Nathan (USA)
Diagnosed with AHP

Fourth Quarter and Full Year 2022 Financial Results

February 23, 2023

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

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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. All statements other than historical statements of fact regarding Alnylam's expectations, beliefs, goals, plans or prospects including, without limitation, expectations regarding Alnylam's aspiration to become a leading biotech company and the planned achievement of its "Alnylam P5x25" strategy, the potential for Alnylam to identify new potential drug development candidates and advance its research and development programs, Alnylam's ability to obtain approval for new commercial products or additional indications for its existing products, and Alnylam's projected commercial and financial performance, should be considered forward-looking statements. 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 Alnylam's business, results of operations and financial condition and the effectiveness or timeliness of Alnylam's efforts to mitigate the impact of the pandemic; Alnylam's ability to successfully execute on its "*Alnylam P^{5}x25*" strategy; Alnylam's ability to discover and develop novel drug candidates and delivery approaches and successfully demonstrate the efficacy and safety of its product candidates; the pre-clinical and clinical results for Alnylam's product candidates; actions or advice of regulatory agencies and Alnylam's ability to obtain and maintain regulatory approval for its product candidates, as well as favorable pricing and reimbursement; successfully launching, marketing and selling Alnylam's approved products globally; delays, interruptions or failures in the manufacture and supply of Alnylam's product candidates or its marketed products; obtaining, maintaining and protecting intellectual property; Alnylam's ability to successfully expand the indication for ONPATTRO or AMVUTTRA in the future; Alnylam's ability to manage its growth and operating expenses through disciplined investment in operations and its ability to achieve a self-sustainable financial profile in the future without the need for future equity financing; Alnylam's ability to maintain strategic business collaborations; Alnylam's 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 a current government investigation and the risk of future government investigations; and unexpected expenditures; as well as those risks more fully discussed in the "Risk Factors" filed with Alnylam's most recent periodic report (Quarterly Report on Form 10-Q or Annual Report on Form 10-K) filed with the SEC and in its other SEC filings. In addition, any forward-looking statements represent Alnylam's views only as of the date of this presentation and should not be relied upon as representing Alnylam's views as of any subsequent date. Alnylam explicitly disclaims any obligation, except to the extent required by law, to update any forward-looking 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. Percentage changes in revenue growth at Constant Exchange Rates, or CER, are non-GAAP financial measures which are presented excluding the impact of changes in foreign currency exchange rates for investors to understand the underlying business performance. CER represents growth calculated as if the exchange rates had remained unchanged from those used during 2021.

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Yvonne Greenstreet, MBChB, MBA

Chief Executive Officer

Overview

Notable Accomplishments in 2022

onpattro® (patisiran) lipid complex injection 10 mg/5 mL
amvuttra® (vutrisiran) injection 25 mg/0.5 mL
GIVLAARI® (givosiran) injection for subcutaneous use 189 mg/mL
OXLUMO® (lumasiran) for injection 94.5 mg/0.5 mL

Combined net product revenues of
$894 million
(35% growth YoY)

APOLLO-B

Reported positive Phase 3 study results in patients with ATTR-CM;
PDUFA date October 8th, 2023

amvuttra® (vutrisiran) injection 25 mg/0.5 mL

FIFTH
RNAi therapeutic approved

3

CTA filings
- **ALN-TTRsc04**
- **ALN-KHK**
- **ALN-PNP**

FAST COMPANY BEST WORKPLACES FOR INNOVATORS 2022
Science 2022 TOP EMPLOYERS
Best Workplaces™ for Women Medium Organisations Great Place To Work. UK 2022
Bloomberg Gender-Equality Index 2022
FORTUNE BEST WORKPLACES FOR WOMEN 2022

Continued recognition of
award winning culture

Initiated first-in-human clinical study of an RNAi therapeutic in CNS
(ALN-APP)

Maintained strong financial position
- **$2.2 billion in cash** at year-end 2022
- Lowered cost of capital via **$1,035 million** convertible financing

1

Label expansion
- **OXLUMO for advanced PH1**

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Multiple Drivers of Future Growth

TTR Franchise Leadership

Expansion Beyond Rare Diseases

Engine for Sustainable Innovation

Liana (Brazil)
Diagnosed with hATTR amyloidosis

Ambitious Five-Year Strategy to Drive Growth

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

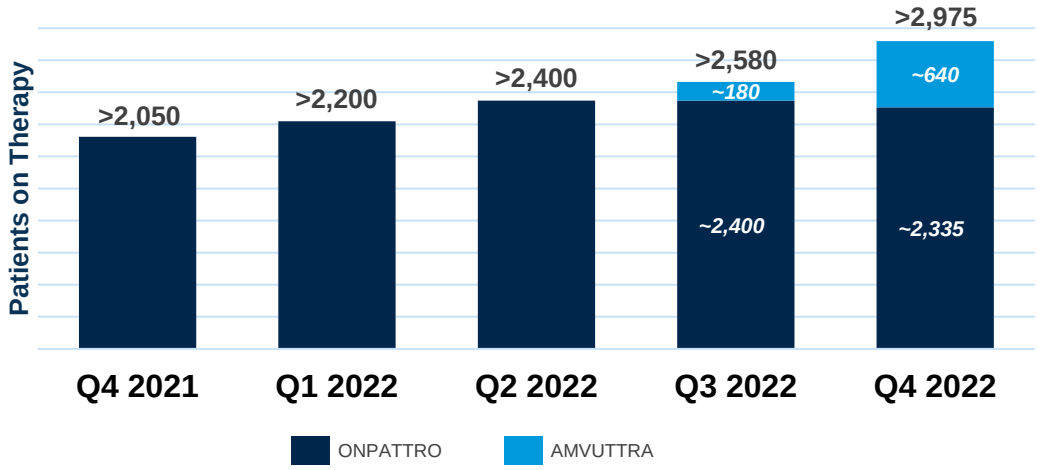
Chief Commercial Officer

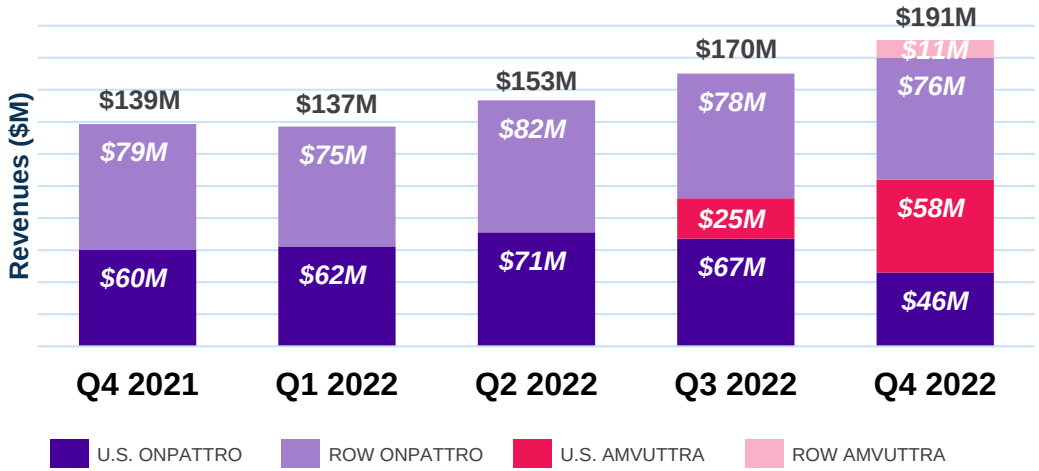
Commercial Highlights

TTR Franchise Update: Year End 2022

$651M
Total TTR Global 2022 Net Product Revenues

>2,975
TTR patients
at YE 2022





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

amvuttra® (vutrisiran) injection 25 mg/0.5 mL

Q4 TTR Franchise Highlights

	YoY % Growth	QoQ % Growth
U.S.	72%	12%
ROW	11%	12%
Global	38%	12%

- U.S. TTR franchise QoQ growth of +12% primarily driven by:
  - Demand growth +19% due to strong AMVUTTRA launch uptake more than offsetting decrease in ONPATTRO demand
  - Inventory dynamics -5% driven by reduction in ONPATTRO inventory in channel
- ROW QoQ growth (+12%) primarily due to AMVUTTRA launch demand & stocking in Germany and Japan
- FX headwinds continued for ROW markets (YoY Global CER[1] growth = 48%)

[1] CER = constant exchange rate, representing growth calculated as if exchange rates had remained unchanged from those used during 2021. CER is a non-GAAP financial measure. A reconciliation of this non-GAAP financial measure to the comparable GAAP measure, as well as additional information regarding our use of non-GAAP financial measures, are available in our press release dated February 23, 2023, which is accessible in the Investors section of our website at www.alnylam.com.

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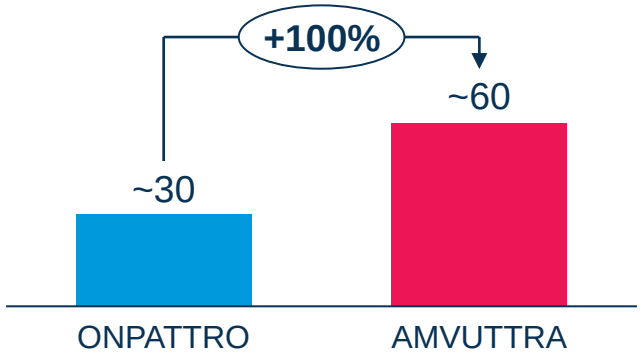
AMVUTTRA® (vutrisiran) Update: Year End 2022

Encouraging Launch Performance Across U.S. and Ex-U.S. Markets

U.S. Start Forms | Doubled "New Start Form" Monthly Average Since Launch

AMVUTTRA® Start Forms Monthly Average



- 760 Amvuttra Start Forms received from launch through December 31, 2022*
- >50% of Start Forms from new patients

U.S. Prescribers | Increasing share of prescribers new to TTR, Balanced Growth Across Account Types

Prescriber base across TTR

- Prior to AMVUTTRA launch, ~500 total prescribers
- Following AMVUTTRA launch, increase by ~30% in prescriber base

Prescriber base for AMVUTTRA

Global Access and Reimbursement

- No significant access headwinds in the U.S.
- J-Code established in U.S. as of Jan 1st 2023
- First international launches in Germany and Japan demonstrate encouraging early signs of strong uptake for AMVUTTRA
- UK reimbursement secured, launch expected in Q1 2023

* Start Forms are an incomplete picture of U.S. demand

AMVUTTRA and ONPATTRO are approved in the U.S. for the PN of hATTR amyloidosis in adults, and in the EU and Japan for the treatment of hATTR amyloidosis in adults with stage 1 or stage 2 polyneuropathy

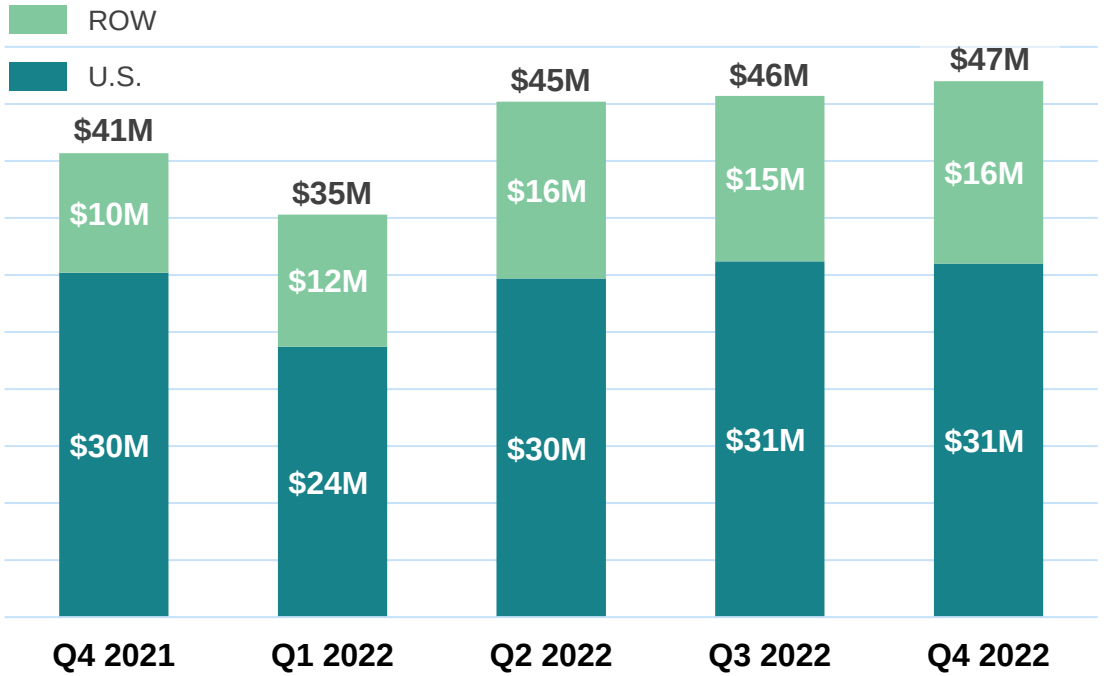
GIVLAARI® (givosiran) Update: Year End 2022

$173M

GIVLAARI Global 2022 Net Product Revenues

>520

Patients Worldwide on Commercial GIVLAARI at YE 2022



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

Q4 Highlights

	YoY % Growth	QoQ % Growth
U.S.	3%	0%
ROW	52%	10%
Global	16%	3%

- U.S. QoQ flat growth primarily due to:
  - Demand growth of +3% driven by an increase in patients on therapy
  - Modest changes in inventory stocking offset increase in patient demand
- ROW QoQ growth +10% due to increase in patient demand and timing of orders in partner markets
- FX headwinds continued for ROW markets (YoY Global CER[1] growth = 22%)

GIVLAARI is approved in the U.S. and Japan for the treatment of adults with acute hepatic porphyria, and in the EU for the treatment acute hepatic porphyria in adults and adolescents aged 12 and above.

[1] CER = constant exchange rate, representing growth calculated as if exchange rates had remained unchanged from those used during 2021. CER is a non-GAAP financial measure. A reconciliation of this non-GAAP financial measure to the comparable GAAP measure, as well as additional information regarding our use of non-GAAP financial measures, are available in our press release dated February 23, 2023, which is accessible in the Investors section of our website at www.alnylam.com.

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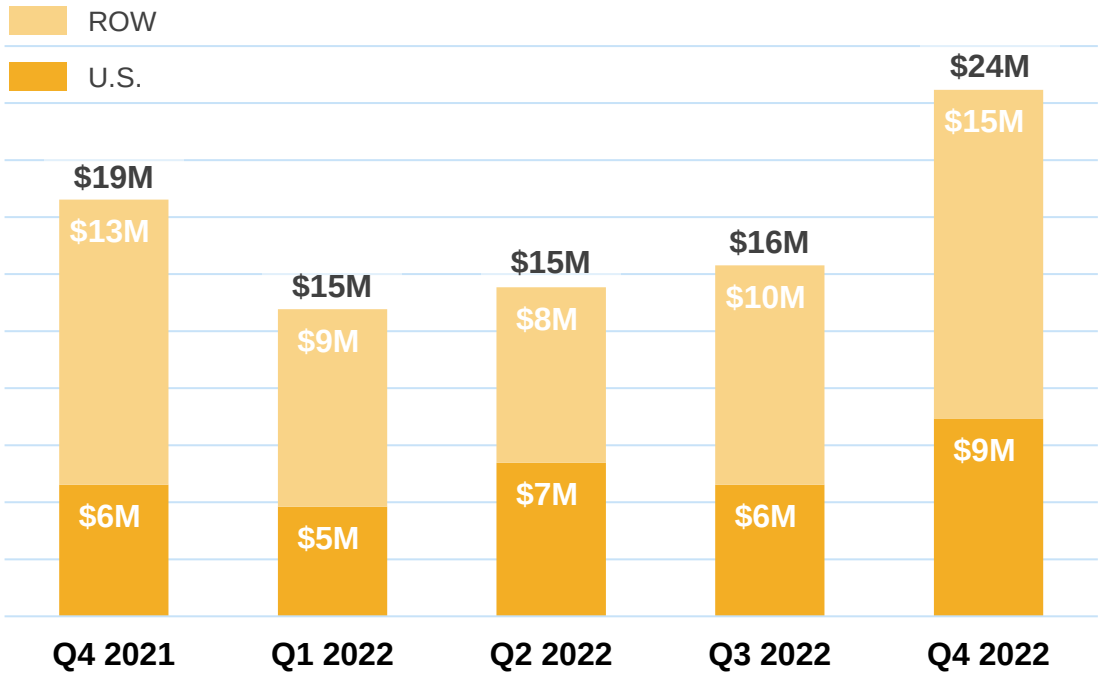
OXLUMO® (lumasiran) Update: Year End 2022

$70M

OXLUMO Global 2022 Net Product Revenues

>280

Patients Worldwide on Commercial OXLUMO at YE 2022



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

Q4 Highlights

	YoY % Growth	QoQ % Growth
U.S.	54%	38%
ROW	12%	50%
Global	24%	45%

- U.S. QoQ growth of +38% primarily impacted by:
  - Demand growth of +34% driven by an increase in patients on therapy and timing of monthly loading dose dynamics
- ROW QoQ growth of +50% driven by strong increase in patients on therapy and timing of orders in partner markets
- FX headwinds continued for ROW markets (YoY Global CER[1] growth = 33%)

OXLUMO is approved in the U.S. for the treatment of primary hyperoxaluria type 1 to lower urinary and plasma oxalate levels in pediatric and adult patients and in the EU for the treatment of primary hyperoxaluria type 1 in all age groups.

[1] CER = constant exchange rate, representing growth calculated as if exchange rates had remained unchanged from those used during 2021. CER is a non-GAAP financial measure. A reconciliation of this non-GAAP financial measure to the comparable GAAP measure, as well as additional information regarding our use of non-GAAP financial measures, are available in our press release dated February 23, 2023, which is accessible in the Investors section of our website at www.alnylam.com.

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Pushkal Garg, M.D.

Chief Medical Officer

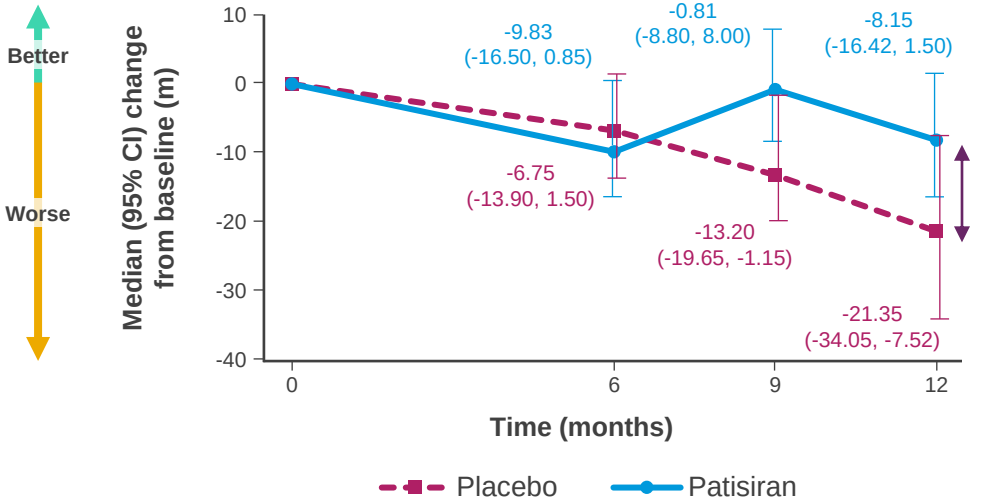
Alnylam Pipeline

APOLLO-B Key Study Results

sNDA Accepted; Potential to Expand Label to Include ATTR Amyloidosis Patients with CM

Patisiran demonstrated statistically significant and clinically meaningful improvements in functional capacity, health status and quality of life compared to placebo at month 12

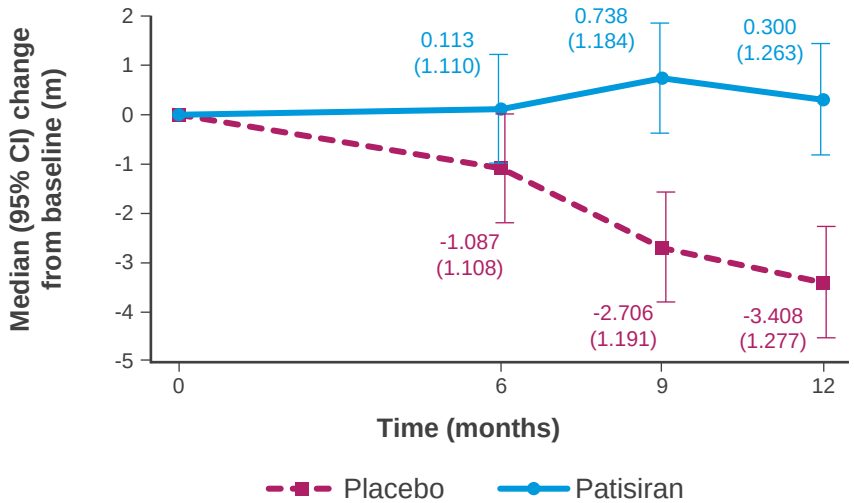
Change from Baseline in 6-MWT[a]



HL estimate of median difference (95% CI): **14.693** (0.693, 28.692) **p=0.0162**

N evaluable				
Placebo	178	178	178	178
Patisiran	181	181	181	181

Change From Baseline in KCCQ-OS using MMRM[b]



LS mean (SEM) difference: **3.709** (1.796) **p=0.0397**

N evaluable				
Placebo	178	170	167	164
Patisiran	181	169	170	170

[a] Primary endpoint analysis based on the stratified Wilcoxon Rank Sum test. Median (95% CI) change from baseline values were based on the observed 6-MWT data and the imputed values; for each patient, the change from baseline was averaged across 100 complete datasets. Missing Month 12 values due to non-COVID-19 death or inability to walk due to progression of ATTR amyloidosis were imputed as the worst 10th percentile change observed across all patients in the double-blind period, capped by the worst possible change for the patient (i.e., 0 minus the patient's baseline 6-MWT). Missing Month 12 data due to other reasons were multiply imputed (assuming data were missing at random) to create 100 complete datasets. At baseline, the median (range) 6-MWT was 358.000 (155.70, 808.00) in the patisiran group and 367.740 (130.00, 740.00) in the placebo group. Abbreviations: 6-MWT, 6-minute walk test; ATTR, transthyretin-mediated; CI, confidence interval; HL, Hodges–Lehmann; m, meters. [b] MMRM model. Missing data not explicitly imputed and assumed to be missing at random. At baseline, the mean (±SD) KCCQ-OS was 69.836 (21.178) in the patisiran group and 70.330 (20.709) in the placebo group. Abbreviations: KCCQ-OS, Kansas City Cardiomyopathy Questionnaire Overall Summary; LS, least squared; MMRM, mixed model repeated measures; SD, standard deviation; SEM, standard error of mean.

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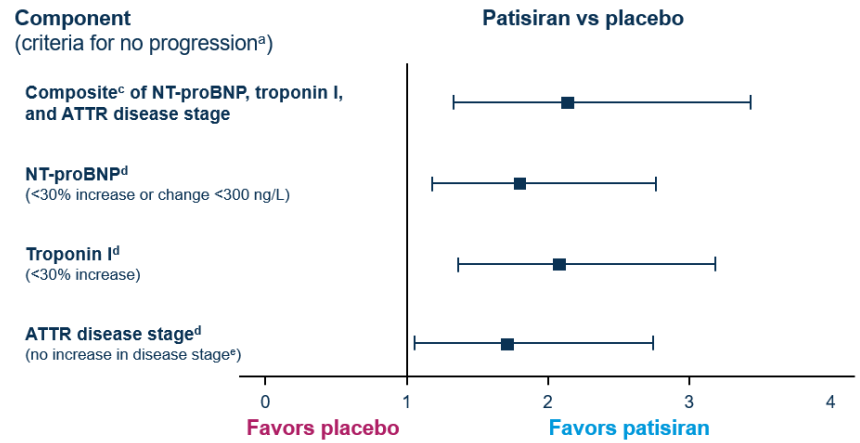
Safety and Exploratory Endpoints Support Therapeutic Potential of Patisiran

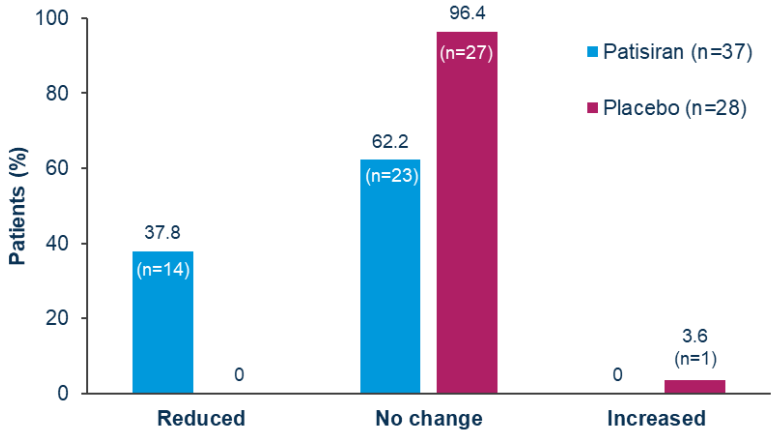
APOLLO-B

- Majority of AEs were mild or moderate in severity
- AEs ≥5% in the patisiran group observed 3% more commonly than in placebo included infusion-related reaction (12.2% vs 9.0%), arthralgia (7.7% vs 4.5%), and muscle spasms (6.6% vs 2.2%)
- Compared with placebo, patisiran demonstrated fewer events within Standardized MedDRA Queries (SMQs) exploring potential cardiac safety issues

Biomarker Based Disease Progression at Month 12[a,b]



Change from Baseline in Perugini Grade at Month 12[c]



[a] Garcia-Pavia P, et al. Eur J Heart Fail. 2021 Jun;23(6):895–905; [b] Patients who are missing Month 12 due to COVID-19 are excluded from analysis. Odds ratio and 95% CI from Cochran–Mantel–Haenszel test stratified by baseline tafamidis use; [c] For the composite parameter, the summary presents the odds ratio (95% CI) of no progression on any component (ie, <30% increase or change <300 ng/L in NT-proBNP AND <30% increase in troponin I AND no increase in ATTR disease stage); [d] For each component, the summary presents the odds ratio (95% CI) of no progression on the specified component (ie, <30% increase or change <300 ng/L for NT-proBNP, <30% increase for troponin I, and no increase for ATTR disease stage); [e] Gillmore JD, et al. Eur Heart J. 2018 Aug;39(30):2799–2806; [f] Analysis includes patients in the patisiran (n=37) and placebo (n=28) arms from the full analysis set with evaluable data at baseline and Month 12. 40 patients in the patisiran group and 37 patients in the placebo group were evaluated at baseline. 37 patients in the patisiran group and 28 patients in the placebo group were evaluated at Month 12.

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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 & recurrent all-cause hospitalizations & urgent HF visits
- 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**

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Vutrisiran Biannual Dosing Regimen

Topline Results and Next Steps

- Evaluated opportunity to develop 50 mg biannual vutrisiran dosing regimen in HELIOS-A Randomized Treatment Extension

- Topline results:
  - Established non-inferiority of 50 mg biannual vs 25 mg quarterly, based on percent TTR reduction through 9 months; however, some TTR recovery noted at end of biannual dosing interval
  - Acceptable safety profile
    - No cardiac, hepatic, or renal safety concerns; 1 SAE of transaminases elevated, considered related
    - 5 deaths on 50 mg biannual and 1 death on 25 mg quarterly*; none considered related to study drug

- Strategic decision not to further advance 50 mg biannual dosing regimen
  - Dynamics of TTR recovery with biannual regimen not supportive of optimal product profile
  - Highly compelling AMVUTTRA 25mg quarterly regimen with commercial performance exceeding expectations
  - Opportunity to focus continued innovation on ALN-TTRsc04, which offers potential for robust and sustained TTR reduction with infrequent dosing

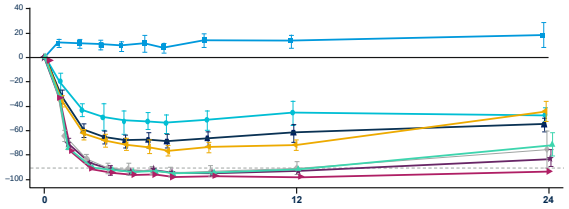
Data cut October 7, 2022

* One death on 25 mg quarterly occurred after patient dropped out of the study

Zilebesiran: Potential Novel Treatment for Patients with Hypertension

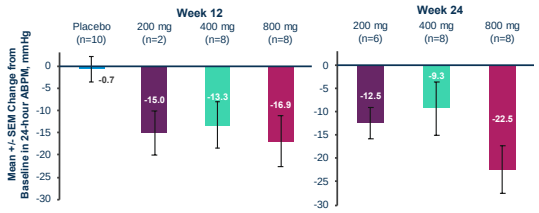
Phase 1 Data Support Compelling Product Profile

Serum AGT Lowering



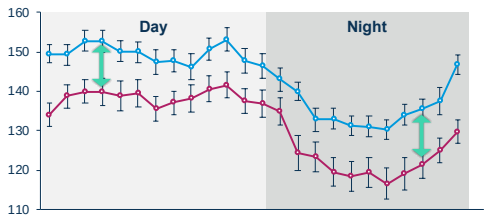
>90% mean serum AGT reduction for 6 months*

Blood Pressure Reduction



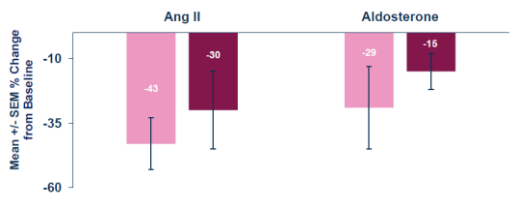
>20 mmHg SBP reduction at 6 months*

Consistent BP Reduction



Tonic BP control demonstrated over 24hr*

Change in RAAS Biomarkers



Durable reduction in Ang II & aldosterone*

KARDIA-1

Monotherapy Phase 2 Study (N = 394)

- Exploring multiple doses and dosing regimens
- Enrollment completed **December 2022**
- Topline results expected **mid-2023**

KARDIA-2

Combination Phase 2 Study (N ~ 630)

- Background treatment standardized with ARB, calcium channel blocker or diuretic
- Enrollment completion expected **early 2023**
- Topline results expected **at or around year-end 2023**

* After single dose of zilebesiran 800mg

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Expanding Beyond Liver with First CNS Program in Clinic

Multiple Patient Populations with High Unmet Need

ALN-APP designed to lower APP production *at its source*, upstream of pathogenic process

Alzheimer's Disease (AD)

- Over 5M people affected by AD in U.S. (30M+ WW)
- Current therapies not shown to halt disease progression
- ALN-APP could reduce both intracellular and extracellular drivers of disease pathology

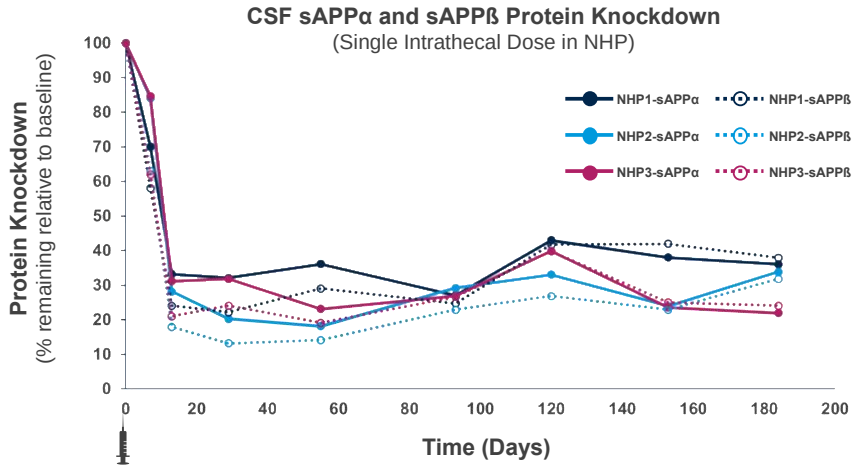
Cerebral Amyloid Angiopathy (CAA)

- Second-leading cause of ICH after hypertension
- No specific treatments available for CAA
- ALN-APP could lower all Aß isoforms including Aß40, primary component of vascular amyloid deposits

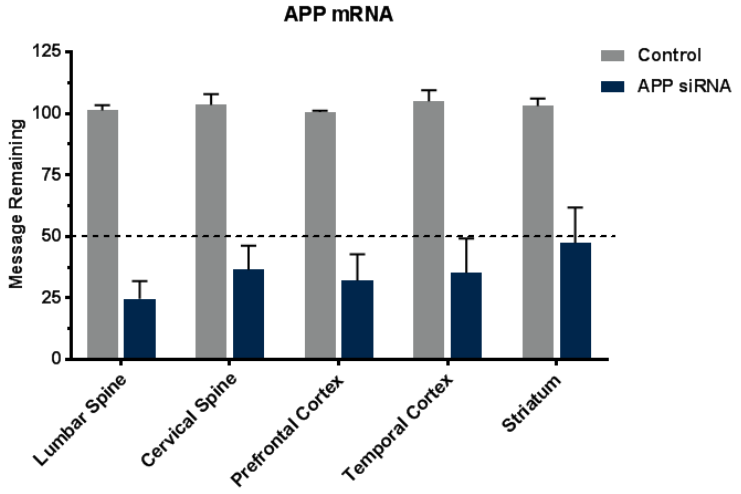
Dose escalation in Part A **ongoing**

Topline Phase 1 data expected **early 2023**

Durable Effect in NHP



Broad Distribution in NHP



APP: amyloid precursor protein

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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]	COMMERCIAL RIGHTS
onpattro (patisiran)	*hATTR Amyloidosis with PN*			●	Global
amvuttra (vutrisiran)	*hATTR Amyloidosis with PN*			●	Global
GIVLAARI (givosiran)	*Acute Hepatic Porphyria*			●	Global
OXLUMO (lumasiran)	*Primary Hyperoxaluria Type 1*			●	Global
LEQVIO (inclisiran)	*Hypercholesterolemia*			●	Milestones & up to 20% Royalties[2]
Patisiran**	*ATTR Amyloidosis with CM*			●	Global
Vutrisiran	*ATTR Amyloidosis with CM*		●		Global
Fitusiran*	*Hemophilia*		●		15-30% Royalties
Cemdisiran (+/- Pozelimab)[3]*	*Complement-Mediated Diseases*		●		Global; Milestone/Royalty
ALN-TTRsc04*	*ATTR Amyloidosis*	●			Global
Belcesiran[4]*	*Alpha-1 Liver Disease*	●			Ex-U.S. option post-Phase 3
ALN-HBV02 (VIR-2218)[5]*	*Hepatitis B Virus Infection*	●			50-50 option post-Phase 2
Zilebesiran*	*Hypertension*	●			Global
ALN-HSD[6]*	*NASH*	●			Royalty
ALN-APP*	*Alzheimer's Disease; Cerebral Amyloid Angiopathy*	●			50-50
ALN-PNP*	*NASH*	●			50-50
ALN-KHK*	*Type 2 Diabetes*	●			Global

[1] Includes marketing application submissions; [2] 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; [3] Alnylam and Regeneron are evaluating potential combinations of the investigational therapeutics cemdisiran and pozelimab; [4] Dicerna is leading and funding development of belcesiran; [5] Vir is leading and funding development of ALN-HBV02; [6] Regeneron is leading and funding development of ALN-HSD; * Not approved for any indication and conclusions regarding the safety or efficacy of the drug have not been established; ** U.S. sNDA accepted; PDUFA Oct. 8, 2023. **As of February 2023**

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Jeff Poulton

Chief Financial Officer

Financial Summary and Upcoming Milestones

Q4 and Full Year 2022 Financial Summary

Financial Results ($ millions)	Q4 2022	Q4 2021	Q4 Reported Growth %	Q4 CER Growth %[3]	FY 2022	FY 2021	FY22 Reported Growth %	FY22 CER Growth %[3]
Net Product Revenues	$262	$199	32%	41%	$894	$662	35%	43%
Net Revenues from Collaborations	$71	$60	18%		$135	$181	-25%	
Royalty Revenues	$3	$0			$8	$1		
Total Revenues	$335	$259	30%	37%	$1,038	$844	23%	29%
Cost of Goods Sold and Collaborations	$51	$38	36%		$169	$140	20%	
Gross Margin	$284	$221	28%		$869	$704	23%	
GM as % of Total Revenues[1]	*85%*	*85%*			*84%*	*83%*		
Non-GAAP R&D Expenses[2]	$245	$211	16%		$791	$724	9%	
Non-GAAP SG&A Expenses[2]	$185	$160	15%		$632	$523	21%	
Non-GAAP Operating Loss[2]	($146)	($150)			($554)	($543)		

Financial Results ($ millions)	Dec 31, 2022	Dec 31, 2021
Cash & Investments[4]	$2,192	$2,436

[1] GM as a % of Total Net Product Revenues for Q4 2022 is 82.4%, Q4 2021 is 83.1%, FY 2022 is 84.3%, FY 2021 is 82.6% (Q4 2022 excludes $5.1M, Q4 2021 excludes $4.0M, FY 2022 excludes $28.6M and FY 2021 excludes $25.1M in 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 are non-GAAP financial measures that exclude from the corresponding GAAP measures costs related to stock-based compensation expense. A reconciliation of these non-GAAP financial measures to the comparable GAAP measures, as well as additional information regarding our use of non-GAAP financial measures, are included in the Appendix to this presentation and in our press release dated February 23, 2023, which is accessible in the Investors section of our website at www.alnylam.com.

[3] Growth rates are at Constant Exchange Rates ("CER"), CER performance is determined by comparing Q4 2022 performance (restated using Q4 2021 exchange rates) to actual Q4 2021 reported performance and by comparing full-year 2022 performance (restated using 2021 exchange rates) to actual full year 2021 reported performance. CER is a non-GAAP financial measure. A reconciliation of this non-GAAP financial measure to the comparable GAAP measure, as well as additional information regarding our use of non-GAAP financial measures, are available in our press release dated February 23, 2023, which is accessible in the Investors section of our website at www.alnylam.com.

[4] Cash, cash equivalents and marketable securities.

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2023 Full Year Guidance[1]

	Guidance	Key Assumptions
Net Product Revenue: ONPATTRO, AMVUTTRA, GIVLAARI, OXLUMO	$1,200M to $1,285M	• Assumes U.S. sNDA approval of patisiran for ATTR amyloidosis with CM by the PDUFA date on October 8th, 2023
Net Product Revenue Growth vs. 2022 at reported Fx rates	*34% to 44%*	• Uses December 31, 2022 Fx rates
Net Product Revenue Growth vs. 2022 at constant exchange rates (i.e., operational growth)[2]	*34% to 44%*	• Uses 2022 actual Fx rates
Net Revenues from Collaborations & Royalties	$100M to $175M	
Non-GAAP Combined R&D and SG&A Expenses[3]	$1,575M to $1,650M	

[1] Our 2023 FY Guidance is based upon December 31, 2022 FX rates including 1 EUR = 1.07 USD and 1 USD = 131 JPY

[2] CER = constant exchange rate, representing growth calculated as if exchange rates had remained unchanged from those used in 2022. CER is a non-GAAP financial measure. Information regarding our use of non-GAAP financial measures is available in our press release dated February 23, 2023, which is accessible in the Investors section of our website at www.alnylam.com.

[3] 2023 Non-GAAP Combined R&D and SG&A Expenses guidance are non-GAAP financial measures that exclude from the corresponding GAAP measures stock-based compensation expense estimated at $215M - $235M. Information regarding our use of non-GAAP financial measures is available in our press release dated February 23, 2023, which is accessible in the Investors section of our website at www.alnylam.com.

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Alnylam 2023 Goals

			Early	Mid	Late
onpattro (patisiran) amvuttra (vutrisiran) GIVLAARI (givosiran) OXLUMO (lumasiran)		*Combined Net Product Revenue Guidance $1,200M – $1,285M*			●
PATISIRAN	ATTR Amyloidosis	FDA Approval of sNDA			●
VUTRISIRAN	ATTR Amyloidosis	Biannual Dosing Regimen Data	✓		
ALN-TTRsc04*	ATTR Amyloidosis	Phase 1 Topline Results			●
ZILEBESIRAN*	Hypertension	Complete KARDIA-2 Enrollment	●		
		KARDIA-1 Phase 2 Topline Results		●	
		KARDIA-2 Phase 2 Topline Results (at or around year-end)			●
ALN-APP*	Alzheimer's Disease	Phase 1 Topline Results	●		
ALN-KHK*	Type 2 Diabetes	Initiate Phase 1 Study	●		
		Phase 1 Topline Results			●
ADDITIONAL PROGRAMS		File 2-4 New INDs			●
PARTNERED PROGRAM MILESTONES					
FITUSIRAN* (Sanofi)	Hemophilia	ATLAS Phase 3 Topline Results			●
ALN-HBV02* (Vir)	Chronic HBV/HDV Infection	Phase 2 Results	●		●
ALN-PNP* (Regeneron)	NASH	Initiate Phase 1 Study	✓		

* 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

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Q4 and Full Year 2022 Financial Results

Q&A Session

Thank You!

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Q4 and Full Year 2022 Financial Results

Appendix

Alnylam Pharmaceuticals, Inc.

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

	Three Months Ended December 31,		Twelve Months Ended December 31,	
	2022	2021[1]	2022	2021[1]
Reconciliation of GAAP to Non-GAAP research and development:				
GAAP Research and development	$ 262,039	$ 229,050	$ 883,015	$ 792,156
Less: Stock-based compensation expenses	(16,944)	(18,537)	(92,161)	(68,415)
Non-GAAP Research and development	$ 245,095	$ 210,513	$ 790,854	$ 723,741
Reconciliation of GAAP to Non-GAAP selling, general and administrative:				
GAAP Selling, general and administrative	$ 210,344	$ 186,382	$ 770,658	$ 620,639
Less: Stock-based compensation expenses	(25,823)	(26,045)	(138,488)	(97,302)
Non-GAAP Selling, general and administrative	$ 184,521	$ 160,337	$ 632,170	$ 523,337
Reconciliation of GAAP to Non-GAAP operating loss:				
GAAP operating loss	$ (188,614)	$ (194,561)	$ (785,072)	$ (708,652)
Add: Stock-based compensation expenses	42,767	44,582	230,649	165,717
Non-GAAP Operating loss	$ (145,847)	$ (149,979)	$ (554,423)	$ (542,935)

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

[1] Beginning in 2022, presentations of non-GAAP financial measures will not include adjustments for upfront payment on license and collaboration agreement. Non-GAAP financial measures for three – and twelve – months ended December 31, 2021 have been adjusted to reflect this updated presentation.

Alnylam Pharmaceuticals, Inc.

Reconciliation of Revenue and Growth at Constant Currency

	December 31, 2022	
	Three Months Ended	Twelve Months Ended
Total net product revenue growth, as reported	32 %	35 %
Add: Impact of foreign currency translation	9	8
Total net product revenue growth at constant currency	41 %	43 %
Total revenue growth, as reported	30 %	23 %
Add: Impact of foreign currency translation	7	6
Total revenue growth at constant currency	37 %	29 %

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

Constant Currency = CER