Third Quarter 2024 Financial Results

October 31, 2024

Agenda

Welcome

- Christine Lindenboom
  Chief Corporate Communications Officer

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 the potential for AMVUTTRA and Alnylam's broader TTR portfolio to serve as a flagship franchise that delivers durable growth and enables investment in R&D, new product development and portfolio diversification for the long term, and ushers in a new phase of growth for Alnylam; Alnylam's potential achievement of its "*Alnylam P^{5}x25*" goals by year end 2025, including its potential to achieve sustainable profitability in the near term, and its ability to become a top-tier biotech driven by a high yielding pipeline of first- and or best-in-class product candidates; the potential for Alnylam to have a robust, self-sustainable pipeline that can deliver meaningful impact to patients across multiple disease areas; the potential for vutrisiran to obtain regulatory approval for the treatment of ATTR amyloidosis with cardiomyopathy; the significant growth opportunity for ONPATTRO and AMVUTTRA in ATTR amyloidosis with polyneuropathy; the potential for Alnylam's RNAi platform to rely on the delivery of siRNA in organs beyond the liver, to address the high unmet need that exists for neurological diseases and to deliver multiple, high-impact new approaches for neurological diseases; the potential for mivelsiran to enable natural clearance of amyloid deposition and to slow, halt or improve the clinical manifestations of Alzheimer's Disease and Cerebral Amyloid Angiopathy; the potential for Alnylam to file INDs for a certain number of programs by the end of 2025; Alnylam's plans to share a Phase 3 development plan for ALN-TTRsc04 in the first quarter of 2025 and to initiate a Phase 2 study for mivelsiran in patients with Alzheimer's disease at or around year end 2024; 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 and the expected range of aggregate annual GAAP and non-GAAP R&D and SG&A expenses for 2024, 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.

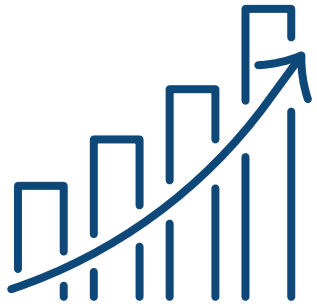
This presentation references generally accepted accounting principles (GAAP), and non-GAAP financial measures. The non-GAAP measures are not in accordance with, or an alternative to, GAAP, and may be different from non-GAAP financial measures used by other companies. Percentage changes in revenue growth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

Q3 2024 Highlights

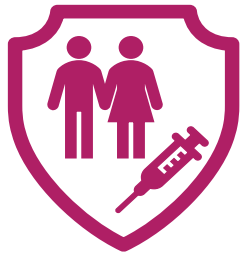


Strong Revenue Growth

- *$420 million net product revenues*
- *34% YoY growth[1]*

Positioned for TTR Leadership

- *Full HELIOS-B results presented*
- *U.S. and EU regulatory submissions completed*
- *Flagship franchise potential*



Steady Pipeline Progress

- *ALN-HTT02 Phase 1 initiation in Huntington's disease*
- *Mivelsiran Phase 1 multidose data in EOAD*

[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.

Alnylam®

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

Commercial Portfolio

Continued Strong Performance in Q3 2024

Overall portfolio

$420M	34%	2%
Combined Net Product Revenue	YoY growth[1] vs. Q3'23	QoQ growth[1] vs. Q2'24

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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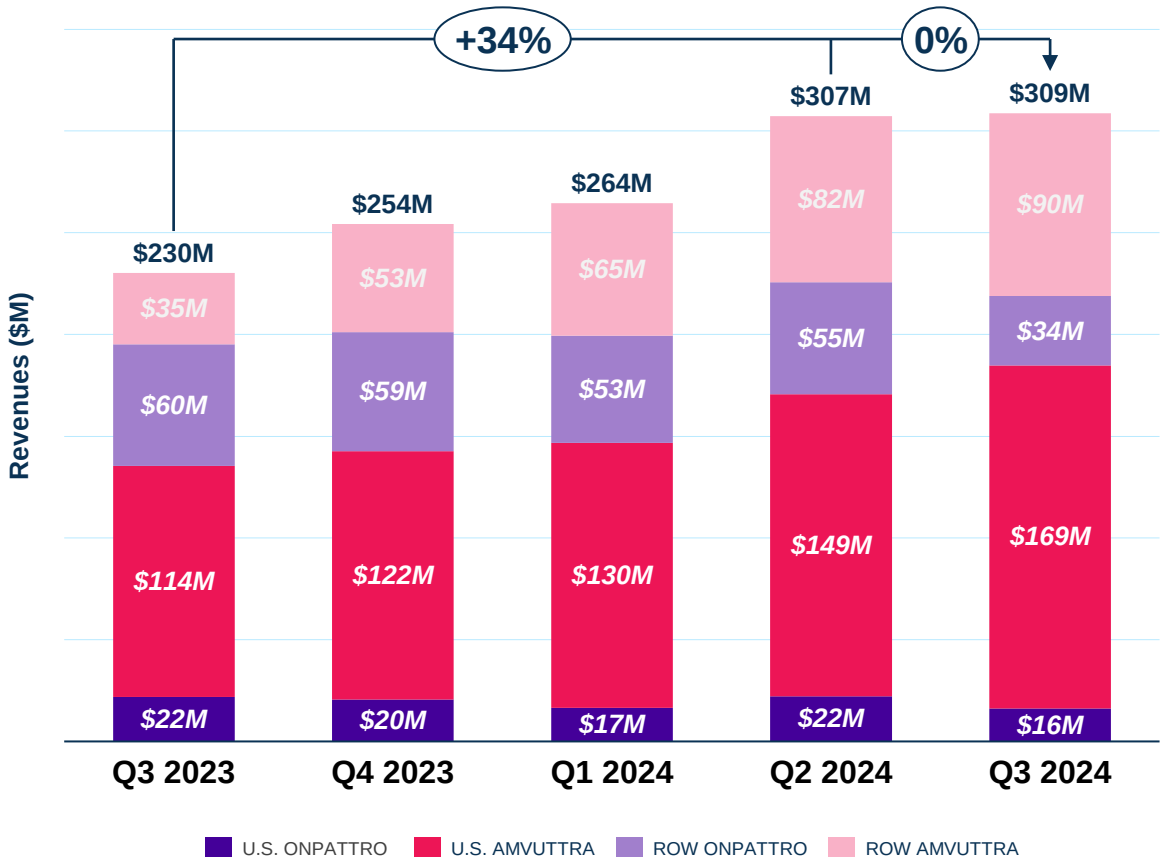
TTR Franchise Update: Q3 2024

$309M
Total TTR
Global Q3 2024
Net Product Revenues



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

amvuttra® (vutrisiran) injection 25 mg/0.5 mL

Q3 TTR Franchise Highlights

	YoY % Growth	QoQ % Growth
U.S.	37%	8%
ROW	31%	-9%
Global	34%	0%

- U.S. TTR franchise YoY growth of +37% driven by:
  - Demand (+31%): continued strong AMVUTTRA demand more than offsetting ONPATTRO decrease due to cannibalization
  - Other (+6%): favorable launch to date gross-to-net adjustment partially offset by negative inventory stocking impact
- ROW YoY growth (+31%):
  - Demand (+27%): continued strong AMVUTTRA demand growth broadly across key ROW markets more than offsetting ONPATTRO decrease due to cannibalization
  - Other (+4%): primarily due to favorable impact from stocking and timing of large orders in partner markets
- Modest FX impact (YoY CER[1] growth = 35%)

[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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We Are On a Path to Leadership in ATTR

Rare yet large, untapped and growing category with significant unmet need

AMVUTTRA is poised to become the standard of care for first line patients in ATTR-CM[1]

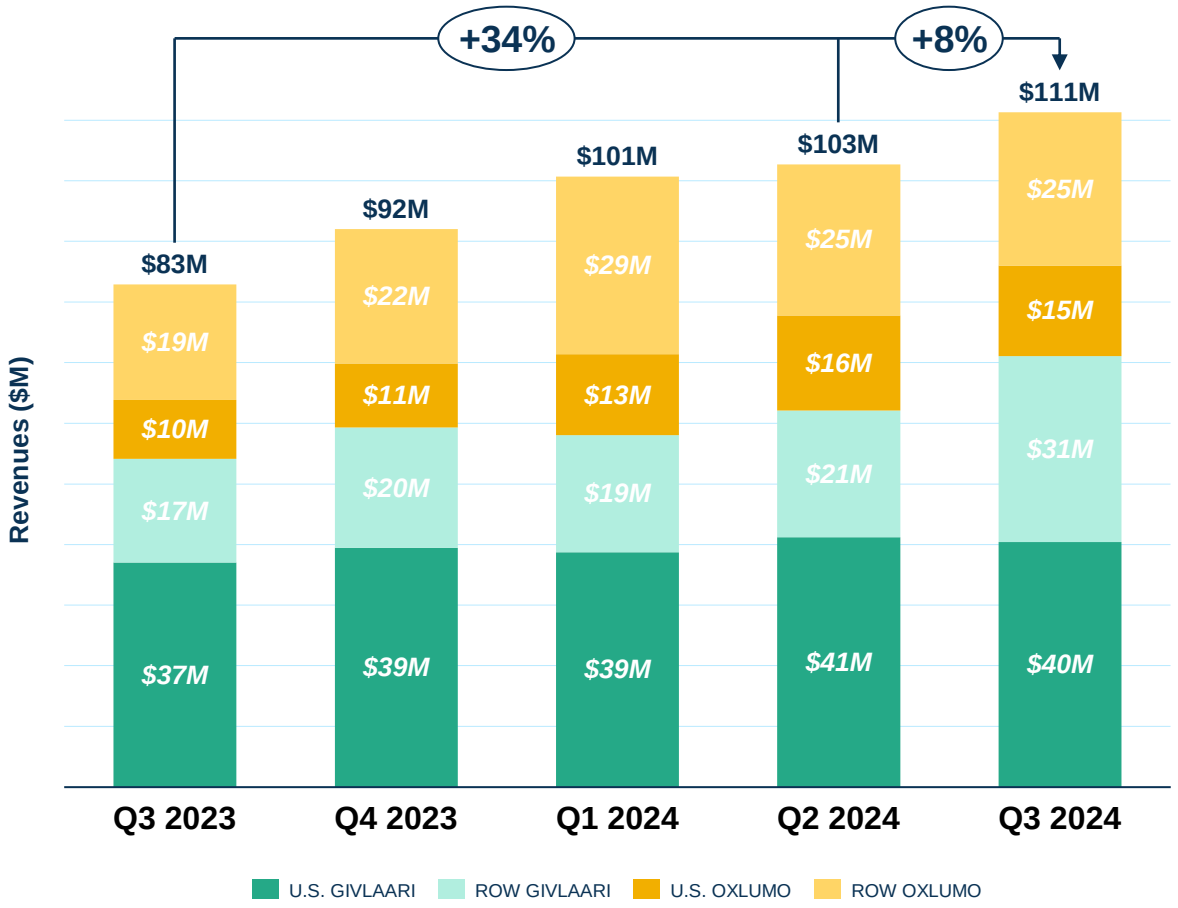
Our success and strong leadership in hATTR-PN position us to be highly competitive in ATTR-CM

We have a deep focus on ATTR and have scaled for a successful launch

[1] Assuming regulatory approval

Rare Franchise Update: Q3 2024

$111M
Total Rare
Global Q3 2024
Net Product Revenues



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

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

Q3 Rare Franchise Highlights

	YoY % Growth	QoQ % Growth
GIVLAARI	31%	14%
OXLUMO	40%	-1%
Total Rare	34%	8%

- GIVLAARI YoY growth of +31% driven by:
  - U.S. (+9%): primarily driven by demand growth (+6%) with additional growth from Q3 '24 price increase
  - ROW (+79%): primarily driven by timing of large orders in partner markets and continued demand growth across EU markets
- OXLUMO YoY growth of +40% driven by:
  - U.S. (+54%): driven by strong demand growth
  - ROW (+33%): primarily driven by strong demand growth across both EU and partner markets
- Modest FX impact (YoY CER[1] growth = 34%)

[1] CER = constant exchange rate, which is a non-GAAP financial measure that represents growth calculated as if exchange rates had remained unchanged from those used during 2023 – see the Financial Summary slide for more information.

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Pushkal Garg, M.D.

Chief Medical Officer

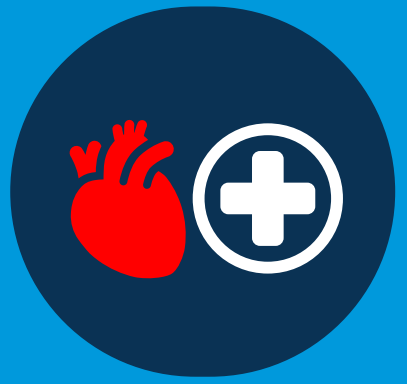
Alnylam Pipeline

HELIOS-B: Compelling Clinical Benefit for Vutrisiran in ATTR-CM

Observed Clinical Benefit Occurs Early and Cascades in Biologically Rational Manner

Rapid TTR Knockdown

Cardiac Biomarkers and Echocardiographic Improvements



Functional, Health Status, and QoL Benefit

Outcomes Benefit

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Vutrisiran Regulatory Filings Submitted in U.S. and EU

HELIOS·B

Priority Review Voucher to accelerate FDA review period

Additional global regulatory submissions – late 2024

Note: Vutrisiran is an investigational therapeutic in development for ATTR-CM, and efficacy and safety in this patient population has not been established or approved by any health authority

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Progress with Mivelsiran (ALN-APP)

Additional sAPPβ Reduction Seen Following Second Administration

Phase 1 (Early-onset Alzheimer's Disease)

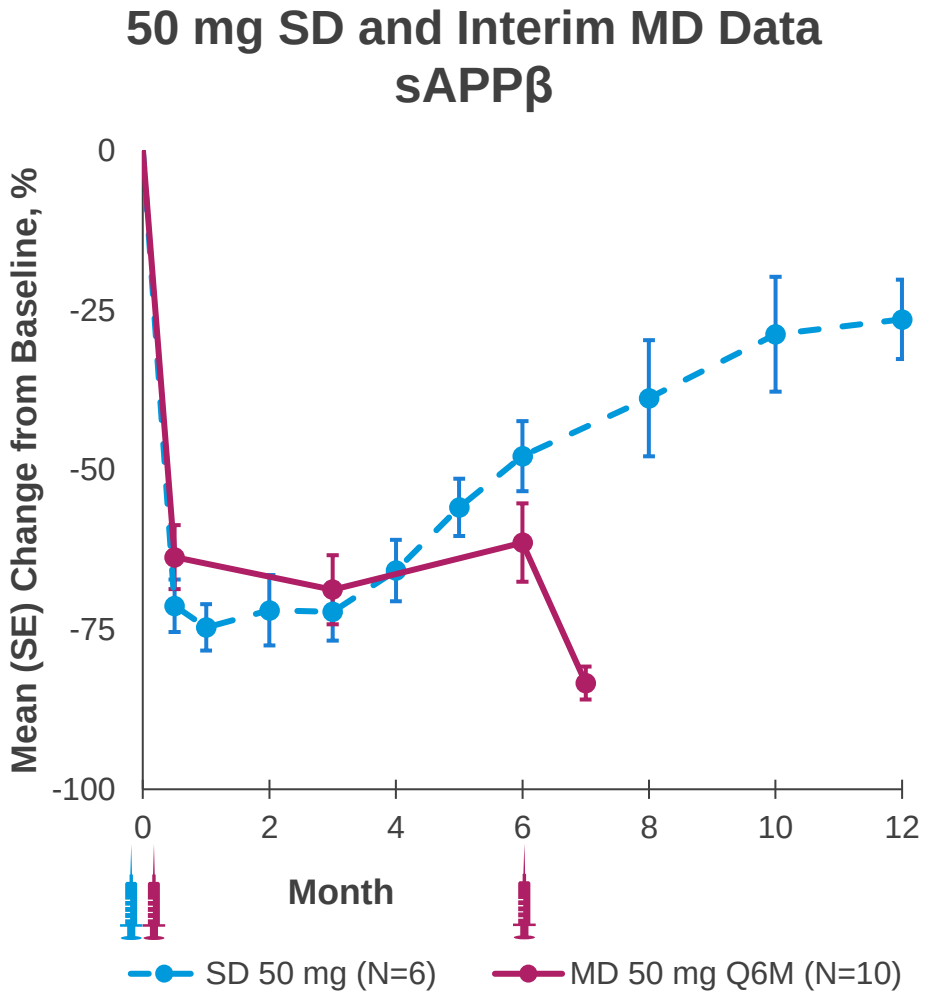
- Rapid, robust, and durable target engagement
  - Up to 92% reduction in sAPPβ at Month 7 with 50 mg Q6M
- Mivelsiran generally well-tolerated
  - No new safety concerns identified
  - No significant abnormalities on CSF safety labs and available data for exploratory biomarker NfL
- Escalation to doses higher than 75 mg in SAD; 3 cohorts now ongoing in MAD

Enrollment ongoing

Phase 2 Cerebral Amyloid Angiopathy

Study in development

Phase 2 Alzheimer's Disease



Data Transfer Date: October 15, 2024. N=5 at Month 2 and Month 4 to Month 12 for SD 50 mg cohort. N=8 at Month 3 and Month 7 for MD 50 mg Q6M cohort.

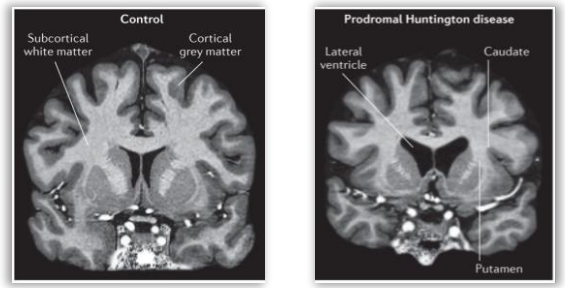
CSF, cerebrospinal fluid; MAD, multiple ascending dose; MD, multiple dose; NfL, neurofilament light chain; Q6M, every 6 months; sAPPβ, soluble amyloid precursor protein beta; SAD, single ascending dose; SD, single dose; SE, standard error.

Expanding Opportunities in CNS

Addressing Unmet Needs in Huntington's Disease

Progressive & Fatal Neurodegenerative Disease

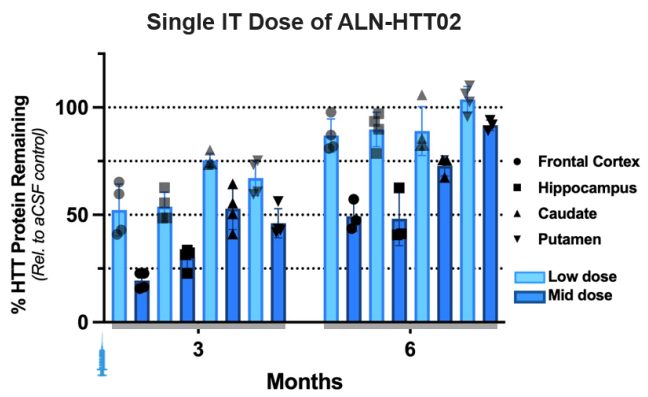
Control Brain

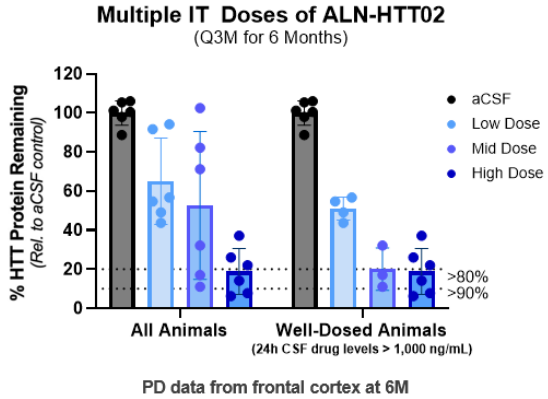


HD Brain

- Huntington's disease (HD) is progressive and fatal, driven by mutant Huntington (HTT)[1,3]
- Both full-length mutant HTT and shorter exon 1 splice isoforms likely contribute to disease pathology[2]
- Investigative HTT-lowering approaches may offer potential to alter the course of HD progression[1,4]

Broad CNS Distribution and Durable HTT-Lowering in NHP[5]





- Widespread distribution across CNS regions
- Durable HTT-lowering, supporting infrequent dosing in the clinic
- Multiple doses well tolerated in NHP
- Encouraging safety profile through 6 months
  - No in-life neurological abnormalities; no elevations in CSF NfL; no elevations in CSF total protein; no adverse microscopic findings

Phase 1 study initiated

[1] Tabrizi SJ, et al. Lancet Neurol. 2022;21(7):645-658. [2] Sampaio C. Parkinsonism Relat Disord. 2024;122:106049. [3] Bates GP, et al. Nat Rev Dis Primers. 2015;1:15005. [4] Ferguson MW, et al. J Cent Nerv Syst Dis. 2022;14:11795735221092517.
[5] Cantley W, et al. Poster Presentation at the European Huntington's Disease Network and Enroll-HD 2024 Meeting. September 12-14, 2024. Strasbourg, France.

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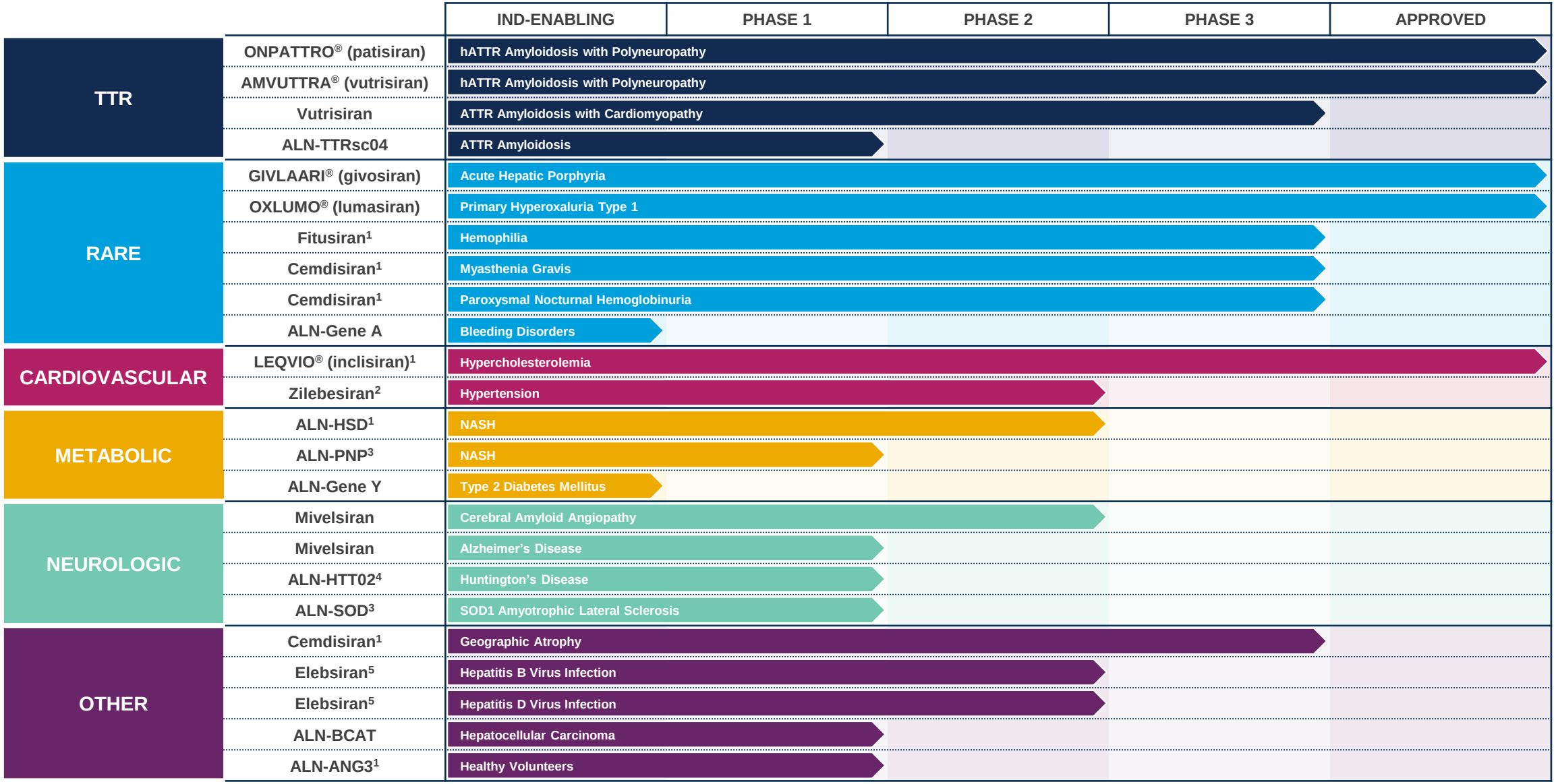
Advancing a Robust and High-Yielding Pipeline of RNAi Therapeutics

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

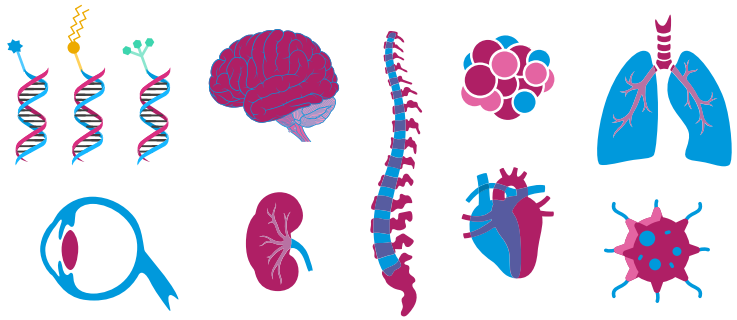


[1] Out-licensed with milestones and/or royalties; [2] Partnered, Alnylam-led development with U.S. profit split and milestones/royalties ex-U.S.; [3] Partner-led with profit split; [4] Partnered, Alnylam-led with profit split; [5] Partner-led with Alnylam option for profit split

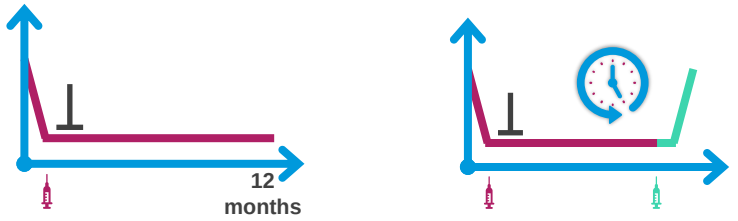
Multiple Sources of Sustainable Innovation Drive Robust Pipeline

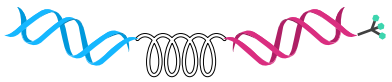
Targeting Nine Alnylam-Led INDs Across Four Tissues by End of 2025

Extrahepatic Delivery



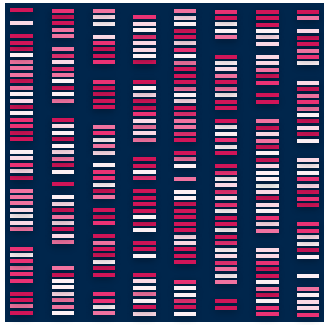
Platform Designs





GEMINI™

Human Genetics

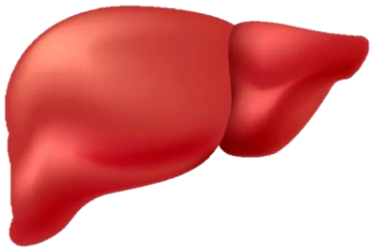


+ Our Future Health

discoverme

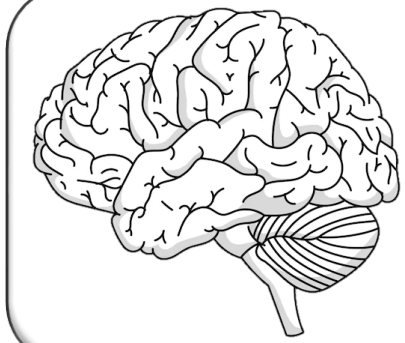
biobank uk

By End of 2025



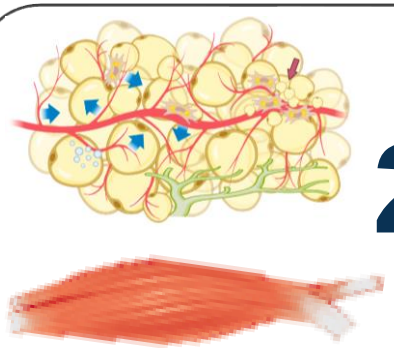
5 new **liver** INDs

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

Q3 2024 Financial Summary

Financial Results ($ millions)	Q3 2024	Q3 2023	Q3 Reported Growth %	Q3 CER Growth %[2]
Net Product Revenues	$420	$313	34%	35%
Net Revenues from Collaborations	$57	$427		
Royalty Revenues	$23	$10		
Total Revenues	$501	$751	-33%	-33%
Product Cost of Goods Sold	$82	$79		
Cost of Collaborations and Royalties	$4	$5		
Total Cost of Goods Sold	$86	$84		
Gross Margin	$415	$666		
Product Sales Gross Margin %[1]	80%	75%		
Non-GAAP R&D Expenses[2]	$251	$224	12%	
Non-GAAP SG&A Expenses[2]	$195	$164	19%	
Non-GAAP Operating Income / (Loss) [2]	($31)	$278		

Financial Results ($ millions)	Sep 30, 2024	Dec 31, 2023
Cash & Investments[3]	$2,780	$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 loss are non-GAAP financial measures that exclude from the corresponding GAAP measures costs related to stock-based compensation expense. CER growth rates represent growth at Constant Exchange Rates, a non-GAAP financial measure determined by comparing Q3 2024 performance (restated using Q3 2023 exchange rates) to actual Q3 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 October 31, 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 Reiterated Full Year Guidance

	FY 2024 Guidance	Key Assumptions
Net Product Revenue[1] ONPATTRO, AMVUTTRA, GIVLAARI, OXLUMO	$1,575M - $1,650M	• Uses June 30, 2024 FX rates
Net Product Revenue Growth vs. 2023 at reported Fx rates[1]	*27% to 33%*	• Uses June 30, 2024 FX rates
Net Product Revenue Growth vs. 2023 at constant exchange rates (i.e., operational growth)[2]	*28% to 34%*	• Uses 2023 actual FX rates
Net Revenues from Collaborations & Royalties	$575M - $650M	
Non-GAAP Combined R&D and SG&A Expenses[3]	$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 October 31, 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 October 31, 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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Q3 2024 Financial Results

Q&A Session

Thank You!

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Q3 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	
	September 30, 2024	**September 30, 2023**
Reconciliation of GAAP to Non-GAAP Research and development:		
GAAP Research and development	$ 270,926	$ 253,179
Less: Stock-based compensation expenses	(19,794)	(29,155)
Non-GAAP Research and development	$ 251,132	$ 224,024
Reconciliation of GAAP to Non-GAAP Selling, general and administrative:		
GAAP Selling, general and administrative	$ 220,993	$ 199,175
Less: Stock-based compensation expenses	(26,010)	(34,782)
Non-GAAP Selling, general and administrative	$ 194,983	$ 164,393
Reconciliation of GAAP to Non-GAAP Operating (loss) income:		
GAAP Operating (loss) income	$ (76,905)	$ 213,867
Add: Stock-based compensation expenses	45,804	63,937
Non-GAAP Operating (loss) income	$ (31,101)	$ 277,804

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

Alnylam Pharmaceuticals, Inc.

Reconciliation of Revenue and Growth at Constant Currency

	September 30, 2024 Three Months Ended
Total TTR net product revenue growth, as reported	34 %
Add: Impact of foreign currency translation	1
Total TTR net product revenue growth at constant currency	35 %
Total Rare net product revenue growth, as reported	34 %
Add: Impact of foreign currency translation	—
Total Rare net product revenue growth at constant currency	34 %
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	(33)%
Add: Impact of foreign currency translation	—
Total revenue growth at constant currency	(33)%

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