrisiran	• Full 18-month results from HELIOS-A Phase 3 study at medical conference in early 2022
Zilebesiran (ALN-AGT)	• Additional Phase 1 data at American Heart Association Scientific Sessions, November 13-15 • Initiate KARDIA-2 Phase 2 study
Lumasiran	• Full results from ILLUMINATE-C Phase 3 study at American Society of Nephrology Kidney Week, Nov 2-7 • Initiate Phase 2 study in patients with recurrent renal stones • Submit regulatory filings with FDA and EMA based on ILLUMINATE-C to strengthen OXLUMO label
ALN-HSD	• Initial Phase 1 safety results in healthy volunteers at Alnylam R&D Day, November 19
Cemdisiran	• Initiate Phase 3 study of cemdisiran/pozelimab combination in myasthenia gravis (led by Regeneron)
ALN-APP	• File CTA
ALN-XDH	• File CTA

Q3 2021 Financial Results

Q&A Session



Alnylam PHARMACEUTICALS

Q3 2021 Financial Results

Appendix

Alnylam Pharmaceuticals, Inc.

Reconciliation of Selected GAAP Measures to Non-GAAP Measures
(In thousands)

	Three Months Ended	
	September 30, 2021	September 30, 2020
Reconciliation of GAAP to Non-GAAP research and development:		
GAAP Research and development	$ 194,572	$ 161,783
Less: Stock-based compensation expenses	(12,417)	(13,703)
Less: Upfront payment on license and collaboration agreement	(10,000)	—
Non-GAAP Research and development	$ 172,155	$ 148,080
Reconciliation of GAAP to Non-GAAP selling, general and administrative:		
GAAP Selling, general and administrative	$ 142,075	$ 167,472
Less: Stock-based compensation expenses	(20,950)	(23,561)
Less: Costs associated with the strategic financing collaboration	—	(763)
Less: Loss on contractual settlement	—	(650)
Less: Change in estimate of contingent liabilities	—	(28,000)
Non-GAAP Selling, general and administrative	$ 121,125	$ 114,498
Reconciliation of GAAP to Non-GAAP operating loss:		
GAAP operating loss	$ (181,677)	$ (225,199)
Add: Stock-based compensation expenses	33,367	37,264
Add: Costs associated with the strategic financing collaboration	—	763
Add: Upfront payment on license and collaboration agreement	10,000	—
Add: Loss on contractual settlement	—	650
Add: Change in estimate of contingent liabilities	—	28,000
Non-GAAP operating loss	$ (138,310)	$ (158,522)

Please note that the figures presented may not sum exactly due to rounding