Fourth Quarter and Full Year 2024 Financial Results

February 13, 2025

Agenda

Welcome

- Christine Lindenboom
  Chief Corporate Communications Officer

Overview

- Yvonne Greenstreet, MBChB, MBA
  Chief Executive Officer

Commercial Highlights

- Tolga Tanguler
  Chief Commercial Officer

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 the potential for 2025 to be a landmark year for Alnylam; Alnylam's aspiration to become a top-tier biotech company and the planned achievement of its "*Alnylam P^{5}x25*" goals; the potential for Alnylam to experience sustainable growth and value creation in the future; Alnylam's ability to obtain approval for new commercial products or additional indications for its existing products, including AMVUTTRA in ATTR-CM; the potential for Alnylam to successfully launch AMVUTTRA in ATTR-CM and for AMVUTTRA become a new standard of care in ATTR-CM and establish a flagship franchise for Alnylam; Alnylam's expectations regarding the safety and efficacy of AMVUTTRA for the treatment of ATTR-CM; the potential for Alnylam to identify new potential drug development candidates and advance its research and development programs and to deliver growth and innovation across a broad range of disease areas and indications, including statements regarding the timing of Alnylam's initiation of Phase 3 clinical trials of nucresiran in ATTR-CM and zilebesiran in hypertension; the advancement by Sanofi of fitusiran through regulatory review and approval and Alnylam's receipt of any royalties on sales of fitusiran; statements regarding the potential profiles and benefits of Alnylam's product candidates; the size of the commercial opportunities for Alnylam's current and any future products; Alnylam's ability to achieve sustainable profitability going forward; and Alnylam's projected commercial and financial performance, including the expected range of combined net product revenues, net revenues from collaboration and royalties, Non-GAAP combined R&D and SG&A expenses and non-GAAP operating income for 2025, 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*" goals; Alnylam's ability to discover and develop novel drug candidates and delivery approaches and successfully demonstrate the efficacy and safety of its product candidates; the pre-clinical and clinical results for Alnylam's product candidates; actions or advice of regulatory agencies and Alnylam's ability to obtain and maintain regulatory approval for its product candidates, as well as favorable pricing and reimbursement; successfully launching, marketing and selling Alnylam's approved products globally; delays, interruptions or failures in the manufacture and supply of Alnylam's product candidates or its marketed products; obtaining, maintaining and protecting intellectual property; Alnylam's ability to successfully expand the approved indications for AMVUTTRA; 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; 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 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.

Yvonne Greenstreet, MBChB, MBA

Chief Executive Officer

Overview

2024 Delivered Strong Progress Across the Business

Portfolio & Pipeline

HELIOS-B

Highly Positive HELIOS-B Phase 3 results

PRIORITY

Global regulatory filings for **vutrisiran,** PDUFA date March 23, 2025

Positive **nucresiran** (ALN-TTRsc04) Phase 1 data supporting potential for best-in-class profile

Positive initial multi-dose results with **mivelsiran**

Initiated cAPPricorn-1 Phase 2 study in CAA

KARDIA

Positive **zilebesiran** Phase 2 results showing significant additive blood pressure lowering

Expanded clinical pipeline with **4 proprietary CTAs:**

- ALN-HTT02
- ALN-AGT-REVERSIR
- ALN-6400
- ALN-4324

Financials & Culture

onpattro (patisiran)

amvuttra (vutrisiran)

GIVLAARI (givosiran)

OXLUMO (lumasiran)

Combined net product revenues: **$1,646 million (33% growth YoY)**

Maintained strong financial position **$2.7 billion in cash** at year-end 2024

The Boston Globe TOP PLACES TO WORK 2015-2024

Continued recognition of **award-winning culture**

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2025: A Landmark Year for Alnylam

Best-in-Class Team + Award-Winning Culture

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Strong Progress Against Ambitious Five-Year Goals

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; 10+ in late stages; 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

Commercial Portfolio – Continued Strong Performance in Q4 2024

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

Q4 2024

$451M
Combined Net Product Revenue

30%
YoY growth[1] vs. Q4'23

7%
QoQ growth[1] vs. Q3'24

Full Year 2024

$1,646M
Combined Net Product Revenue

33%
YoY growth[1] vs. FY'23

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

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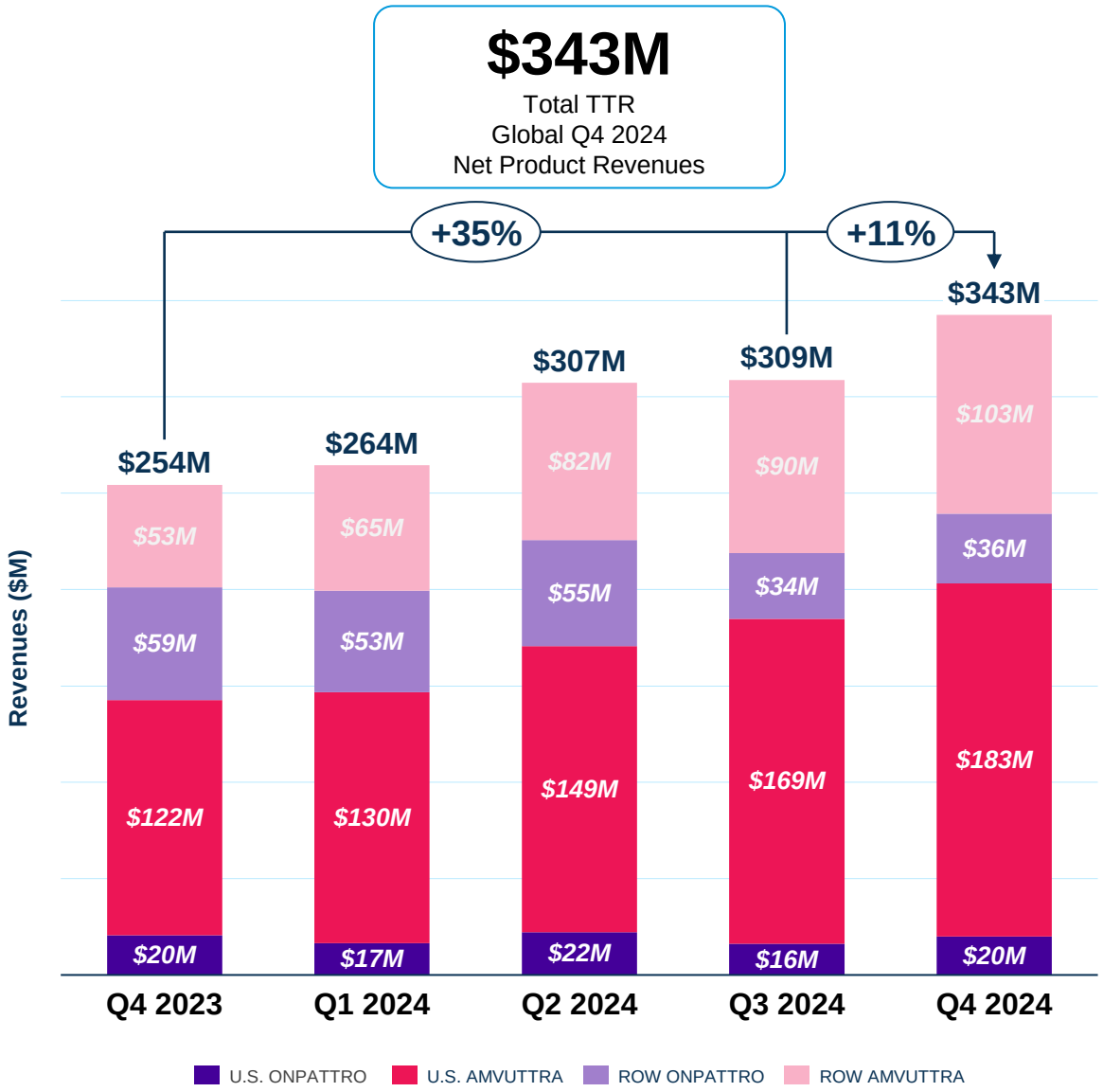
TTR Franchise Update: Q4 2024



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

amvuttra® (vutrisiran) injection 25 mg/0.5 mL

Q4 TTR Franchise Highlights

	YoY % Growth	QoQ % Growth
U.S.	42%	10%
ROW	25%	12%
Global	35%	11%

- U.S. TTR franchise YoY growth of +42% driven by:
  - Demand (+34%): continued strong AMVUTTRA demand more than offsetting ONPATTRO decrease due to cannibalization
  - GTN (+10%): favorable gross-to-net adjustments booked in Q4'24
  - Inventory (-2%): unfavorable impact driven by inventory stocking dynamics
- ROW YoY growth (+25%):
  - Demand (+27%): continued strong AMVUTTRA demand growth broadly across key international markets more than offsetting ONPATTRO decrease due to cannibalization
  - Other (-2%): primarily due to unfavorable price / GTN impacts in Europe, partially offset by positive stocking dynamics and timing of orders in partner markets
- Minimal (+1%) 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 2023 – see the Financial Summary slide for more information.

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2025 TTR Franchise Guidance

2025 Guidance

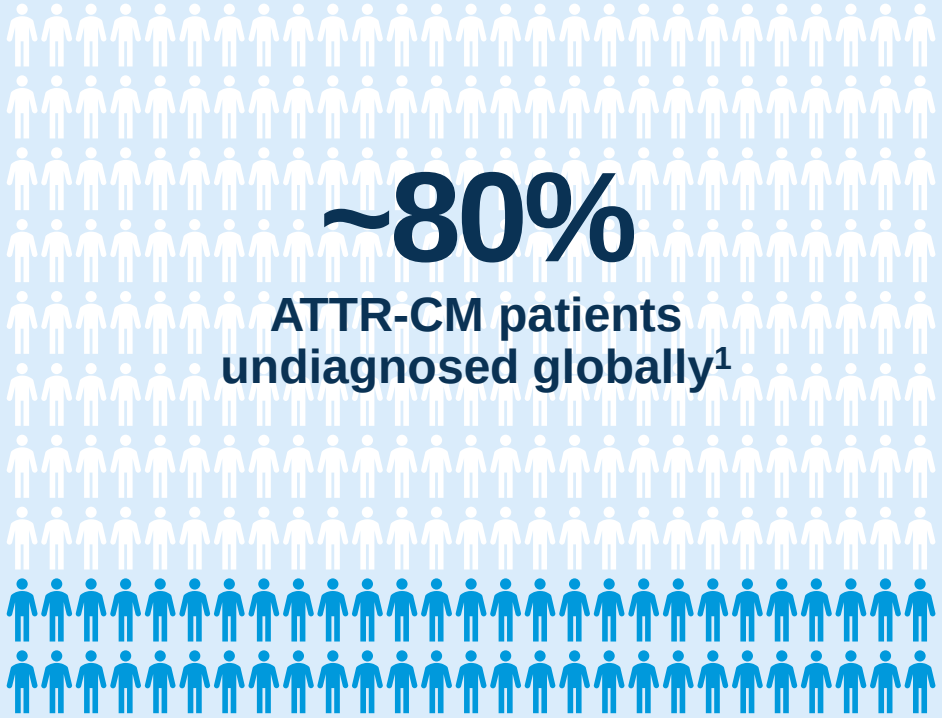
$1,600 to $1,725 Million

Total TTR Net Product Revenues (PN & CM*)
(ONPATTRO, AMVUTTRA)

* Guidance assumes FDA approval of the sNDA for vutrisiran for the treatment of adults with ATTR amyloidosis with cardiomyopathy by the March 23, 2025 PDUFA target action date.

Disrupting an Expanding Growth Market

Significant Unmet Patient Need



Highly Differentiated AMVUTTRA Value Proposition

- **RAPID KNOCKDOWN** of TTR works upstream, at the source
- **36% RRR** in all-cause mortality in contemporary treatment setting
- **Early & consistent** preservation of function and QoL
- Only **4** doses per year

[1] Information based on Alnylam modeling data

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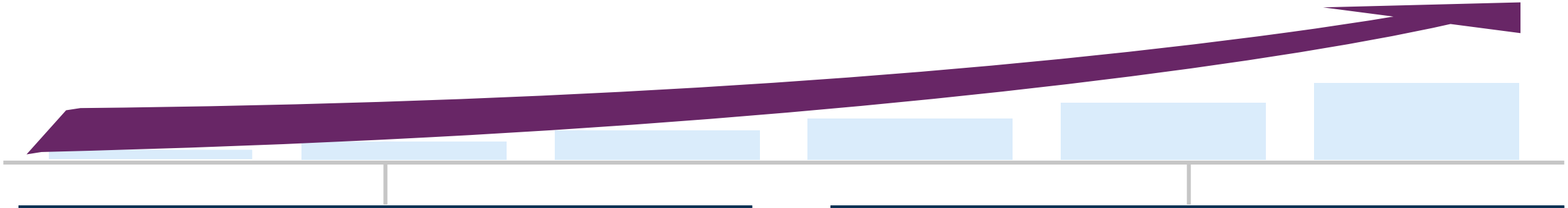
Approaching Launch with Durable Success in Mind



Pre-Launch Preparation
(Ongoing)

Optimizing access pathways at ~170 priority health systems (label contingent)

Bolstering a broad ecosystem of alternative sites of care

Scaled up field teams across commercial and medical

Post Approval
(Late Mar – Dec'25)

Securing **health systems formulary approval**

Finalizing VBAs for ATTR-CM

Disciplined and compliant go-to-market execution upon approval

Communicating Progress

PDUFA, US Launch

Final Label & Launch Readiness Indicators

Q1’25 Earnings

Initial Customer Feedback

Q2’25 Earnings

Early Launch Indicators

Q3’25 Earnings

Customer Utilization

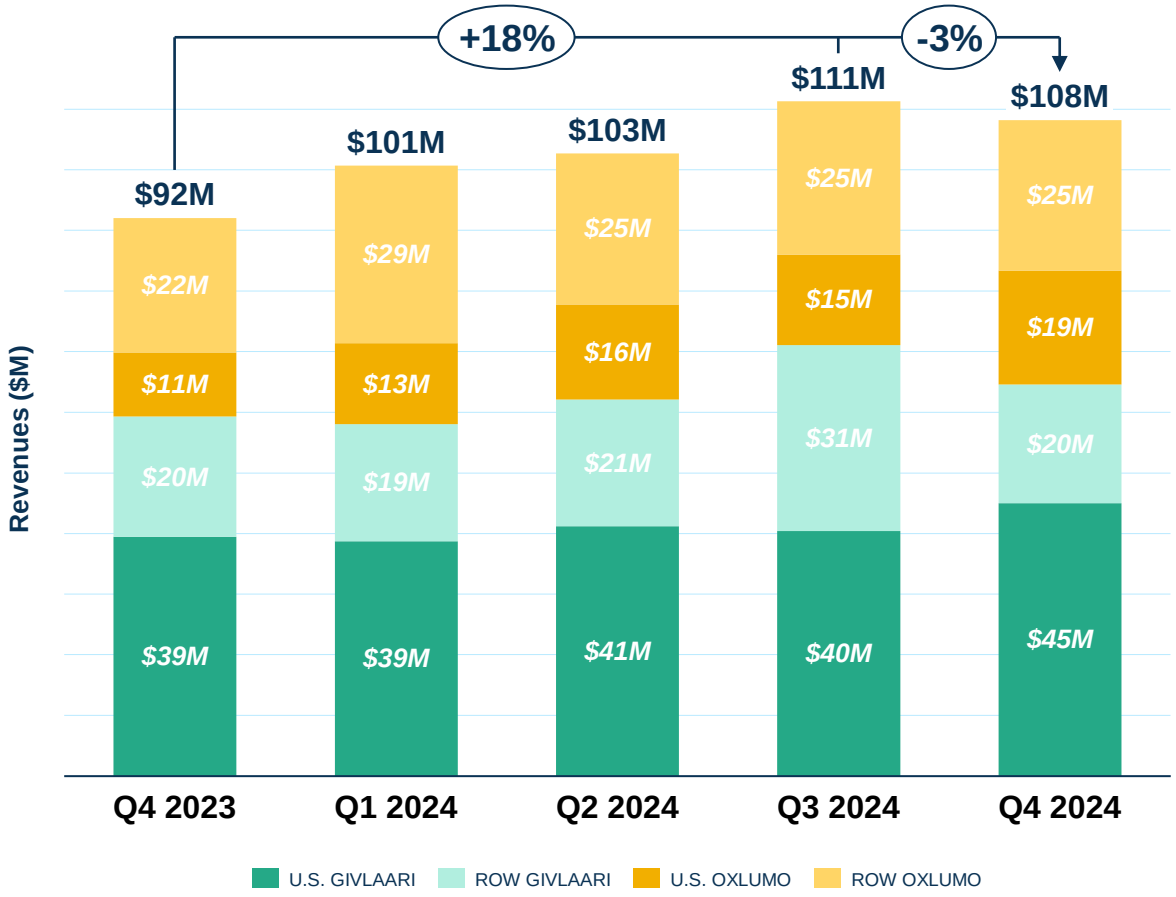
2025 Guidance

$1,600 to $1,725 Million

Total TTR Net Product Revenues

Rare Franchise Update: Q4 2024

$108M
Total Rare
Global Q4 2024
Net Product Revenues



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

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

Q4 Rare Franchise Highlights

	YoY % Growth	QoQ % Growth
GIVLAARI	9%	-9%
OXLUMO	33%	8%
Total Rare	18%	-3%

- GIVLAARI YoY growth of +9% driven by:
  - U.S. (+14%): primarily driven by demand growth (+10%) with additional growth favorably impacted by inventory stocking dynamics
  - ROW (-1%): demand growth in European markets offset by gross to net adjustments in partner markets.
- OXLUMO YoY growth of +33% driven by:
  - U.S. (+77%): primarily driven by strong demand growth (+47%) with additional growth driven by positive gross to net pricing adjustments in Q4'24 and inventory stocking dynamics
  - ROW (+12%): primarily driven by strong demand growth partially offset by gross to net price adjustments in Europe
- Minimal (+1%) FX impact (YoY CER[1] growth = 17%)

[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

Pipeline

Vutrisiran Regulatory Status

On Track Toward Early 2025 Launch

- ✓ Submitted sNDA within 90 days of topline results
- ✓ sNDA under Priority Review
- ✓ PDUFA date March 23, 2025

Pursuing Rapid Ex-U.S. Launches

- ✓ Parallel filings achieved in all major regions, including Europe and Japan
- ✓ Priority Review granted in Japan
- ✓ Launches in Germany and Japan expected 2H25

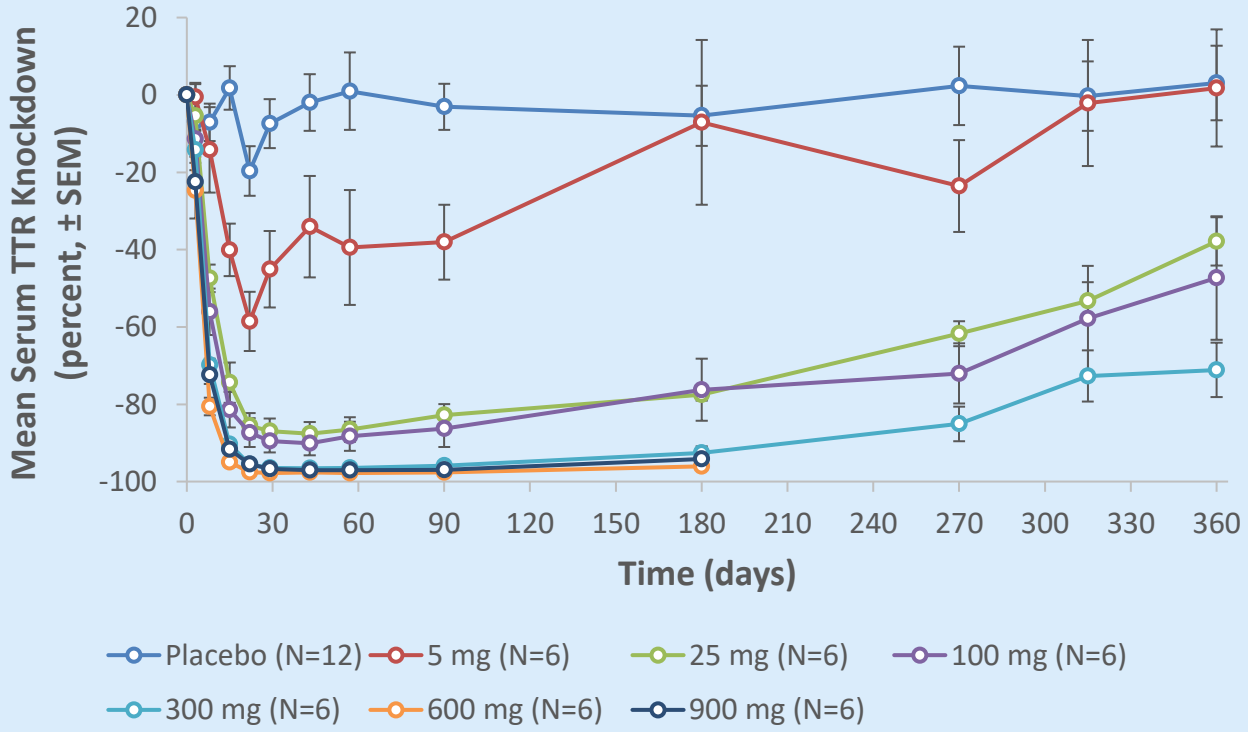
Nucresiran (ALN-TTRsc04) Offers Potential for Best-in-Class Profile

Continued Innovation to Secure Franchise Leadership

Emerging Profile

- ✓ **>95% TTR Knockdown**
- ✓ **Biannual or annual dosing** to optimize patient experience
- ✓ **Encouraging safety** profile to date

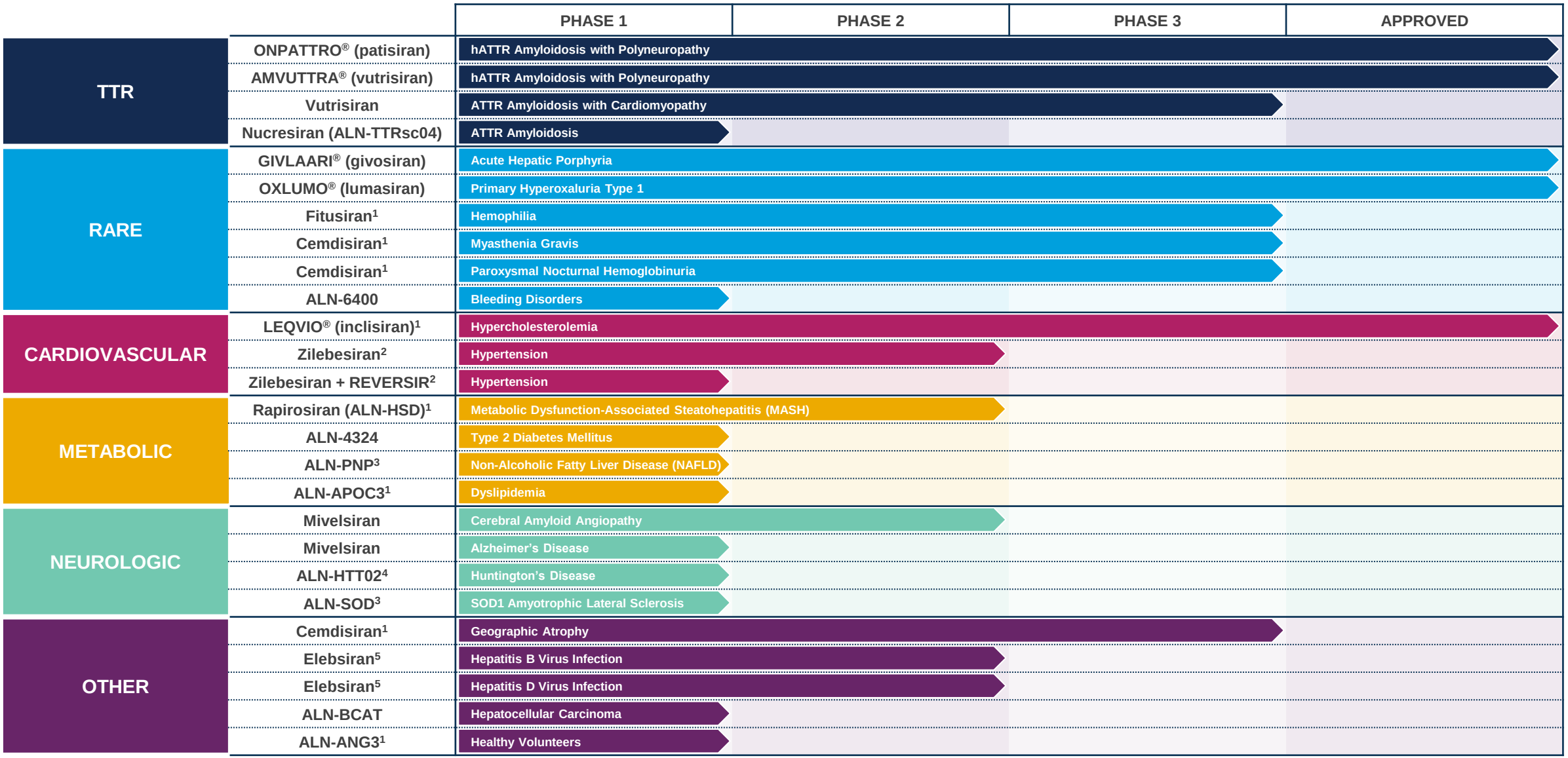
Encouraging Phase 1 Data[1]



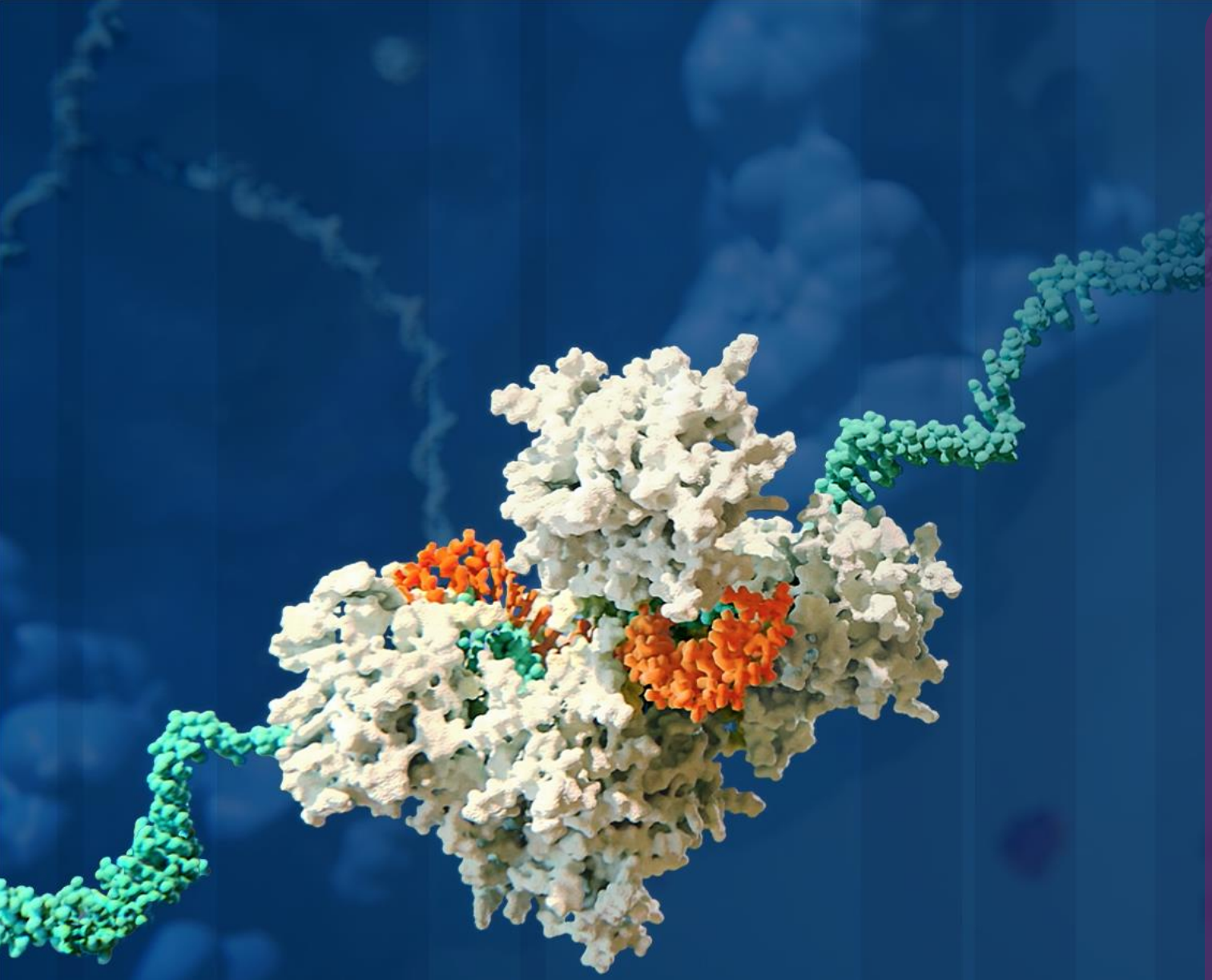
Phase 3 study initiation in ATTR-CM expected in first half of 2025

1. Murad et al., AHA 2024

Robust and High-Value Pipeline of RNAi Therapeutics



** Vutrisiran and fitusiran are under regulatory review. [1] Out-licensed with milestones and/or royalties; [2] Partnered, Alnylam-led development with U.S. profit split and milestones/royalties ex-U.S.; [3] Partner-led with profit split; [4] Partnered, Alnylam-led with profit split; [5] Partner-led with Alnylam option for profit split*



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R&D Day

February 25, 2025

9:00 am ET

This event will be webcast

Jeff Poulton

Chief Financial Officer

Financial Summary and Upcoming Milestones

Q4 and Full Year 2024 Financial Summary

Financial Results ($ millions)	Q4 2024	Q4 2023	Q4 Reported Growth %	Q4 CER Growth %[2]	FY 2024	FY 2023	FY24 Reported Growth %	FY24 CER Growth %[2]
Net Product Revenues	$451	$346	30%	29%	$1,646	$1,241	33%	33%
Net Revenues from Collaborations	$107	$76			$510	$546		
Royalty Revenues	$35	$17			$92	$41		
Total Revenues	$593	$440	35%	34%	$2,248	$1,828	23%	23%
Product Cost of Goods Sold	$103	$72			$307	$268		
Cost of Collaborations and Royalties	$0	$14			$17	$42		
Total Cost of Goods Sold	$103	$86			$323	$310		
Gross Margin	$490	$354			$1,925	$1,518		
Product Sales Gross Margin %[1]	*77%*	*79%*			*81%*	*78%*		
Non-GAAP R&D Expenses[2]	$260	$253	3%		$998	$907	10%	
Non-GAAP SG&A Expenses[2]	$244	$175	39%		$831	$671	24%	
Non-GAAP Operating (Loss) Income [2]	($14)	($74)			$95	($60)		

Financial Results ($ millions)	Dec 31, 2024	Dec 31, 2023
Cash & Investments[3]	$2,695	$2,439

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

[2] Non-GAAP R&D expenses, Non-GAAP SG&A expenses and Non-GAAP 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 Q4 2024 performance (restated using Q4 2023 exchange rates) to actual Q4 2023 reported performance and by comparing full-year 2024 performance (restated using 2023 exchange rates) to actual full-year 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 February 13, 2025, 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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2025 Full-Year Guidance

Item	FY 2025 Guidance	Key Assumptions
Total TTR Product Revenues (PN & CM) (ONPATTRO, AMVUTTRA)	$1,600 to $1,725 million	• AMVUTTRA-CM approval and launch in U.S. by FDA PDUFA date (March 23) • AMVUTTRA-CM approval and launch in Germany & Japan 2H 2025
Total Rare Product Revenues (GIVLAARI, OXLUMO)	$450 to $525 million	
Total Combined Net Product Revenues[1]	**$2,050 to $2,250 million**	
Net Product Revenues Growth vs. 2024 at Reported Fx Rates[1]	*25% to 37%*	• Uses December 31, 2024 Fx rates
Net Product Revenues Growth vs. 2024 at constant exchange rates (i.e., operational growth)[2]	*26% to 39%*	• Uses 2024 actual Fx rates
Net Revenues from Collaborations & Royalties	**$650 to $750 million**	• Achievement of $300M KARDIA-6 CVOT milestone with Roche • Fitusiran approval by FDA PDUFA date (March 28)
Non-GAAP Combined R&D and SG&A Expenses[3]	**$2,100 to $2,200 million**	
Non-GAAP Operating Income[3]	**Achieve profitability**	

[1] Our 2025 FY Guidance is based upon December 31, 2024 FX rates including 1 EUR = 1.04 USD and 1 USD = 157 JPY

[2] CER = constant exchange rate, representing growth calculated as if exchange rates had remained unchanged from those used in 2024. CER is a non-GAAP financial measure

[3] 2025 Non-GAAP Combined R&D and SG&A Expenses and Non-GAAP Operating Income guidance are non-GAAP financial measures that exclude from the corresponding GAAP measures stock-based compensation expense estimated at $270M - $330M.

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Alnylam 2025 Goals

onpattro (patisiran) / amvuttra (vutrisiran) / GIVLAARI (givosiran) / OXLUMO (lumasiran)		Combined Net Product Revenue Guidance $2,050M – $2,250M	**2025**
VUTRISIRAN	ATTR Amyloidosis	U.S. FDA Approval	**PDUFA date March 23, 2025**
		Additional Global Approvals (Japan, EU)	**Q2, Q3**
NUCRESIRAN* **(ALN-TTRsc04)**	ATTR Amyloidosis	Initiate Phase 3 Study in ATTR-CM	**H1**
ZILEBESIRAN*	Hypertension	KARDIA-3 Phase 2 Results	**H2**
		Initiate Phase 3 CVOT	**H2**
MIVELSIRAN*	Cerebral Amyloid Angiopathy and Alzheimer's Disease	Interim Phase 1 Part B Data in EOAD	**H2**
		Initiate Phase 2 Study in AD	**H2**
ALN-6400*	Bleeding Disorders	Initiate Phase 2 Study	**H2**
ADDITIONAL PROGRAMS		File ≥4 New INDs	**2025**
KEY PARTNER-LED PROGRAM MILESTONES			
FITUSIRAN* (Sanofi)	Hemophilia	U.S. FDA Approval	**PDUFA date March 28, 2025**
ELEBSIRAN* (Vir)	Chronic HBV/HDV	Initiate Phase 3 study in HDV	**H1**
		Phase 2 HBV Functional Cure Results	**Q2**
CEMDISIRAN* (Regeneron)	Complement-Mediated Diseases	Phase 3 MG Results	**H2**

** Not approved for any indication and conclusions regarding the safety or effectiveness of these drugs have not been established.*
EOAD = Early Onset Alzheimer's Disease; MG = Myasthenia Gravis

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Q4 and Full Year 2024 Financial Results

Q&A Session


Silence disease
Amplify life™
Alnylam®

Q4 and Full Year 2024 Financial Results

Appendix

Alnylam Pharmaceuticals, Inc.

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

	Three Months Ended December 31,		Twelve Months Ended December 31,	
	2024	**2023**	**2024**	**2023**
Reconciliation of GAAP to Non-GAAP research and development:				
GAAP Research and development	$ 300,169	$ 272,141	$ 1,126,232	$ 1,004,415
Less: Stock-based compensation expenses	(40,625)	(19,085)	(127,749)	(97,273)
Non-GAAP Research and development	$ 259,544	$ 253,056	$ 998,483	$ 907,142
Reconciliation of GAAP to Non-GAAP selling, general and administrative:				
GAAP Selling, general and administrative	$ 295,339	$ 198,123	$ 975,526	$ 795,646
Less: Stock-based compensation expenses	(51,020)	(22,909)	(144,335)	(124,407)
Non-GAAP Selling, general and administrative	$ 244,319	$ 175,214	$ 831,191	$ 671,239
Reconciliation of GAAP to Non-GAAP operating loss:				
GAAP operating loss	$ (105,159)	$ (116,404)	$ (176,885)	$ (282,175)
Add: Stock-based compensation expenses	91,645	41,994	272,084	221,680
Non-GAAP Operating (loss) income	$ (13,514)	$ (74,410)	$ 95,199	$ (60,495)

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

Alnylam Pharmaceuticals, Inc.

Reconciliation of Product Revenue and Growth at Constant Currency

	December 31, 2024	
	Three Months Ended	Twelve Months Ended
Total TTR net product revenue growth, as reported	35 %	34 %
Add: Impact of foreign currency translation	(1)	—
Total TTR net product revenue growth at constant currency	34 %	34 %
Total Rare net product revenue growth, as reported	18 %	29 %
Add: Impact of foreign currency translation	(1)	(1)
Total Rare net product revenue growth at constant currency	17 %	28 %
Total net product revenue growth, as reported	30 %	33 %
Add: Impact of foreign currency translation	(1)	—
Total net product revenue growth at constant currency	29 %	33 %
Total revenue growth, as reported	35 %	23 %
Add: Impact of foreign currency translation	(1)	—
Total revenue growth at constant currency	34 %	23 %

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