Second Quarter 2025 Financial Results

July 31, 2025

Agenda

Welcome

- **Christine Akinc**
  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 Research & Development 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 drive sustainable growth and value creation for years to come; Alnylam's ability to be a long-term leader in TTR amyloidosis; the ability of Alnylam's R&D engine to deliver sustainable innovation and value creation; Alnylam's ability to achieve sustainable profitability; AMVUTTRA's position as a flagship commercial franchise with robust and durable long-term growth potential; the expectation that international markets will contribute to the launch of AMVUTTRA in ATTR-CM in the second half of 2025; Alnylam's ability to achieve the "*Alnylam P^{5}x25*" goals by the end of 2025; Alnylam's ability to make AMVUTTRA the first-line treatment of choice for ATTR-CM; Alnylam's ability to achieve significant revenue growth going forward; Alnylam's ability to establish itself as a unique, top-tier biotech company delivering sustainable innovation for many years to come; Alnylam's ability to deliver long-term, innovation-driven growth; the potential for Alnylam to advance its research and development programs, and the timing of the initiation and readout of clinical trials of any of Alnylam's product candidates and of any approval and launch of any of Alnylam's product candidates; the expectation that the grant of Fast Track Designation to nucresiran will enable a more streamlined review process; the potential of Alnylam's pipeline to deliver multiple blockbuster opportunities and meaningful impact to patients for many years to come; and Alnylam's projected commercial and financial performance, including the revised expected range of TTR, Rare and combined net product revenues, net revenues from collaboration and royalties, combined Non-GAAP 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 sustainable profitability; 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®

Positioned for Success Through 2025 and Beyond

Best-in-Class Team ✚ Award-Winning Culture

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Durable TTR Leadership Drove Q2 Performance

Innovative Pipeline Advancing

TTR Leadership

$544M
(+77% YoY)
Q2 Total TTR Net Revenues

~1,400
ATTR-CM Patients Receiving AMVUTTRA
(as of June 30, 2025)

Growth Through Innovation

ATTR-CM
nucresiran
Initiated TRITON-CM Phase 3 Study

Alzheimer's Disease
mivelsiran
Announced Phase 1 Multidose Results

Type 2 Diabetes
ALN-4324
Initiated Phase 1 Study

Strong Financial Performance

$672M
(+64% YoY)
Q2 Total Net Product Revenues

$2,650M to $2,800M
(+$575M/ +27% midpoint)
Increased 2025 Total Net Product Revenue Guidance

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Continued Progress Against Fulfillment of Ambitious 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

Accelerating Performance in Q2 2025

Strong Growth Achieved Across Franchises and Regions

Q2 2025 Overall Portfolio

$672M
Total Net Product Revenues

+64%
YoY growth[1]
vs. Q2'24

+43%
QoQ growth[1]
vs. Q1'25

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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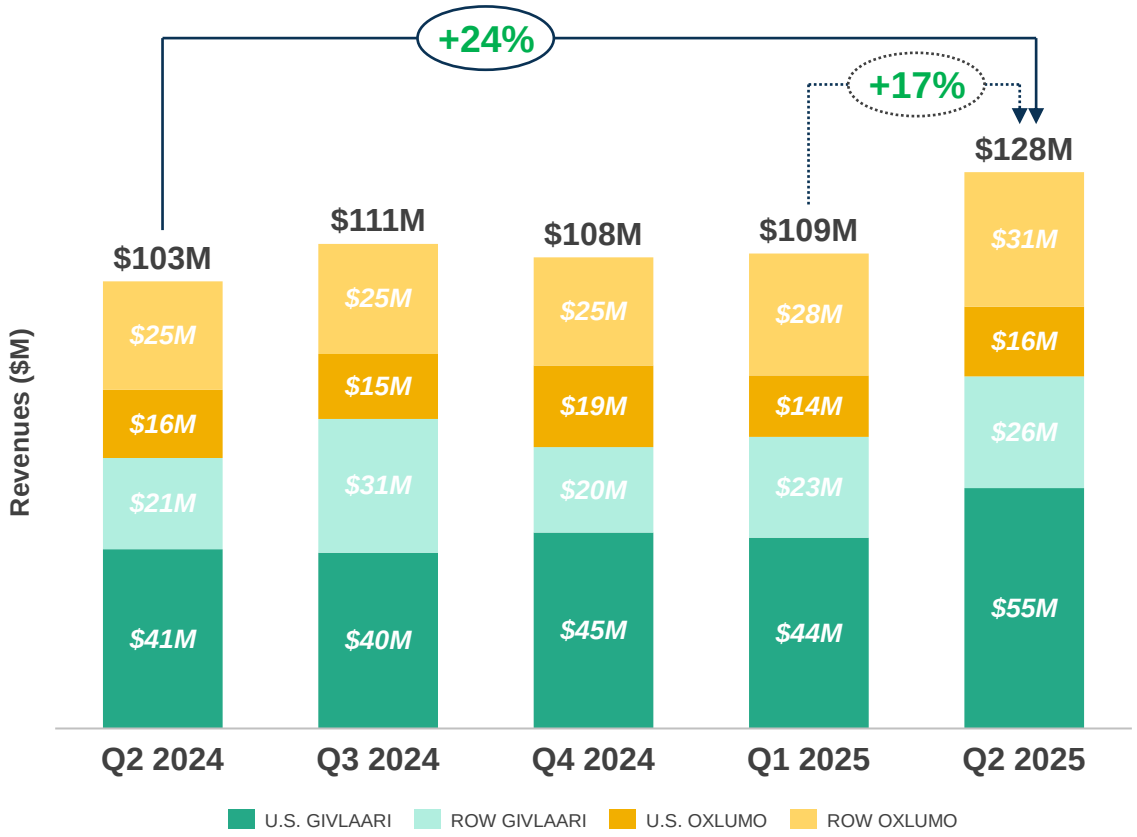
Q2 2025: Driving Consistent Rare Franchise Growth

$128M
Total Rare
Global Q2 2025
Net Product Revenues



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

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

Q2 2025 Rare Franchise Highlights

	YoY % Growth	QoQ % Growth
GIVLAARI	**30%**	21%
OXLUMO	**15%**	11%
TOTAL Rare	**24%**	17%

- GIVLAARI YoY +30% growth highlights:
  - ~18% YoY increase in global patients on therapy
  - U.S. growth favorably impacted by a gross-to-net adjustment in Q2
- OXLUMO YoY +15% growth highlights:
  - ~16% YoY increase in global patients on therapy
- Modest FX tailwind -1% (YoY CER[1] growth = 23%)

[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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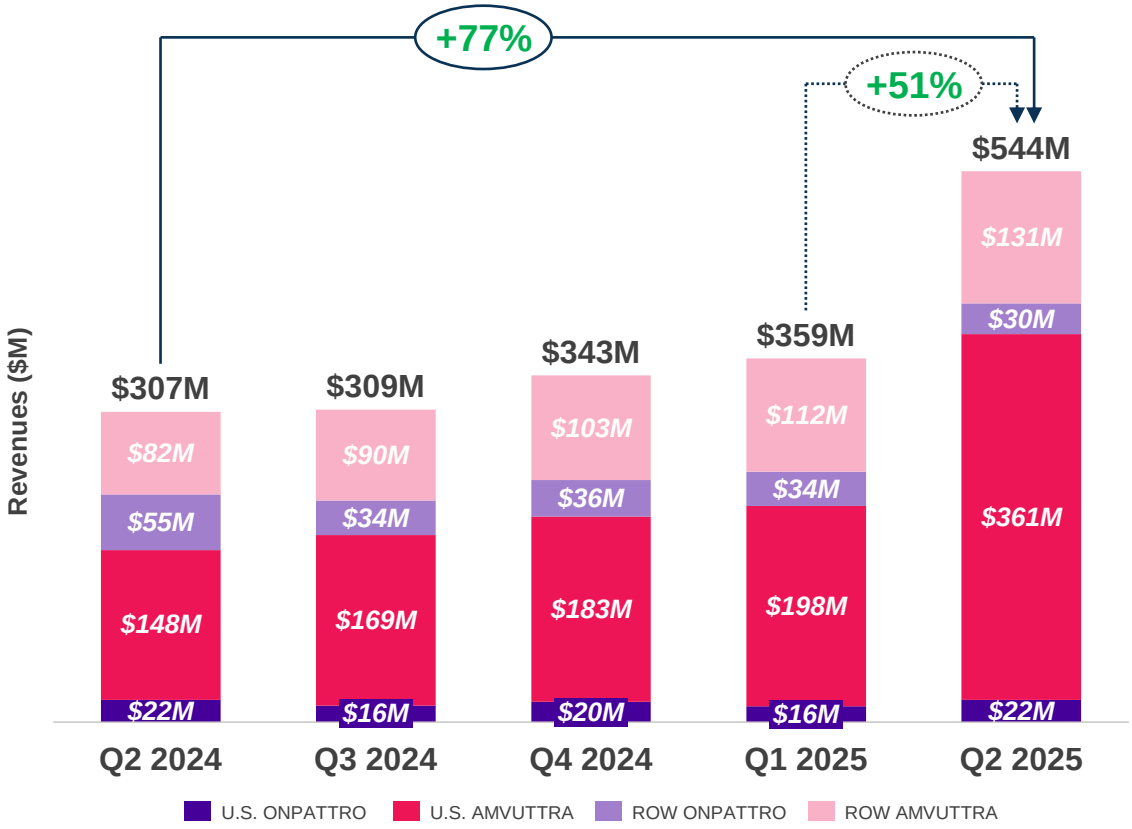
Q2 2025: Growth Inflection Driven by U.S. ATTR-CM Launch

$544M
Total TTR
Global Q2 2025
Net Product Revenues



amvuttra (vutrisiran) injection 25 mg/0.5 mL

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

Q2 2025 TTR Franchise Highlights

	YoY % Growth	QoQ % Growth
U.S.	**125%**	**80%**
ROW	**18%**	10%
Global	**77%**	51%

- U.S. Q2 '25 vs. Q1 '25 (QoQ) +80% growth highlights:
  - Substantial demand growth driven by ATTR-CM launch: ~1,400 CM patients on therapy at end of Q2, and ~$150M ATTR-CM Q2 revenue
  - Demand driven inventory channel build (~$25M benefit vs. Q1) offset by increase in gross-to-net deductions
- U.S. Q2 '25 vs. Q2 '24 (YoY) +125% growth highlights:
  - 115% demand growth driven primarily by ATTR-CM launch
  - Additional 10% growth due to demand driven inventory channel build
- ROW YoY +18% growth primarily driven by continued hATTR-PN patient growth with no ATTR-CM sales occurring in Q2 '25
- Modest FX tailwind -2% (YoY CER[1] growth = 75%)

[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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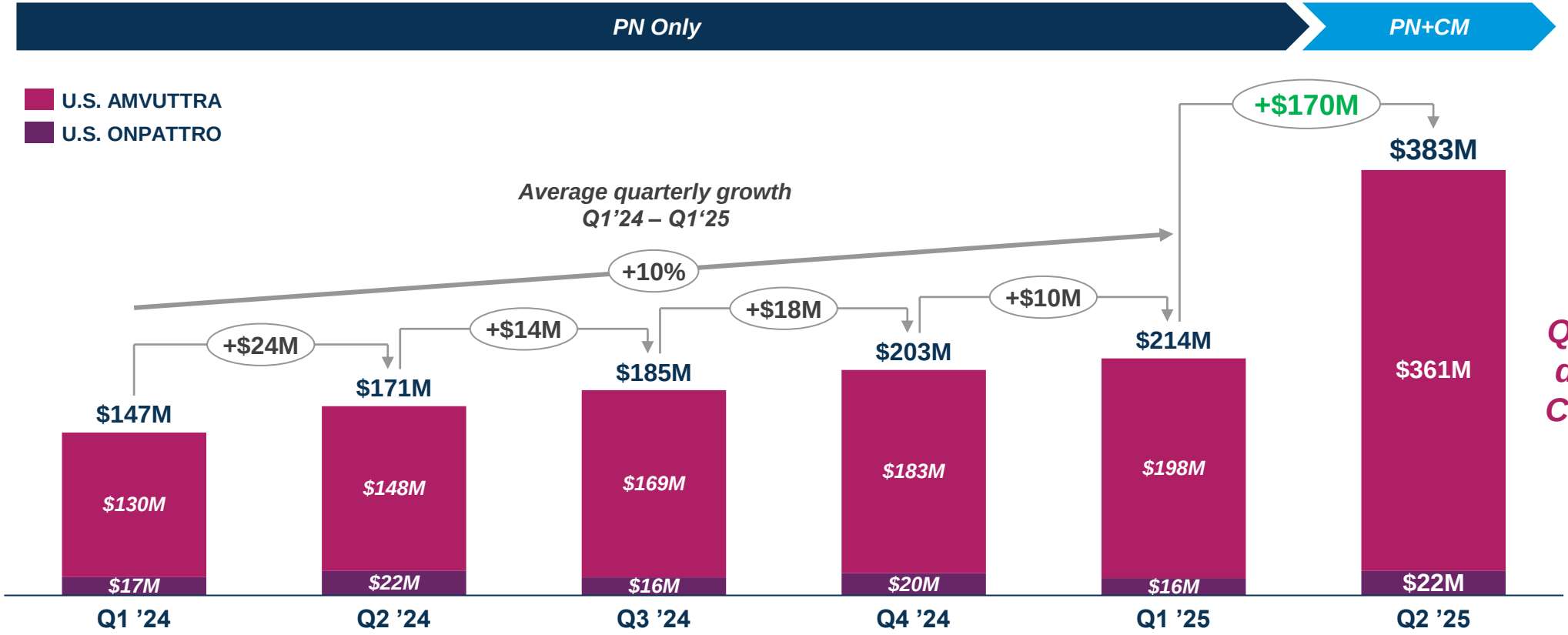
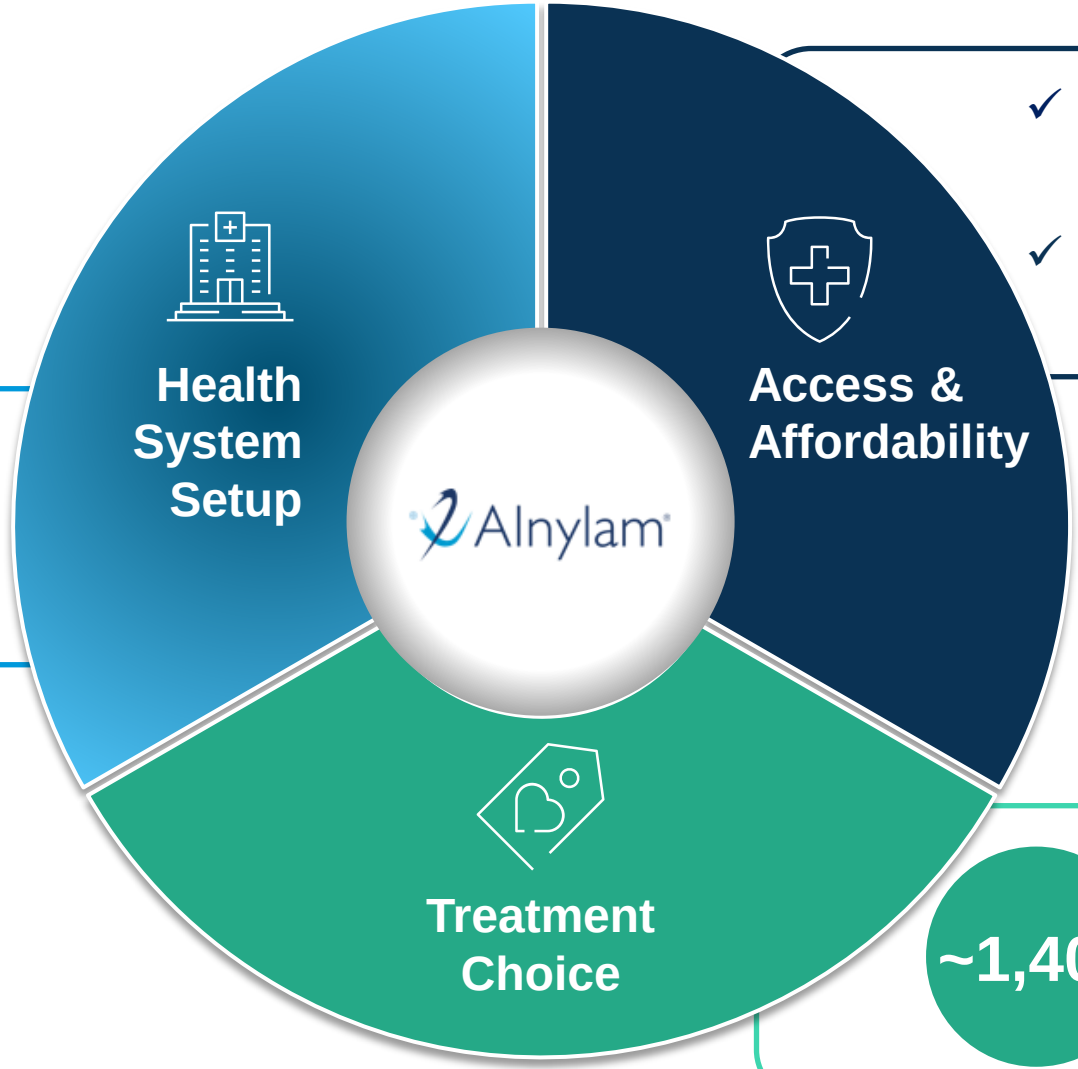
Q2 2025: Step Change in Growth Indicates ~$150 Million in U.S. ATTR-CM Launch Revenue



Q2 growth driven by CM launch

QoQ Growth	3%	16%	8%	10%	5%	**80%**
YoY Growth	35%	40%	37%	42%	45%	**125%**

ATTR-CM U.S. Launch Focused on 3 Key Enablers



- ✓ **AMVUTTRA on Formulary** for majority of ~170 priority Health Systems

- ✓ **Large Majority** of U.S. patients covered for AMVUTTRA in 1L
- ✓ **Most patients pay $0** in out-of-pocket costs

~1,400 **CM patients** on therapy with AMVUTTRA in Q2

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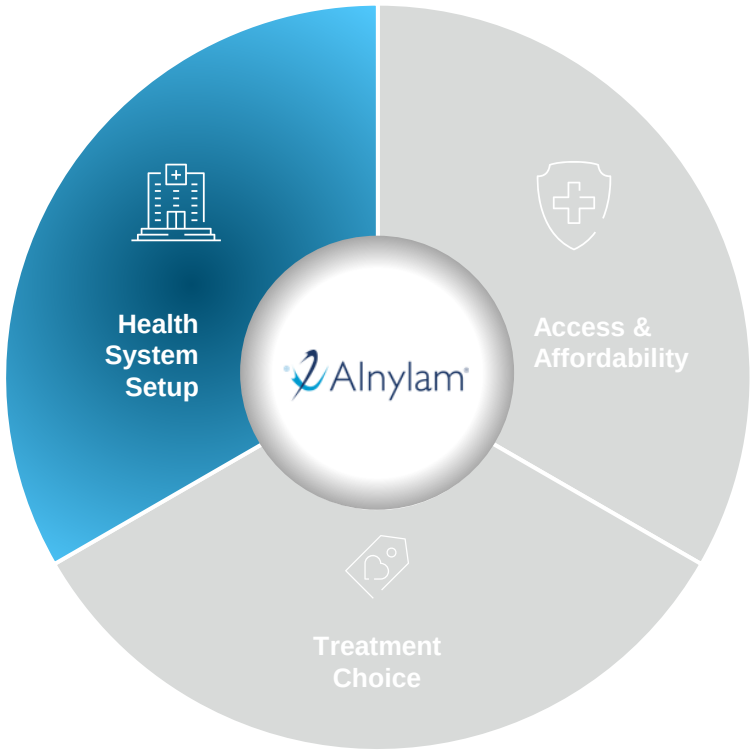
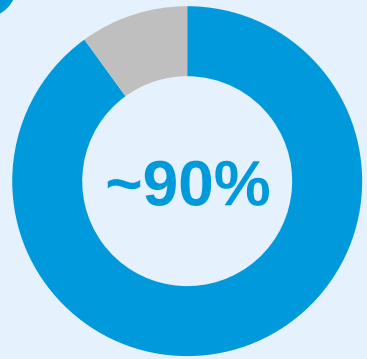
ATTR-CM | Rapid Progress on Health System Setup



AMVUTTRA on formulary for **majority of ~170** priority Health Systems

>2,000

Alternate Sites of Care enabled



U.S. patients able to receive AMVUTTRA within ~10 miles of home

Source: Data on file

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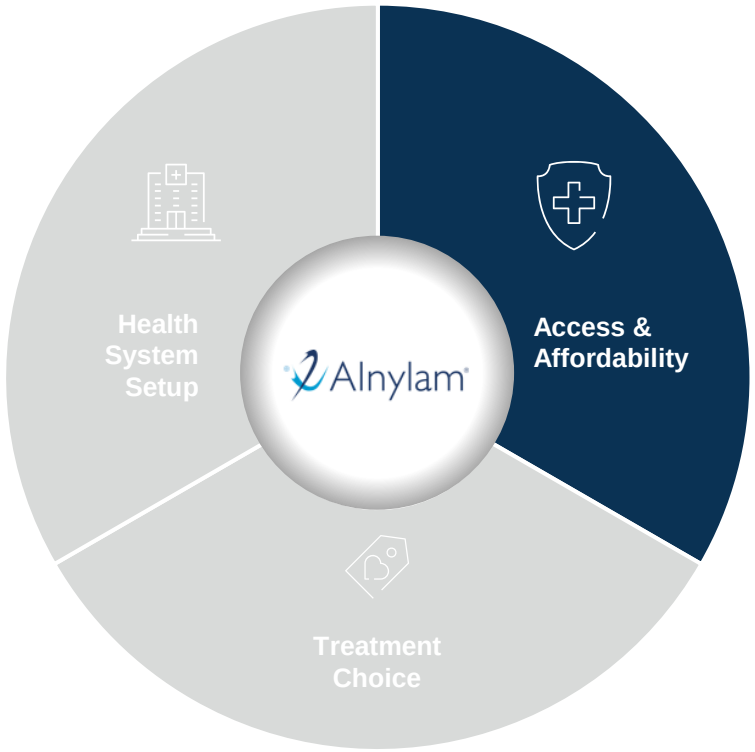
ATTR-CM | Patients Are Accessing AMVUTTRA in First Line



Large majority of U.S. patients have first-line payer coverage
(no step through required)

Most patients have paid

$0

out of pocket

Confirmed utilization across **all payer segments**

Source: Payer policy updates as of Q2'25, Alnylam Assist data on file

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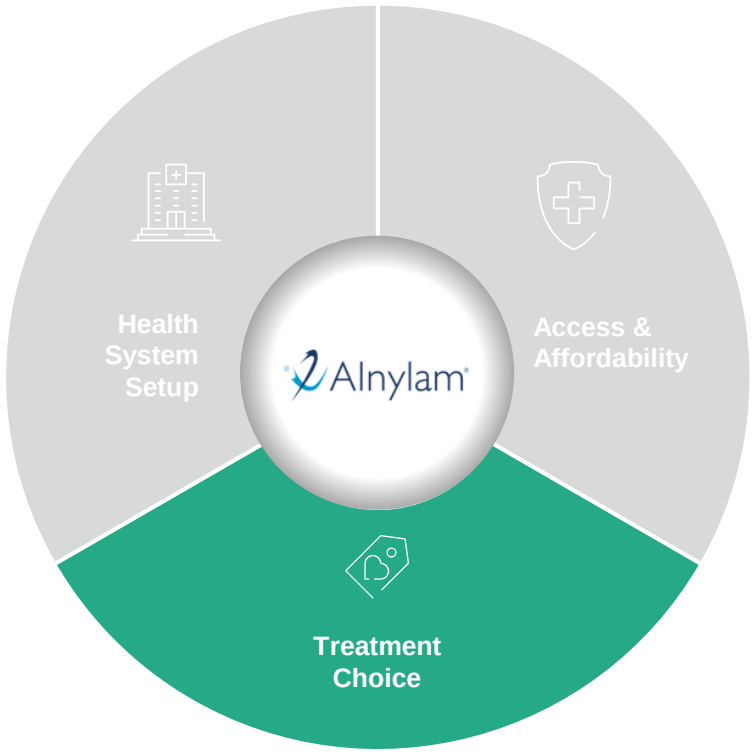
ATTR-CM | HCPs & Patients Are Choosing AMVUTTRA



~1,400

CM patients on therapy with AMVUTTRA in Q2

Broad & balanced utilization

(i.e., New To Treatment & Stabilizer Progressor; Academic & Community)

3X increase in total AMVUTTRA prescribers QoQ

Source: Data on file

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Strong Launch Progress Expected to Drive Sustainable Growth

✓ Well positioned for TTR leadership

✓ Growing & underserved category

✓ Expanding impact with ROW ATTR-CM launches

Pipeline

Pushkal Garg, M.D.
Chief Research & Development Officer

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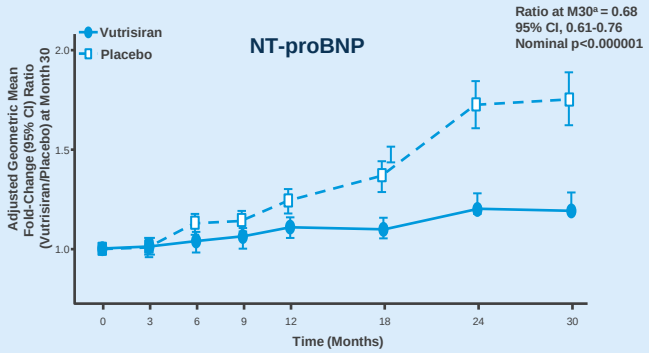
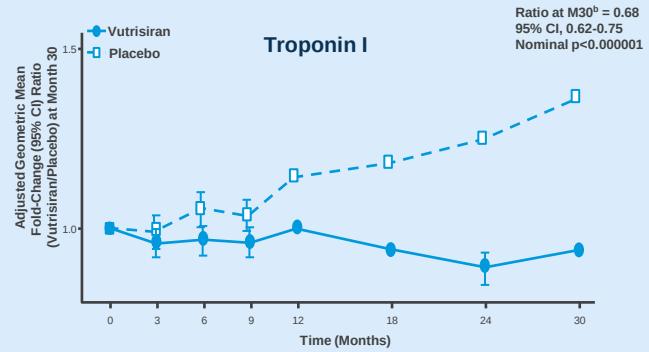
Additional Data from HELIOS-B Continue to Drive Confidence in AMVUTTRA's Clinically Differentiated Profile

Biomarkers[1]

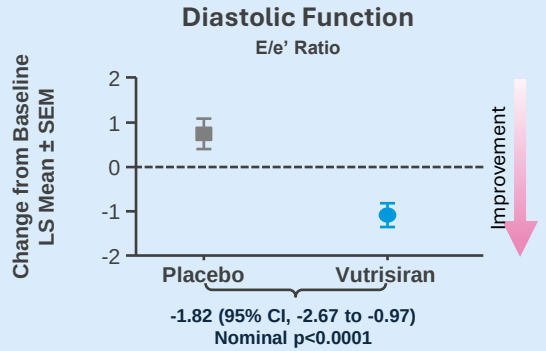
Vutrisiran improved NT-proBNP and Troponin I levels vs. placebo

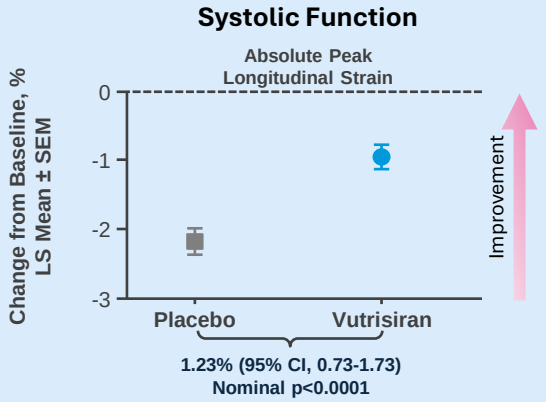




Cardiac Structure & Function[2]

Vutrisiran was associated with improvements in echocardiographic assessments at month 30

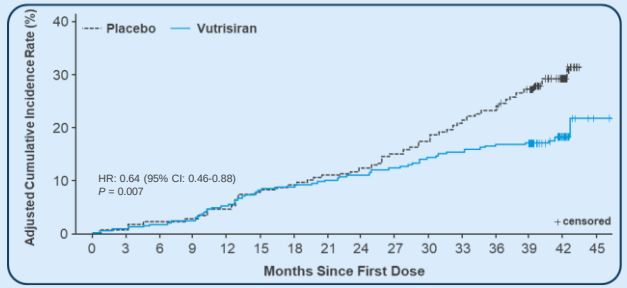




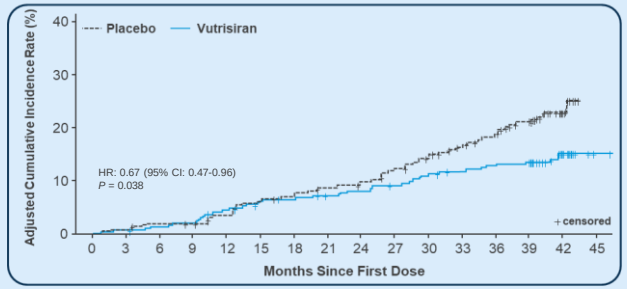
Survival[3]

Vutrisiran reduced all-cause & cardiovascular mortality through month 42

ACM Risk Reduction of 36% Through 42 Months in the Overall Population



CVM Risk Reduction of 33% Through 42 Months in the Overall Population



[1] Maurer, et al. HFSA 2024. [2] Jering, et al. HFSA 2024. [3] Witteles, et al. JACC 2025.

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Nucresiran TRITON Phase 3 Program

Next-generation silencer with potential for greater TTR knockdown, improved efficacy, and biannual dosing

TRITON-CM
ATTR-CM CLINICAL STUDY

CVO primary endpoint (event driven)

Targeting Launch ~2030

- Randomized, double-blind, event-driven outcomes study
- **Initiated**

U.S. FDA Fast Track Designation

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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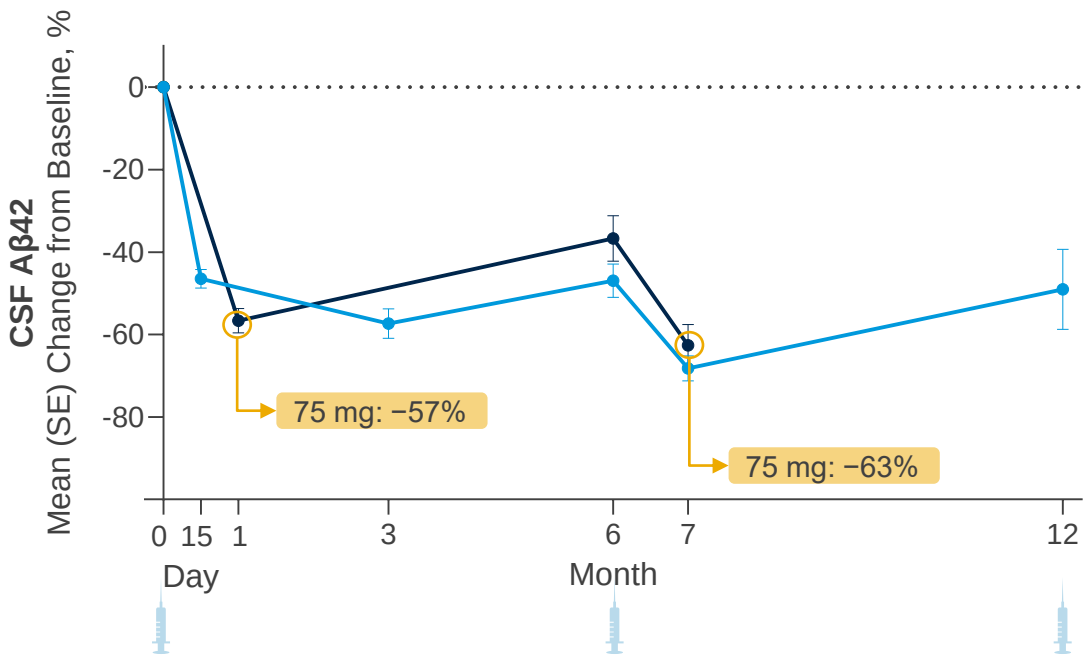
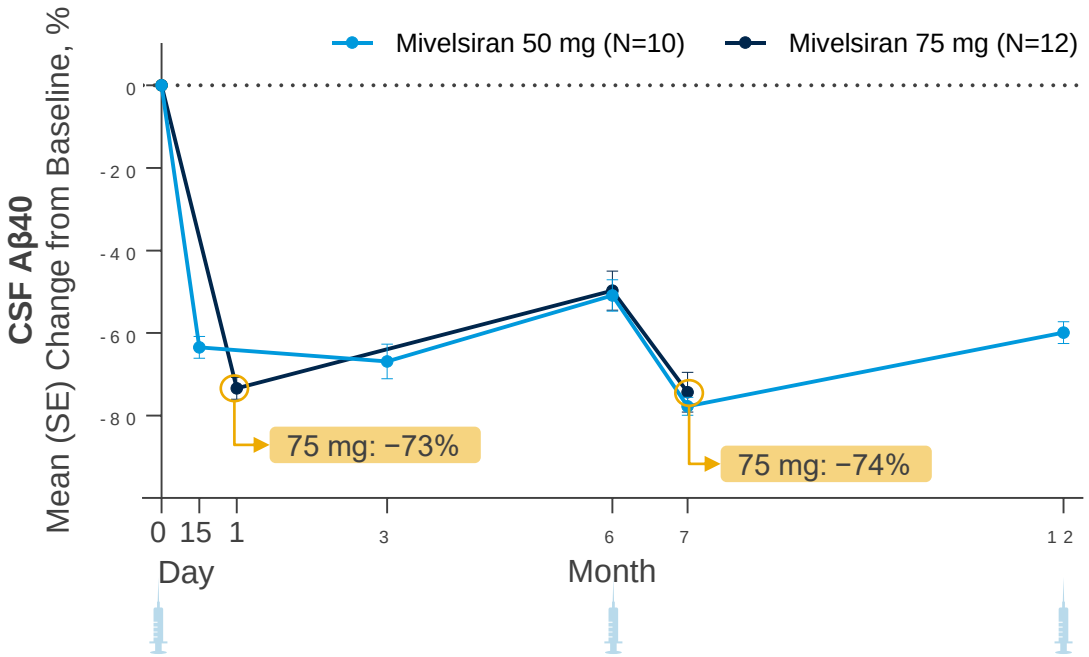
Mivelsiran: Durable Knockdown and Tolerability Observed >1 Year

Multiple Doses of Mivelsiran Provided Additional Reductions in CSF Aβ42 and Aβ40 Levels





Encouraging Safety and Tolerability Profile

- Majority of AEs were nonserious, mild or moderate, and deemed unrelated to the study drug
- No serious or severe AEs were deemed related to study drug
- The two most common AEs were procedural pain and procedural headache
- No notable increases in CSF WBCs, protein or NfL

Data shown as of May 15, 2025. Time points with an n of <3 are not plotted.
Aβ, amyloid-beta; Aβ40, Aβ peptide length 40 amino acids; Aβ42, Aβ peptide length 42 amino acids; CSF, cerebrospinal fluid; SE, standard error.

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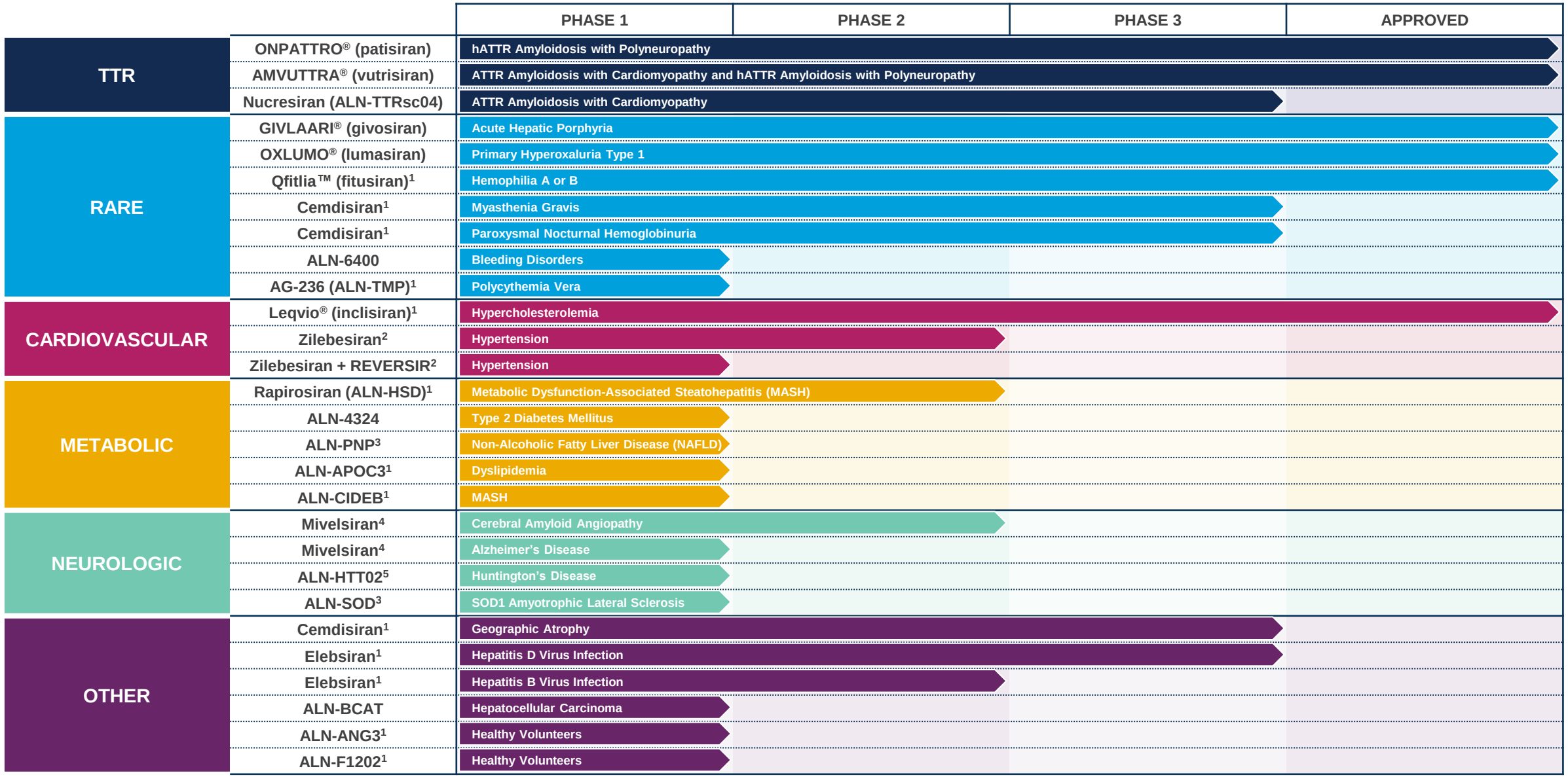
Robust and High-Value Pipeline of RNAi Therapeutics



[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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Q2 2025 Financial Summary

($ in millions except where noted as percentages)	Q2 2024	Q2 2025	Q2 2025 vs Q2 2024 (Reported)	Q2 2025 vs Q2 2024 (CER[2])
Total Net Product Revenues	$410	**$672**	***64%***	***62%***
Net Revenues from Collaborations & Royalties	249	**101**	***(59%)***	
Collaboration Revenue	227	61	*(73%)*	
Royalty Revenue	22	40	*78%*	
Total Revenues	660	**774**	***17%***	
Total Cost of Goods Sold, Collaborations & Royalties	69	**143**		
Gross Margin on Product Revenues	*84%*	*79%*		
Gross Margin on Total Revenues	*90%*	*82%*		
Non-GAAP Combined R&D and SG&A Expenses[1]	453	**535**	***18%***	
R&D	246	274	*11%*	
SG&A	207	261	*26%*	
Non-GAAP Operating Income	138	**95**		
Non-GAAP Operating Margin	*21%*	***12%***		
Non-GAAP Net Income	74	**44**		

($ in millions)	Q4 2024	Q2 2025
Cash, Cash Equivalents & Marketable Securities (period end)	2,695	**2,858**

[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 July 31, 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 Q2 2025 performance (restated using Q2 2024 exchange rates) to actual Q2 2024 reported performance.

2025 Full-Year Guidance Upgraded

Item	Prior FY 2025 Guidance	Updated FY 2025 Guidance
Total Net Product Revenues[1]	**$2,050 to $2,250 million**	**$2,650 to $2,800 million**
• Total Rare Net Product Revenues (GIVLAARI, OXLUMO)	$450 to $525 million	$475 to $525 million
• Total TTR Net Product Revenues (PN & CM) (AMVUTTRA, ONPATTRO)	$1,600 to $1,725 million	$2,175 to $2,275 million
Net Product Revenues Growth vs. 2024 at Reported FX Rates[1]	*25% to 37%*	*61% to 70%*
Net Product Revenues Growth vs. 2024 at constant exchange rates (i.e., operational growth)[2]	*26% to 39%*	*59% to 68%*
Net Revenues from Collaborations & Royalties	**$650 to $750 million**	**Reiterate FY Guidance**
Non-GAAP Combined R&D and SG&A Expenses[3]	**$2,100 to $2,200 million**	**Reiterate FY Guidance**
Non-GAAP Operating Income[3]	**Achieve profitability**	**Reiterate FY Guidance**

[1] Our 2025 FY Guidance is based upon June 30, 2025 FX rates including 1 EUR = 1.17 USD and 1 USD = 144 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 in the Prior FY 2025 Guidance, and $345M - $375M in the Updated FY 2025 Guidance.

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2025 Full-Year Guidance Upgraded

Item	Prior FY 2025 Guidance	Updated FY 2025 Guidance
Total Net Product Revenues[1]	$2,850 to $2,950 million	$2,850 to $2,900 million
Net … at R…		
Net … exc…		
Net…		
No… SG…		
Non-GAAP Operating Income[3]	Achieve profitability	Reiterate FY Guidance

TTR Franchise Growth

2023	+~$300M	2024	+~$1,000M	2025
$912M		$1,223M		$2,225M
(actual)		*(actual)*		*(TTR guidance midpoint)*
PN only		***PN only***		***PN+CM***

[1] *Our 2025 FY Guidance is based upon June 30, 2025 FX rates including 1 EUR = 1.17 USD and 1 USD = 144 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 in the Prior FY 2025 Guidance, and $345M - $375M in the Updated FY 2025 Guidance.*

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Alnylam 2025 Goals

amvuttra (vutrisiran) · onpattro (patisiran) · GIVLAARI (givosiran) · OXLUMO (lumasiran)		Combined Net Product Revenue Guidance $2,650M – $2,800M	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

Q&A Session

Q2 2025 Financial Results

Alnylam®


Silence disease
Amplify life™
Alnylam®

Appendix

Q2 2025 Financial Results

Alnylam Pharmaceuticals, Inc.

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

	Three Months Ended	
	June 30, 2025	June 30, 2024
Reconciliation of GAAP to Non-GAAP Research and development expenses:		
GAAP Research and development expenses	$ 323,621	$ 294,142
Less: Stock-based compensation expenses	(49,552)	(48,115)
Non-GAAP Research and development expenses	$ 274,069	$ 246,027
Reconciliation of GAAP to Non-GAAP Selling, general and administrative expenses:		
GAAP Selling, general and administrative expenses	$ 323,314	$ 248,397
Less: Stock-based compensation expenses	(62,128)	(41,173)
Non-GAAP Selling, general and administrative expenses	$ 261,186	$ 207,224
Reconciliation of GAAP to Non-GAAP Income (loss) from operations:		
GAAP (Loss) income from operations	$ (16,199)	$ 48,614
Add: Stock-based compensation expenses	111,680	89,288
Non-GAAP Operating income	$ 95,481	$ 137,902
Reconciliation of GAAP to Non-GAAP Net income (loss):		
GAAP Net loss	$ (66,277)	$ (16,889)
Add: Stock-based compensation expenses	111,680	89,288
Add: Realized and unrealized loss on marketable equity securities	1,350	1,367
Less: Income tax effect of GAAP to non-GAAP reconciling items	(2,631)	—
Non-GAAP Net income	$ 44,122	$ 73,766

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

	June 30, 2025
	Three Months Ended
Total TTR net product revenue growth, as reported	77 %
Add: Impact of foreign currency translation	(2)
Total TTR net product revenue growth at constant currency	75 %
Total Rare net product revenue growth, as reported	24 %
Add: Impact of foreign currency translation	(1)
Total Rare net product revenue growth at constant currency	23 %
Total net product revenue growth, as reported	64 %
Add: Impact of foreign currency translation	(2)
Total net product revenue growth at constant currency	62 %
Total revenue growth, as reported	17 %
Add: Impact of foreign currency translation	(1)
Total revenue growth at constant currency	16 %

Constant Currency = Constant Exchange Rate, or CER