



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

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 P⁵x25*" 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 P⁵x25*" 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.

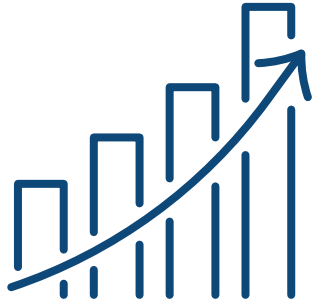
This presentation references non-GAAP financial measures. These measures are not in accordance with, or an alternative to, GAAP, and may be different from non-GAAP financial measures used by other companies. Percentage changes in revenue growth at Constant Exchange Rates, or CER, are non-GAAP financial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



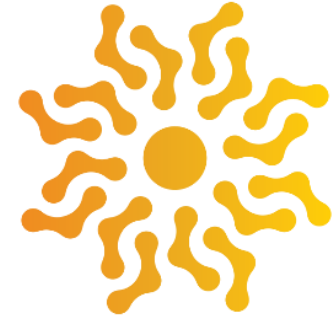
Strong Revenue Growth

- *\$410 million net product revenues*
- *34% YoY growth¹*



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



Patients: Over 0.5 million on Aynylam 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: $\geq 40\%$ revenue CAGR through YE 2025

Profitability: Achieve sustainable non-GAAP profitability within period

SAVE THE DATE

 Alnylam[®]

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
Combined Net Product Revenue

34%
YoY growth¹ vs. Q2'23

12%
QoQ growth¹ vs. Q1'24

TTR Franchise

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

amvuttra
(vutrisiran) injection
25 mg/0.5 mL

Rare Franchise

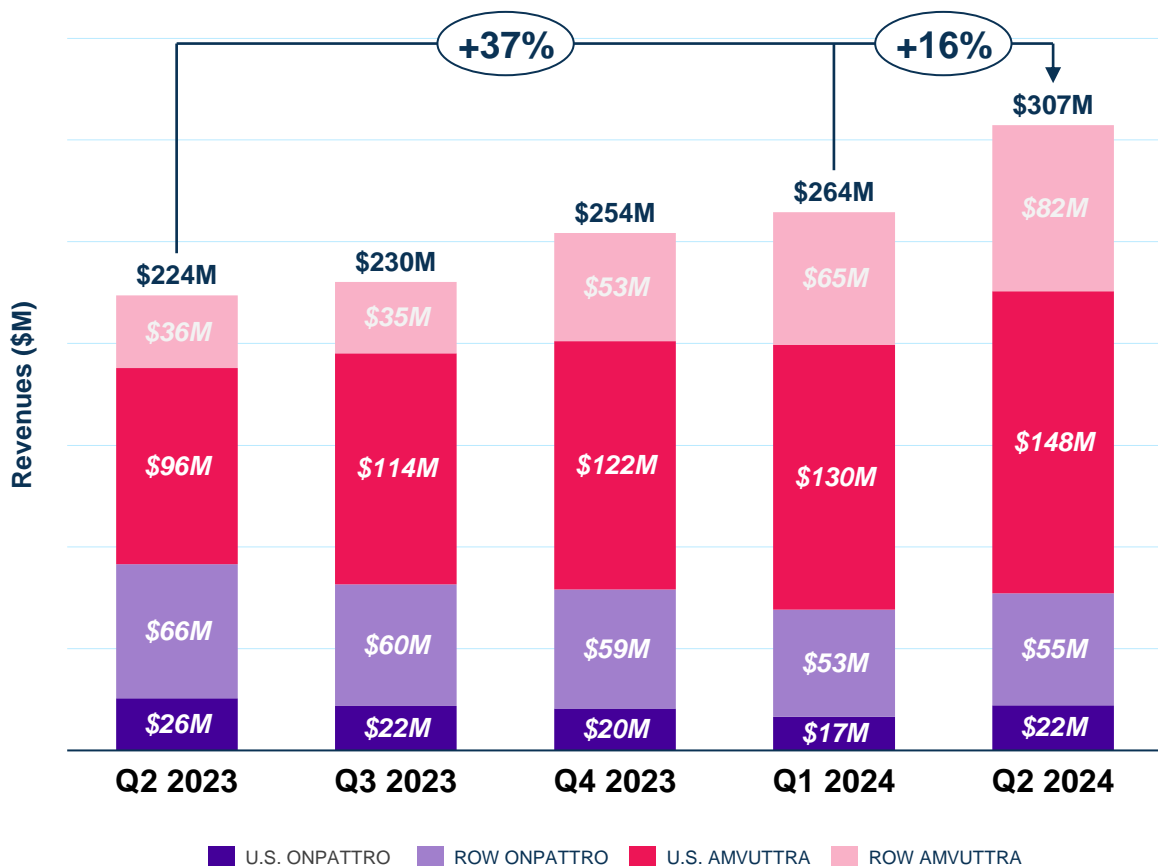
GIVLAARI[®]
(givosiran) injection for subcutaneous use
189 mg/mL

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

TTR Franchise Update: Q2 2024

\$307M
Total TTR
Global Q2 2024
Net Product Revenues

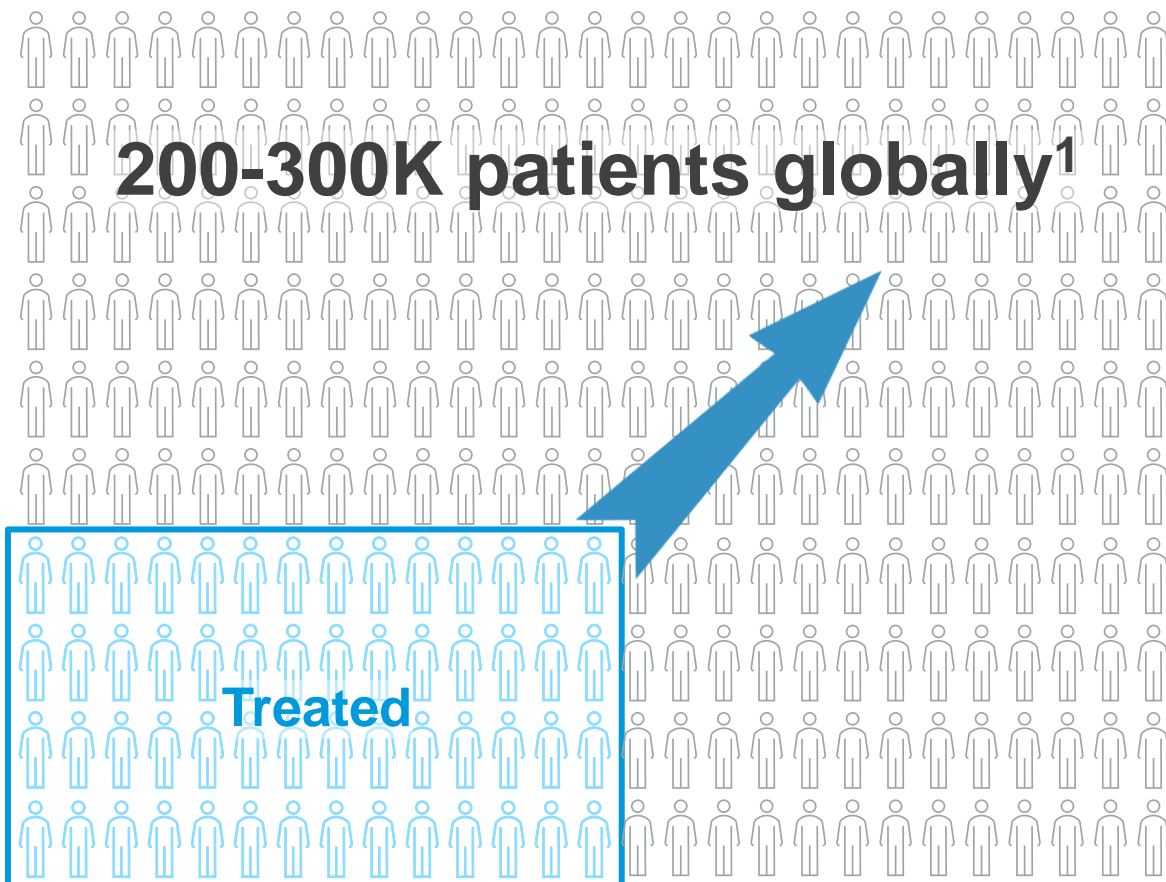


Q2 TTR Franchise Highlights

	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 CER¹ growth = 39%)

Significant Unmet Need Remains Among ATTR-CM Patients



~80%

**ATTR-CM patients
untreated globally¹**

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

**Opportunity
for Additional
Treatment Options**

- HCPs prioritize impact on mortality, CV events and functional capacity²
- Looking for better symptomatic and QoL impact, and greater impact on disease progression²

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

Features Physicians Consistently Look for in a First-Line Therapy¹

- ✓ 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.

Anylam 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

Established Patient Support Services

Optimized time to therapy, strong compliance



Deep experience with TTR Centers

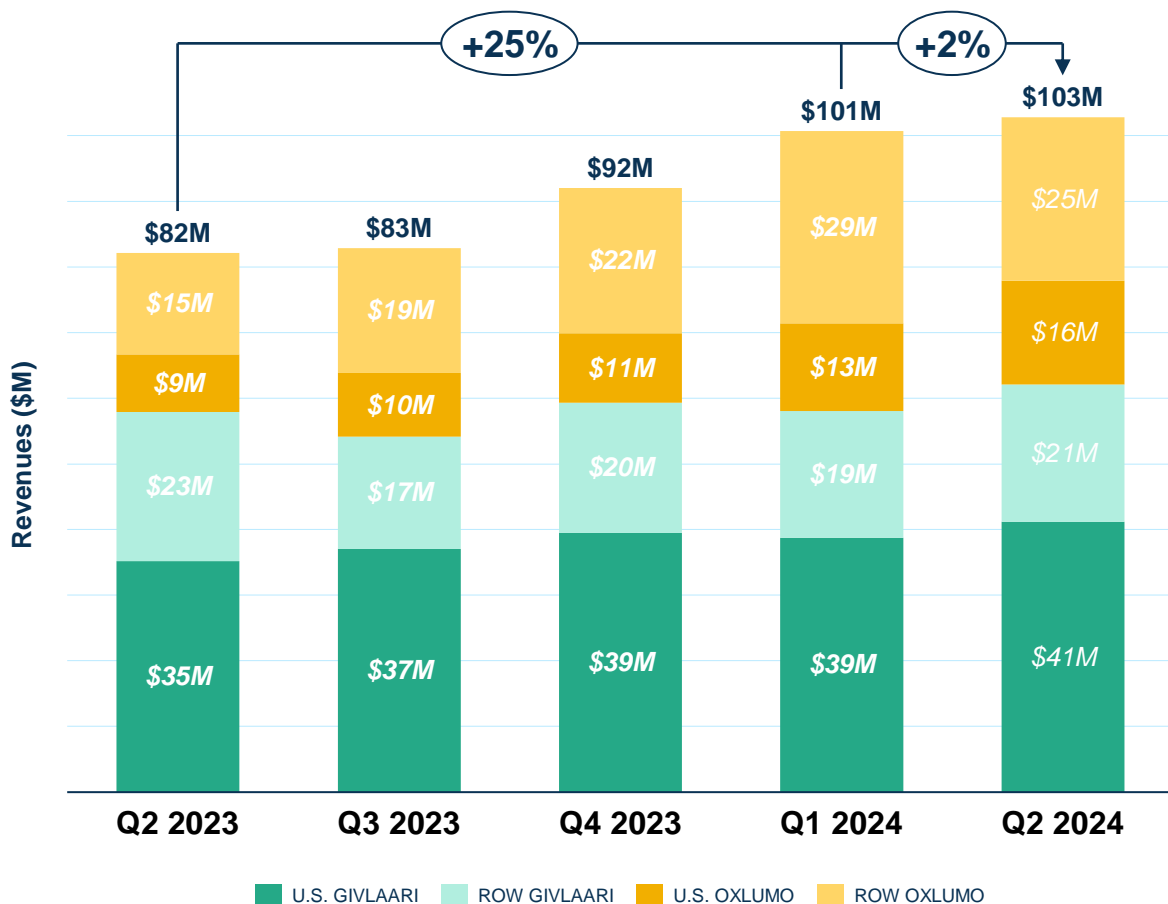
Well positioned to serve unmet needs of ATTR-CM patients

Strong Payer and Health Systems Partnerships

Exceptional patient access through excellence in account management and clinical education

Rare Franchise Update: Q2 2024

\$103M
Total Rare
Global Q2 2024
Net Product Revenues



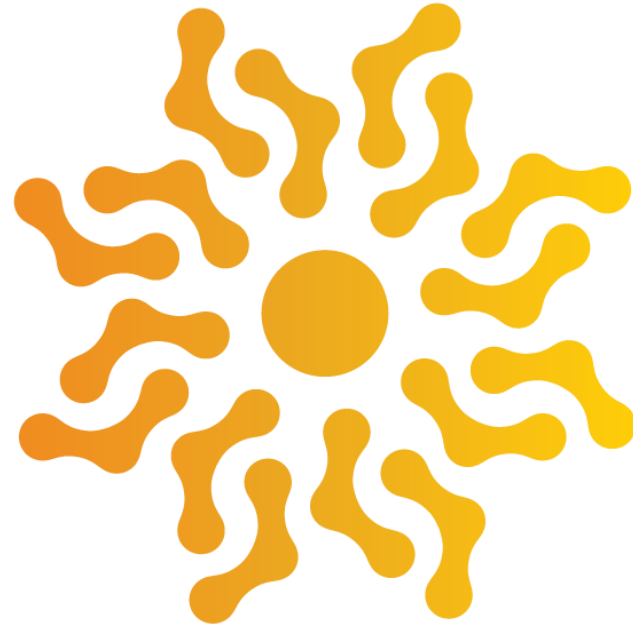
Q2 Rare Franchise Highlights

	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 CER¹ growth = 26%)



Pushkal Garg, M.D.
Chief Medical Officer
Anylam Pipeline

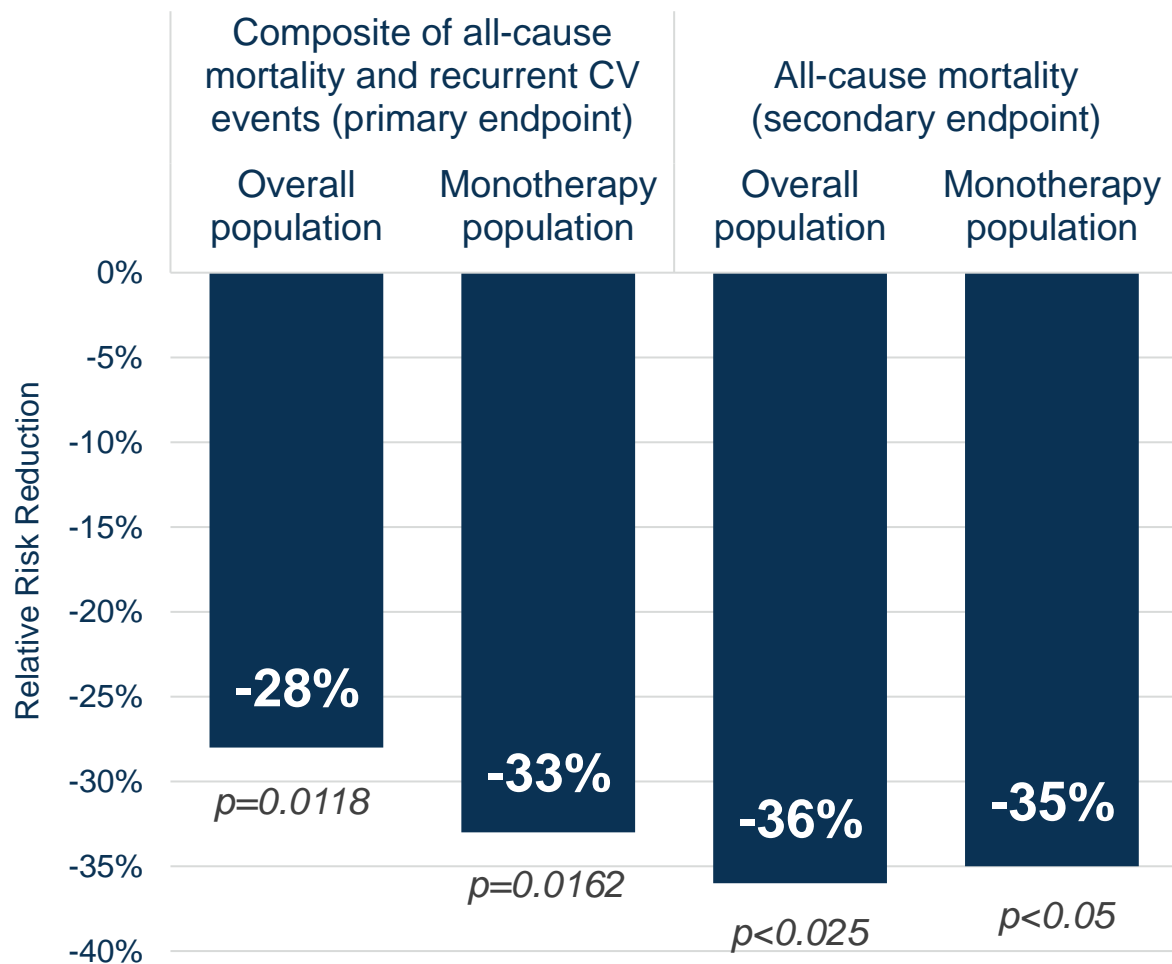


HELIOS · B

POSITIVE TOPLINE RESULTS

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

Relative Risk Reduction Versus Placebo

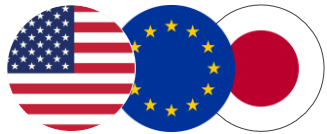


- ✓ Clinically significant benefits on 6MWT, KCCQ, and NYHA class – key measures of disease progression
- ✓ Consistent effects observed in all key subgroups, including baseline tafamidis
- ✓ Encouraging safety and tolerability, consistent with established profile

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

ALN-HTT02*
Huntington's Disease

ALN-SOD‡
Amyotrophic Lateral Sclerosis

ALN-Gene A
Bleeding Disorders

ALN-Gene Y
Type 2 Diabetes Mellitus

Phase 1

ALN-TTRsc04
ATTR Amyloidosis

ALN-KHK
Type 2 Diabetes Mellitus

**Mivelsiran
(ALN-APP)**
Alzheimer's Disease

ALN-PNP†
NASH

ALN-BCAT
Hepatocellular Carcinoma

Phase 2

Zilebesiran*
Hypertension

ALN-HSD^
NASH

**Elebsiran‡
(ALN-HBV02/VIR-2218)**
Hepatitis B Virus Infection

**Elebsiran‡
(ALN-HBV02/VIR-2218)**
Hepatitis D Virus Infection

**Mivelsiran
(ALN-APP)**
Cerebral Amyloid Angiopathy

Phase 3

Vutrisiran
ATTR Amyloidosis with CM

Fitusiran^
Hemophilia

**Cemdisiran
(pozelimab combo)^**
Myasthenia Gravis

**Cemdisiran
(pozelimab combo)^**
Paroxysmal Nocturnal Hemoglobinuria

Approved

onpattro
(patisirán)
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

LEQVIO
(inclisiran)
injection
284 mg/1.5 mL

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

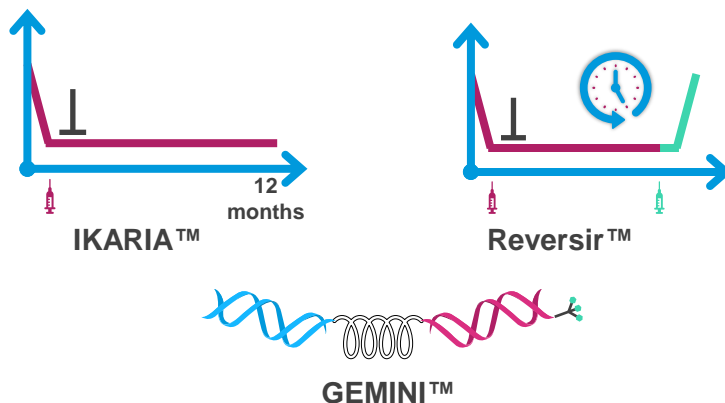
Multiple Sources of Sustainable Innovation Drive Robust Pipeline

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

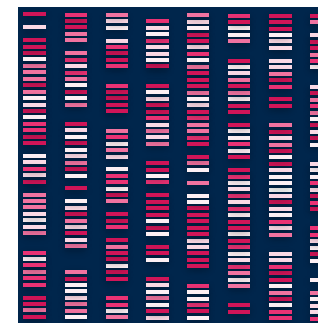
Extrahepatic Delivery



Platform Designs



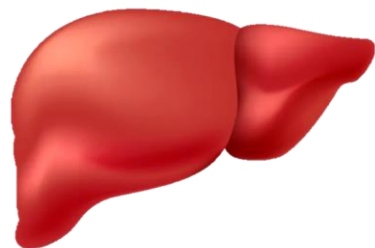
Human Genetics



+
Our
Future
Health

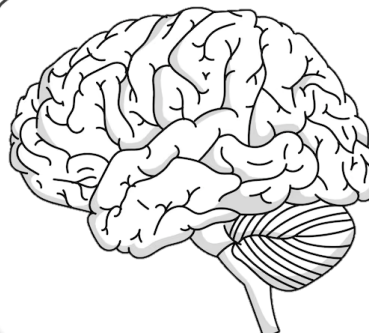


By End of 2025



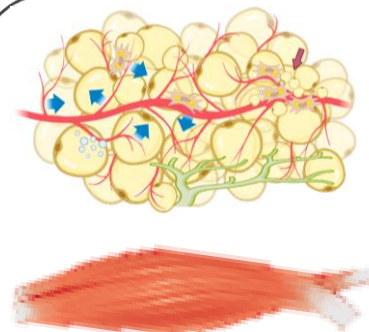
5 new liver
INDs

10+ including
partnered programs



2 new CNS
INDs

3+ including
partnered programs



2 new tissues
with INDs



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		
<i>Product Sales Gross Margin %¹</i>	<i>84%</i>	<i>75%</i>		
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.

2024 Updated Full Year Guidance


	Prior FY 2024 Guidance	Updated FY 2024 Guidance
Net Product Revenue¹ ONPATTRO, AMVUTTRA, GIVLAARI, OXLUMO	\$1,400M - \$1,500M	\$1,575M - \$1,650M
<i>Net Product Revenue Growth vs. 2023 at reported FX rates¹</i>	<i>13% to 21%</i>	<i>27% to 33%</i>
<i>Net Product Revenue Growth vs. 2023 at constant exchange rates (i.e., operational growth)²</i>	<i>13% to 21%</i>	<i>28% to 34%</i>
Net Revenues from Collaborations & Royalties	\$325M - \$425M	\$575M - \$650M
Non-GAAP Combined R&D and SG&A Expenses³	\$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.

Anylam 2024 Goals

			Early	Mid	Late
			<i>Combined Net Product Revenue Guidance</i> \$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



Q2 2024 Financial Results

Q&A Session

| || **Thank You!**



Q2 2024 Financial Results

Appendix

Anylam 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	<u>\$ 246,027</u>	<u>\$ 215,725</u>
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	<u>\$ 207,224</u>	<u>\$ 171,688</u>
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)	<u>\$ 137,902</u>	<u>\$ (154,029)</u>



Anylam 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	<u>39 %</u>
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	<u>26 %</u>
Total net product revenue growth, as reported	34 %
Add: Impact of foreign currency translation	1
Total net product revenue growth at constant currency	<u>35 %</u>
Total revenue growth, as reported	107 %
Add: Impact of foreign currency translation	1
Total revenue growth at constant currency	<u>108 %</u>