First Quarter 2025 Financial Results

May 1, 2025

Agenda

Welcome

- **Christine Lindenboom**
  Chief Corporate Communications Officer

Overview

- **Yvonne Greenstreet, M.D., 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 Alnylam to experience sustainable growth and value creation in 2025 and for years to come; the future potential of Alnylam's TTR franchise and the potential for Alnylam to be the leader in TTR; Alnylam's aspiration to become a unique, top-tier biotech company delivering sustainable innovation to patients for many years to come and the planned achievement of its "*Alnylam P^{5}x25*" goals by the end of 2025, including to achieve sustainable non-GAAP profitability beginning in 2025; the potential success of Alnylam's launch of AMVUTTRA in ATTR-CM, including Alnylam's ability to establish access and health systems formulary coverage for AMVUTTRA in ATTR-CM and for HCPs to prescribe AMVUTTRA for ATTR-CM; the potential size of the addressable patient population for ATTR-CM and the size of Alnylam's opportunity in ATTR-CM; the potential receipt of additional regulatory approvals for AMVUTTRA in ATTR-CM and the timing of any such regulatory approvals; the potential for RNAi therapeutics to have a bright future across of broad range of diseases; the potential for Alnylam to identify new potential drug development candidates and advance its research and development programs, including zilebesiran and nucresiran, and the timing of the initiation and readout of clinical trials of any of Alnylam's product candidates; the potential success of any clinical trials of nucresiran and the potential for nucresiran to receive regulatory approval(s) and/or launch in any indication; Alnylam's ability to achieve delivery of RNAi therapeutics to every major tissue by 2030; the potential impact of tariffs now in place and any future tariffs on Alnylam's business and Alnylam's ability to absorb the impact of such tariffs; the potential impact of other policies, including FDA personnel reorganization and other biotech industry initiatives, on Alnylam's business; and Alnylam's projected commercial and financial performance, including the expected range of TTR, Rare and 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 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 2024 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.

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, is a non-GAAP financial measure which is 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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Overview

Yvonne Greenstreet, M.D., MBA

Chief Executive Officer

Alnylam®

Strong Q1 Financial Results and Significant Advancement Toward Our Goal of Becoming the Global TTR Leader

Commercial Execution

Combined net product revenues:
$469 million
(28% growth YoY)

Primarily driven by U.S. TTR (+45% growth YoY)

Portfolio Advancement

Regulatory approvals of **AMVUTTRA®** (vutrisiran) in ATTR-CM and **Qfitlia™** for Hemophilia A or B[1]

amvuttra (vutrisiran) injection 25 mg/0.5 mL

Qfitlia (fitusiran) injection 50 mg/0.5 mL

Reiterated Guidance

On track to meet 2025 financial guidance, including:

Combined net product revenues of **$2,050 million to $2,250 million**

Achieve non-GAAP **profitability**

[1] *Qfitlia partnered with Sanofi*

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Positioned for Success Through 2025 and Beyond

Best-in-Class Team + Award-Winning Culture

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Continued 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

Commercial Highlights

Tolga Tanguler
Chief Commercial Officer

Alnylam Continued To Deliver Strong Performance in Q1’25

Growth Achieved Across Franchises; Primarily Driven by U.S. TTR Franchise

Q1 2025 Overall Portfolio

$469 M
Combined Net Product Revenues

+28%
YoY growth[1]
vs. Q1’24

+4%
QoQ growth[1]
vs. Q4’24

TTR Franchise

amvuttra (vutrisiran) injection 25 mg/0.5 mL

onpattro (patisiran) lipid complex injection 10 mg/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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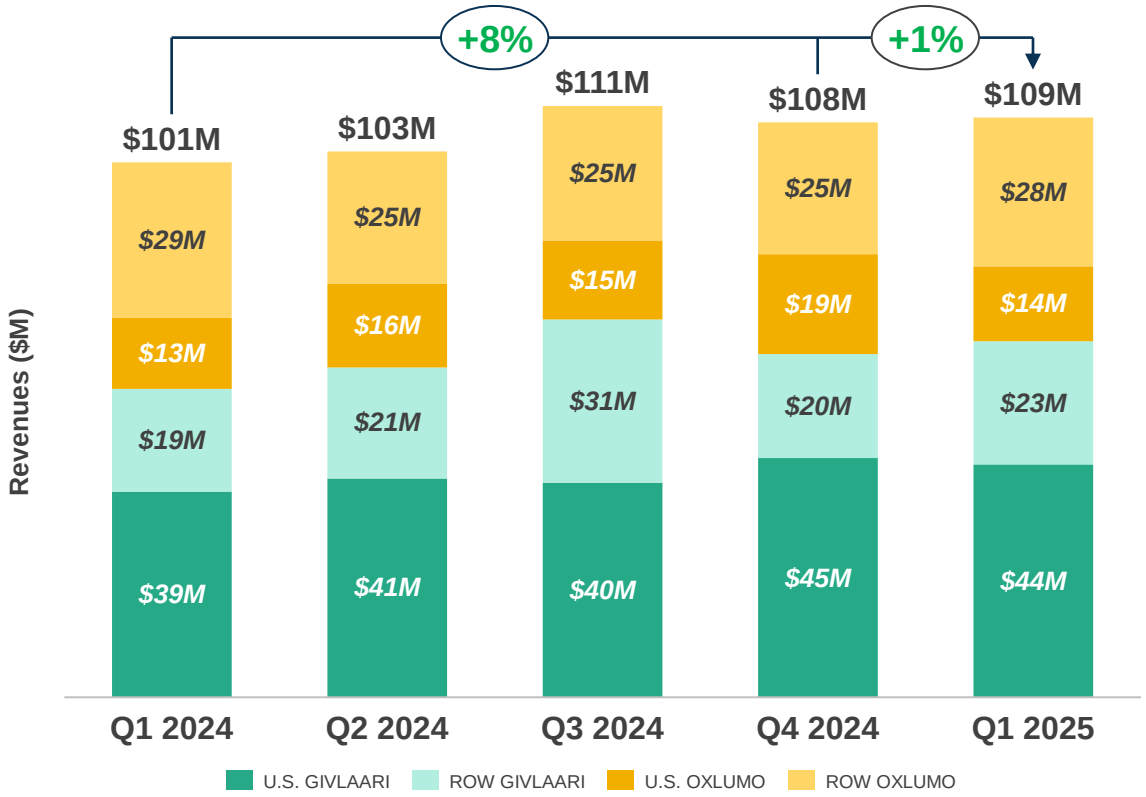
Q1 2025: Rare Franchise Demand Growth Remains Healthy

$109M
Total Rare
Global Q1 2025
Net Product Revenues



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

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

Q1 2025 Rare Franchise Highlights

	YoY % Growth	QoQ % Growth
GIVLAARI	**15%**	4%
OXLUMO	**-1%**	-3%
Total Rare	**8%**	1%

- GIVLAARI YoY +15% growth highlights:
  - Demand driven by ~15% YoY increase in global patients on therapy
  - US growth favorably impacted by gross to net adjustment
- OXLUMO YoY -1% growth highlights:
  - ~20% YoY increase in global patients on therapy
  - Increase in patient demand offset by gross to net adjustments in European markets and timing of orders in partner markets
- Modest FX headwind -3% (YoY CER[1] growth = 11%)

[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 2024 – see the Financial Summary slide for more information.

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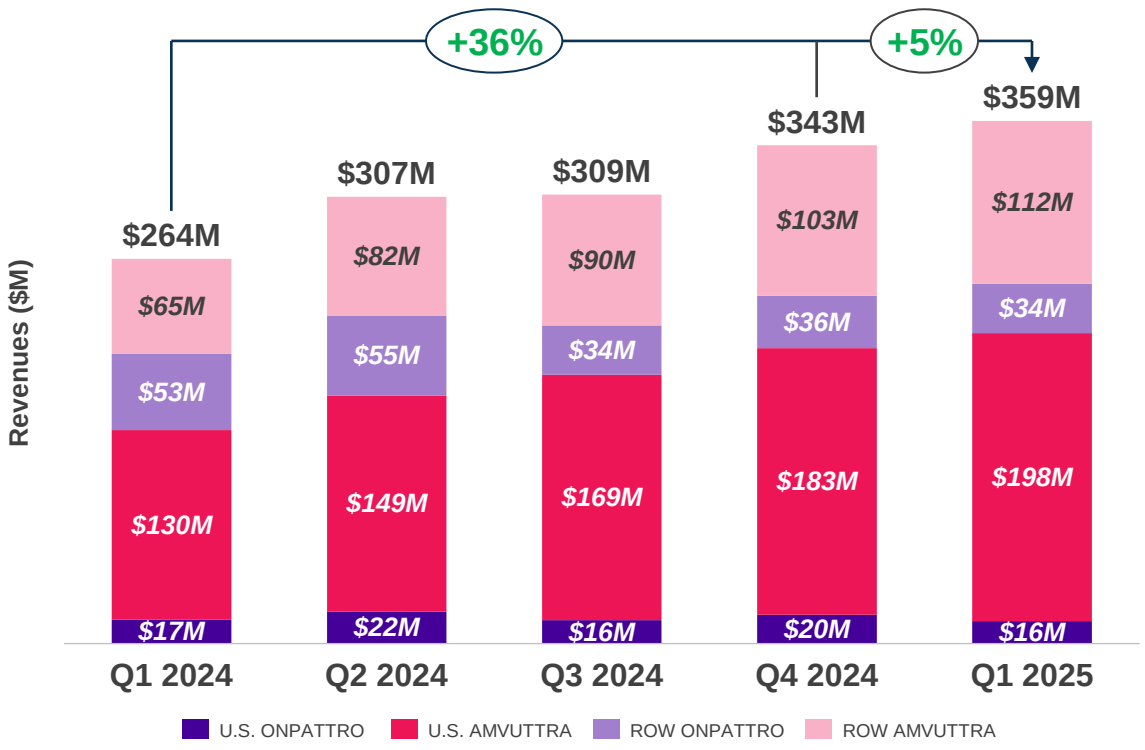
Q1 2025: Robust 36% TTR Growth Driven by U.S. Performance

$359M
Total TTR
Global Q1 2025
Net Product Revenues



amvuttra (vutrisiran) injection 25 mg/0.5 mL

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

Q1 2025 TTR Franchise Highlights

	YoY % Growth	QoQ % Growth
U.S.	**45%**	5%
ROW	**24%**	5%
Global	**36%**	5%

- U.S. YoY +45% growth highlights:
  - Demand +32%, Inventory +6%, Gross-to-Net +7%
  - Captured ~70% of new to treatment hATTR-PN patients in Q1
  - No ATTR-CM sales in Q1 as launch initiated late March
- ROW YoY +24% growth highlights:
  - Primarily demand driven +21%
  - Partner markets growth benefited from initial launch in Australia
  - Preparing for ATTR-CM launch in Japan and Germany in 2H 2025
- Modest FX headwind -2% (YoY CER[1] growth = 38%)

[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 2024 – see the Financial Summary slide for more information.

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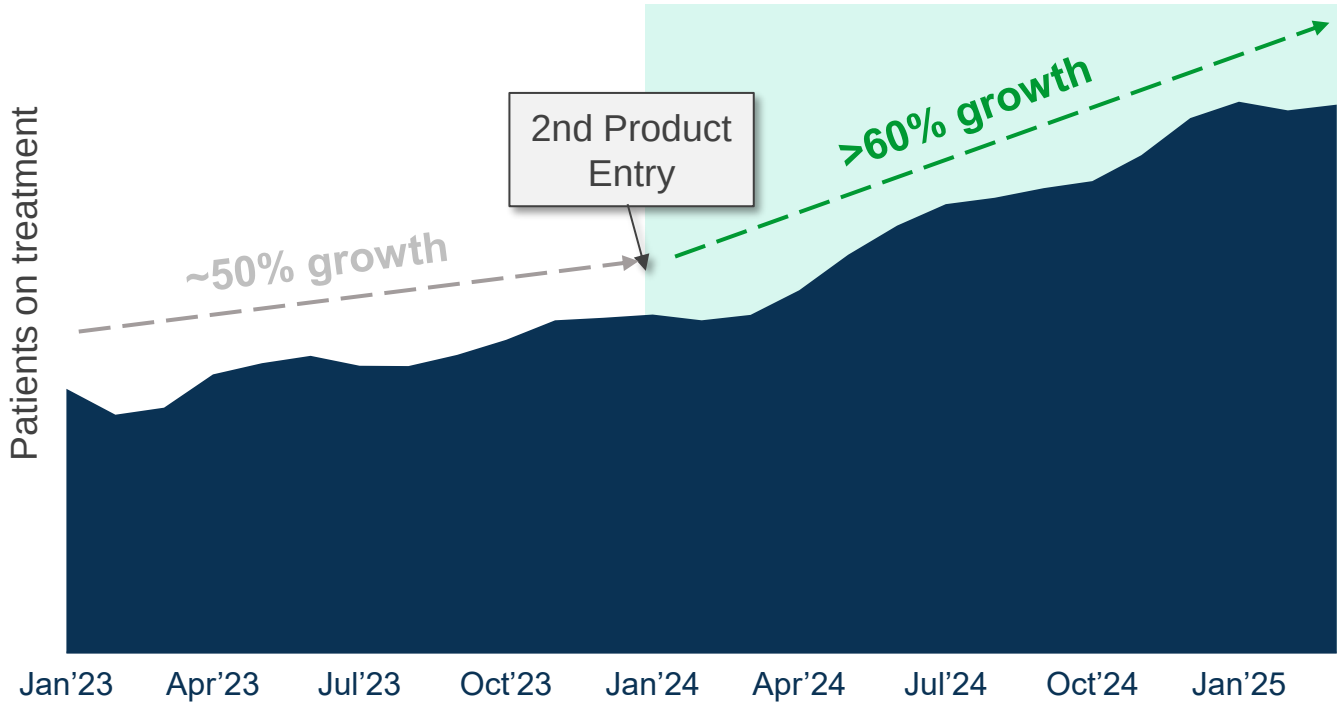
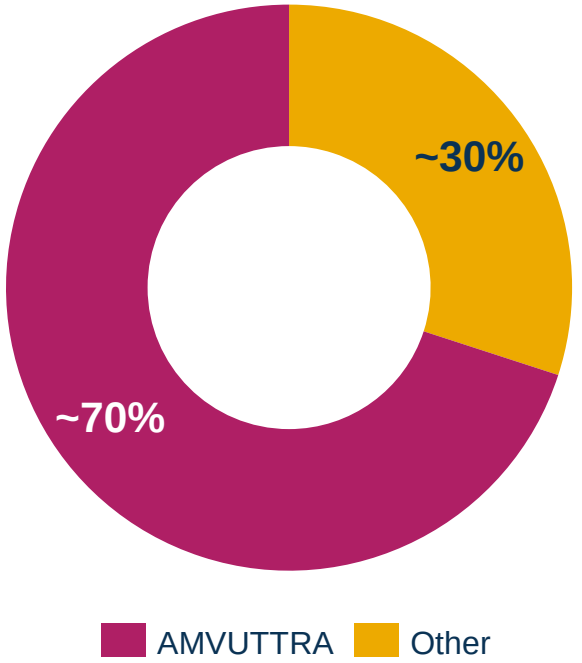
hATTR-PN | AMVUTTRA Drives Category Growth and Leads New Patient Share in U.S.

PN category growth accelerated as expected



AMVUTTRA captured ~70% of new patient starts in Q1'25

hATTR-PN U.S. New Patient Share in Q1'25



Sources: Claims data analysis, data on file as of Q1'25

ATTR-CM | Momentum Building for Second Half of 2025

Optimizing access pathways at ~170 priority health systems (~80% of Rx volume)

Treatment sites expansion (2x increase since Q4'24, achieving >2,000 sites[1])

Continued payer engagements (e.g., VBA expansion into ATTR-CM) ***on track***

Health systems formulary approval (via Pharmacy & Therapeutics Committees) ***on track***

[1] *Represents alternate sites of care*

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ATTR-CM | U.S. Launch Off To A Strong Start

Access & Affordability

Patients Are Accessing AMVUTTRA Across Payer Mix

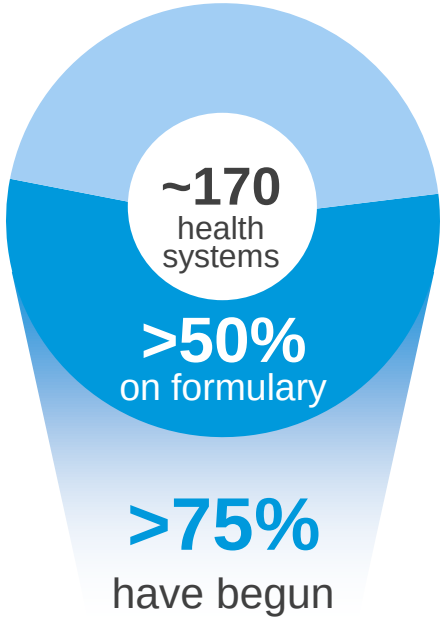
Commercial, Medicare FFS, and Medicare Advantage

Majority of lives are covered by **VBAs that include ATTR-CM**

$0 co-pay
for majority of patients

Health System Formulary Coverage

Rapid Progress on Formulary Inclusion



Treatment Choice

AMVUTTRA's First-Line Profile Is Resonating

~60% of HCPs agree that silencing TTR gives ATTR patients optimal outcomes

Broad Patient Uptake

New To Treatment	Stabilizer Progressor
Academic	Community

Sources: Claims data analysis, data on file as of Q1'25

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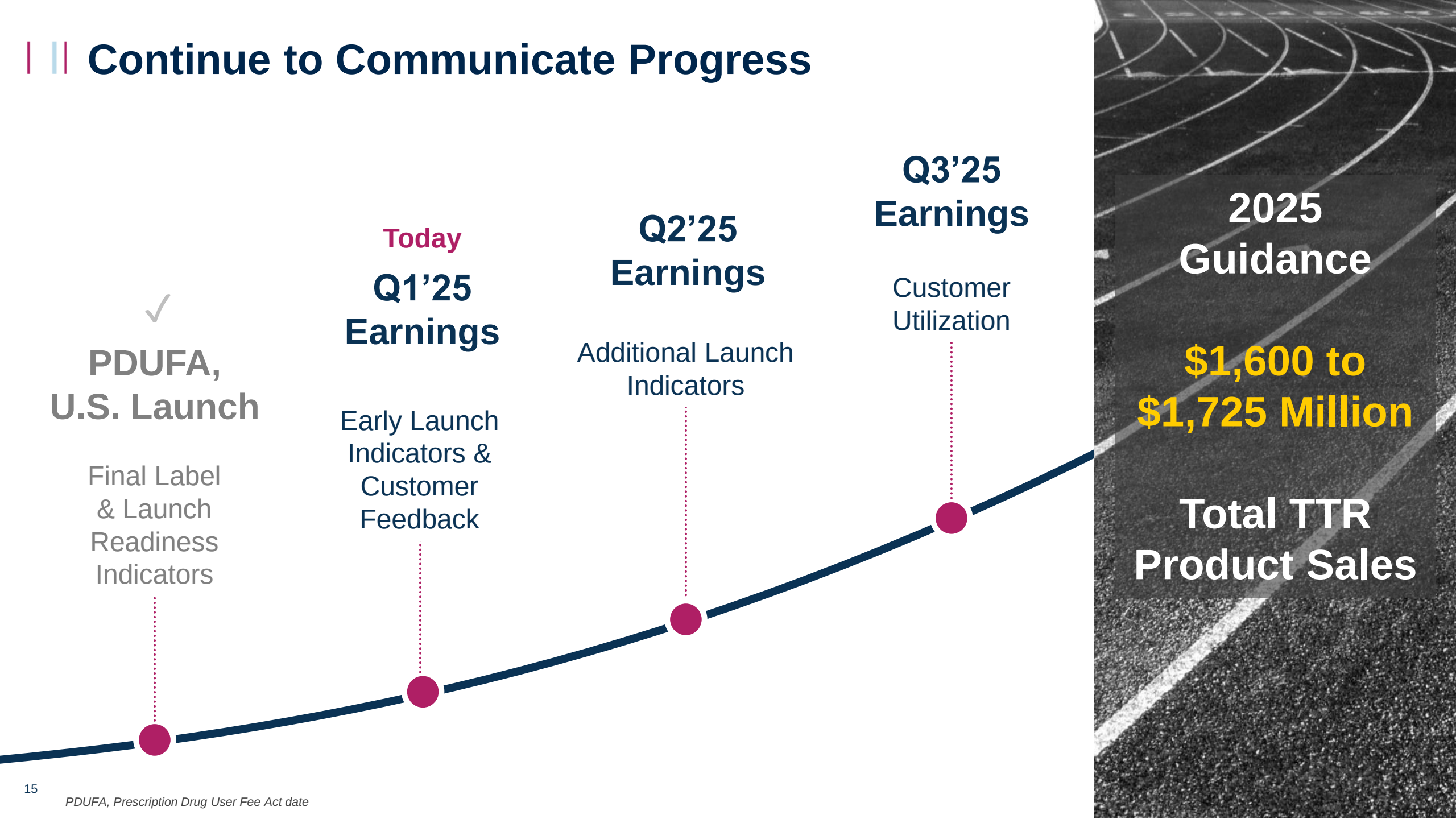
Continue to Communicate Progress



PDUFA, Prescription Drug User Fee Act date

Pipeline

Pushkal Garg, M.D.
Chief Medical Officer

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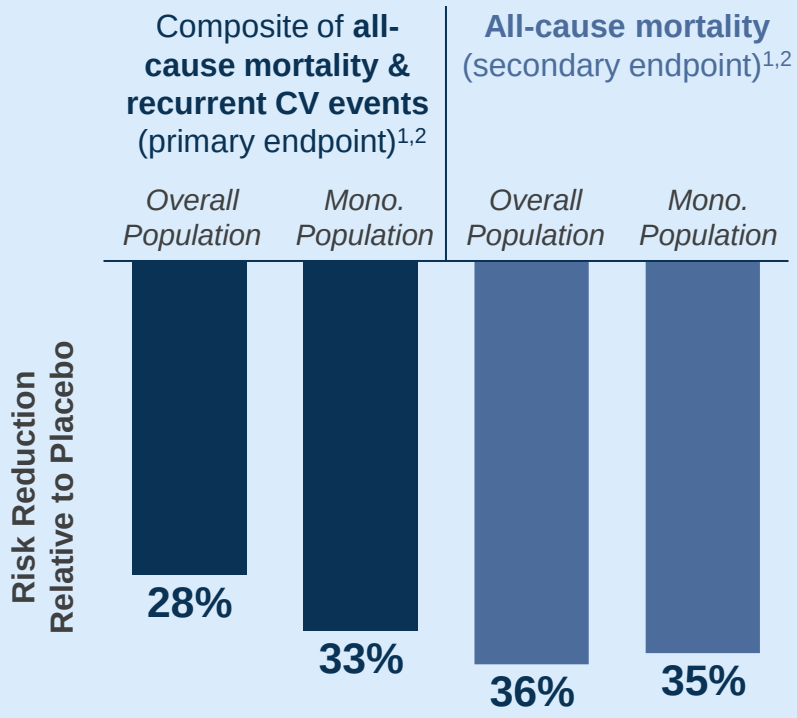
AMVUTTRA Therapeutic Profile Supports First-Line Potential

Population Representative of Today's Patients

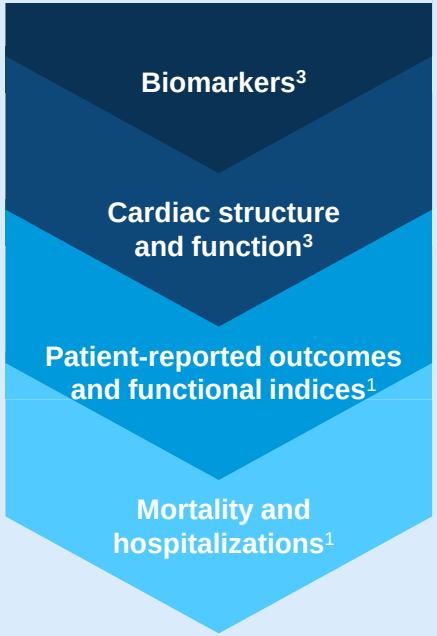
~50%
of patients were on **tafamidis** at baseline or during DB period

~30%
of patients started **SGLT2** inhibitors during DB period

~80%
of patients were on **diuretics** at baseline and ~50% had intensification or initiation of diuretics after 1st dose



Broad Impact on ATTR-CM Parameters with Substantial Improvement of CV Outcomes



4 subcutaneous doses per year

Primary composite endpoint assessed over 33-36 months. Secondary all-cause mortality endpoint assessed over 33-42 months.

References: [1] Fontana et al. N Engl J Med. 2025;392(1):33-44; [2] Fontana et al. ESC Congress 2024. London, UK; [3] Fontana et al. N Engl J Med. 2025;392(1):33-44 (supplement).

AMVUTTRA Regulatory Progress

U.S.

APPROVED

Brazil

APPROVED

European Union

POSITIVE CHMP OPINION

Japan

expected Q2 2025

United Kingdom

expected Q3 2025

Canada

expected Q4 2025

Additional countries

expected 2026-2027

Continued Evidence Generation from HELIOS-B to Support AMVUTTRA Differentiation

Echocardiographic Parameters[1]

- Vutrisiran improved diastolic function and attenuated declines in LV and RV systolic function at 18 months

Baseline Heart Failure Severity[2]

- Consistent benefit across range of baseline disease severities
- Greatest benefit observed in patients with earlier, less severe disease

JACC

Functional Capacity, Health Status, Quality of Life[3]

- Significantly more vutrisiran patients maintained or improved functional capacity, health status, and quality of life over 30 months compared to placebo

JACC

[1] *Jerring, et al. ACC 2025;* [2] *Maurer, et al. ACC 2025;* [3] *Sheikh, et al. ACC 2025*

Nucresiran TRITON Phase 3 Program

Potential to Launch in hATTR-PN Ahead of ATTR-CM

TRITON-CM
ATTR-CM CLINICAL STUDY

CVO primary endpoint (event driven)

Assumed Launch ~2030

- Randomized, double-blind, event-driven outcomes study
- Initiation expected first half 2025

TRITON-PN
hATTR-PN CLINICAL STUDY

mNIS+7 primary endpoint

Targeting Launch several years earlier

- Exploring efficient designs; history of innovative designs with HELIOS-A FPI to top line in ~2 years
- Initiation expected late 2025

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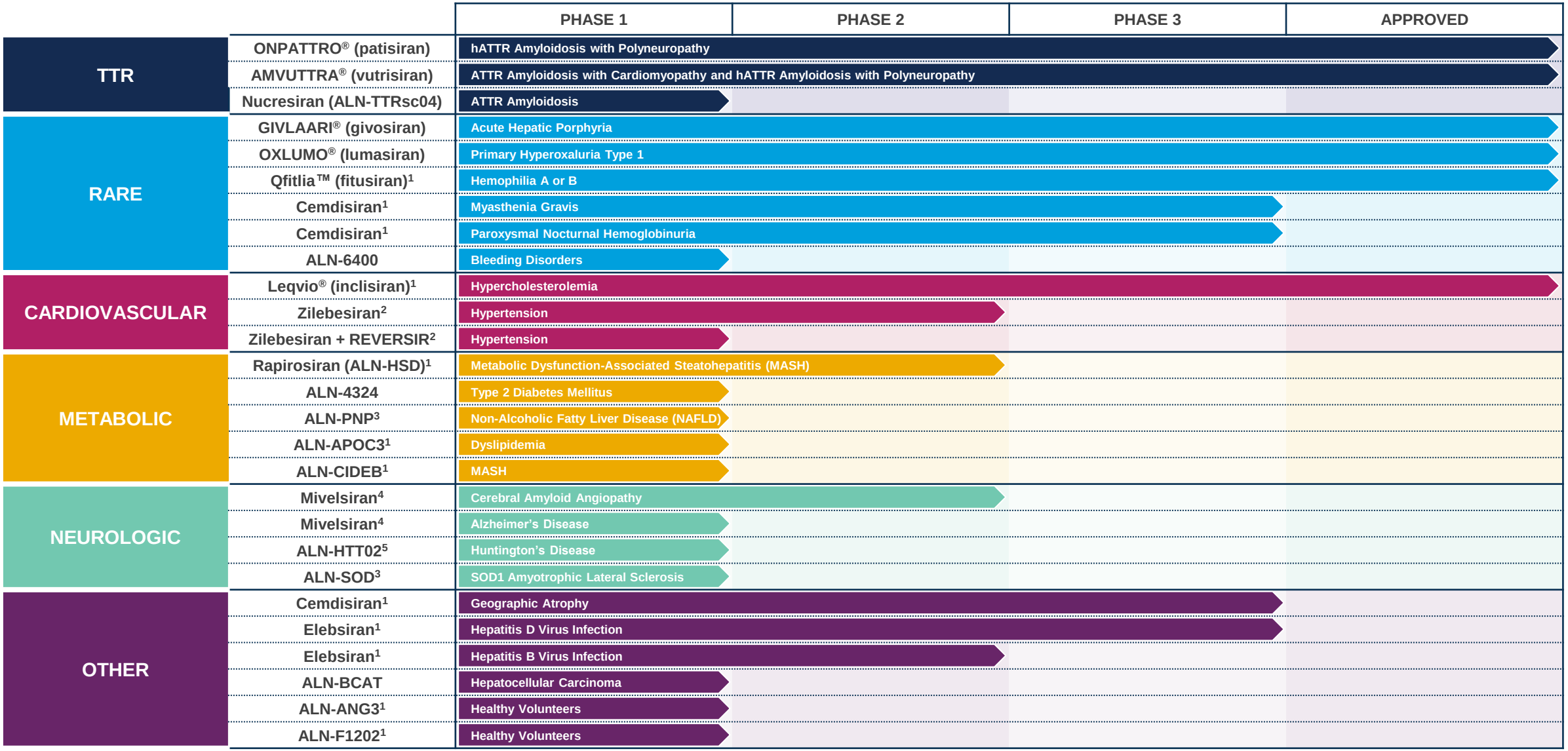
Robust and High-Value Pipeline of RNAi Therapeutics



[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] Product developed as part of collaboration with Regeneron [5] Partnered, Alnylam-led with profit split

Financial Summary and Upcoming Milestones

Jeff Poulton
Chief Financial Officer

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Q1 2025 Financial Summary

($ in millions except where noted as percentages)	Q1 2024	Q1 2025	Q1 2025 vs Q1 2024 (Reported)	Q1 2025 vs Q1 2024 (CER[2])
Total Combined Net Product Revenues	$365	**$469**	***28%***	***30%***
Net Revenues from Collaborations & Royalties	129	**126**	***(3%)***	
Collaboration Revenue	119	99	*(16%)*	
Royalty Revenue	11	26	*149%*	
Total Cost of Goods Sold, Collaborations & Royalties	66	**71**		
Gross Margin on Product Revenues	*85%*	*85%*		
Gross Margin on Total Revenues	*87%*	*88%*		
Non-GAAP Combined R&D and SG&A Expenses[1]	426	**448**	***5%***	
R&D	242	241	-	
SG&A	185	207	*12%*	
Non-GAAP Operating Income	2	**75**		
Non-GAAP Operating Margin	*0%*	***13%***		
Non-GAAP Net Loss	(21)	**(1)**		

($ in millions)	Q4 2024	Q1 2025
Cash, Cash Equivalents & Marketable Securities (period end)	2,695	**2,632**

[1] 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. 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 1, 2025, which is accessible in the Investors section of our website at www.alnylam.com.

[2] CER growth rates represent growth at Constant Exchange Rates, a non-GAAP financial measure determined by comparing Q1 2025 performance (restated using Q1 2024 exchange rates) to actual Q1 2024 reported performance.

2025 Full-Year Guidance

Item	FY 2025 Guidance	Key Assumptions
Total TTR Net Product Revenues (PN & CM) (AMVUTTRA, ONPATTRO)	$1,600 to $1,725 million	• AMVUTTRA-CM approval and launch in Germany and Japan in the second half of 2025
Total Rare Net 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 for remainder of year forecast
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 CVOT milestone with Roche
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

amvuttra (vutrisiran) / onpattro (patisiran) / GIVLAARI (givosiran) / OXLUMO (lumasiran)		Combined Net Product Revenue Guidance $2,050M – $2,250M	2025
VUTRISIRAN	ATTR Amyloidosis	U.S. FDA Approval	**March 20, 2025** ✓
		Additional Global Approvals (Japan, EU)	**Q2, Q3**
NUCRESIRAN* **(ALN-TTRsc04)**	ATTR Amyloidosis	Initiate Phase 3 Study in ATTR-CM	**H1**
		Initiate Phase 3 Study in hATTR-PN	**H2**
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	**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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Q&A Session

Q1 2025 Financial Results

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Silence disease
Amplify life™
Alnylam®

Appendix

Q1 2025 Financial Results

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Alnylam Pharmaceuticals, Inc.

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

	Three Months Ended	
	March 31, 2025	March 31, 2024
Reconciliation of GAAP to Non-GAAP Research and development:		
GAAP Research and development	$ 265,122	$ 260,995
Less: Stock-based compensation expenses	(23,798)	(19,215)
Non-GAAP Research and development	$ 241,324	$ 241,780
Reconciliation of GAAP to Non-GAAP Selling, general and administrative:		
GAAP Selling, general and administrative	$ 239,949	$ 210,797
Less: Stock-based compensation expenses	(32,914)	(26,132)
Non-GAAP Selling, general and administrative	$ 207,035	$ 184,665
Reconciliation of GAAP to Non-GAAP Income (loss) from operations:		
GAAP Income (loss) from operations	$ 18,077	$ (43,435)
Add: Stock-based compensation expenses	56,712	45,347
Non-GAAP Operating income	$ 74,789	$ 1,912
Reconciliation of GAAP to Non-GAAP Net loss:		
GAAP Net loss	$ (57,479)	$ (65,935)
Add: Stock-based compensation expenses	56,712	45,347
Add: Unrealized loss (gain) on marketable equity securities	956	(78)
Less: Income tax effect of GAAP to non-GAAP reconciling items	(1,476)	—
Non-GAAP Net loss	$ (1,287)	$ (20,666)
Reconciliation of GAAP to Non-GAAP Net loss per common share - basic and diluted:		
GAAP Net loss per common share — basic and diluted	$ (0.44)	$ (0.52)
Add: Stock-based compensation expenses	0.44	0.36
Add: Unrealized loss (gain) on marketable equity securities	0.01	—
Less: Income tax effect of GAAP to non-GAAP reconciling items	(0.01)	—
Non-GAAP Net loss per common share — basic and diluted	$ (0.01)	$ (0.16)

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

	March 31, 2025 Three Months Ended
Total TTR net product revenue growth, as reported	36 %
Add: Impact of foreign currency translation	2
Total TTR net product revenue growth at constant currency	38 %
Total Rare net product revenue growth, as reported	8 %
Add: Impact of foreign currency translation	3
Total Rare net product revenue growth at constant currency	11 %
Total net product revenue growth, as reported	28 %
Add: Impact of foreign currency translation	2
Total net product revenue growth at constant currency	30 %

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