Nathan (USA)
Diagnosed with AHP

Third Quarter 2023 Financial Results

November 2, 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 P^{5}x25*" 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; 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, including vutrisiran; actions or advice of regulatory agencies and Alnylam's ability to obtain and maintain regulatory approval for its product candidates, including vutrisiran, 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; delays or interruptions in the supply of resources needed to advance Alnylam's research and development programs, including as may arise from recent disruptions in the supply of non-human primates; obtaining, maintaining and protecting intellectual property; Alnylam's ability to successfully expand the indication 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 Roche, Novartis, Sanofi, Regeneron and Vir; the outcome of litigation; the risks of future government investigations; and unexpected expenditures; as well as those risks more fully discussed in the "Risk Factors" filed with Alnylam's 2022 Annual Report on Form 10-K filed with the Securities and Exchange Commission (SEC), as may be updated from time to time in Alnylam's subsequent Quarterly Reports on Form 10-Q and in its other SEC filings. In addition, any forward-looking statements represent Alnylam's views only as of today and should not be relied upon as representing its 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 2022.

Yvonne Greenstreet, MBChB, MBA

Chief Executive Officer

Overview

SAVE THE DATE

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R&D Day

December 13, 2023

8:30 am ET (held virtually)

Registration information forthcoming

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

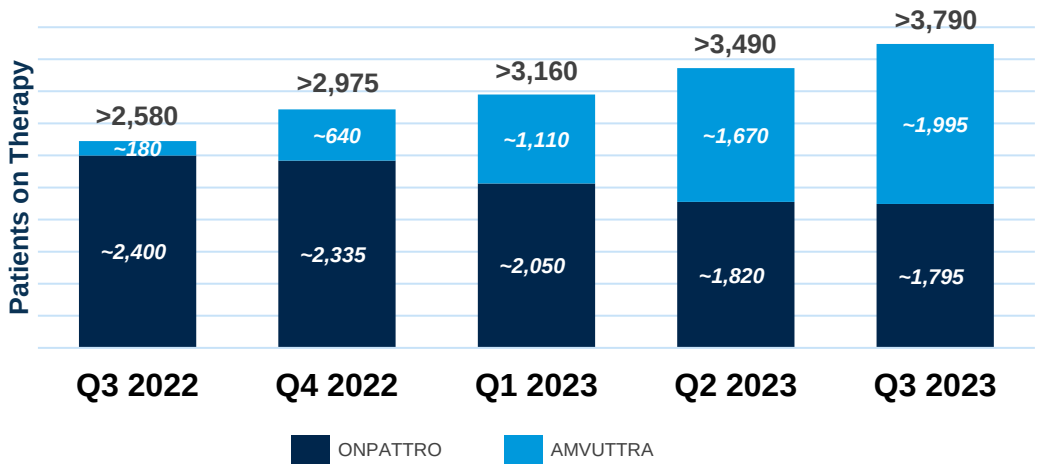
Chief Commercial Officer

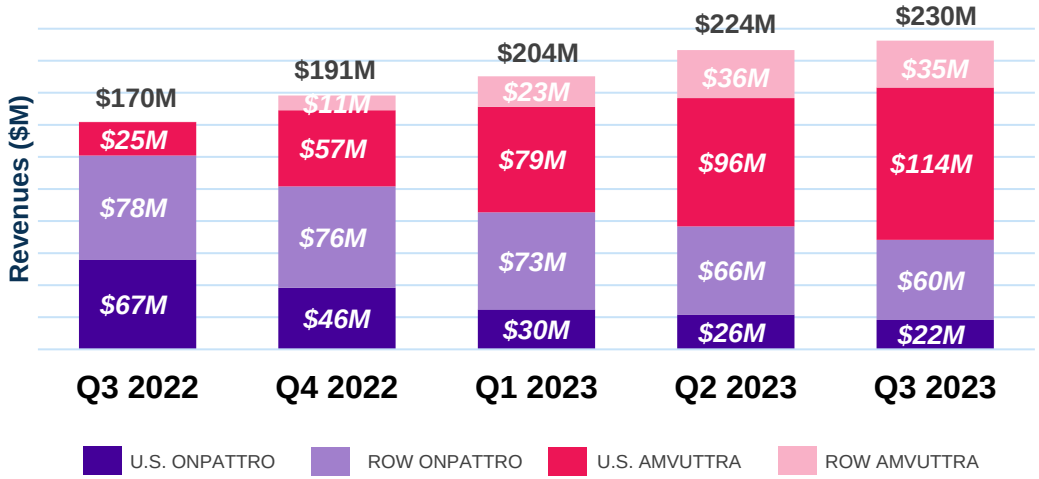
Commercial Highlights

TTR Franchise Update: Q3 2023

$230M
Total TTR
Global Q3 2023
Net Product Revenues

>3,790
Total TTR patients worldwide at end of Q3 2023





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

amvuttra® (vutrisiran) injection 25 mg/0.5 mL

Q3 TTR Franchise Highlights

	YoY % Growth	QoQ % Growth
U.S.	47%	11%
ROW	22%	-7%
Global	35%	3%

- U.S. QoQ +11% growth driven by:
  - Demand (+6%): continued strong AMVUTTRA demand more than offsetting ONPATTRO cannibalization
  - Inventory (+5%): increase in inventory value in the distribution channel driven by AMVUTTRA stocking
- ROW QoQ -7% decline driven by:
  - Steady demand growth offset primarily by pricing adjustments (Germany), destocking (Japan) and timing of orders in partner markets
  - AMVUTTRA now launched in all major ROW markets following recent Spain and Italy launches
- Modest FX impact (YoY CER[1] growth = 34%)

[1] CER = constant exchange rate, which is a non-GAAP financial measure that represents growth calculated as if exchange rates had remained unchanged from those used during 2022 – see the Financial Summary slide for more information.

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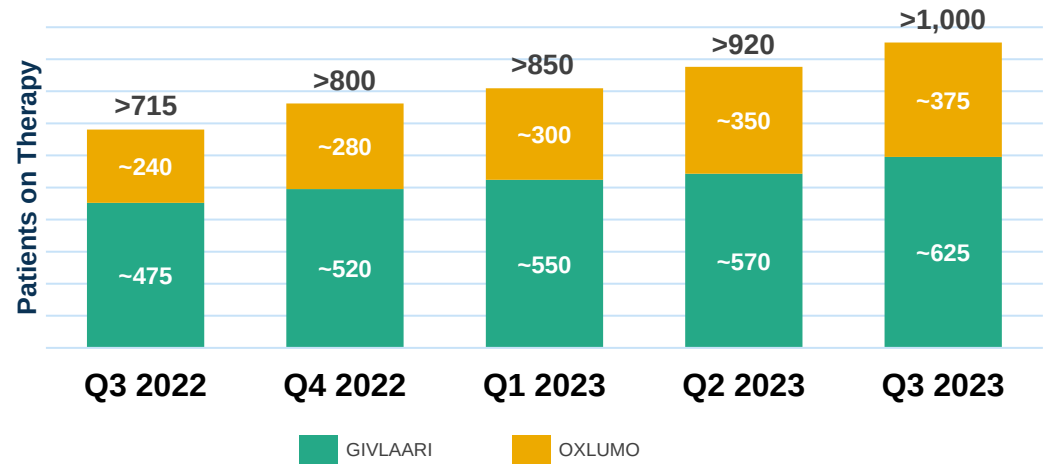
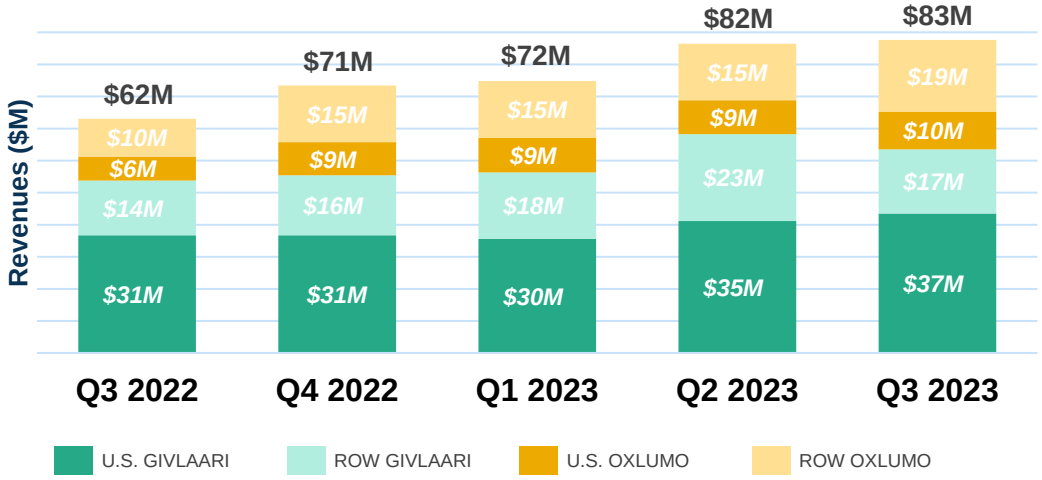
Ultra Rare Franchise Update: Q3 2023

$83M
Total Ultra Rare
Global Q3 2023
Net Product Revenues

>1,000
Total Ultra Rare
patients worldwide
at end of Q3 2023





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

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

Q3 Ultra Rare Franchise Highlights

	YoY % Growth	QoQ % Growth
GIVLAARI	19%	-6%
OXLUMO	75%	19%
Total Ultra Rare	33%	1%

- GIVLAARI QoQ decline of -6% driven by:
  - U.S. (+5%): increased demand
  - ROW (-25%): primarily driven by timing of orders in partner markets (i.e., large Q2 order) and higher gross to net deductions
- OXLUMO QoQ growth of +19% driven by:
  - U.S. (+10%): demand growth (+16%) partially offset by reduced inventory in the distribution channel
  - ROW (+23%): increased demand and partner market order timing
- Modest FX impact (YoY CER[1] growth = 31%)

[1] CER = constant exchange rate, which is a non-GAAP financial measure that represents growth calculated as if exchange rates had remained unchanged from those used during 2022 – see the Financial Summary slide for more information.

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Pushkal Garg, M.D.

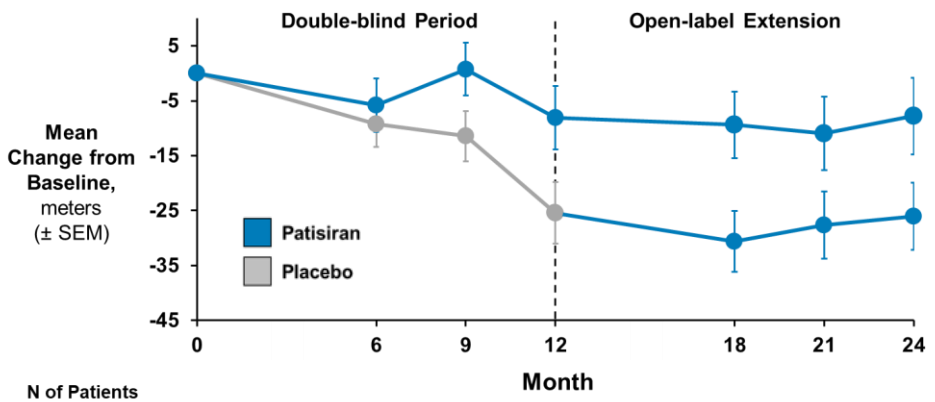
Chief Medical Officer

Alnylam Pipeline

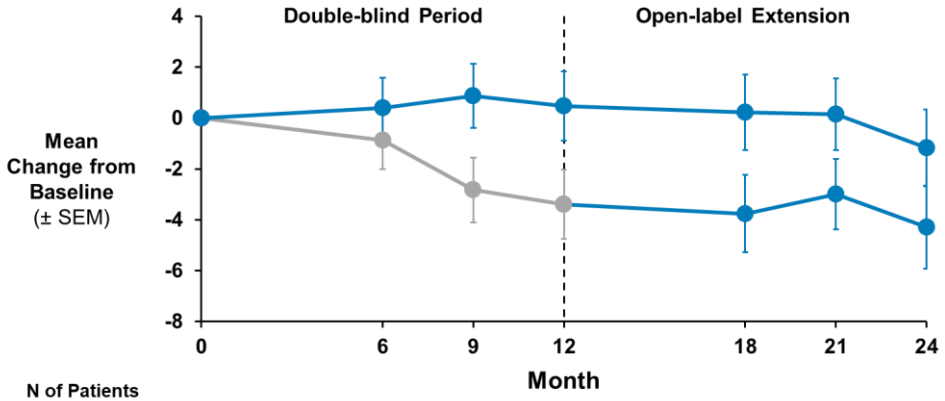
APOLLO-B Phase 3 Study (Open-Label Extension)

Treatment Effect of Patisiran Sustained at 24 Months

6-MWT



KCCQ



Maurer, et al. HFSA 2023

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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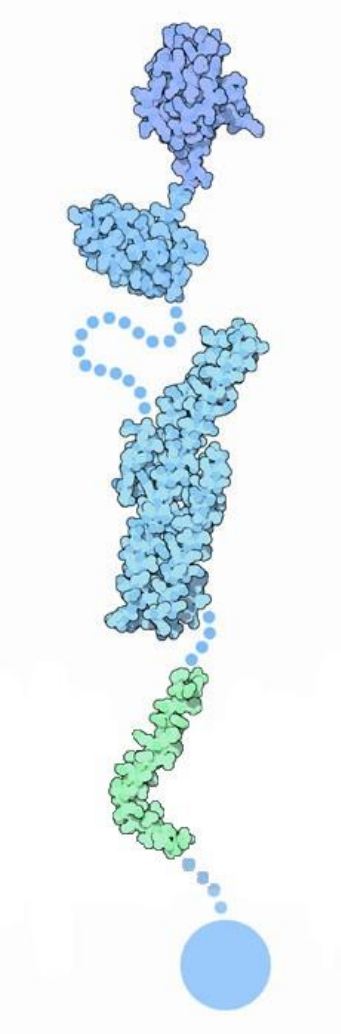
Amyloid Precursor Protein (APP)

Target for Alzheimer's Disease and Cerebral Amyloid Angiopathy



APP: One target, two distinct pathological processes

- ☑ Genetically validated target for AD and CAA
- ☑ Soluble biomarkers of target engagement (sAPPα and sAPPβ) in CSF
- ☑ Significant patient population with high unmet need in both diseases
  - AD: Over 5M people affected in U.S. (over 30M worldwide)
  - CAA: Second leading cause of intracerebral hemorrhage

Alzheimer's Disease (AD)

- APP mutations and duplications cause Early Onset AD
- Amyloid deposits in brain tissue, tau tangles in neurons, neurodegeneration

Cerebral Amyloid Angiopathy (CAA)

- APP mutations cause hereditary CAA
- Amyloid deposits in walls of vessels in CNS and results in cerebral hemorrhages and cognitive impairment

APP Protein Structure courtesy of David S. Goodsell and the RCSB Protein Data Bank

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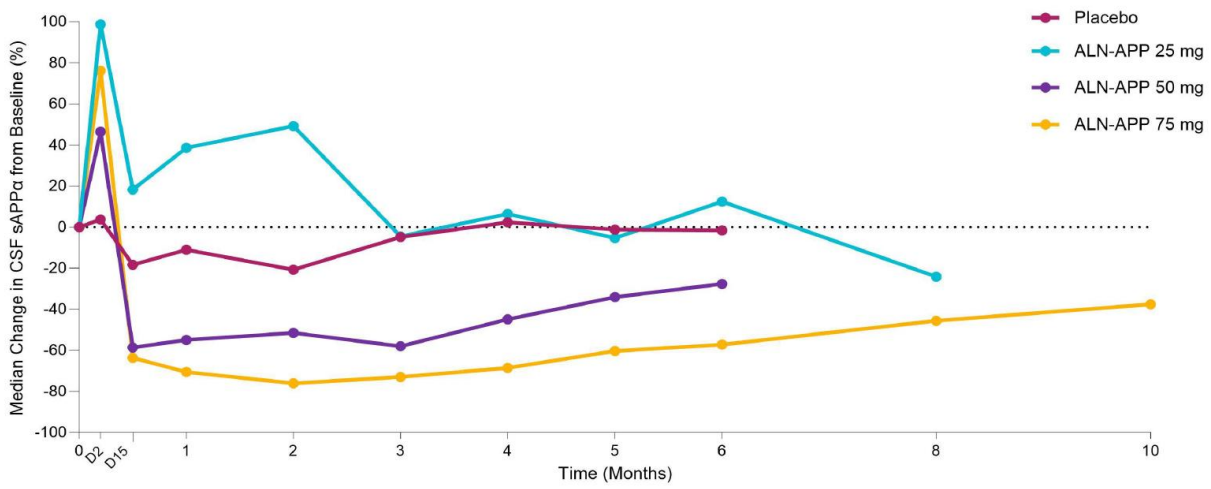
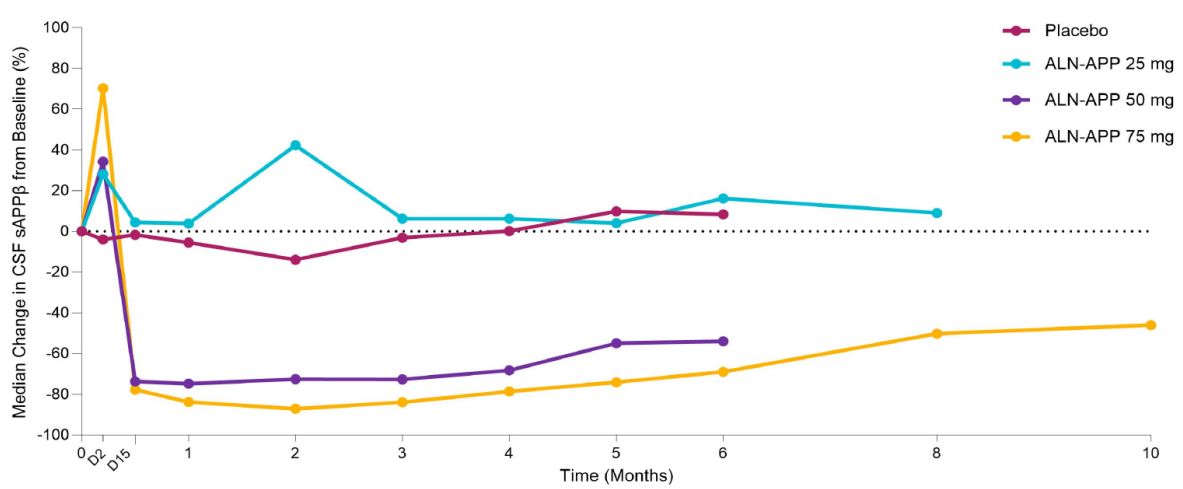
ALN-APP Phase 1 Results

Rapid and Sustained Reductions in CSF sAPPα and sAPPβ

Median Percent Change from Baseline in CSF sAPPα



Median Percent Change from Baseline in CSF sAPPβ



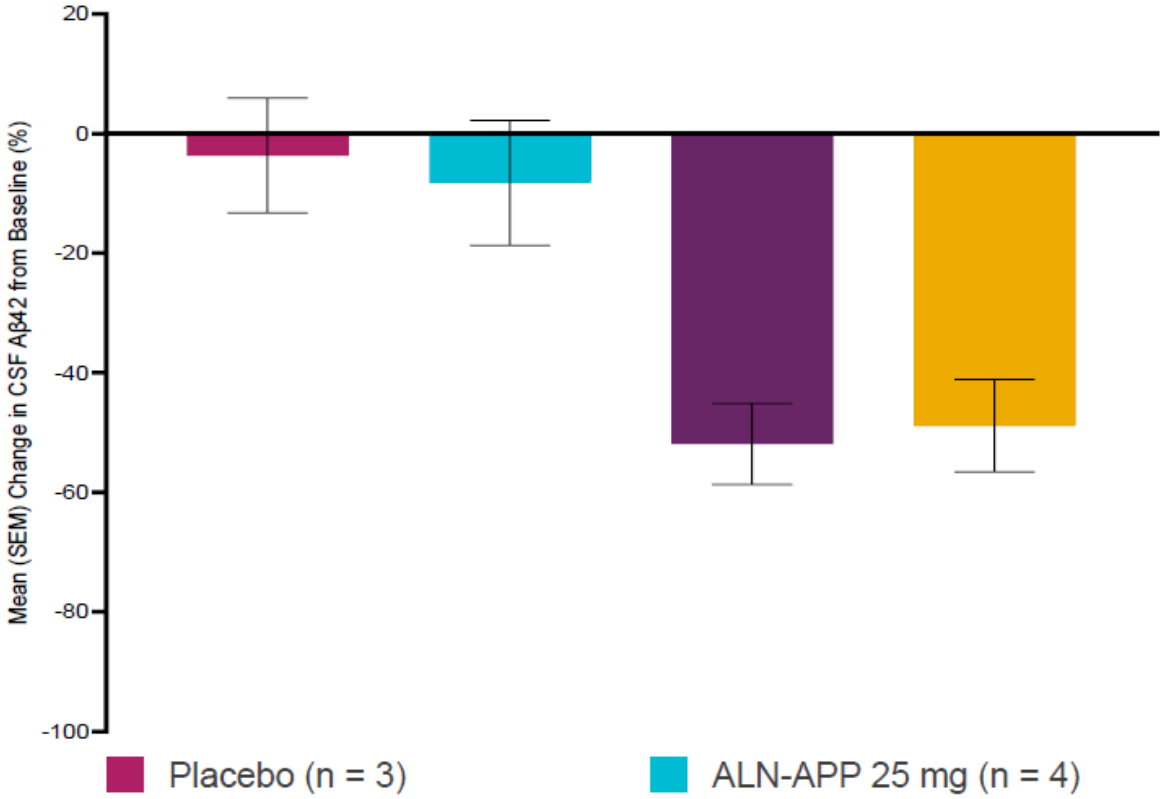
- All AEs were mild or moderate in severity
- No deaths, SUSARs, or treatment or study discontinuations occurred
- One individual in the 50mg or PBO cohort had two mild AEs that were deemed drug-related by the investigator and included post-LP headache and post-LP nausea, both of which resolved on the same day

CSF, cerebrospinal fluid; D, Day; sAPP, soluble amyloid precursor protein; SEM, standard error of the mean.

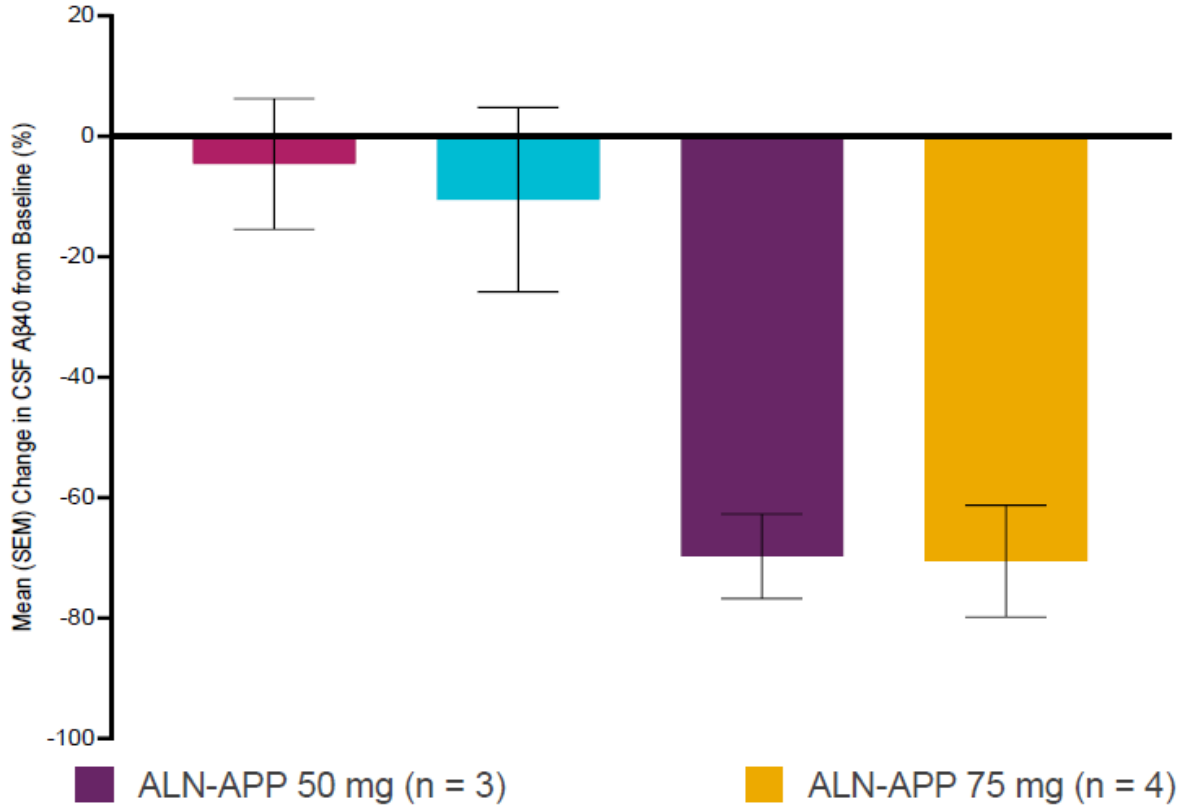
[a]Data shown as of October 6, 2023.

Robust Reductions in CSF Aβ42 and Aβ40 at Month 2

Median Change from Baseline in CSF Aβ42



Median Change from Baseline in CSF Aβ40



- CSF safety biomarkers, routine lab assessments, and preliminary data for the exploratory biomarker neurofilament light chain (NfL) all continued to show no concerning trends

Data shown as of August 17, 2023
Data is not shown for later timepoints owing to the limited number of patients with data from Month 3
Aβ40, amyloid beta peptide length 40 amino acids; Aβ42, amyloid beta peptide length 42 amino acids; CSF, cerebrospinal fluid; SEM, standard error of the mean

Zilebesiran Phase 2 KARDIA Program

KARDIA$_1$

Monotherapy Phase 2 Study (N = 394)

- Enrollment completed December 2022
- Positive topline results announced Sept. 2023
- Full results to be presented at **AHA 2023**

KARDIA$_2$

Combination Phase 2 Study (N = 672)

- Enrollment completed June 2023
- Topline results expected **early 2024**

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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]
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*	●			U.S. 50-50; Ex-U.S. Royalties
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] Novo Nordisk 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. **As of November 2023**

Jeff Poulton

Chief Financial Officer

Financial Summary and Upcoming Milestones

Q3 2023 Financial Summary

Financial Results ($ millions)	Q3 2023	Q3 2022	Q3 Reported Growth %	Q3 CER Growth %[2]
Net Product Revenues	$313	$232	35%	33%
Net Revenues from Collaborations	$427	$29		
Royalty Revenues	$10	$3		
Total Revenues	$751	$264	184%	182%
Product Cost of Goods Sold	$79	$37		
Cost of Collaborations and Royalties	$5	$5		
Gross Margin	$666	$223		
Product Sales Gross Margin %[1]	*75%*	*84%*		
Non-GAAP R&D Expenses[2]	$224	$192	16%	
Non-GAAP SG&A Expenses[2]	$164	$161	2%	
Non-GAAP Operating Income / (Loss) [2]	$278	($130)		

Financial Results ($ millions)	Sep 30, 2023	Dec 31, 2022
Cash & Investments[3]	$2,406	$2,192

[1] Product Sales GM % calculation excludes Cost of Collaborations and Royalties associated with Net Revenues from Collaborations.

[2] Non-GAAP R&D expenses, SG&A expenses and operating income / (loss) are non-GAAP financial measures that exclude from the corresponding GAAP measures costs related to stock-based compensation expense. CER growth rates represent growth at Constant Exchange Rates, a non-GAAP financial measure determined by comparing Q3 2023 performance (restated using Q3 2022 exchange rates) to actual Q3 2022 reported performance. 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 November 2, 2023, which is accessible in the Investors section of our website at www.alnylam.com.

[3] Cash, cash equivalents and marketable securities.

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2023 Updated Full Year Guidance[1]

	Prior FY 2023 Guidance	Updated FY 2023 Guidance
Net Product Revenue: ONPATTRO, AMVUTTRA, GIVLAARI, OXLUMO	$1,200M to $1,285M	No change
Net Product Revenue Growth vs. 2022 at reported Fx rates	*34% to 44%*	No change
Net Product Revenue Growth vs. 2022 at constant exchange rates (i.e., operational growth)[2]	*34% to 44%*	No change
Net Revenues from Collaborations & Royalties	$100M to $175M	$575M to $625M
Non-GAAP Combined R&D and SG&A Expenses[2]	$1,575M to $1,650M	No change

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

[2] Constant exchange rate (CER) is a non-GAAP financial measure that represents growth calculated as if exchange rates had remained unchanged from those used during 2022. 2023 Non-GAAP Combined R&D and SG&A Expenses guidance is a non-GAAP financial measure that excludes from the corresponding GAAP measures stock-based compensation expense estimated at $215M - $235M. See the Financial Summary slide for more information about our use of non-GAAP financial measures.

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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*			●
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		✓	
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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Q3 2023 Financial Results

Q&A Session

Thank You!

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Q3 2023 Financial Results

Appendix

Alnylam Pharmaceuticals, Inc.

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

	Three Months Ended	
	September 30, 2023	September 30, 2022
Reconciliation of GAAP to Non-GAAP research and development:		
GAAP research and development	$ 253,179	$ 245,371
Less: Stock-based compensation expenses	(29,155)	(52,962)
Non-GAAP research and development	$ 224,024	$ 192,409
Reconciliation of GAAP to Non-GAAP selling, general and administrative:		
GAAP selling, general and administrative	$ 199,175	$ 235,859
Less: Stock-based compensation expenses	(34,782)	(75,156)
Non-GAAP selling, general and administrative	$ 164,393	$ 160,703
Reconciliation of GAAP to Non-GAAP operating income (loss):		
GAAP operating income (loss)	$ 213,867	$ (258,040)
Add: Stock-based compensation expenses	63,937	128,118
Non-GAAP operating income (loss)	$ 277,804	$ (129,922)

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

Alnylam Pharmaceuticals, Inc.

Reconciliation of Revenue and Growth at Constant Currency

	Three Months Ended September 30, 2023
Total TTR net product revenue growth, as reported	35%
Add: Impact of foreign currency translation	(1)
Total TTR net product revenue growth at constant currency	34%
Total Ultra Rare net product revenue growth, as reported	33%
Add: Impact of foreign currency translation	(2)
Total Ultra Rare net product revenue growth at constant currency	31%
Total net product revenue growth, as reported	35%
Add: Impact of foreign currency translation	(2)
Total net product revenue growth at constant currency	33%
Total revenue growth, as reported	184%
Add: Impact of foreign currency translation	(2)
Total revenue growth at constant currency	182%

Please note that the figures presented may not sum exactly due to rounding
Constant Currency = CER

Summary of Accounting Conclusion for the Roche Transaction

Transaction Consideration	P&L Impact
$310 million upfront payment	Recognized in collaboration revenue when license agreement signed (Q3 2023)
Development milestones	Recognized in collaboration revenue when achieved
Commercial milestones	Recognized in collaboration revenue when achieved
40 / 60 global development cost share	Alnylam records 100% of R&D expense; 60% reimbursement of R&D expense recognized in collaboration revenue as incurred
50 / 50 U.S. profit (or loss) split	Recognized in collaboration revenue*
Tiered low double-digit royalties on ex-U.S. sales	Recognized as royalty revenue

* Preliminary and subject to change.