Nathan (USA)
Diagnosed with AHP

First Quarter 2022 Financial Results

April 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

- Pushkal Garg, M.D.
  Chief Medical Officer

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 potential launch of vutrisiran for the treatment of hATTR amyloidosis patients with polyneuropathy, if approved by the FDA and other regulatory authorities, the potential opportunity for RNAi therapeutics in prevalent diseases, the achievement of additional pipeline and regulatory milestones, including relating to ongoing clinical studies of patisiran, vutrisiran and zilebesiran, delayed enrollment in the zilebesiran KARDIA-1 Phase 2 study and expected timing for topline data, and the initiation of clinical studies for ALN-APP and ALN-XDH, as well as the expected range of net product revenues, as updated, and net revenues from collaborations and royalties for 2022, and the expected range of aggregate annual GAAP and non-GAAP R&D and SG&A expenses for 2022, as updated, 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 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 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, including vutrisiran; obtaining, maintaining and protecting intellectual property; our ability to successfully expand the indication for OXLUMO, ONPATTRO (and potentially vutrisiran, if approved) 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.

Yvonne Greenstreet, MBChB, MBA

Chief Executive Officer

Overview

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

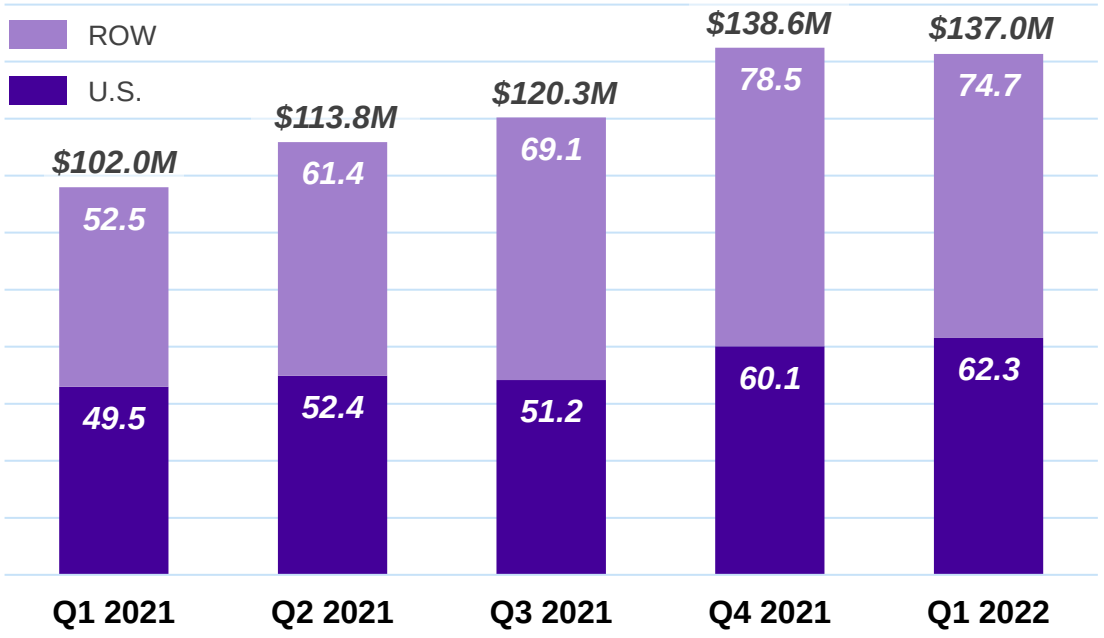
ONPATTRO® (patisiran) Update: Q1 2022

$137M

ONPATTRO Global Q1 2022 Net Product Revenues

>2,200

Patients Worldwide on Commercial ONPATTRO at end of Q1 2022



Q1 Highlights

	YoY % Growth	QoQ % Growth
U.S.	26%	4%
ROW	42%	-5%
Global	34%	-1%

- Steady patient growth continues across key markets
- U.S. QoQ growth of 4% impacted by:
  - Demand growth +7% due to an increase in patients on therapy partially offset by COVID impact on compliance
  - Inventory stocking dynamics (-6%)
  - Modest decrease in gross to net deductions (+3%)
- ROW patient growth offset by higher Q1 gross to net deductions following Q4 non-recurring benefits and foreign exchange

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

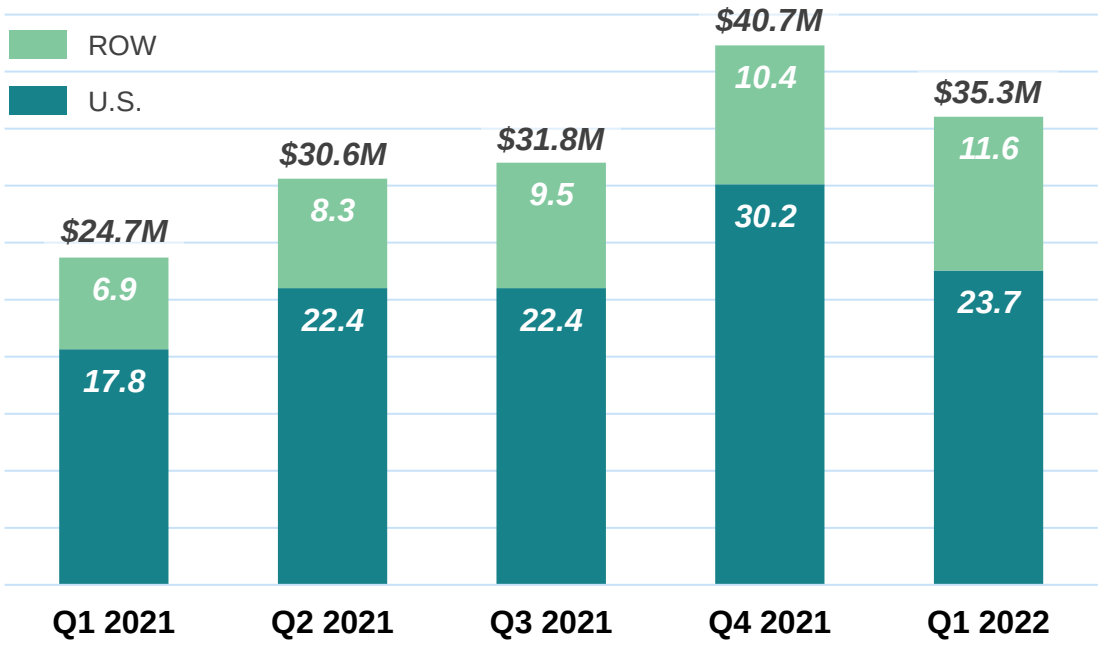
GIVLAARI® (givosiran) Update: Q1 2022

$35M

GIVLAARI Global Q1 2022 Net Product Revenues

>400

Patients Worldwide on Commercial GIVLAARI at end of Q1 2022



Q1 Highlights

	YoY % Growth	QoQ % Growth
U.S.	33%	-22%
ROW	68%	11%
Global	43%	-13%

- U.S. QoQ growth of -22% impacted by:
  - Flat demand growth, despite 5% growth in patients, due to COVID impacted lower patient compliance
  - Inventory stocking dynamics (-15%)
  - Increase in gross to net deductions in Q1 following Q4 non-recurring benefits (-7%)
- ROW growth primarily driven by new patient adds in key markets, including launch in UK, offset by foreign exchange

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

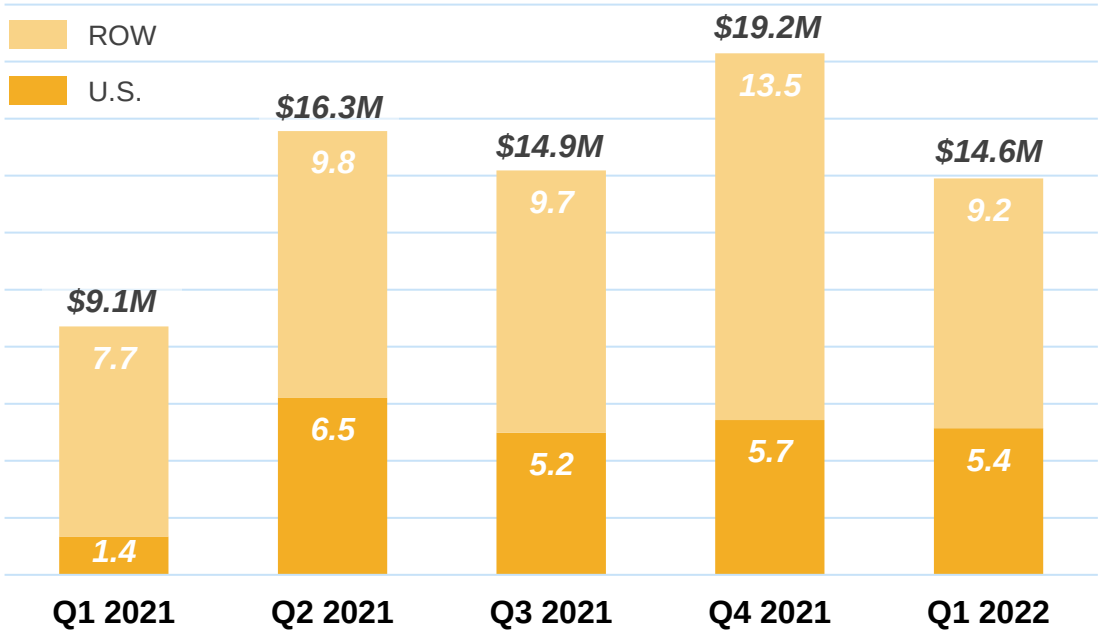
OXLUMO® (lumasiran) Update: Q1 2022

$15M

OXLUMO Global Q1 2022 Net Product Revenues

>160

Patients Worldwide on Commercial OXLUMO at end of Q1 2022



Q1 Highlights

	YoY % Growth	QoQ % Growth
U.S.	284%	-5%
ROW	19%	-32%
Global	59%	-24%

- U.S. QoQ growth of -5% impacted by:
  - Demand growth +6% due to an increase in patients on therapy
  - Increase in gross to net deductions (-11%)
- ROW patient growth offset by higher Q1 gross to net deductions following Q4 non-recurring benefits, timing of orders in partner markets, and foreign exchange

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

Pushkal Garg, M.D.
Chief Medical Officer

Alnylam Pipeline

Patisiran APOLLO-B Phase 3 Study

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

N = 360
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 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

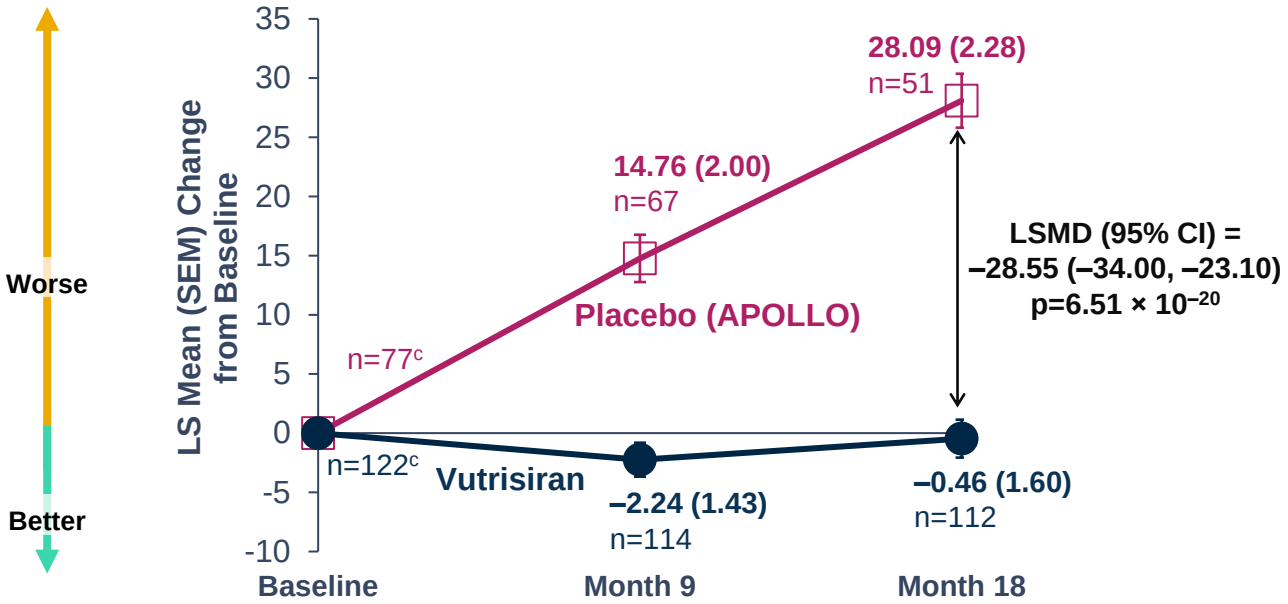
10-MWT, 10-meter walk test; ATTRv, transthyretin-mediated amyloidosis (v for variant); hATTR, hereditary transthyretin-mediated amyloidosis; IV, intravenous; KPS, Karnofsky performance status; mBMI, modified body mass index; mNIS+7, modified Neuropathy Impairment Score +7; NIS, Neuropathy Impairment 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.

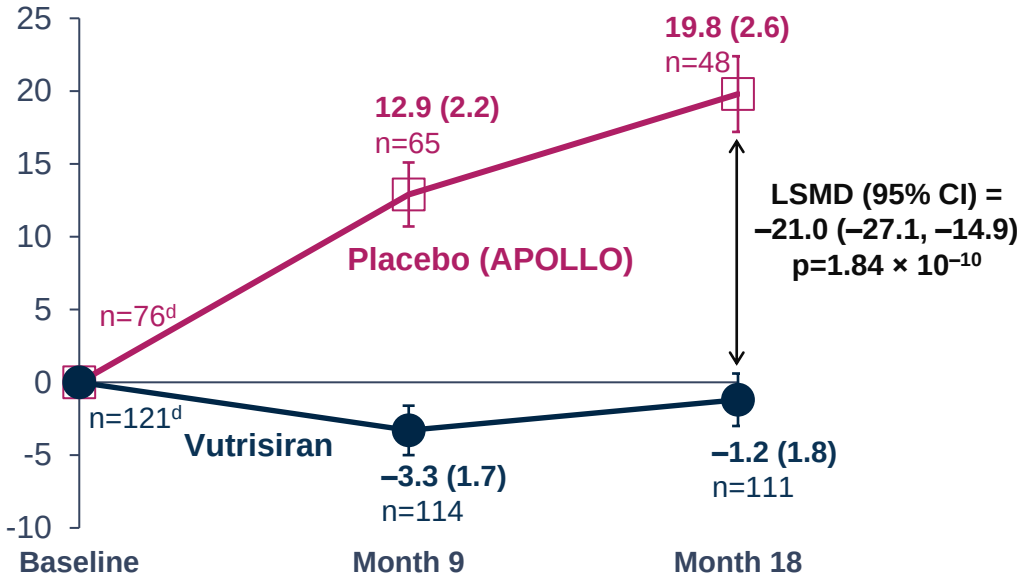
Statistically Significant Improvement in Neuropathy Impairment and Quality of Life with Vutrisiran vs External Placebo at Month 18

- Improvement was observed across all prespecified patient subgroups, components, and subdomains of mNIS+7 and Norfolk QOL-DN (data not shown)
- Improvement relative to baseline[a] in mNIS+7 (48.3% [vutrisiran] vs 3.9% [placebo]) and Norfolk QOL-DN (56.8% vs 10.4%)
- Consistent treatment effects in vutrisiran and patisiran groups in HELIOS-A (data not shown)

mNIS+7 LS Mean Change from Baseline[b]



Norfolk QOL-DN LS Mean Change from Baseline[b]



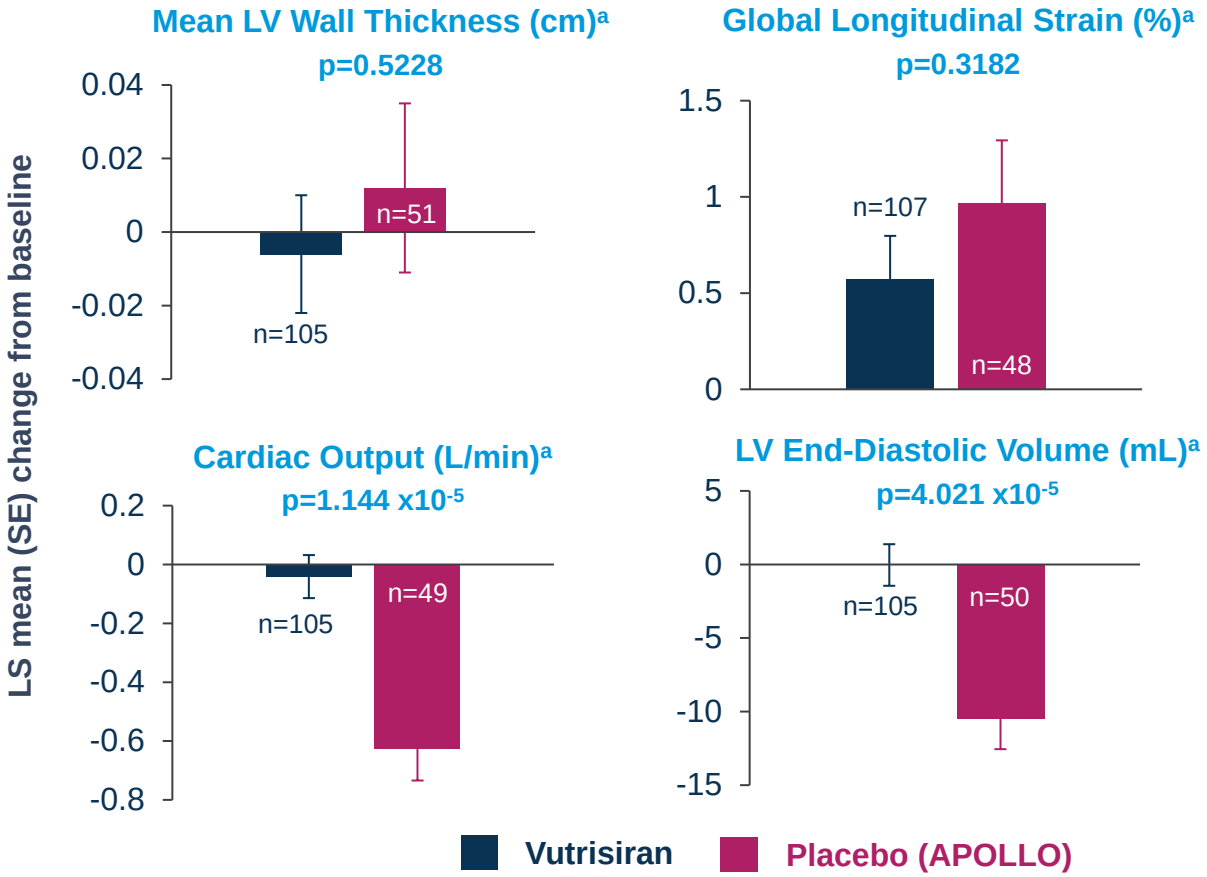
[a]Improvement defined as patients with <0-point increase from baseline to 18 months. [b]mITT population (all randomized patients who received any amount of study drug). Value of n is the number of evaluable patients at each timepoint. Data plotted for mNIS+7 and Norfolk QOL-DN at Month 9 are ANCOVA/multiple imputation model data and data plotted at Month 18 are MMRM model data. **[c]At baseline, the mean (±SD) mNIS+7 was 60.6 (36.0) in the vutrisiran group and 74.6 (37.0) in the external placebo group. [d]At baseline, the mean (±SD) Norfolk QOL-DN score was 47.1 (26.3) in the vutrisiran group and 55.5 (24.3) in the external placebo group.**

ANCOVA, analysis of covariance; CI, confidence interval; LS, least squares; LSMD, LS mean difference; mITT, modified intent-to-treat; MMRM, mixed model for repeated measures; mNIS+7, modified Neuropathy Impairment Score +7; Norfolk QOL-DN, Norfolk Quality of Life-Diabetic Neuropathy; SD, standard deviation; SEM, standard error of the mean. Adams, et al. SFNP 2022

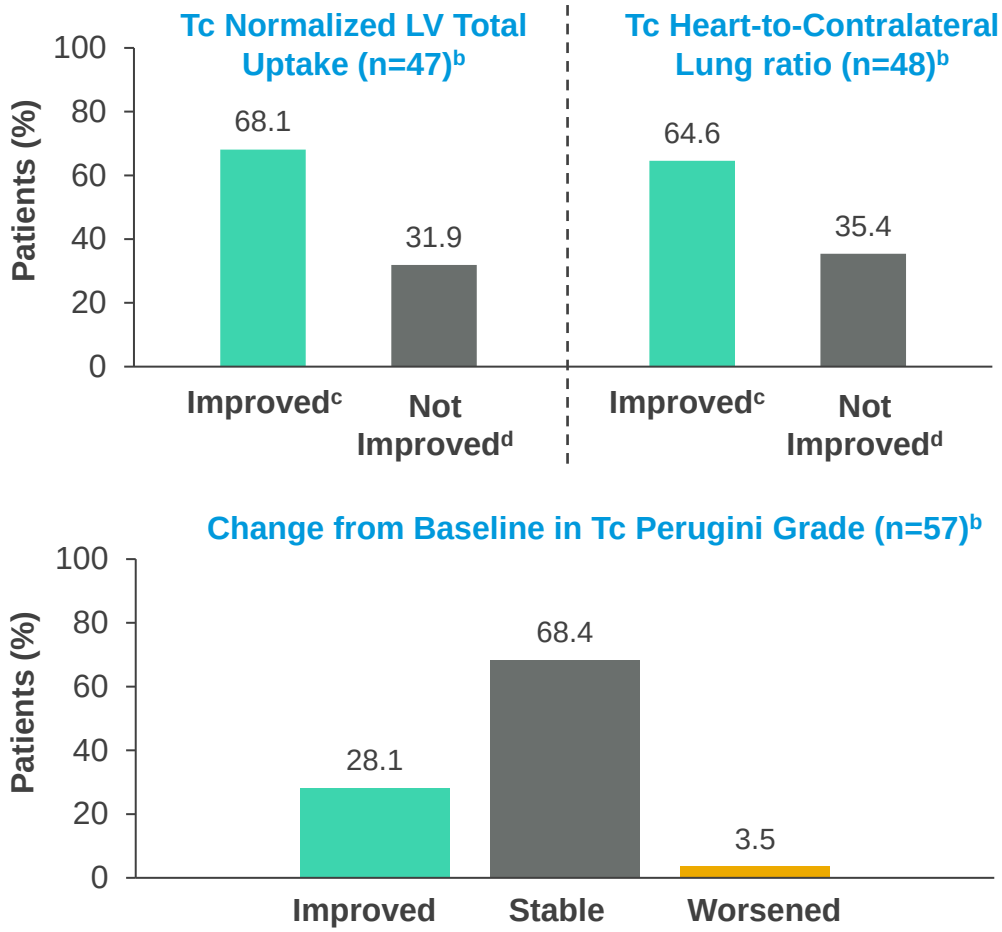
Exploratory Imaging Parameters

Potential Evidence of Reduction in Amyloid Burden

Vutrisiran trended toward improvement in all echocardiographic parameters, compared with external placebo group



Reduced cardiac technetium uptake on scintigraphy imaging shown in majority of assessable vutrisiran patients



[a] mITT population. P-values are nominal. [b] Patients from the mITT population for whom the relevant 18 month data were available. [c] Improved: <0 increase from baseline. [d] Not improved: ≥0 increase from baseline. Adams, et al. SFNP 2022

HELIOS-A Safety Summary[a]

Majority of AEs mild or moderate in severity

- No drug-related discontinuations or deaths
- Three study discontinuations (2.5%) due to AEs in the vutrisiran arm (two due to death, as previously reported; one due to heart failure), none of which were considered related to study drug
  - One death due to COVID-19 pneumonia and the other due to iliac artery occlusion
- As previously reported, two SAEs deemed related to vutrisiran by investigators:
  - Dyslipidemia and urinary tract infection
- AEs ≥10% in the vutrisiran group included fall, pain in extremity, diarrhea, peripheral edema, urinary tract infection, arthralgia, and dizziness
- Injection-site reactions were reported in 5 patients (4.1%) receiving vutrisiran; all were mild and transient
- No safety signals regarding liver function tests, hematology, or renal function related to vutrisiran

HELIOS-A Safety Summary[a]

	APOLLO	HELIOS-A	
At least one event, n (%)	Placebo (n=77)	Vutrisiran (n=122)	Patisiran (n=42)
AEs	75 (97.4)	119 (97.5)	41 (97.6)
SAEs	31 (40.3)	32 (26.2)	18 (42.9)
Severe AEs	28 (36.4)	19 (15.6)	16 (38.1)
AEs leading to treatment discontinuation	11 (14.3)	3 (2.5)	3 (7.1)
AEs leading to stopping study participation	9 (11.7)	3 (2.5)	2 (4.8)
Deaths	6 (7.8)	2 (1.6)	3 (7.1)

[a] Data reported during 18-month treatment period.

AE, adverse event; SAE, serious AE. Adams, et al. SFNP 202

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

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**
- Expected to complete enrollment in **early 2023** with topline data expected **mid-2023**

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
- Study initiated **November 2021**
- Expected to complete enrollment at or around **year-end 2022**

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]
Vutrisiran*	*hATTR Amyloidosis with PN*			●	Global
Patisiran	*ATTR Amyloidosis with CM*		●		Global
Vutrisiran*	*ATTR Amyloidosis with CM*		●		Global
Vutrisiran[7]*	*Stargardt Disease*		○		Global
Fitusiran*	*Hemophilia*		●		15-30% Royalties
Lumasiran	*Severe PH1* *Recurrent Renal Stones*	●		●	Global
Cemdisiran (+/- Pozelimab)[8]*	*Complement-Mediated Diseases*		●		50-50; Milestone/Royalty
Belcesiran[9]*	*Alpha-1 Liver Disease*	●			Ex-U.S. option post-Phase 3
ALN-HBV02 (VIR-2218)[10]*	*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] Phase 3 study of vutrisiran in Stargardt Disease expected to initiate in late 2022; [8] Cemdisiran and pozelimab are each currently in Phase 2 development; Alnylam and Regeneron are evaluating potential combinations of these two investigational therapeutics; [9] Dicerna is leading and funding development of belcesiran; [10] 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 April 2022

Alnylam Clinical Development Pipeline

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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] Phase 3 study of vutrisiran in Stargardt Disease expected to initiate in late 2022; [8] Cemdisiran and pozelimab are each currently in Phase 2 development; Alnylam and Regeneron are evaluating potential combinations of these two investigational therapeutics; [9] Dicerna is leading and funding development of belcesiran; [10] 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 April 2022

Jeff Poulton

Chief Financial Officer

Financial Summary and Upcoming Milestones

Q1 2022 Financial Summary

Financial Results ($ millions)	Q1 2022	Q1 2021	Reported Growth %	CER Growth %[3]
Net Product Revenues	$186.9	$135.8	38%	43%
Net Revenues from Collaborations	$25.9	$41.8	(38%)	
Royalty Revenues	$0.4	-	-	
Total Revenues	$213.3	$177.6	20%	24%
Cost of Goods Sold and Collaborations	$35.6	$31.1	15%	
Gross Margin	$177.6	$146.5	21%	
GM as % of Total Revenues[1]	*83.3%*	*82.5%*	-	
Non-GAAP R&D Expenses[2]	$158.3	$161.5	(2%)	(1%)
Non-GAAP SG&A Expenses[2]	$136.8	$115.5	18%	20%
Non-GAAP Operating Loss [2]	($117.4)	($130.6)	(10%)	(15%)

Financial Results ($ millions)	Mar 31, 2022	Dec 31, 2021
Cash & Investments[4]	$2,239.6	$2,435.6

[1] GM as a % of Total Net Product Revenues is 87.4% and 83.0% for Q1 2022 and Q1 2021, respectively (excludes $12.2M and $8.0M of Cost of Collaborations and Royalties for Q1 2022 and Q1 2021, 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.
[3] Growth rates are at Constant Exchange Rates ("CER"), CER performance is determined by comparing Q1 2022 performance (restated using Q1 2021 exchange rates) to actual Q1 2022 reported performance.
[4] Cash, cash equivalents and marketable securities
See Appendix for a reconciliation between GAAP and non-GAAP measures

2022 Updated Full Year Guidance

	Prior FY 2022 Guidance[1]	Updated FY 2022 Guidance[2]
Net Product Revenue (ONPATTRO, GIVLAARI, OXLUMO, vutrisiran)[3]	$900M – $1,000M	$870M – $930M
Net Revenues from Collaborations & Royalties	$175M – $225M	No change
Non-GAAP Combined R&D and SG&A Expenses[4]	$1,400M – $1,500M	$1,390M – $1,450M

[1] Our Prior FY 2022 Guidance utilized January 31, 2022 FX rates of: 1 EUR = 1.12 USD; 1 GBP = 1.34 USD; 1 CHF = 1.08 USD; 1 CAD = 0.79 USD, 1 USD = 115 JPY
[2] Our Updated 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] Assuming FDA approval of vutrisiran by the July 14, 2022 PDUFA goal date
[4] 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) 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		*Combined Net Product Revenue Guidance $870 million – $930 million (includes vutrisiran)*			●
PATISIRAN	hATTR/ATTR Amyloidosis	APOLLO-B Phase 3 Topline Results		●	
		File sNDA for ATTR-CM			●
VUTRISIRAN*	hATTR/ATTR Amyloidosis	FDA Approval (7/14/22 PDUFA)		●	
		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

Q1 2022 Financial Results

Q&A Session

Q1 2022 Financial Results

Appendix

Alnylam Pharmaceuticals, Inc.

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

	Three Months Ended	
	March 31, 2022	March 31, 2021
Reconciliation of GAAP to Non-GAAP research and development:		
GAAP Research and development	$ 169,893	$ 185,899
Less: Stock-based compensation expenses	(11,617)	(24,375)
Non-GAAP Research and development	$ 158,276	$ 161,524
Reconciliation of GAAP to Non-GAAP selling, general and administrative:		
GAAP Selling, general and administrative	$ 154,471	$ 146,859
Less: Stock-based compensation expenses	(17,676)	(31,315)
Non-GAAP Selling, general and administrative	$ 136,795	$ 115,544
Reconciliation of GAAP to Non-GAAP operating loss:		
GAAP operating loss	$ (146,732)	$ (186,254)
Add: Stock-based compensation expenses	29,293	55,690
Non-GAAP operating loss	$ (117,439)	$ (130,564)

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 Currency

	Three Months Ended March 31, 2022
Net product revenues as reported	38 %
Less: Impact of foreign currency translation	5
Net product revenues growth at constant currency	43 %
Total revenues as reported	20 %
Less: Impact of foreign currency translation	4
Total revenues growth at constant currency	24 %
Non-GAAP Research and development as reported	(2)%
Less: Impact of foreign currency translation	1
Non-GAAP research and development at constant currency	(1)%
Non-GAAP Selling, general and administrative as reported	18 %
Less: Impact of foreign currency translation	2
Non-GAAP selling, general and administrative at constant currency	20 %
Non-GAAP operating loss as reported	(10)%
Less: Impact of foreign currency translation	(5)
Non-GAAP operating loss at constant currency	(15)%

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