First Quarter 2024 Financial Results

May 2, 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 top-tier biotech company, the potential for Alnylam to identify new potential drug development candidates and advance its research and development programs, Alnylam's ability to obtain approval for new commercial products or additional approved indications for its existing commercial products, 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, the expected timing of topline data from the HELIOS-B Phase 3 clinical study, whether the HELIOS-B Phase 3 clinical study will deliver positive results and the potential of AMVUTTRA to have a market leading profile, including an impactful clinical profile, for the treatment of ATTR cardiomyopathy if approved, and the planned achievement of 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 ALN-APP; 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; the direct or indirect impact of the COVID-19 global pandemic or any future pandemic on Alnylam's business, results of operations and financial condition; 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.

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Yvonne Greenstreet, MBChB, MBA

Chief Executive Officer

Overview

Ambitious Five-Year Strategy to Drive Growth

Alnylam P5x25

Patients: Over 0.5 million on Alnylam RNAi therapeutics globally

Products: 6+ marketed products in rare and prevalent diseases

Pipeline: Over 20 clinical programs, with 10+ in late stages and 4+ INDs per year

Performance: ≥40% revenue CAGR through YE 2025

Profitability: Achieve sustainable non-GAAP profitability within period

Tolga Tanguler

Chief Commercial Officer

Commercial Highlights

Commercial Portfolio Strong Start into 2024

Overall portfolio

$365M
Combined Net Product Revenue

32%
YoY growth[1] vs. Q1.23

5%
QoQ growth[1] vs. Q4.23

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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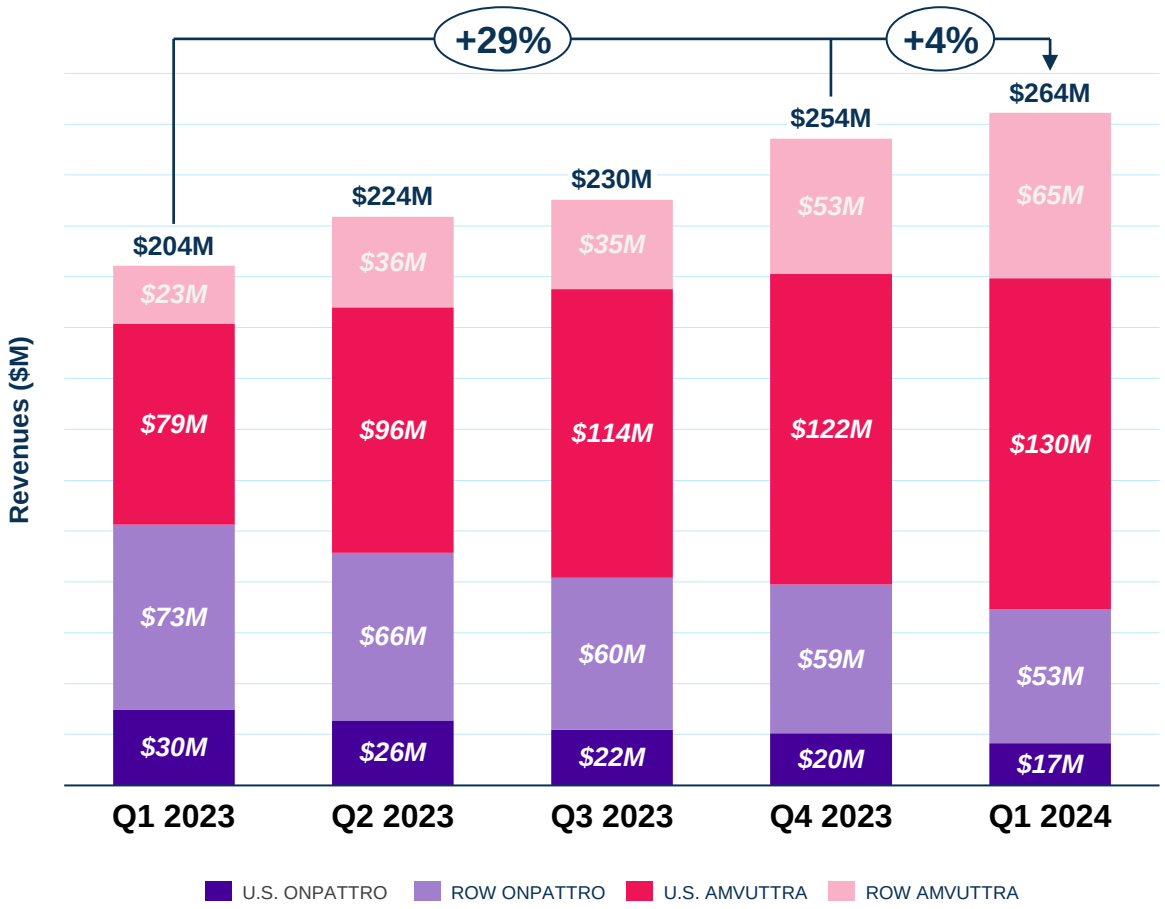
TTR Franchise Update: Q1 2024

$264M
Total TTR
Global Q1 2024
Net Product Revenues



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

amvuttra® (vutrisiran) injection 25 mg/0.5 mL

Q1 TTR Franchise Highlights

	YoY % Growth	QoQ % Growth
U.S.	35%	3%
ROW	23%	5%
Global	29%	4%

- U.S. TTR franchise YoY growth +35% driven by:
  - Demand (+39%): continued strong AMVUTTRA demand more than offsetting decrease in ONPATTRO due to cannibalization
  - Inventory (-4%): driven by lower AMVUTTRA and ONPATTRO channel inventory dynamics
- ROW YoY growth +23% driven by:
  - Demand growth in AMVUTTRA with favorable impacts in Italy and Spain following Q4'23 successful launches
  - Partially offset by negative price impacts primarily in Germany due to end of free pricing period for AMVUTTRA in Q2'23
- Modest FX impact (YoY CER[1] growth = 30%)

[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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AMVUTTRA is Clear Market Leader in Treatment of hATTR-PN

Awareness & Diagnosis

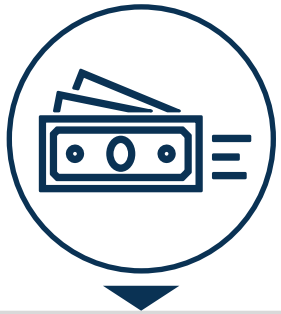
~80% of patients remain undiagnosed and/or untreated

Driving category growth

Treatment Choice

>50% growth in prescribers compared to Q1 2023

Flexibility to treat patients in hospital, at outpatient clinic, or at home*



Access

>99% of patients have confirmed access

~70% of patients have no out-of-pocket costs

Adherence & Compliance

>95% of patients comply with the AMVUTTRA dosing regimen and remain on therapy

hATTR: hereditary transthyretin-mediated; PN: polyneuropathy; *Individual patient coverage varies based on insurance plan

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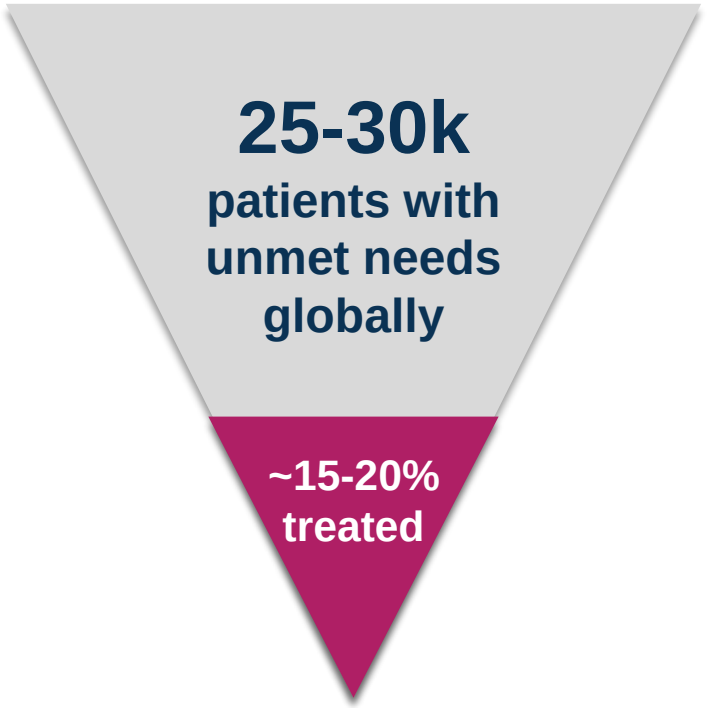
Significant Growth Opportunity in hATTR-PN

hATTR PN under treated and under diagnosed[1]



Winning product profile

- **Rapidly knocked down TTR** as early as **three weeks**, with a mean TTR knockdown of **88%** over 18 months[2]
- The only treatment than can **reverse the PN manifestations** of hATTR amyloidosis with **4 doses per year[2]**
- **Accessible and affordable** for most patients, regardless of insurance type

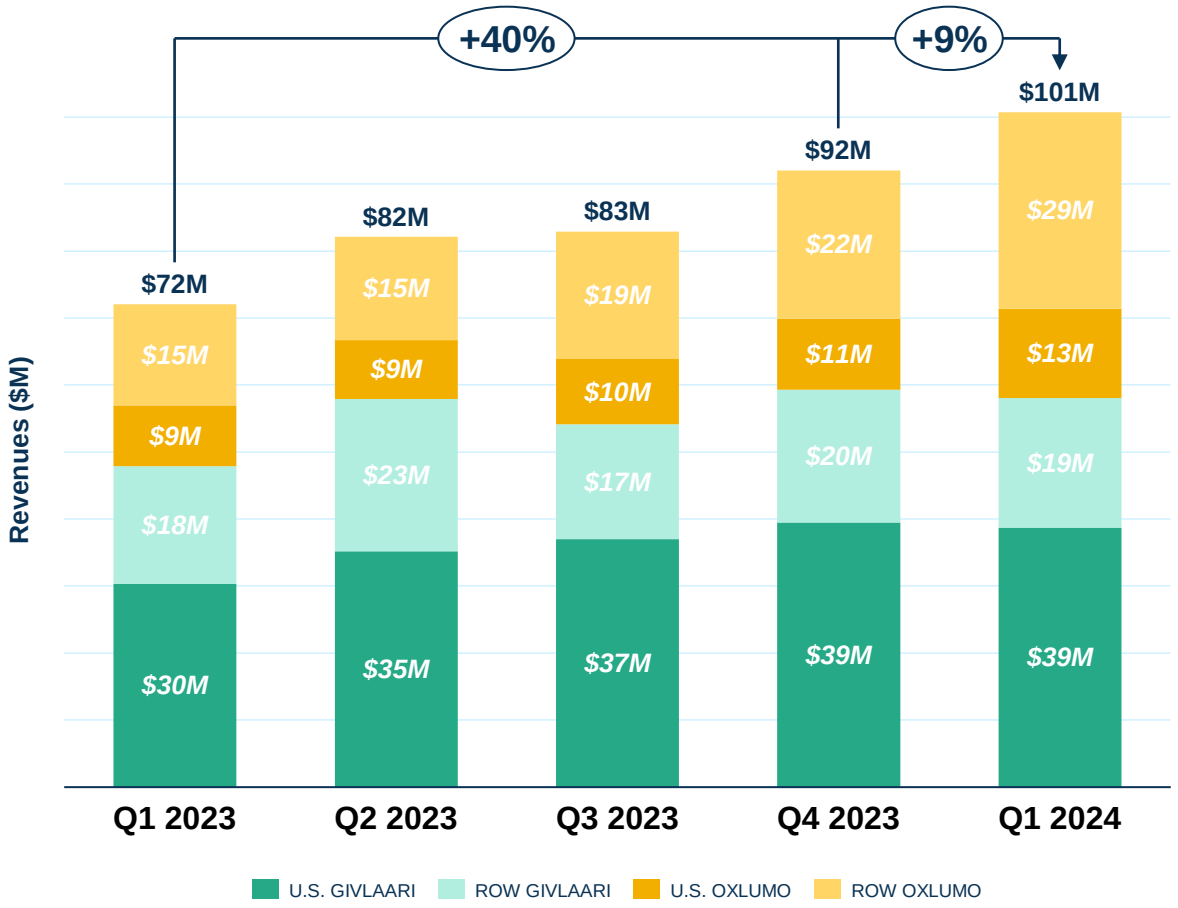
Expanding our reach

Launched patient DTC campaign to increase awareness of disease and benefits of AMVUTTRA

[1] Based on Alnylam estimates from interviews with key opinion leaders, THAOS registry, recent clinical trials and literature; [2] Adams, et al. Amyloid 2023.
hATTR: hereditary transthyretin-mediated; PN: polyneuropathy; TTR: transthyretin. DTC: Direct to Consumer
AMVUTTRA (vutrisiran) is approved in the U.S. for the treatment of adults with hATTR amyloidosis with polyneuropathy. For additional information about AMVUTTRA, including the risks of AMVUTTRA, see Full Prescribing Information.

Rare Franchise Update: Q1 2024

$101M
Total Rare
Global Q1 2024
Net Product Revenues



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

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

Q1 Rare Franchise Highlights

	YoY % Growth	QoQ % Growth
GIVLAARI	21%	-2%
OXLUMO	77%	30%
Total Rare	40%	9%

- GIVLAARI YoY growth +21% driven by:
  - U.S. (+28%): primarily due to demand growth and modest additional favorability from lower gross to net deductions
  - ROW (+10%): primarily due to demand growth partially offset by increased gross to net deductions
- OXLUMO YoY growth of +77% driven by:
  - U.S. (+47%): primarily due to demand growth and modest additional favorability from lower gross to net deductions
  - ROW (+94%): driven by strong demand, one-time positive gross to net adjustment, and timing of orders in partner markets
  - Given the nature of the Q1 ROW gross to net deductions and partner market favorability, we anticipate lower OXLUMO global sales in Q2
- Modest 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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Pushkal Garg, M.D.

Chief Medical Officer

Alnylam Pipeline

Vutrisiran HELIOS·B Phase 3 Study

Randomized, Double-Blind Outcomes Study in ATTR Amyloidosis Patients with Cardiomyopathy

N = 655

Patient Population

- ATTR amyloidosis; wild-type or any TTR mutation
- Confirmed cardiomyopathy and medical history of symptomatic heart failure
- NYHA ≤ III; minimum walk and NT-proBNP limits at baseline
- 40% of patients on tafamidis at baseline

1:1 RANDOMIZATION

Vutrisiran
SC q3M
25 mg

or

Placebo
SC q3M

Primary Endpoint

- Composite outcome of all-cause mortality and recurrent CV events, assessed when last patient reaches Month 33, in:
  - Overall population
  - Monotherapy population

Secondary Endpoints

- 6-MWT distance
- Kansas City Cardiomyopathy Questionnaire score
- All-cause mortality
- NYHA Class

Topline results expected **late June/early July 2024**

Assuming positive results,
sNDA submission expected **late 2024**

HELIOS·B

ClinicalTrials.gov Identifier: NCT04153149

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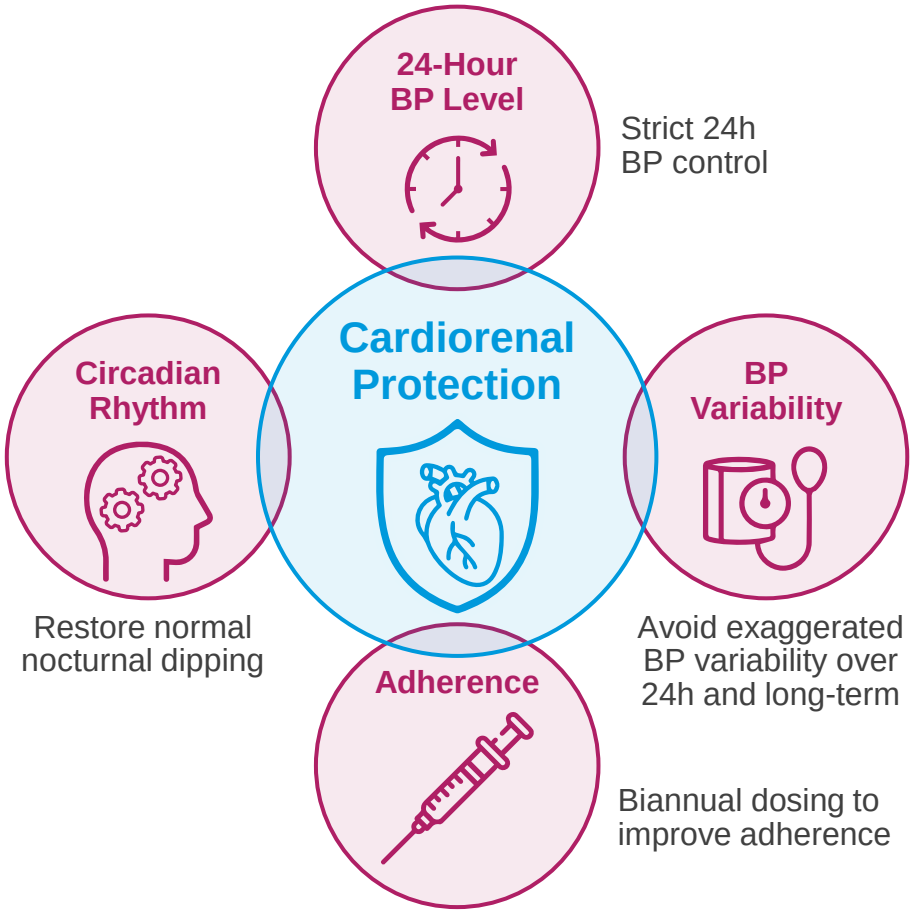
Uncontrolled Hypertension is a Global Health Crisis

Leading Preventable Risk Factor for Cardiovascular Morbidity and Mortality

- **~219MM** adults with primary hypertension[1]
- Hypertension is the **leading cause of cardiovascular morbidity and mortality in the world**[2,3]
- Up to **80%** have uncontrolled disease[4,5]
- **Variability in BP, lack of nighttime dipping, poor medication adherence** further exacerbate CV risk[6]

Targeting Tonic BP Control to Reduce Cardiovascular and Renal Risks



[1] Extrapolated for 7 major markets (7MM) based on proportion of US hypertension population with prior history of CVD or Framingham Risk Score of >10%, excluding patients with history of stroke and women of child-bearing potential; [2] Zhou B et al. Nat Rev Cardiol 2021;18:785–802; [3] Danaei G et al. PLoS Med 2009;6:e1000058; [4] Available from: www.who.int/news-room/fact-sheets/detail/hypertension (Accessed September 14, 2023); [5] Centers for Disease Control and Prevention. Estimated hypertension prevalence, treatment, and control among U.S. adults. 2022. Available from: https://millionhearts.hhs.gov/data-reports/hypertension-prevalence.html (Accessed September 14, 2023); [6] Ettehad D et al. Lancet 2006; 387: 957-67

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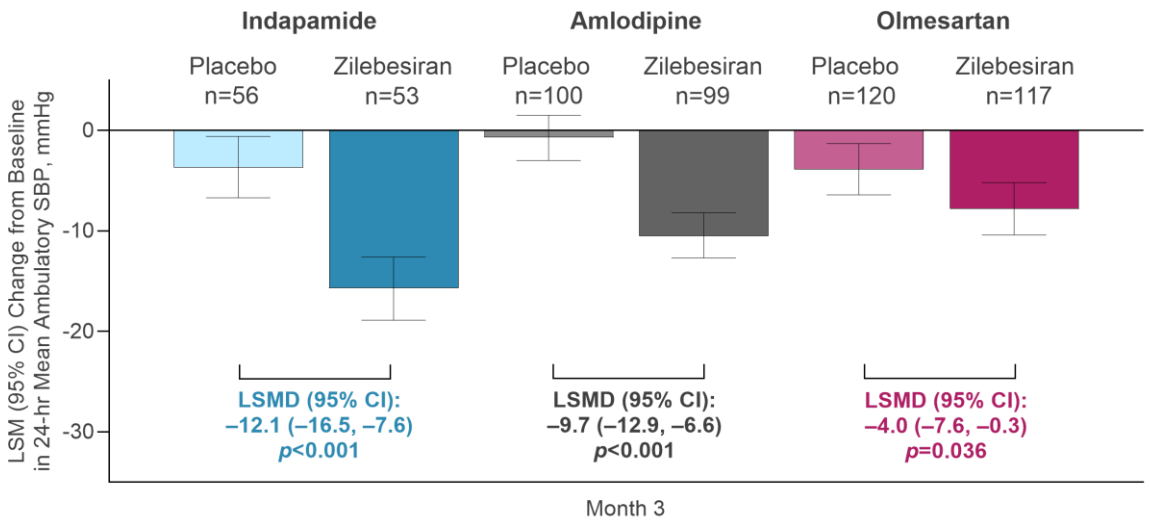
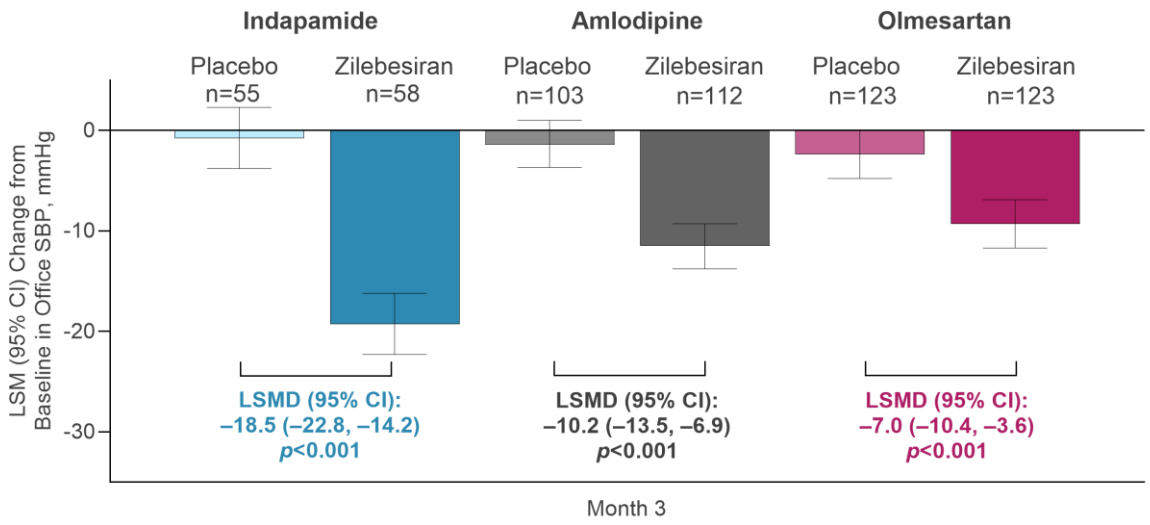
Zilebesiran Continues to Demonstrate Potential to Transform Treatment of Hypertension

KARDIA-2 Phase 2 Results: Blood Pressure Reduction as Add-On Therapy

Primary Endpoint: 24-hour Mean Ambulatory SBP Reduction at Month 3*



Secondary Endpoint: Office SBP Reduction at Month 3*



- Generally well tolerated
- Increased rate of mild hyperkalemia, hypotension, and eGFR decline >30%; most non-serious, transient, and resolved without intervention.

* Blood pressure assessed while patients were receiving or within 2 weeks of stopping any rescue medication is censored.

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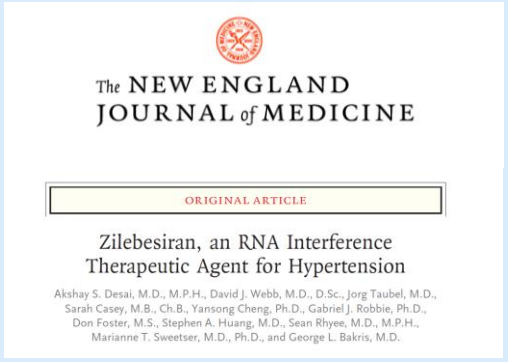
Zilebesiran Clinical Development Plan

Exploring Power of Tonic Blood Pressure Control to Improve Cardiovascular Outcomes

Phase 1

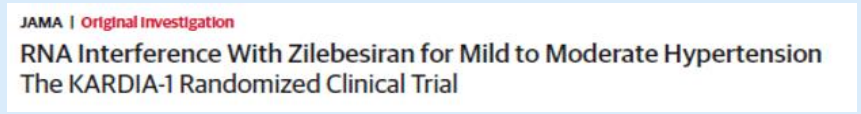
Zilebesiran safety, tolerability, and PK/PD in patients with mild-to-moderate hypertension[1]



Phase 2

KARDIA-1

Zilebesiran monotherapy in pts with mild-to-mod HTN[2]



KARDIA-2

Zilebesiran in combination with single antihypertensive in patients with mild-to-moderate hypertension[3]

Results Presented ACC April 7th, 2024

KARDIA-3

Zilebesiran in combination with ≥2 antihypertensives in high CV risk patients with uncontrolled hypertension

Initiated February 2024

Phase 3

Cardiovascular Outcomes Trial (CVOT)

Study in patients with uncontrolled hypertension at high CV risk, evaluating composite MACE endpoint

Launch with label to reduce cardiovascular morbidity and mortality

Expected ~2030

The safety and efficacy of zilebesiran have not been established or evaluated by the FDA, EMA or any other health authority. Launch assumes positive clinical trial results and regulatory approval. MACE, major adverse cardiovascular event; [1] Desai AS, et al. N Engl J Med. 2023;389:228-238; [2] Bakris GL, et al. JAMA. 2024;331(9):740–749; [3] Bakris et al. ACC Scientific Sessions 2024

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-SOD1‡
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® (patisiran) 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, 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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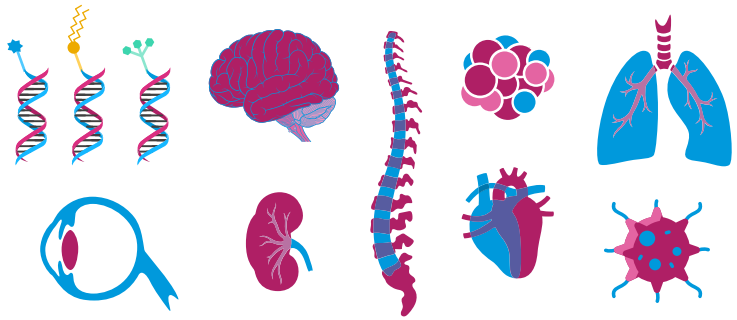
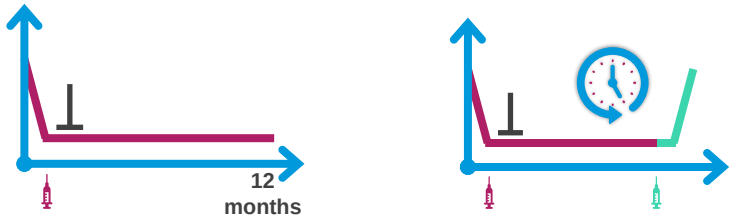
Multiple Sources of Sustainable Innovation Drive Robust Pipeline

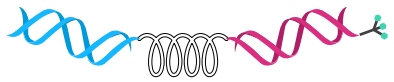
Targeting Nine Alnylam-Led INDs Across Four Tissues by End of 2025

Extrahepatic Delivery



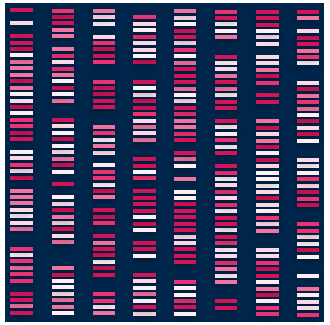
Platform Designs





GEMINI™

Human Genetics

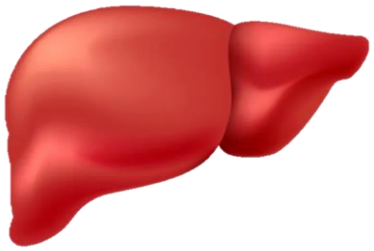


+ Our Future Health

discoverme

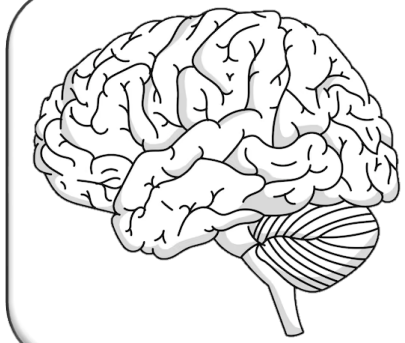
biobank uk

By End of 2025



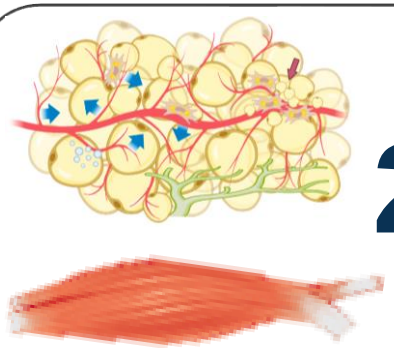
5 new **liver** INDs

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

Q1 2024 Financial Summary

Financial Results ($ millions)	Q1 2024	Q1 2023	Q1 Reported Growth %	Q1 CER Growth %[2]
Net Product Revenues	$365	$276	32%	32%
Net Revenues from Collaborations	$119	$36		
Royalty Revenues	$11	$7		
Total Revenues	$494	$319	55%	55%
Product Cost of Goods Sold	$55	$41		
Cost of Collaborations and Royalties	$11	$13		
Total Cost of Goods Sold	$66	$55		
Gross Margin	$428	$264		
Product Sales Gross Margin %[1]	*85%*	*85%*		
Non-GAAP R&D Expenses[2]	$242	$214	13%	
Non-GAAP SG&A Expenses[2]	$185	$160	15%	
Non-GAAP Operating Profit (Loss)[2]	$2	($110)		

Financial Results ($ millions)	Mar 31, 2024	Dec 31, 2023
Cash & Investments[3]	$2,371	$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 profit (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 Q1 2024 performance (restated using Q1 2023 exchange rates) to actual Q1 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 May 2, 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

	Guidance	Key Assumptions
Net Product Revenue[1] ONPATTRO, AMVUTTRA, GIVLAARI, OXLUMO	$1,400M to $1,500M	• Uses January 31, 2024 FX rates
Net Product Revenue Growth vs. 2023 at reported Fx rates[1]	*13% to 21%*	• Uses January 31, 2024 FX rates
Net Product Revenue Growth vs. 2023 at constant exchange rates (i.e., operational growth)[2]	*13% to 21%*	• Uses 2023 actual FX rates
Net Revenues from Collaborations & Royalties	$325M to $425M	
Non-GAAP Combined R&D and SG&A Expenses[3]	$1,675M to $1,775M	

[1] Our 2024 FY Guidance is based upon January 31, 2024 FX rates including 1 EUR = 1.08 USD and 1 USD = 147 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 May 2, 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 $1,400M – $1,500M*			●
VUTRISIRAN	ATTR Amyloidosis	HELIOS-B Topline Results (*late June/early July*)		●	
		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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Q1 2024 Financial Results

Q&A Session

Thank You!

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Q1 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	
	March 31, 2024	March 31, 2023
Reconciliation of GAAP to Non-GAAP Research and development:		
GAAP Research and development	$ 260,995	$ 230,569
Less: Stock-based compensation expenses	(19,215)	(16,232)
Non-GAAP Research and development	$ 241,780	$ 214,337
Reconciliation of GAAP to Non-GAAP Selling, general and administrative:		
GAAP Selling, general and administrative	$ 210,797	$ 183,659
Less: Stock-based compensation expenses	(26,132)	(23,715)
Non-GAAP Selling, general and administrative	$ 184,665	$ 159,944
Reconciliation of GAAP to Non-GAAP Operating gain (loss):		
GAAP Operating loss	$ (43,435)	$ (149,807)
Add: Stock-based compensation expenses	45,347	39,947
Non-GAAP Operating gain (loss)	$ 1,912	$ (109,860)

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 March 31, 2024
Total TTR net product revenue growth, as reported	29 %
Add: Impact of foreign currency translation	1
Total TTR net product revenue growth at constant currency	30 %
Total Rare net product revenue growth, as reported	40 %
Add: Impact of foreign currency translation	(1)
Total Rare net product revenue growth at constant currency	39 %
Total net product revenue growth, as reported	32 %
Add: Impact of foreign currency translation	—
Total net product revenue growth at constant currency	32 %
Total revenue growth, as reported	55 %
Add: Impact of foreign currency translation	—
Total revenue growth at constant currency	55 %

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