Second Quarter 2024 Financial Results

August 1, 2024

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, statements regarding Alnylam's aspiration to become a leading global biotech company, the potential for Alnylam to identify new potential drug development candidates and advance its research and development programs, Alnylam's estimations regarding the size of the potential patient population and the number of patients who are dissatisfied with their current treatment regimens; Alnylam's expectations regarding the safety and efficacy of vutrisiran for the treatment of ATTR amyloidosis with cardiomyopathy, including its potential to be standard of care in ATTR-CM; the potential for vutrisiran to obtain regulatory approval for the treatment of ATTR amyloidosis with cardiomyopathy; the expected timing of the presentation of full data from the HELIOS-B clinical trial and the filing of a U.S. Supplemental New Drug Application for vutrisiran in by mid- to late 2024; Alnylam's plans to use a Priority Review Voucher in connection with the Supplemental New Drug Application for vutrisiran; the potential for vutrisiran's clinical profile to support first-line positioning in newly diagnosed patients and in those patients who continue to experience disease progression with stabilizers; the potential for vutrisiran to have a market-leading profile in ATTR-CM; and Alnylam's projected commercial and financial performance, including the expected range of net product revenues and net revenues from collaborations and royalties for 2024, the expected range of aggregate annual GAAP and non-GAAP R&D and SG&A expenses for 2024, and the advancement towards its "*Alnylam P^{5}x25*" strategy, 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, risks and uncertainties relating to: 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, zilebesiran, and mivelsiran; 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; obtaining, maintaining and protecting intellectual property; Alnylam's ability to successfully expand the approved indications for 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 risk of future government investigations; and unexpected expenditures; as well as those risks more fully discussed in the "Risk Factors" filed with Alnylam's 2023 Annual Report on Form 10-K filed with the Securities and Exchange Commission (SEC) and in other filings that Alnylam makes with the SEC. 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.

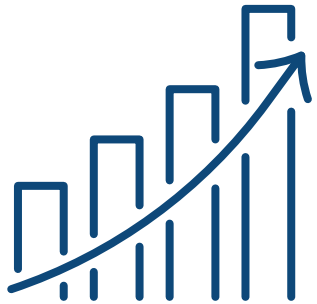
This presentation references non-GAAP financial measures. These measures are not in accordance with, or an alternative to, GAAP, and may be different from non-GAAP financial measures used by other companies. Percentage changes in revenue growth at Constant Exchange Rates, or CER, are non-GAAP financial 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 the prior fiscal year.

Yvonne Greenstreet, MBChB, MBA

Chief Executive Officer

Overview

Q2 2024 Highlights

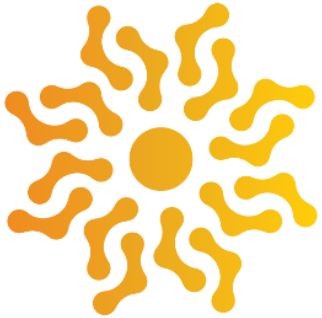


Strong Revenue Growth

- *$410 million net product revenues*
- *34% YoY growth[1]*

Increased Financial Guidance

- *11% increase in net product revenue guidance at midpoint*



Positive HELIOS-B Topline Results

- *Potential for standard of care*
- *Well positioned to address significant unmet need in ATTR-CM*
- *Anchor commercial franchise*

[1] With FX impact. For growth at CER = constant exchange rate – see the Financial Summary slide for more information

Note: The safety and efficacy of AMVUTTRA (vutrisiran) for the treatment of ATTR amyloidosis with cardiomyopathy have not been established or evaluated by the FDA, EMA or any other health authority.

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

SAVE THE DATE

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TTR Investor Day

October 9, 2024

8:30 am ET | NYC & Webcast

Registration information forthcoming

Tolga Tanguler

Chief Commercial Officer

Commercial Highlights

Commercial Portfolio

Continued Strong Performance in Q2 2024

Overall Portfolio

$410M	34%	12%
Combined Net Product Revenue	YoY growth[1] vs. Q2'23	QoQ growth[1] vs. Q1'24

TTR Franchise

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

amvuttra® (vutrisiran) injection 25 mg/0.5 mL

Rare Franchise

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

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

[1] With FX impact. For growth at CER = constant exchange rate – see the Financial Summary slide for more information

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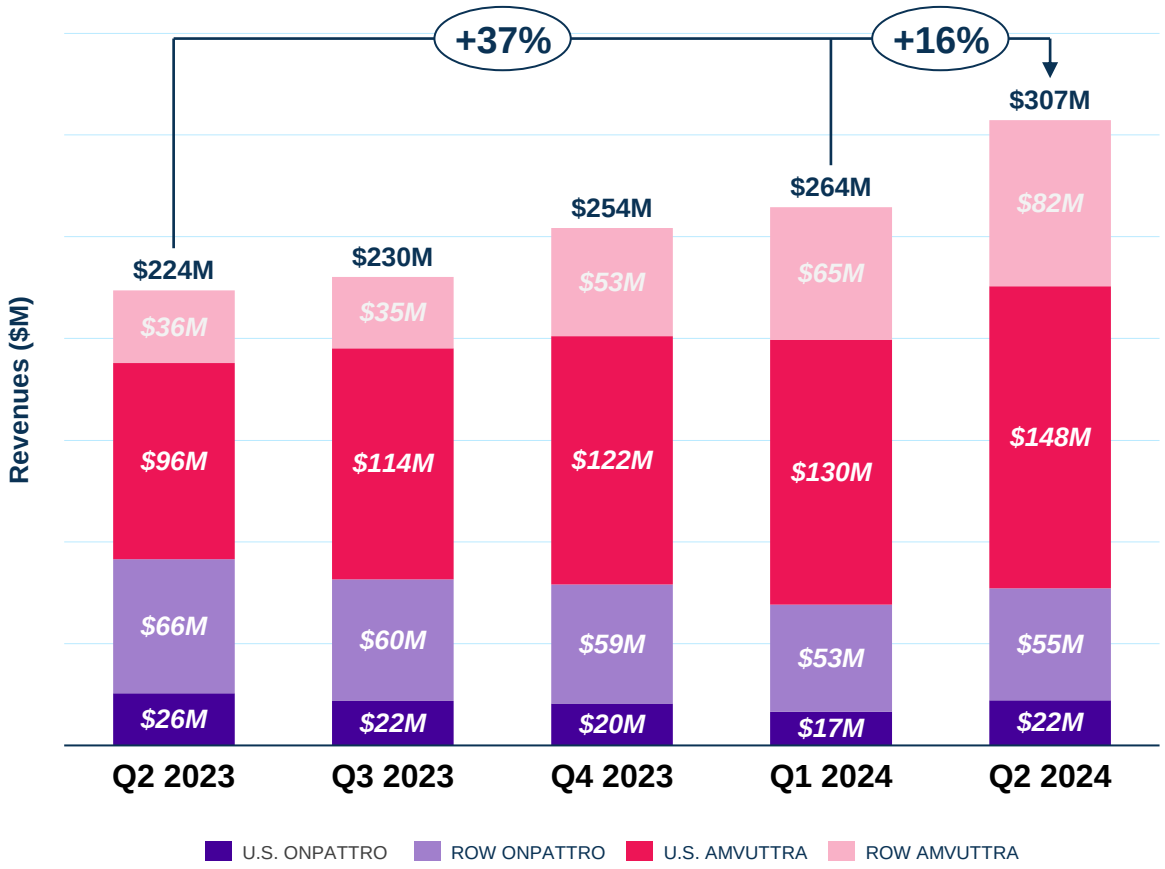
TTR Franchise Update: Q2 2024

$307M
Total TTR
Global Q2 2024
Net Product Revenues



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.	40%	16%
ROW	35%	16%
Global	37%	16%

- U.S. TTR franchise YoY growth of +40% driven by:
  - Demand (+34%): continued strong AMVUTTRA demand more than offsetting decrease in ONPATTRO due to cannibalization
  - Price (+5%): favorable gross-to-net adjustment driven by reduction in ONPATTRO value-based agreement
- ROW YoY growth (+35%):
  - Demand: continued strong AMVUTTRA demand growth broadly across key ROW markets more than offsetting decrease in ONPATTRO due to cannibalization
  - Inventory: positive impact driven by stocking dynamics and timing of large orders in certain partner markets (e.g. Brazil)
- Modest negative FX impact (YoY CER[1] growth = 39%)

[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 2023 – see the Financial Summary slide for more information.

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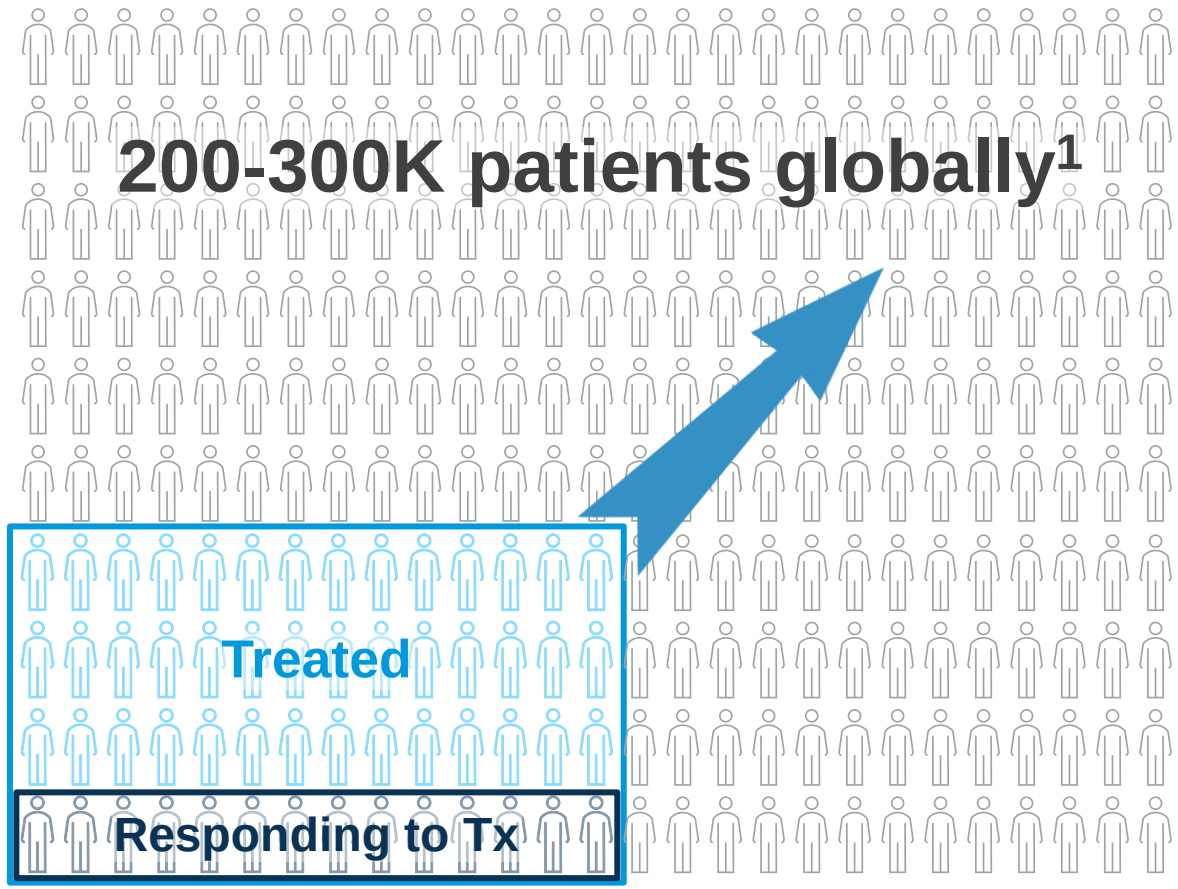
Significant Unmet Need Remains Among ATTR-CM Patients



~80%

ATTR-CM patients untreated globally[1]

- Diagnostic rates rapidly improving
- Analogues suggest competition accelerates category growth

~75%

Patients have partial or no response to current treatment, per HCPs[2]

- HCPs prioritize impact on mortality, CV events and functional capacity[3]
- Looking for better symptomatic and QoL impact, and greater impact on disease progression[3]

[1] ATTR-CM, based on Alnylam modeling data, 2. Alnylam market research with HCPs (n=530), 3. Alnylam Market Research with HCPs (n = 100)

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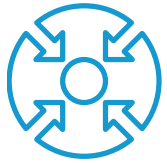
Vutrisiran Well Positioned for Market-Leading Profile in ATTR-CM

Features Physicians Consistently Look for in a First-Line Therapy[1]

- ✓ Efficacy
  - Clinical Outcomes
  - Symptomology, QoL, Function
- ✓ Safety/Tolerability
- ✓ Ease of Use
- ✓ Access

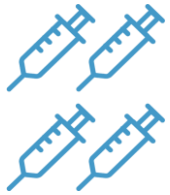


Unique MOA

- **Targeted RNAi mechanism** enables **rapid knockdown** of pathogenic protein at the source
- Works **upstream of approved medicine**

Data Support Potential First-Line Use

- Significant reduction in **mortality** and **CV hospitalizations**
- Substantial impact on **measures of disease progression**
- **Consistent effects** across all key trial subgroups
- **Encouraging safety,** consistent with established profile



Only 4 Doses per Year

- **Quarterly, subcutaneous dosing,** supporting strong adherence, aligning with MD visits
- **Site of care flexibility**

Favorable Payer Dynamics

- **Part B** coverage expected to result in majority of patients having **$0 out-of-pocket costs**
- Monotherapy favored by payers prior to tafamidis LOE

[1] Alnylam market research with HCPs (n=530)

Note: The safety and efficacy of AMVUTTRA (vutrisiran) for the treatment of ATTR amyloidosis with cardiomyopathy have not been established or evaluated by the FDA, EMA or any other health authority.

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Alnylam Prepared to Move Quickly for Rapid Impact with Proven Commercial Engine in TTR Franchise

Focused Customer-Facing Teams

Delivering seamless customer experiences, differentiating in competitive landscape

Deep experience with TTR Centers

Well positioned to serve unmet needs of ATTR-CM patients

Established Patient Support Services

Optimized time to therapy, strong compliance

Strong Payer and Health Systems Partnerships

Exceptional patient access through excellence in account management and clinical education

Note: The safety and efficacy of AMVUTTRA (vutrisiran) for the treatment of ATTR amyloidosis with cardiomyopathy have not been established or evaluated by the FDA, EMA or any other health authority.

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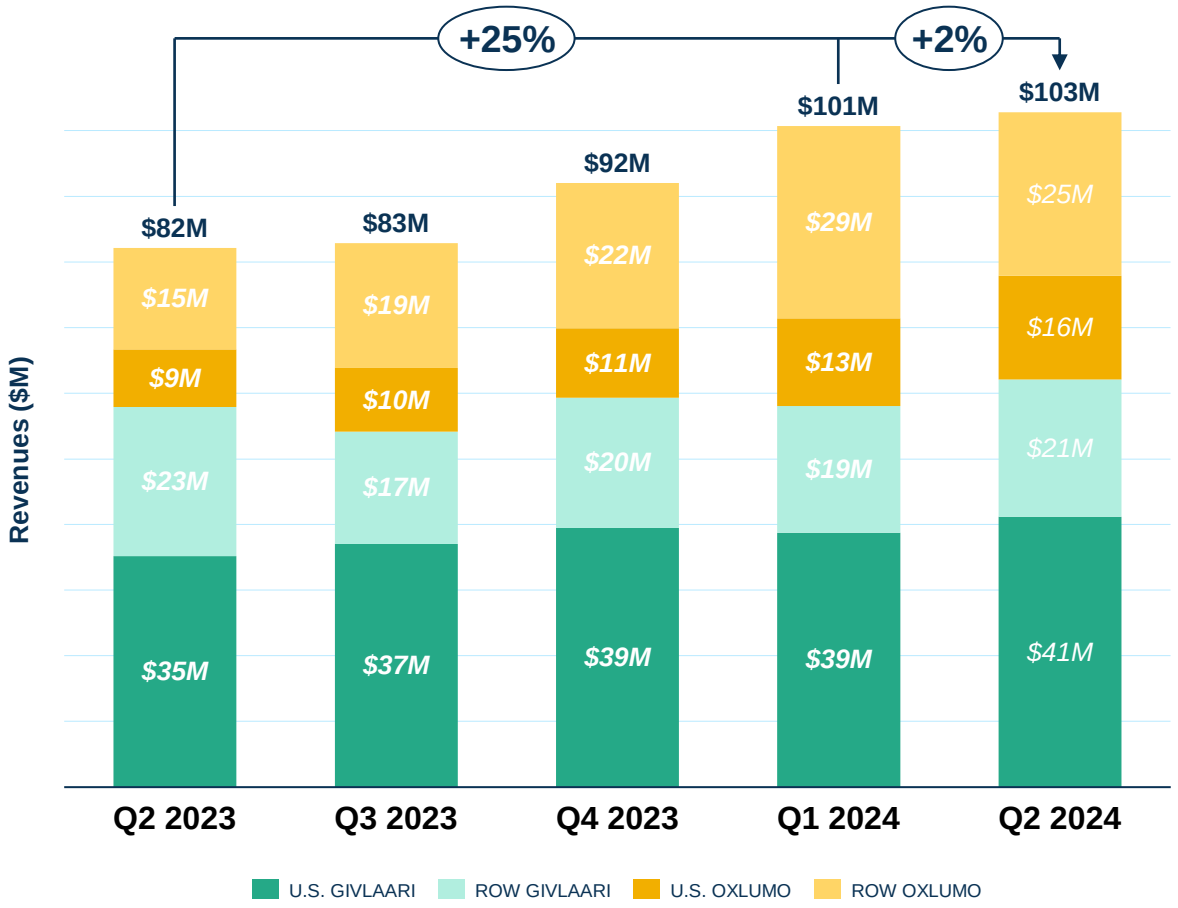
Rare Franchise Update: Q2 2024

$103M
Total Rare
Global Q2 2024
Net Product Revenues



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

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

Q2 Rare Franchise Highlights

	YoY % Growth	QoQ % Growth
GIVLAARI	7%	7%
OXLUMO	68%	-5%
Total Rare	25%	2%

- GIVLAARI YoY growth of +7% driven by:
  - U.S. (+17%): primarily driven by demand growth with additional contribution from lower gross-to-net deductions
  - ROW (-8%): demand growth across EU markets more than offset by timing of large orders in certain partner markets (e.g. Brazil)
- OXLUMO YoY growth of +68% driven by:
  - U.S. (+79%): driven by strong demand growth
  - ROW (+61%): driven by strong demand growth across both EU and partner markets
- Modest FX impact (YoY CER[1] growth = 26%)

[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 2023 – see the Financial Summary slide for more information.

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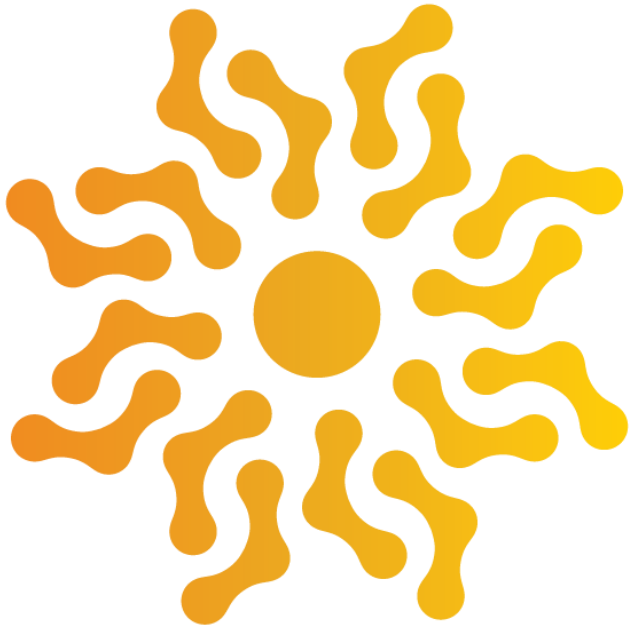
Pushkal Garg, M.D.

Chief Medical Officer

Alnylam Pipeline



HELIOS-B

POSITIVE TOPLINE RESULTS

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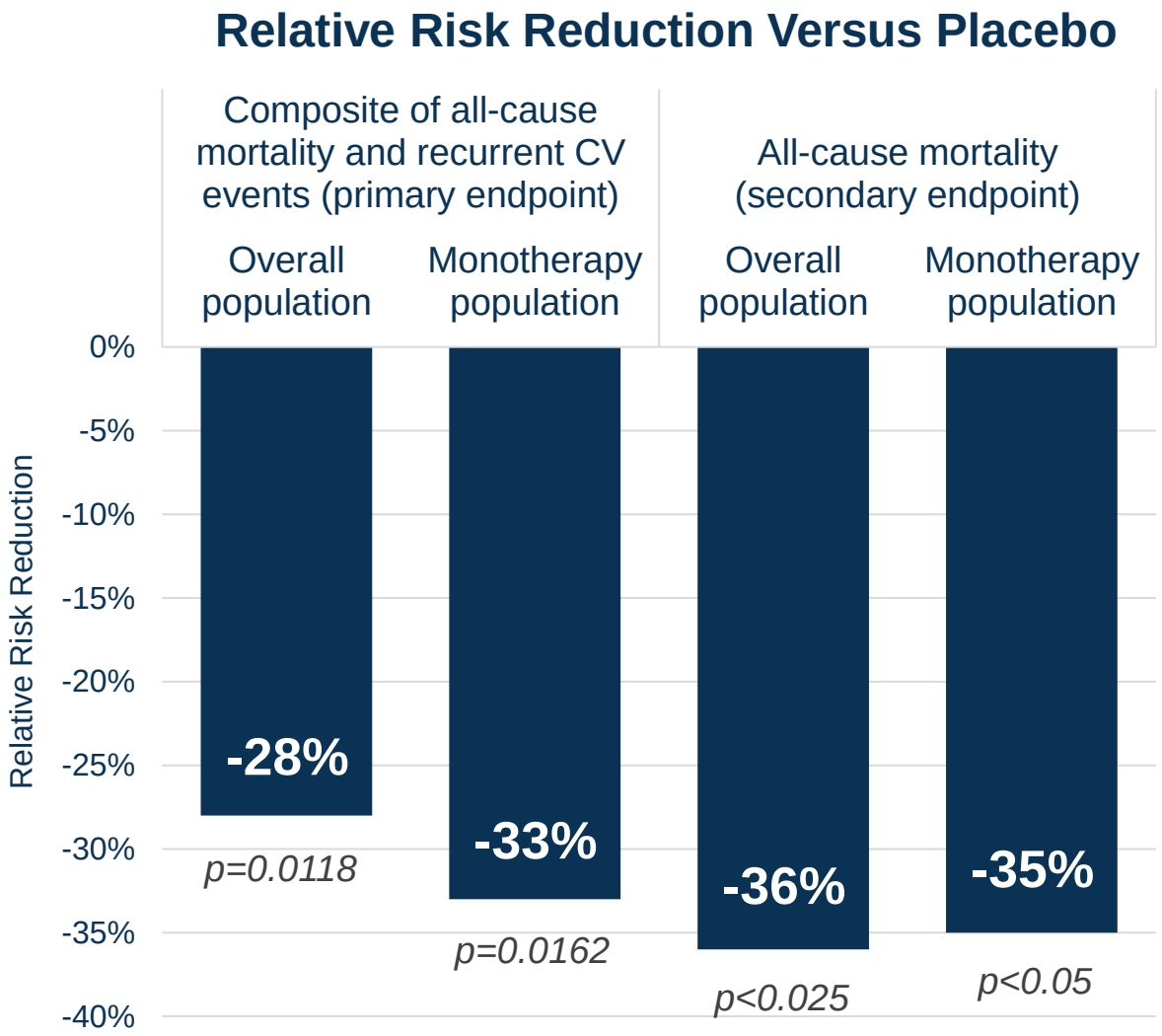
Data Support Potential for Vutrisiran as Standard of Care in ATTR-CM



- Clinically significant benefits on 6MWT, KCCQ, and NYHA class – key measures of disease progression
- Consistent effects observed in all key subgroups, including baseline tafamidis
- Encouraging safety and tolerability, consistent with established profile

Primary composite endpoint of all-cause mortality and recurrent CV events included data up to 36 months; Secondary endpoint of all-cause mortality included data up to 42 months.

Note: The safety and efficacy of AMVUTTRA (vutrisiran) for the treatment of ATTR amyloidosis with cardiomyopathy have not been established or evaluated by the FDA, EMA or any other health authority.

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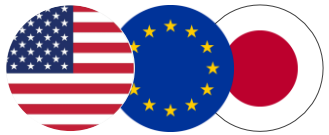
Next Steps

HELIOS-B Full Results – ESC Congress (August 30, London)



Global Regulatory Submissions – Late 2024

Priority Review Voucher to Accelerate FDA Review

Advancing a Robust and High-Yielding Pipeline of RNAi Therapeutics

Positioned to Deliver Strong Growth and Innovation Across Multiple Disease Areas and Indications

IND-enabling	Phase 1	Phase 2	Phase 3	Approved
ALN-HTT02* Huntington's Disease	**ALN-TTRsc04** ATTR Amyloidosis	**Zilebesiran*** Hypertension	**Vutrisiran** ATTR Amyloidosis with CM	onpattro® (patisiran) lipid complex injection 10 mg/5 mL
ALN-SOD‡ Amyotrophic Lateral Sclerosis	**ALN-KHK** Type 2 Diabetes Mellitus	**ALN-HSD^** NASH	**Fitusiran^** Hemophilia	amvuttra® (vutrisiran) injection 25 mg/0.5 mL
ALN-Gene A Bleeding Disorders	**Mivelsiran (ALN-APP)** Alzheimer's Disease	**Elebsiran‡ (ALN-HBV02/VIR-2218)** Hepatitis B Virus Infection	**Cemdisiran (pozelimab combo)^** Myasthenia Gravis	GIVLAARI® (givosiran) injection for subcutaneous use 189 mg/mL
ALN-Gene Y Type 2 Diabetes Mellitus	**ALN-PNP†** NASH	**Elebsiran‡ (ALN-HBV02/VIR-2218)** Hepatitis D Virus Infection	**Cemdisiran (pozelimab combo)^** Paroxysmal Nocturnal Hemoglobinuria	OXLUMO® (lumasiran) for injection 94.5 mg/0.5 mL
	ALN-BCAT Hepatocellular Carcinoma	**Mivelsiran (ALN-APP)** Cerebral Amyloid Angiopathy		LEQVIO® ^ (inclisiran) injection 284 mg/1.5 mL

* Partnered, Alnylam-led with profit split † Partner-led with profit split ‡ Partner-led with Alnylam option for profit split ^ Partner-led with Milestones/Royalties

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Partnered Program Updates

sanofi

FITUSIRAN

Hemophilia

- Regulatory filings submitted in China, Brazil, and U.S.
- FDA target action date March 28, 2025

REGENERON

CEMDISIRAN

Complement-Mediated Diseases

- Regeneron gained exclusive rights to monotherapy
- Alnylam received $10M upfront; eligible to receive certain regulatory milestones, and low double-digit royalties on sales, if approved

MIVELSIRAN

Alzheimer's Disease & Cerebral Amyloid Angiopathy

- Alnylam assumed full global development and commercialization rights in all indications post opt out by Regeneron of further co-development and co-commercialization
- Regeneron eligible to receive low double-digit royalties on sales of mivelsiran, if approved

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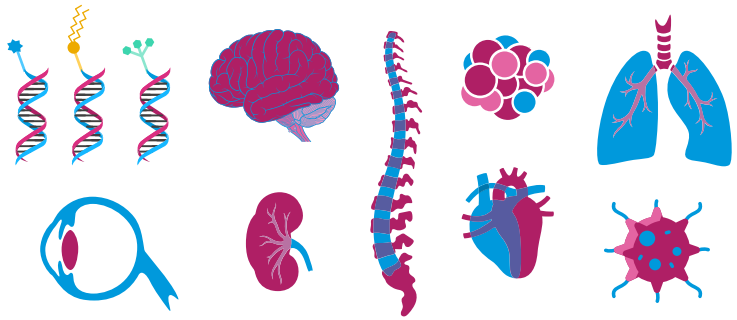
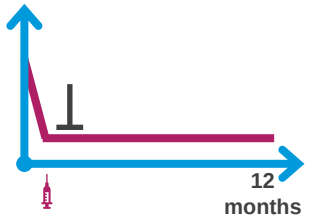
Multiple Sources of Sustainable Innovation Drive Robust Pipeline

Targeting Nine Alnylam-Led INDs Across Four Tissues by End of 2025

Extrahepatic Delivery

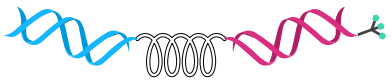


Platform Designs



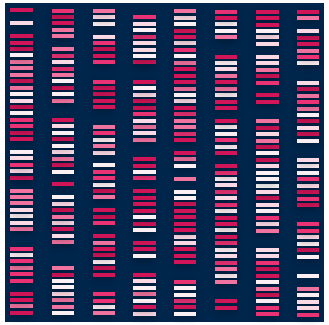
IKARIA™

Reversir™



GEMINI™

Human Genetics

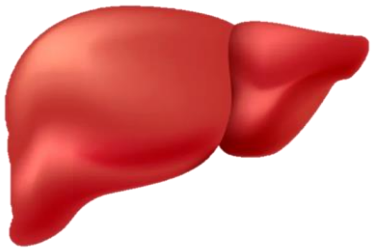


+ Our Future Health

discoverme

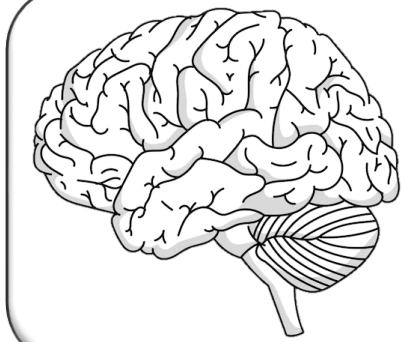
biobank uk

By End of 2025



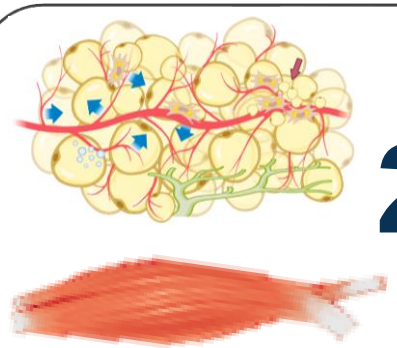
5 new **liver** INDs

10+ including partnered programs



2 new **CNS** INDs

3+ including partnered programs



2 **new tissues** with INDs

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Jeff Poulton

Chief Financial Officer

Financial Summary and Upcoming Milestones

Q2 2024 Financial Summary

Financial Results ($ millions)	Q2 2024	Q2 2023	Q2 Reported Growth %	Q2 CER Growth %[2]
Net Product Revenues	$410	$306	34%	35%
Net Revenues from Collaborations	$227	$6		
Royalty Revenues	$22	$7		
Total Revenues	$660	$319	107%	108%
Product Cost of Goods Sold	$67	$75		
Cost of Collaborations and Royalties	$1	$10		
Total Cost of Goods Sold	$69	$85		
Gross Margin	$591	$233		
Product Sales Gross Margin %[1]	*84%*	*75%*		
Non-GAAP R&D Expenses[2]	$246	$216	14%	
Non-GAAP SG&A Expenses[2]	$207	$172	21%	
Non-GAAP Operating Income / (Loss)[2]	$138	($154)		

Financial Results ($ millions)	Jun 30, 2024	Dec 31, 2023
Cash & Investments[3]	$2,625	$2,439

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

[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. CER growth rates represent growth at Constant Exchange Rates, a non-GAAP financial measure determined by comparing Q2 2024 performance (restated using Q2 2023 exchange rates) to actual Q2 2023 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 1, 2024, 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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2024 Updated Full Year Guidance

	Prior FY 2024 Guidance	Updated FY 2024 Guidance
Net Product Revenue[1] ONPATTRO, AMVUTTRA, GIVLAARI, OXLUMO	$1,400M - $1,500M	$1,575M - $1,650M
Net Product Revenue Growth vs. 2023 at reported FX rates[1]	*13% to 21%*	*27% to 33%*
Net Product Revenue Growth vs. 2023 at constant exchange rates (i.e., operational growth)[2]	*13% to 21%*	*28% to 34%*
Net Revenues from Collaborations & Royalties	$325M - $425M	$575M - $650M
Non-GAAP Combined R&D and SG&A Expenses[3]	$1,675M - $1,775M	$1,775M - $1,875M

[1] Our 2024 FY Guidance is based upon June 30, 2024 FX rates including 1 EUR = 1.07 USD and 1 USD = 161 JPY

[2] CER = constant exchange rate, representing growth calculated as if exchange rates had remained unchanged from those used in 2023. CER is a non-GAAP financial measure. Information regarding our use of non-GAAP financial measures is available in our press release dated August 1, 2024, which is accessible in the Investors section of our website at www.alnylam.com.

[3] 2024 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 $225M - $275M. Information regarding our use of non-GAAP financial measures is available in our press release dated May 2, 2024, which is accessible in the Investors section of our website at www.alnylam.com.

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Alnylam 2024 Goals

			Early	Mid	Late
onpattro (patisiran) amvuttra (vutrisiran) GIVLAARI (givosiran) OXLUMO (lumasiran)		*Combined Net Product Revenue Guidance $1,575M – $1,650M*			●
VUTRISIRAN	ATTR Amyloidosis	HELIOS-B Topline Results		✓	
		sNDA Submission			●
ALN-TTRsc04*	ATTR Amyloidosis	Initiate Phase 3 ATTR-CM Study			●
ZILEBESIRAN*	Hypertension	KARDIA-2 Phase 2 Topline Results	✓		
		Initiate KARDIA-3 Phase 2 Study	✓		
MIVELSIRAN* **(ALN-APP)**	Alzheimer's Disease	Interim Phase 1 Part B Multi-Dose Results			●
		Initiate Phase 2 Study			●
	Cerebral Amyloid Angiopathy	Initiate Phase 2 Study	✓		
ALN-KHK*	Type 2 Diabetes	Initiate Phase 1 Part B	✓		
ALN-BCAT*	Hepatocellular Carcinoma	Initiate Phase 1 Study	●		
ADDITIONAL PROGRAMS		File 3 New INDs			●
KEY PARTNER-LED PROGRAM MILESTONES					
FITUSIRAN* (Sanofi)	Hemophilia	NDA Submission	2024 ✓		
ELEBSIRAN* (Vir)	Chronic HBV/HDV Infection	Phase 2 Results	Q2 ✓ | Q4 ●		

* 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 2024 Financial Results

Q&A Session

Thank You!

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Q2 2024 Financial Results

Appendix

Alnylam Pharmaceuticals, Inc.

Reconciliation of Selected GAAP Measures to Non-GAAP Measures
(In thousands, except per share amounts)

	Three Months Ended	
	June 30, 2024	June 30, 2023
Reconciliation of GAAP to Non-GAAP Research and development:		
GAAP Research and development	$ 294,142	$ 248,526
Less: Stock-based compensation expenses	(48,115)	(32,801)
Non-GAAP Research and development	$ 246,027	$ 215,725
Reconciliation of GAAP to Non-GAAP Selling, general and administrative:		
GAAP Selling, general and administrative	$ 248,397	$ 214,689
Less: Stock-based compensation expenses	(41,173)	(43,001)
Non-GAAP Selling, general and administrative	$ 207,224	$ 171,688
Reconciliation of GAAP to Non-GAAP Operating income (loss):		
GAAP Operating income (loss)	$ 48,614	$ (229,831)
Add: Stock-based compensation expenses	89,288	75,802
Non-GAAP Operating income (loss)	$ 137,902	$ (154,029)

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, 2024
Total TTR net product revenue growth, as reported	37 %
Add: Impact of foreign currency translation	2
Total TTR net product revenue growth at constant currency	39 %
Total Rare net product revenue growth, as reported	25 %
Add: Impact of foreign currency translation	1
Total Rare net product revenue growth at constant currency	26 %
Total net product revenue growth, as reported	34 %
Add: Impact of foreign currency translation	1
Total net product revenue growth at constant currency	35 %
Total revenue growth, as reported	107 %
Add: Impact of foreign currency translation	1
Total revenue growth at constant currency	108 %

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