Nathan (USA)
Diagnosed with AHP

Second Quarter 2023 Financial Results

August 3, 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, or public health emergency 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; 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; delays or interruptions in the supply of resources needed to advance Alnylam's research and development programs, including as may arise from the recent disruptions in the supply of non-human primates; 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 Roche, 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 2022.

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Yvonne Greenstreet, MBChB, MBA

Chief Executive Officer

Overview

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

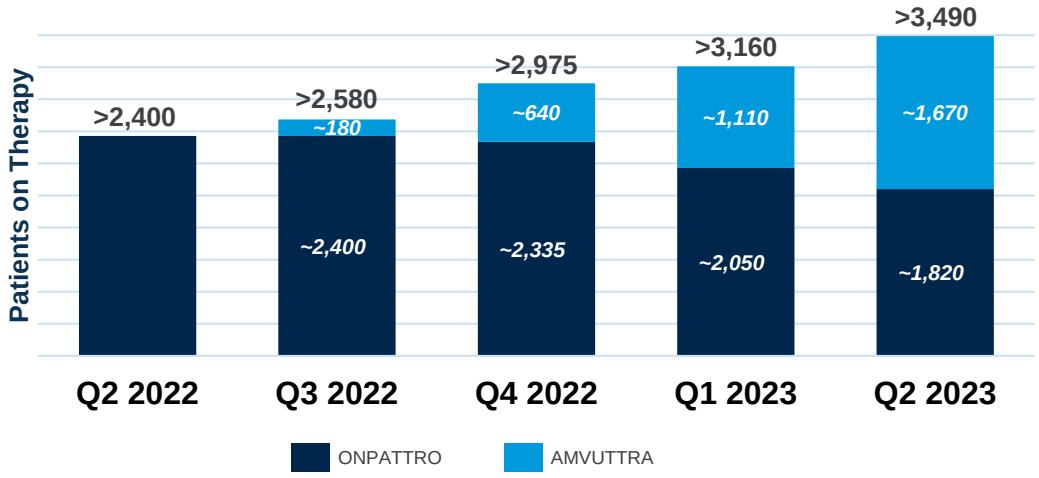
Chief Commercial Officer

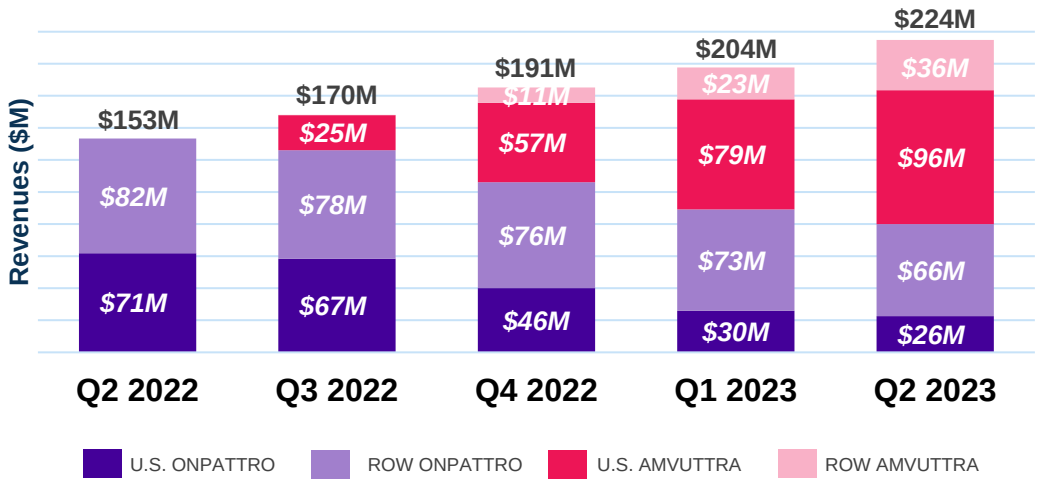
Commercial Highlights

TTR Franchise Update: Q2 2023

$224M
Total TTR
Global Q2 2023
Net Product Revenues

>3,490
Total TTR patients
worldwide at end of
Q2 2023





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

amvuttra® (vutrisiran) injection 25 mg/0.5 mL

Q2 TTR Franchise Highlights

	YoY % Growth	QoQ % Growth
U.S.	72%	12%
ROW	23%	6%
Global	46%	9%

- U.S. TTR franchise QoQ growth of +12% driven by:
  - Demand (+15%): continued strong AMVUTTRA demand more than offsetting decrease in ONPATTRO due to cannibalization
  - Inventory (-2%): modest reduction of both ONPATTRO and AMVUTTRA channel inventory
- ROW QoQ growth (+6%): AMVUTTRA launch demand in Japan and UK; ONPATTRO demand in markets where AMVUTTRA is not yet available
- Modest FX impact (YoY CER[1] growth = 47%)

[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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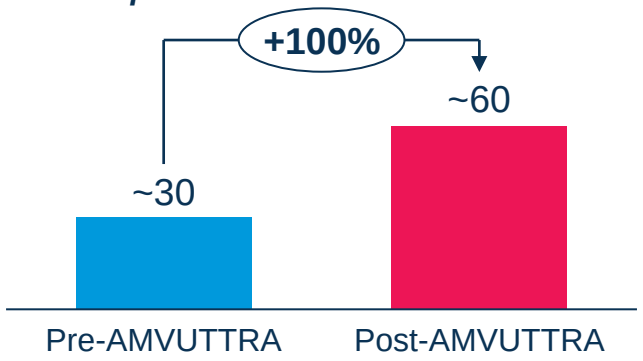
Strong U.S. TTR Commercial Execution 12 Months Post AMVUTTRA Launch

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

***New* TTR Start Forms Monthly Average pre & post AMVUTTRA launch**



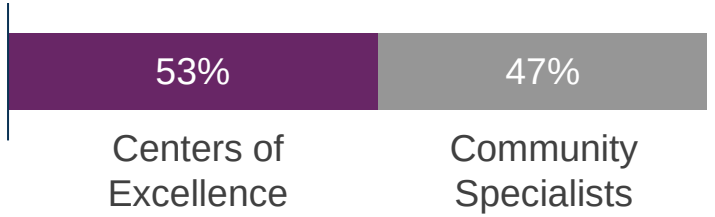
- Additionally, ONPATTRO switching has been robust with > 67% of ONPATTRO patients in U.S. having switched or initiated a switch to AMVUTTRA LTD

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

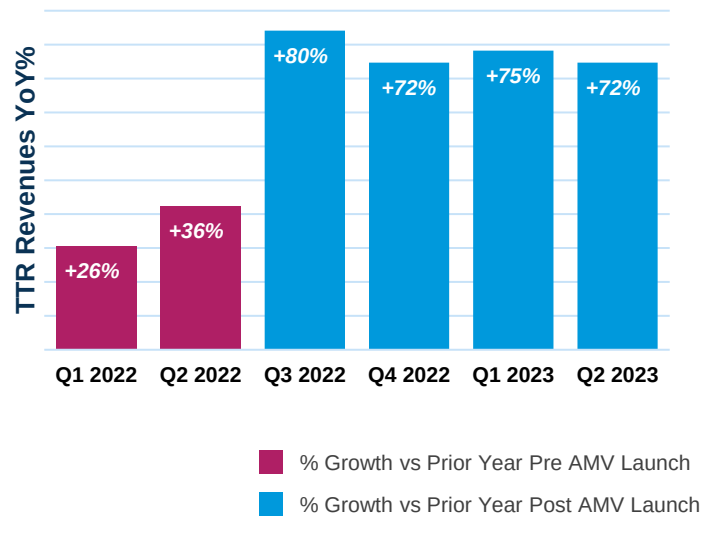
Prescriber base across TTR

- Prior to AMVUTTRA launch, ~500 total prescribers
- Following AMVUTTRA launch, increase by ~50% in prescriber base

Prescriber base for AMVUTTRA



Accelerating Growth for U.S. TTR-PN Franchise



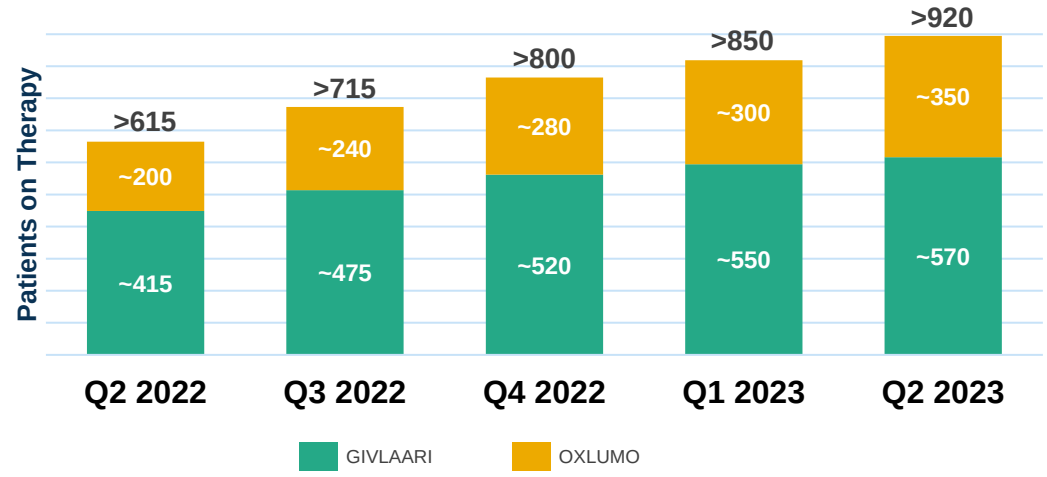
* Start Forms are an incomplete picture of U.S. demand

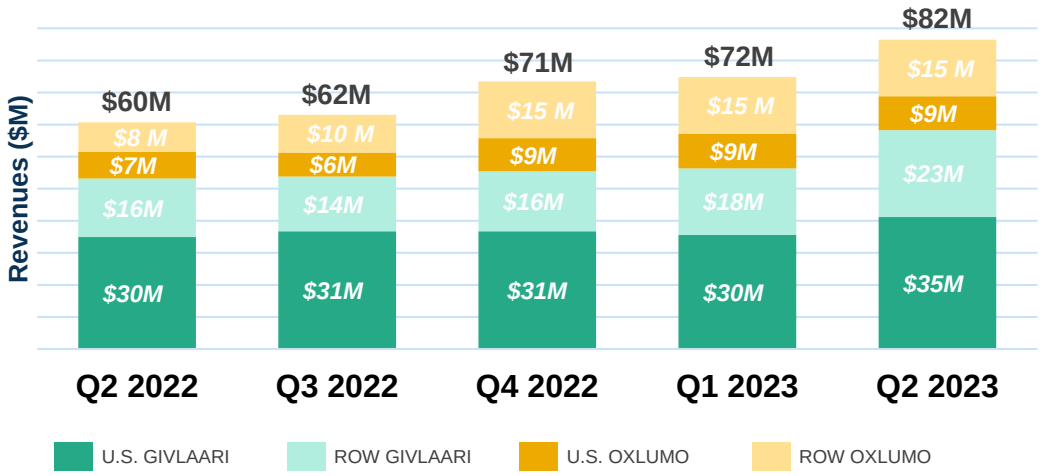
AMVUTTRA and ONPATTRO are approved in the U.S. for the PN of hATTR amyloidosis in adults

Ultra Rare Franchise Update: Q2 2023

$82M
Total Ultra Rare Global Q2 2023 Net Product Revenues

>920
Total Ultra Rare patients worldwide at end of Q2 2023





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

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

Q2 Ultra Rare Franchise Highlights

	YoY % Growth	QoQ % Growth
GIVLAARI	28%	21%
OXLUMO	62%	0%
Total Ultra Rare	37%	14%

- GIVLAARI QoQ growth of +21% driven by:
  - U.S. (+16%): increased patients and higher compliance
  - ROW (+29%): increased demand and partner market order timing
- OXLUMO flat QoQ growth driven by:
  - U.S. (-3%): fewer patients on loading dose regimen
  - ROW (+2%): partner market order timing
- Neutral FX impact (YoY CER[1] growth = 37%)

[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

TTR Franchise Phase 3 Program

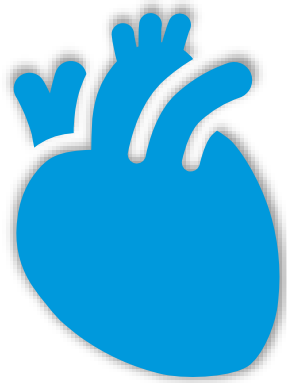
Randomized, Double-Blind, Placebo-Controlled Studies in ATTR Amyloidosis Patients with Cardiomyopathy

APOLLO-B

patisiran

N = 360
hereditary & wild-type
6-minute walk test
12 months

Results presented at
ISA and HFSA – September 2022



HELIOS-B

vutrisiran

N = 655
hereditary & wild-type
mortality & cardiovascular events
30 months

Enrollment **complete**

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

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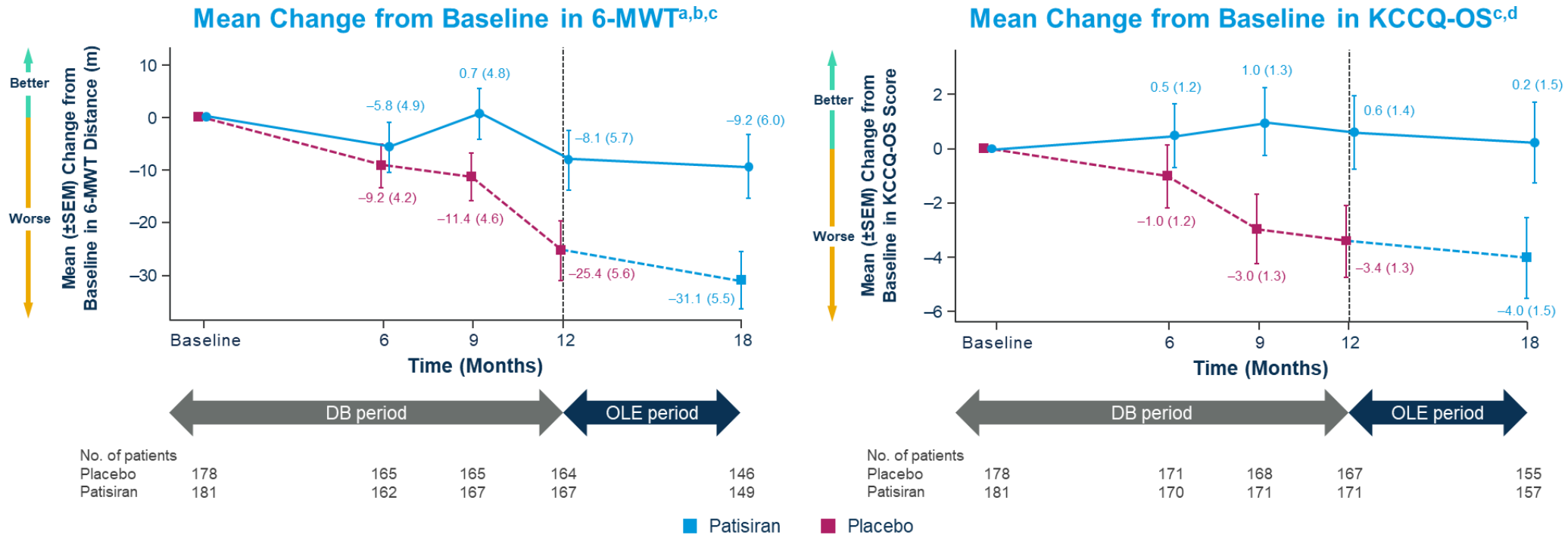
APOLLO-B 18-Month Results

Changes from Baseline in Functional Capacity (6-MWT) and Health Status and QOL (KCCQ-OS)



- The majority of AEs were mild or moderate in severity
- The most common related AE was infusion-related reactions (14.1% of patients)
- The safety profile of patisiran was consistent with previous findings with no new safety concerns identified
- The type and nature of cardiac events observed were consistent with the underlying disease and with those reported during the DB period

[a]Baseline is defined as the last non-missing value available prior to first dose of study drug in the DB period. All patients received patisiran after Month 12. [b]Assessments where the timer was stopped after ≤4 minutes or conducted using unapproved walking aid are excluded from the analysis. [c]Visits with complete data collection are presented. [d]Baseline is defined as the last non-missing value available on or before the date of first dose of study drug in the DB period. All patients received patisiran after Month 12. **Abbreviations**: 6-MWT, 6-minute walk test; DB, double-blind; KCCQ-OS, Kansas City Cardiomyopathy Questionnaire-Overall Summary; OLE, open-label extension; QOL, quality of life; SEM, standard error of the mean.

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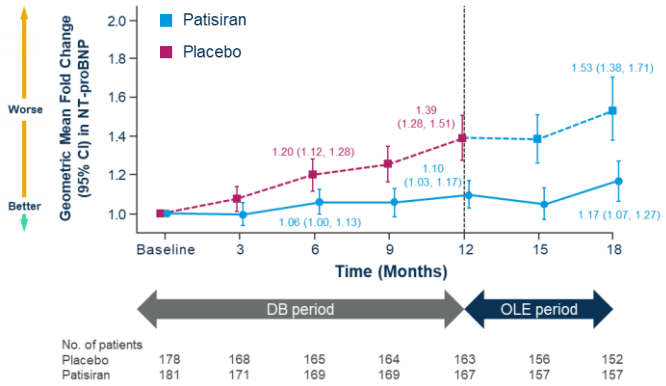
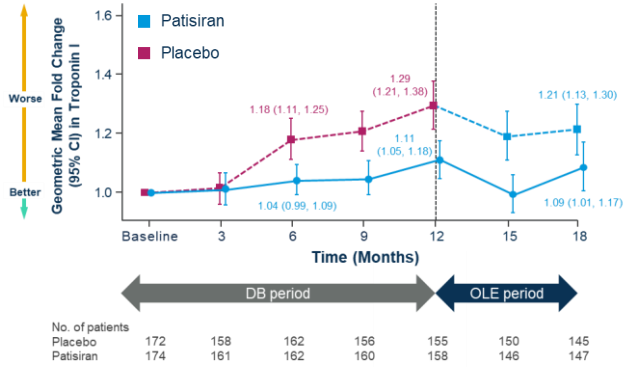
APOLLO-B 18-Month Results

Cardiac Biomarkers (NT-proBNP, Troponin I) and Composite Endpoints

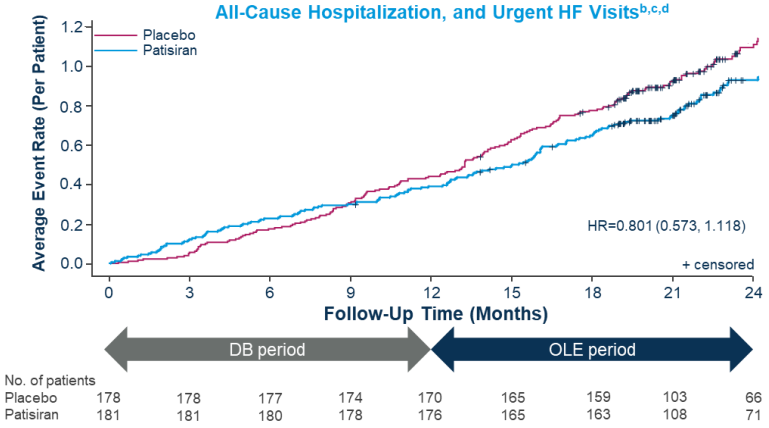
Geometric Mean Fold Change from Baseline in NT-proBNP[a]



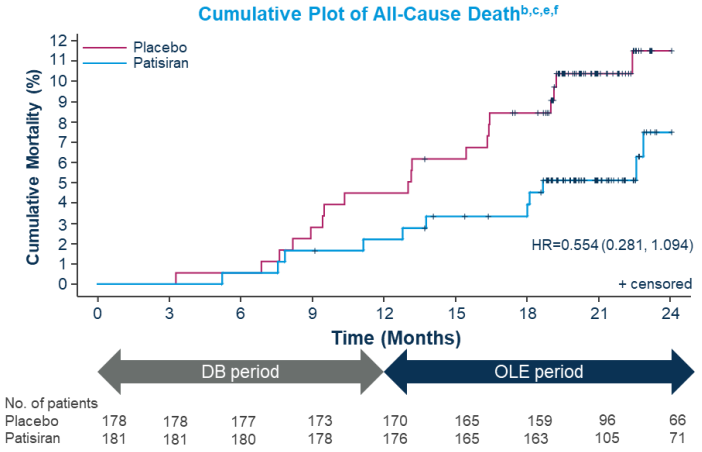
Geometric Mean Fold Change from Baseline in Troponin I[a]



Mean Cumulative Function Plot of All-Cause Mortality, All-Cause Hospitalization, and Urgent HF Visits[b,c,d]



Cumulative Plot of All-Cause Death[b,c,e,f]



[a]Visits with complete data collection are presented. Baseline is defined as the last non-missing value available on or before the date of first dose of study drug in the DB period. All patients received patisiran after Month 12. [b]Heart transplantation and left ventricular assist device placement are handled in the same manner as death. Deaths, hospitalizations, and urgent HF visits due to COVID-19 are excluded from analysis. For patients who discontinued treatment during the DB period, events occurring after Day 417 are excluded. For patients who discontinued treatment during the OLE period, events occurring more than 90 days after last patisiran dose are excluded. The figure is truncated at Day 731; events that occurred after Day 731 are included in the estimate of the HR but not shown in the figure. [c]The analysis was based on the ITT principle and analyzed each treatment arm from initial randomization through the cut-off date, ignoring entry into the OLE. [d]The HR is derived using the modified Andersen–Gill model stratified by baseline tafamidis use, including randomized treatment arm, type of ATTR amyloidosis, baseline NYHA class, and age group as covariates. An HR <1 represents a favorable outcome for patisiran. [e]The HR is derived using the Cox proportional hazards model including randomized treatment as a covariate. [f]4 and 2 deaths in patients initially randomized to placebo and patisiran, respectively, that occurred after Day 731 are included in the estimate of HR but not shown in the figure. **Abbreviations**: CI, confidence interval; DB, double-blind; NT-proBNP, N-terminal prohormone of B-type natriuretic peptide; OLE, open-label extension.

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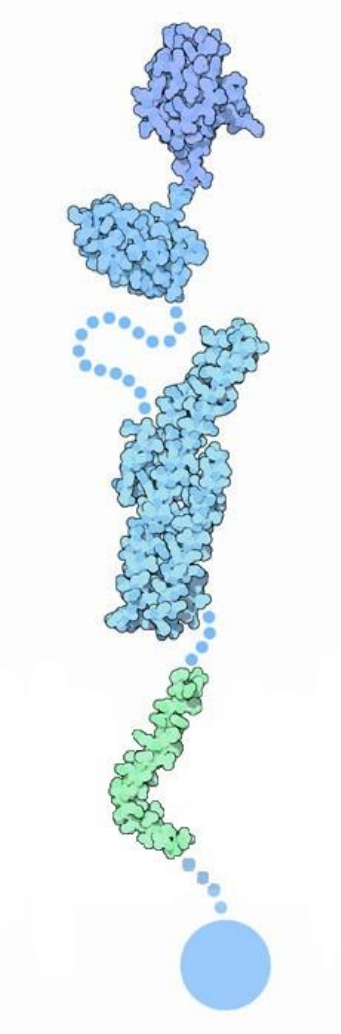
Amyloid Precursor Protein (APP)

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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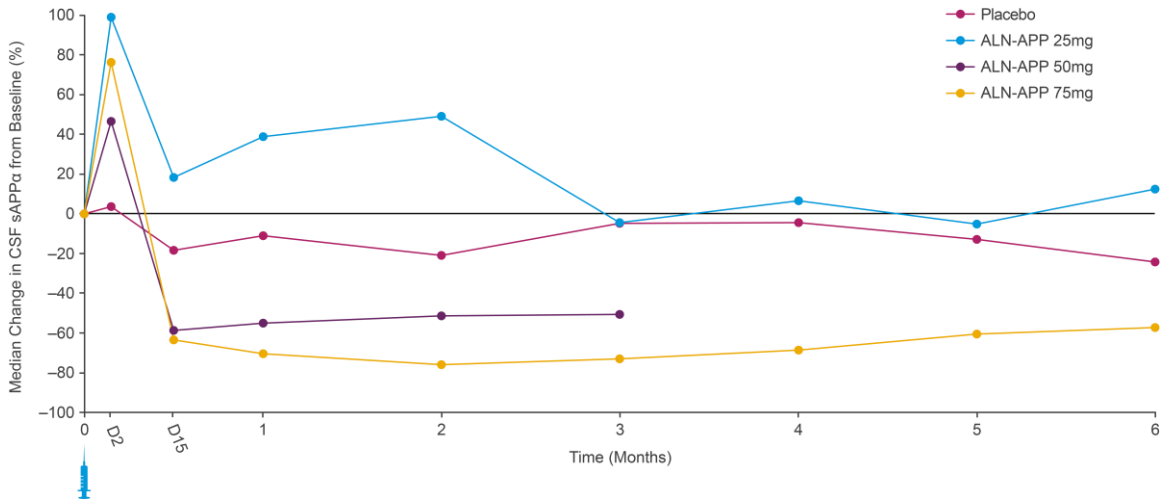
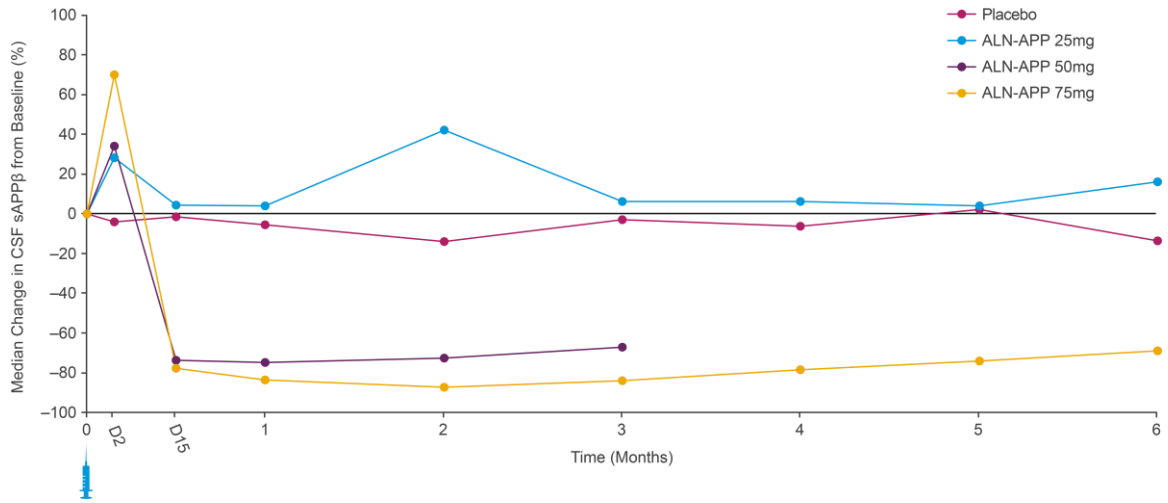
ALN-APP Phase 1 Results

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 June 29, 2023.

Zilebesiran Updates

Clinical Progress and Significant Collaboration Agreement

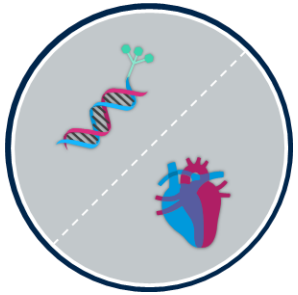
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Zilebesiran, an RNA Interference Therapeutic Agent for Hypertension

Akshay S. Desai, M.D., M.P.H., David J. Webb, M.D., D.Sc., Jorg Taubel, M.D., Sarah Casey, M.B., Ch.B., Yansong Cheng, Ph.D., Gabriel J. Robbie, Ph.D., Don Foster, M.S., Stephen A. Huang, M.D., Sean Rhyee, M.D., M.P.H., Marianne T. Sweetser, M.D., Ph.D., and George L. Bakris, M.D.

Alnylam® PHARMACEUTICALS



Roche

KARDIA-1

Monotherapy Phase 2 Study (N = 394)

- Enrollment completed December 2022; topline results expected mid-2023; full results to be presented at future medical conference

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]
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*	●			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; ** U.S. sNDA accepted; PDUFA Oct. 8, 2023. **As of August 2023**

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Jeff Poulton

Chief Financial Officer

Financial Summary and Upcoming Milestones

Q2 2023 Financial Summary

Financial Results ($ millions)	Q2 2023	Q2 2022	Q2 Reported Growth %	Q2 CER Growth %[2]
Net Product Revenues	$306	$214	43%	44%
Net Revenues from Collaborations	$6	$9		
Royalty Revenues	$7	$2		
Total Revenues	$319	$225	42%	43%
Product Cost of Goods Sold	$75	$34		
Cost of Collaborations and Royalties	$10	$7		
Gross Margin	$233	$184		
Product Sales Gross Margin %[1]	*75%*	*84%*		
Non-GAAP R&D Expenses[2]	$216	$195	11%	
Non-GAAP SG&A Expenses[2]	$172	$150	14%	
Non-GAAP Operating Loss [2]	($154)	($161)		

Financial Results ($ millions)	Jun 30, 2023	Dec 31, 2022
Cash & Investments[3]	$2,058	$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 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 Q2 2023 performance (restated using Q2 2022 exchange rates) to actual Q2 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 August 3, 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 Reiterated 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[1]
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[2]	$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] 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*			●
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		●	
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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Q2 2023 Financial Results

Q&A Session

Thank You!

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Q2 2023 Financial Results

Appendix

Alnylam Pharmaceuticals, Inc.

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

	Three Months Ended	
	June 30, 2023	June 30, 2022
Reconciliation of GAAP to Non-GAAP research and development:		
GAAP research and development	$ 248,526	$ 205,712
Less: Stock-based compensation expenses	(32,801)	(10,638)
Non-GAAP research and development	$ 215,725	$ 195,074
Reconciliation of GAAP to Non-GAAP selling, general and administrative:		
GAAP selling, general and administrative	$ 214,689	$ 169,984
Less: Stock-based compensation expenses	(43,001)	(19,833)
Non-GAAP selling, general and administrative	$ 171,688	$ 150,151
Reconciliation of GAAP to Non-GAAP operating loss:		
GAAP operating loss	$ (229,831)	$ (191,686)
Add: Stock-based compensation expenses	75,802	30,471
Non-GAAP operating loss	$ (154,029)	$ (161,215)

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 June 30, 2023
Total TTR net product revenue growth, as reported	46 %
Add: Impact of foreign currency translation	1
Total TTR net product revenue growth at constant currency	47 %
Total Ultra Rare net product revenue growth, as reported	37 %
Add: Impact of foreign currency translation	—
Total Ultra Rare net product revenue growth at constant currency	37 %
Total net product revenue growth, as reported	43 %
Add: Impact of foreign currency translation	1
Total net product revenue growth at constant currency	44 %
Total revenue growth, as reported	42 %
Add: Impact of foreign currency translation	1
Total revenue growth at constant currency	43 %

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