Nathan (USA)
Diagnosed with AHP

Second Quarter 2022 Financial Results

July 28, 2022

Alnylam®@20

Agenda

Welcome

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

Overview

- Yvonne Greenstreet, MBChB, MBA
  Chief Executive Officer

Commercial Highlights

- Tolga Tanguler
  Chief Commercial Officer

Alnylam Pipeline

- Akshay Vaishnaw, M.D., Ph.D.
  President

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, our ability to attain financial self-sustainability, the drivers of our future growth potential, including the potential of our TTR franchise, including the launch of AMVUTTRA in the U.S. for the treatment of the polyneuropathy of hATTR amyloidosis in adults, and the ongoing review and potential approval of vutrisiran by other regulatory authorities, the expected timing of topline data from the APOLLO-B Phase 3 clinical study, the achievement of additional pipeline milestones and data, including relating to ongoing clinical studies of vutrisiran, zilebesiran, lumasiran, cemdisiran, ALN-HBV02 (Vir 2218), ALN-HSD, ALN-APP and ALN-XDH, the initiation of a Phase 3 clinical study for vutrisiran in Stargardt disease and the filing of an IND for ALN-TTRsc04, the expected range of net product revenues and net revenues from collaborations and royalties for 2022, the expected range of aggregate annual GAAP and non-GAAP R&D and SG&A expenses for 2022, and the potential impact of foreign exchange rates on our results, growth rates and 2022 guidance. 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 recent leadership transition on our ability to 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 and GEMINI platforms, and successfully demonstrate the efficacy and safety of our product candidates; the pre-clinical and clinical results for our product candidates, including patisiran and vutrisiran; actions or advice of regulatory agencies and our ability to obtain and maintain regulatory approval for our product candidates, including vutrisiran and lumasiran, 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, AMVUTTRA or OXLUMO 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; the impact of foreign exchange rates on our results; 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 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 and realized and unrealized (gains) losses on marketable equity securities. 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 realized and 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.

Percentage changes in revenue growth at Constant Exchange Rates, or CER, are presented excluding the impact of changes in foreign currency exchange rates for investors to understand the underlying business performance. The current period's foreign currency revenue values are converted into U.S. dollars using the average exchange rates from the prior period.

Yvonne Greenstreet, MBChB, MBA

Chief Executive Officer

Overview

The fifth RNAi therapeutic is

NOW APPROVED

amvuttra™
(vutrisiran) injection
25 mg/0.5 mL

2022 Expected to Deliver Multiple Catalysts with Value-Creation Potential

Full 18-Month HELIOS-A Phase 3 Results with Vutrisiran	January 21, 2022 Société Francophone du Nerf Périphérique ✓
Cemdisiran Phase 2 Data in IgA Nephropathy	Early 2022 ✓
FDA Approval of Vutrisiran	Mid-2022 ✓
APOLLO-B Phase 3 Results with Patisiran	***Within next three weeks***
ALN-HSD Phase 1 Part B Topline Results in NASH Patients	Mid-2022
Vutrisiran Biannual Dose Regimen Data	Late 2022
ALN-APP Phase 1 Topline Results	Late 2022
ALN-XDH Phase 1 Topline Results	Late 2022

Early is Q1-Q2, Mid is Q2-Q3, and Late is Q3-Q4

Multiple Drivers of Future Growth

TTR Franchise Leadership

Expansion into Prevalent Diseases

Engine for Sustainable Innovation

Andreas (Sweden)
Diagnosed with hATTR amyloidosis

Alnylam P5X25

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

Tolga Tanguler

Chief Commercial Officer

Commercial Highlights

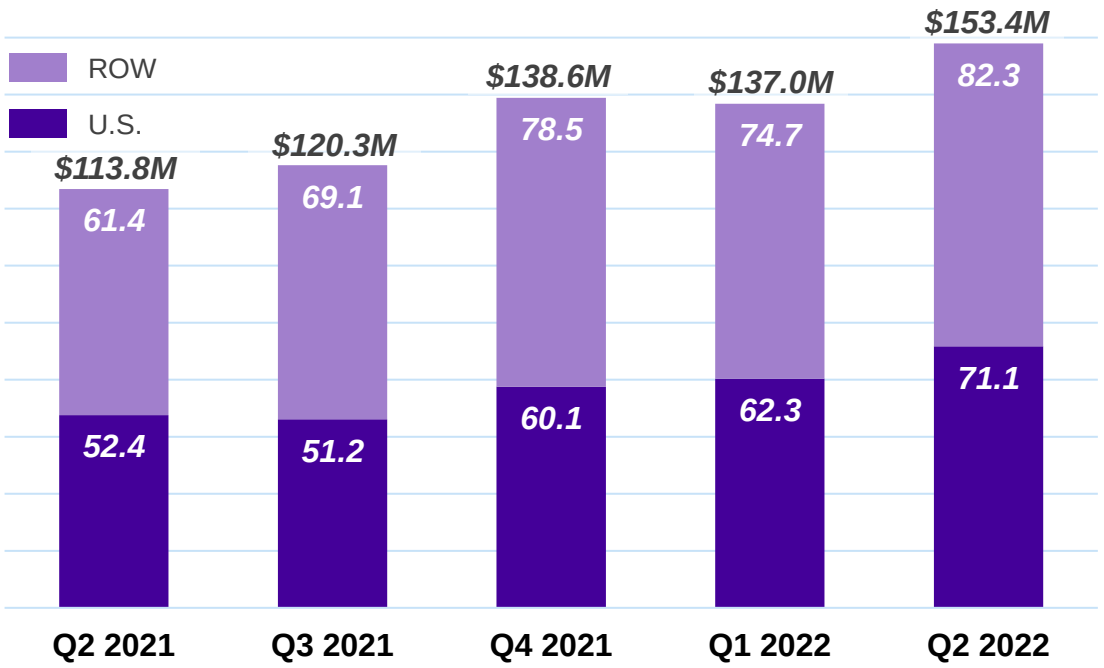
ONPATTRO® (patisiran) Update: Q2 2022

$153M

ONPATTRO Global Q2 2022 Net Product Revenues

>2,400

Patients Worldwide on Commercial ONPATTRO at end of Q2 2022



Q2 Highlights

	YoY % Growth	QoQ % Growth
U.S.	36%	14%
ROW	34%	10%
Global	35%	12%

- Steady patient growth continues across key markets
- U.S. QoQ growth of 14% primarily due to an increase in patients on therapy and improved patient compliance following COVID impacted Q1
- ROW QoQ growth of 10% favorably impacted by growth in patients on therapy and timing of orders in partner markets
- Strengthening USD continues to create FX headwind for ROW markets (YoY CER[1] growth = 42%)
- AMVUTTRA first commercial sales will occur in Q3 following June 13, 2022 U.S. approval

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

[1] CER = constant exchange rate, representing growth calculated as if exchange rates had remained unchanged from those used in Q2 2021.

AMVUTTRA™ (vutrisiran) Update: Initial Launch Progress

Promising Early Indicators Following U.S. Approval on June 13

PERFORMANCE

HCP & PATIENT OUTREACH

HEALTH SYSTEMS & PAYERS

EARLY HIGHLIGHTS

Encouraging early demand signal

- 133 Start Forms received from launch through July 22, 2022*
  - ~1/3 from new patients / ~2/3 from ONPATTRO switch
  - >20% sourced from new prescribers
- Product available in channel from early July

Initial promotion / education efforts

- >61,000 HCPs and Patients reached with launch messages within 48 hours
- Peer to peer educational programs underway reaching hundreds of physicians

Positive payer interactions

- ~60% of top tier Health Systems have initiated the formulary process
- 1st payer policy published (~24M covered lives)
- Anticipate permanent J-code will be established January 1, 2023

* Start Forms are an incomplete picture of U.S. demand
AMVUTTRA is approved in the U.S. for the PN of hATTR amyloidosis in adults

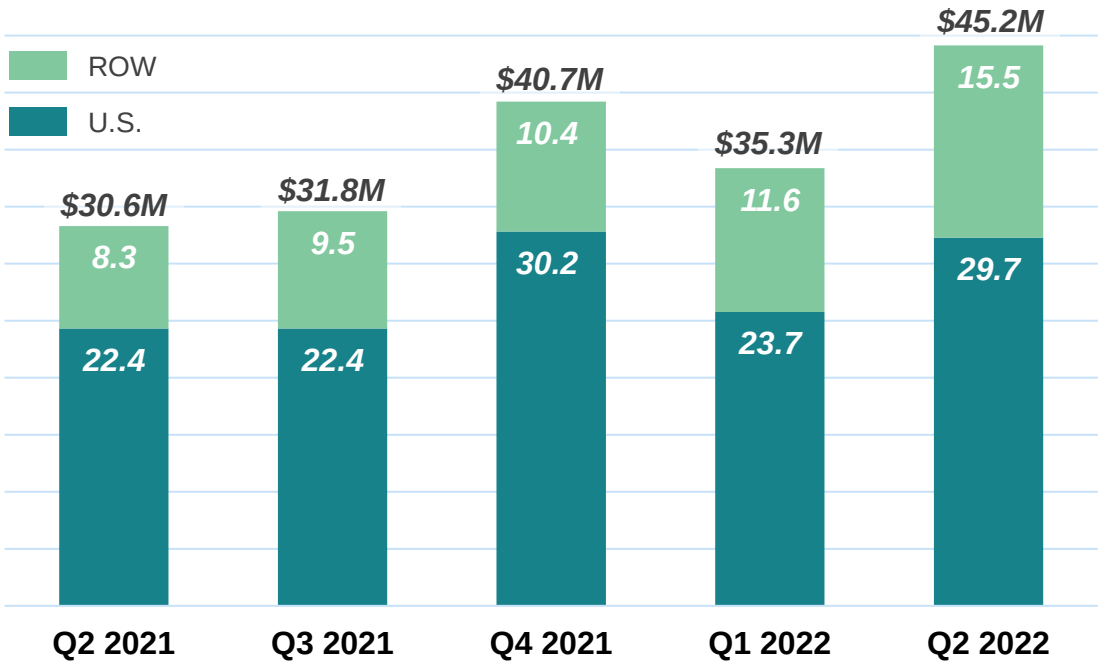
GIVLAARI® (givosiran) Update: Q2 2022

$45M

GIVLAARI Global Q2 2022 Net Product Revenues

>420

Patients Worldwide on Commercial GIVLAARI at end of Q2 2022



Q2 Highlights

	YoY % Growth	QoQ % Growth
U.S.	33%	25%
ROW	87%	34%
Global	47%	28%

- U.S. QoQ growth of 25% impacted by:
  - Demand growth +12% due to an increase in patients on therapy and improved patient compliance following COVID impacted Q1
  - Inventory stocking dynamics (+8%) and modest decrease in gross to net deductions (+5%)
- ROW QoQ growth of 34% favorably impacted by increased demand, including from late Q1 UK launch, and a decrease in gross to net deductions
- Strengthening USD continues to create FX headwind for ROW markets (YoY CER[1] growth = 53%)

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

[1] CER = constant exchange rate, representing growth calculated as if exchange rates had remained unchanged from those used in Q2 2021.

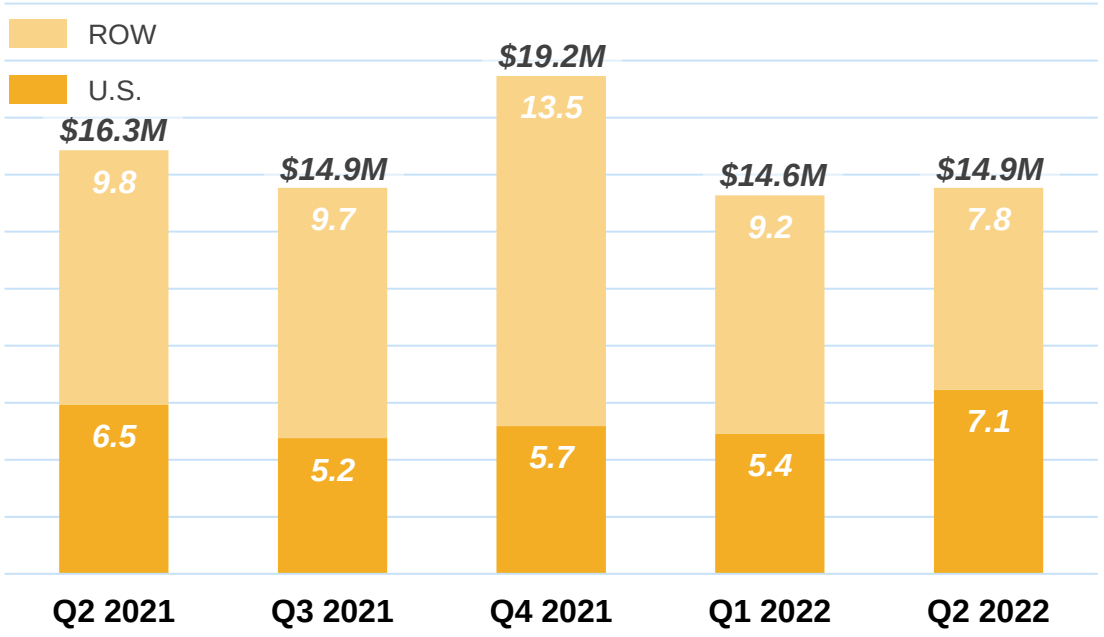
OXLUMO® (lumasiran) Update: Q2 2022

$15M

OXLUMO Global Q2 2022 Net Product Revenues

>200

Patients Worldwide on Commercial OXLUMO at end of Q2 2022



Q2 Highlights

	YoY % Growth	QoQ % Growth
U.S.	9%	32%
ROW	-20%	-15%
Global	-9%	2%

- U.S. QoQ growth of 32% primarily due to increase in patient demand, stocking dynamics, and reduced gross to net deductions
- ROW QoQ growth of -15% despite strong patient growth due to an increase in gross to net deductions and the timing of orders in partner markets
- Global YoY growth of -9%, despite doubling of patients, due to higher proportion of patients on monthly loading dose in Q2 2021 and lower net pricing in international markets in Q2 2022
- Strengthening USD continues to create FX headwind for ROW markets (YoY CER[1] growth = -4%)

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

[1] CER = constant exchange rate, representing growth calculated as if exchange rates had remained unchanged from those used in Q2 2021.

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

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 (KCCQ-OS)
- Death and hospitalization outcomes

Selected Exploratory Endpoints

- Cardiac biomarkers

12-Month Treatment Extension

ClinicalTrials.gov Identifier: NCT03997383

APOLLO-B

Enrollment complete

Topline results expected
within next three weeks

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 Patients with Hereditary ATTR Amyloidosis with Polyneuropathy

HELIOS·A

- As previously reported, the primary endpoint of change from baseline in mNIS+7 at Month 9 was met[1]

Patient Population
N=164

- 18–85 years old
- hATTR amyloidosis with polyneuropathy; any *TTR* mutation
- NIS 5–130 and PND ≤IIIB
- KPS ≥60%
- Prior tetramer stabilizer use permitted

3:1 RANDOMIZATION

Stratification:
TTR V30M vs non-V30M
Baseline NIS <50 vs ≥50

n=122

Vutrisiran
25 mg
SC Q3M

or

n=42

Reference comparator
(patisiran)
0.3 mg/kg
IV Q3W

Efficacy Assessments

Vutrisiran vs APOLLO Placebo

Primary Endpoint (at Month 9; previously presented[1])
- Change from baseline in mNIS+7[a]

Secondary Endpoints
Change from baseline in:
- mNIS+7 at Month 18
- Norfolk QOL-DN[b] at Months 9 and 18
- 10-MWT[c] at Months 9 and 18
- mBMI[d] at Month 18
- R-ODS[e] at Month 18

Selected Exploratory Endpoints
- Change from baseline in cardiac biomarkers, echocardiographic parameters to Month 18
- Change from baseline in Tc scintigraphy measures to Month 18[f]

Vutrisiran vs HELIOS-A Patisiran

Secondary Endpoint
- % serum TTR reduction to Month 18

[a]Higher scores of mNIS+7 indicate more neurologic impairment (range, 0 to 304). [b]Higher scores of Norfolk QOL-DN indicate worse quality of life (range, −4 to 136). [c]10-MWT speed (m/s) = 10 meters/mean time (seconds) taken to complete two assessments at each visit, imputed as 0 for patients unable to perform the walk; lower speeds indicate worse ambulatory function. [d]Lower scores of mBMI ([weight in kg/m^2] x serum albumin g/L) indicate worse nutritional status. [e]Lower scores of R-ODS indicate more disability (range, 0 to 48). [f]Tc scintigraphy was only performed at select sites, comparison to baseline, not placebo

10-MWT, 10-meter walk test; ATTRv, transthyretin-mediated amyloidosis (v for variant); hATTR, hereditary transthyretin-mediated amyloidosis; IV, intravenous; KPS, Karnofsky performance status; mBMI, modified body mass index; mNIS+7, modified Neuropathy Impairment Score +7; NIS, Neuropathy Impairment Score; Norfolk QOL-DN, Norfolk Quality of Life-Diabetic Neuropathy; PND, polyneuropathy disability; Q3M, every 3 months; Q3W, every 3 weeks; R-ODS, Rasch-built Overall Disability Scale; SC, subcutaneous; Tc, technetium; TTR, transthyretin.

1. Adams D et al. *Neurology* 2021;96(15 Supplement):1234.

Vutrisiran HELIOS·B Phase 3 Study

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

N = 655
Patient Population

- ATTR amyloidosis; wild-type or any TTR mutation
- 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

Topline results on 30-month endpoint expected **early 2024**

Study includes optional interim analysis

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 with PN[2]*		●	Global
GIVLAARI (givosiran)	*Acute Hepatic Porphyria[3]*		●	Global
OXLUMO (lumasiran)	*Primary Hyperoxaluria Type 1[4]*		●	Global
LEQVIO (inclisiran)	*Hypercholesterolemia[5]*		●	Milestones & up to 20% Royalties[6]
amvuttra (vutrisiran)	*hATTR Amyloidosis with PN[7]*		●	Global
Patisiran	*ATTR Amyloidosis with CM*	●		Global
Vutrisiran	*ATTR Amyloidosis with CM*	●		Global
Vutrisiran[8]*	*Stargardt Disease*	○		Global
Fitusiran*	*Hemophilia*	●		15-30% Royalties
Lumasiran	*Severe PH1 Recurrent Renal Stones*		●	Global
Cemdisiran (+/- Pozelimab)[9]*	*Complement-Mediated Diseases*	●		50-50; Milestone/Royalty
Belcesiran[10]*	*Alpha-1 Liver Disease*			Ex-U.S. option post-Phase 3
ALN-HBV02 (VIR-2218)[11]*	*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] Approved in the U.S. for the treatment of heterozygous familial hypercholesterolemia (HeFH) or clinical atherosclerotic cardiovascular disease (ASCVD) and in the EU for the treatment of hypercholesterolemia or mixed dyslipidemia; [6] 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; [7] Approved in the U.S. for the PN of hATTR amyloidosis in adults [8] Phase 3 study of vutrisiran in Stargardt Disease expected to initiate in late 2022; [9] Cemdisiran and pozelimab are each currently in Phase 2 development; Alnylam and Regeneron are evaluating potential combinations of these two investigational therapeutics; [10] Dicerna is leading and funding development of belcesiran; [11] 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 July 2022

Alnylam Clinical Development Pipeline

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Fitusiran*	*Hemophilia*		●		15-30% Royalties
Lumasiran	*Severe PH1 Recurrent Renal Stones*	●		●	Global
Cemdisiran (+/- Pozelimab)[9]*	*Complement-Mediated Diseases*		●		50-50; Milestone/Royalty
Belcesiran[10]*	*Alpha-1 Liver Disease*	●			Ex-U.S. option post-Phase 3
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Zilebesiran (ALN-AGT)*	*Hypertension*	●			Global
ALN-HSD*	*NASH*	●			50-50
ALN-APP*	*Alzheimer's Disease; Cerebral Amyloid Angiopathy*	●			50-50
ALN-XDH*	*Gout*	●			Global

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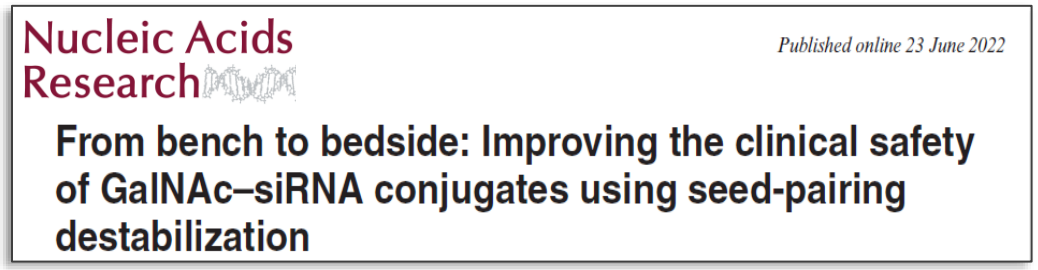
As of July 2022

Progress with Platform Innovation

Alnylam Proprietary Advances in Delivery and Target Discovery

- Leveraging Alnylam's decades long investment in the siRNA delivery platform, this paper describes lipid conjugates suitable for clinical development for targets in CNS, eye, lung
- Potential for lipid conjugates to other organs being studied



- We further expand on our approach to improve the specificity of GalNAc-siRNA conjugates using seed-pairing destabilization

- Alnylam discovered target in UK Biobank
- *INHBE* loss of function improves waist-to-hip ratio, a surrogate for abdominal fat that impacts risk for type 2 diabetes and heart disease

Jeff Poulton

Chief Financial Officer

Financial Summary and Upcoming Milestones

Q2 2022 Financial Summary

Financial Results ($ millions)	Q2 2022	Q2 2021	Reported Growth %	CER Growth %[3]
Net Product Revenues	$214	$161	33%	40%
Net Revenues from Collaborations	$9	$59	(85%)	
Royalty Revenues	$2	$0		
Total Revenues	$225	$221	2%	7%
Cost of Goods Sold and Collaborations	$41	$39	5%	
Gross Margin	$184	$182	1%	
GM as % of Total Revenues[1]	*82%*	*82%*		
Non-GAAP R&D Expenses[2]	$195	$170	15%	16%
Non-GAAP SG&A Expenses[2]	$150	$126	19%	21%
Non-GAAP Operating Loss [2]	($161)	($114)	41%	36%

Financial Results ($ millions)	Jun 30, 2022	Dec 31, 2021
Cash & Investments[4]	$2,111	$2,436

[1] GM as a % of Total Net Product Revenues is 84.1% and 87.5% for Q2 2022 and Q2 2021, respectively (excludes $6.8M and $8.5M of Cost of Collaborations and Royalties for Q2 2022 and Q2 2021, respectively).
[2] Non-GAAP R&D expenses, non-GAAP SG&A expenses and non-GAAP operating loss exclude costs related to stock-based compensation expense.
[3] Growth rates are at Constant Exchange Rates ("CER"), CER is determined by comparing Q2 2022 performance (restated using Q2 2021 exchange rates) to actual Q2 2022 reported performance. CER is a Non-GAAP measure.
[4] Cash, cash equivalents and marketable securities
See Appendix for a reconciliation between GAAP and non-GAAP measures

2022 Financial Guidance Reiterated

	FY 2022 Guidance[1,2]
Net Product Revenue (ONPATTRO, GIVLAARI, OXLUMO, AMVUTTRA)	$870M – $930M
Net Revenues from Collaborations & Royalties	$175M – $225M
Non-GAAP Combined R&D and SG&A Expenses[3]	$1,390M – $1,450M

[1] As of April 28, 2022

[2] Our FY 2022 Guidance utilizes April 18, 2022 FX rates of: 1 EUR = 1.08 USD; 1 GBP = 1.31 USD; 1 CHF = 1.06 USD; 1 CAD = 0.79 USD, 1 USD = 126 JPY

[3] 2022 Non-GAAP Combined R&D and SG&A Expenses guidance excludes stock-based compensation expense estimated at $230 million to $250 million

Alnylam 2022 Goals

			Early	Mid	Late
onpattro (patisiran) GIVLAARI (givosiran) OXLUMO (lumasiran) amvuttra (vutrisiran)		*Combined Net Product Revenue Guidance $870 million – $930 million*			●
PATISIRAN	hATTR/ATTR Amyloidosis	APOLLO-B Phase 3 Topline Results		●	
		File sNDA for ATTR with cardiomyopathy			●
VUTRISIRAN*	hATTR/ATTR Amyloidosis	FDA Approval		✓	
		U.S. Launch		✓	
		EMA Approval		●	
		Biannual Dose Regimen Data			●
	Stargardt Disease	Initiate Phase 3 in Stargardt Disease			●
ALN-TTRsc04*	ATTR Amyloidosis	File IND			●
		Initiate Phase 1 Study			●
LUMASIRAN	PH1, Recurrent Renal Stones	Complete Enrollment in Phase 2 Study in Recurrent Renal Stones			●
INCLISIRAN	Hypercholesterolemia	FDA Approval (1/1/22 PDUFA)	✓		
CEMDISIRAN* (+/- POZELIMAB)	Complement-Mediated Diseases	Phase 2 Monotherapy Results in IgA Nephropathy	✓		
		Initiate Phase 3 Combination Study in PNH	✓		
ZILEBESIRAN*	Hypertension	Complete KARDIA-2 Enrollment (at or around year-end)			●
ALN-HBV02 (VIR-2218)*	Chronic HBV Infection	Phase 2 Combination Results	✓		●
ALN-HSD*	NASH	Phase 1 Part B Topline Results		●	
ALN-APP*	Alzheimer's Disease	Initiate Phase 1 Study	✓		
		Phase 1 Topline Results			●
ALN-XDH*	Gout	Initiate Phase 1 Study	✓		
		Phase 1 Topline Results			●
ADDITIONAL PROGRAMS		File 2-4 new INDs	●	●	●

* Not approved for any indication and conclusions regarding the safety or effectiveness of these drugs have not been established

Early is Q1-Q2, Mid is Q2-Q3, and Late is Q3-Q4

Q2 2022 Financial Results

Q&A Session

Q2 2022 Financial Results

Appendix

Alnylam Pharmaceuticals, Inc.

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

	Three Months Ended		Six Months Ended	
	June 30, 2022	June 30, 2021	June 30, 2022	June 30, 2021
Reconciliation of GAAP to Non-GAAP research and development:				
GAAP Research and development	$ 205,712	$ 182,635	$ 375,605	$ 368,534
Less: Stock-based compensation expenses	(10,638)	(13,086)	(22,255)	(37,461)
Non-GAAP Research and development	$ 195,074	$ 169,549	$ 353,350	$ 331,073
Reconciliation of GAAP to Non-GAAP selling, general and administrative:				
GAAP Selling, general and administrative	$ 169,984	$ 145,323	$ 324,455	$ 292,182
Less: Stock-based compensation expenses	(19,833)	(18,992)	(37,509)	(50,307)
Non-GAAP Selling, general and administrative	$ 150,151	$ 126,331	$ 286,946	$ 241,875
Reconciliation of GAAP to Non-GAAP operating loss:				
GAAP Operating loss	$ (191,686)	$ (146,160)	$ (338,418)	$ (332,414)
Add: Stock-based compensation expenses	30,471	32,078	59,764	87,768
Non-GAAP Operating loss	$ (161,215)	$ (114,082)	$ (278,654)	$ (244,646)

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

Alnylam Pharmaceuticals, Inc.

Reconciliation of Revenue and Operating Expense Growth at Constant Exchange Rate (CER)*

	June 30, 2022	
	Three Months Ended	Six Months Ended
ONPATTRO net product revenue growth, as reported	35 %	35 %
Less: Impact of foreign currency translation	7	6
ONPATTRO net product revenue growth at constant currency	42 %	41 %
GIVLAARI net product revenue growth, as reported	47 %	45 %
Less: Impact of foreign currency translation	6	5
GIVLAARI net product revenue growth at constant currency	53 %	50 %
OXLUMO net product revenue growth, as reported	(9)%	16 %
Less: Impact of foreign currency translation	5	6
OXLUMO net product revenue growth at constant currency	(4)%	22 %
Total net product revenue growth, as reported	33 %	35 %
Less: Impact of foreign currency translation	7	6
Total net product revenue growth at constant currency	40 %	41 %

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

** Constant Exchange Rate (CER) representing growth calculated as if the exchange rates had remained unchanged from those used in the second quarter 2021. CER is a Non-GAAP measure.*