Third Quarter 2025 Financial Results

October 30, 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, Alnylam's confidence in the long-term strength and sustainability of its TTR franchise, and the prospects for RNAi therapeutics to become the standard of care in TTR amyloidosis; Alnylam's ability to sustain profitability going forward; Alnylam's confidence in the launch of AMVUTTRA in ATTR-CM and the performance of its other commercial products for the remainder of 2025; the expectation that Alnylam will launch AMVUTTRA in ATTR-CM in jurisdictions outside the U.S. in 2026, that the majority of ex-U.S. launches will begin in 2026, and that additional AMVUTTRA markets will come online in ATTR-CM in the years ahead; Alnylam's ability to achieve the "*Alnylam P^{5}x25*" goals and to evolve into a top-tier biotech company; Alnylam's ability to establish AMVUTTRA as the first-line treatment for ATTR-CM; the belief that ATTR-CM is a growing and underserved category; Alnylam's ability to achieve significant revenue growth going forward; Alnylam's ability to build a pipeline that has the potential to drive sustainable growth and long-term value creation; the potential multi-billion dollar opportunities within Alnylam's pipeline and the ability of Alnylam's R&D engine to deliver sustainable innovation and value creation for many years to come; the potential for Alnylam to successfully advance its research and development programs; the timing of the initiation and readout of clinical trials of any of Alnylam's product candidates and of any approval and commercial launch of any of Alnylam's product candidates; the potential product profiles and benefits of Alnylam's product candidates, including zilebesiran and ALN-6400; the number of patients who will be enrolled in the ZENITH clinical trial; and Alnylam's projected commercial and financial performance, including the revised expected range of TTR and combined net product revenues, and Non-GAAP operating expense guidance 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; the possibility of unfavorable new clinical data and further analyses of existing clinical data; interim and preliminary data; the possibility that clinical data are subject to differing interpretations and assessments by regulatory agencies; 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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TTR Leadership Drove Q3 Results and Increase to FY25 Guidance

TTR Leadership

$724M
+135% YoY
Q3 Total TTR Net Revenues

$543M
+194% YoY
U.S. Q3 Total TTR Net Revenues

Growth Through Innovation

Hypertension
zilebesiran
Initiated ZENITH Phase 3 Trial

Alzheimer's/ Tauopathies
ALN-5288
Initiated Phase 1 Trial

hATTR-PN
nucresiran
Initiating TRITON-PN Phase 3 Trial Early Q4

Strong Financial Performance

$851M
(+103% YoY)
Q3 Total Net Product Revenues

$2,950M to $3,050M
(+$275M/ +10% midpoint)
Increased 2025 Total Net Product Revenue Guidance

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Tremendous Progress on *Alnylam P5x25* 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

Robust Performance in Q3 2025

Strong Growth Achieved Across Franchises and Regions

Q3 2025 Overall Portfolio

$851M
Combined Net Product Revenues

+103%
YoY growth[1]
vs. Q3'24

+27%
QoQ growth[1]
vs. Q2'25

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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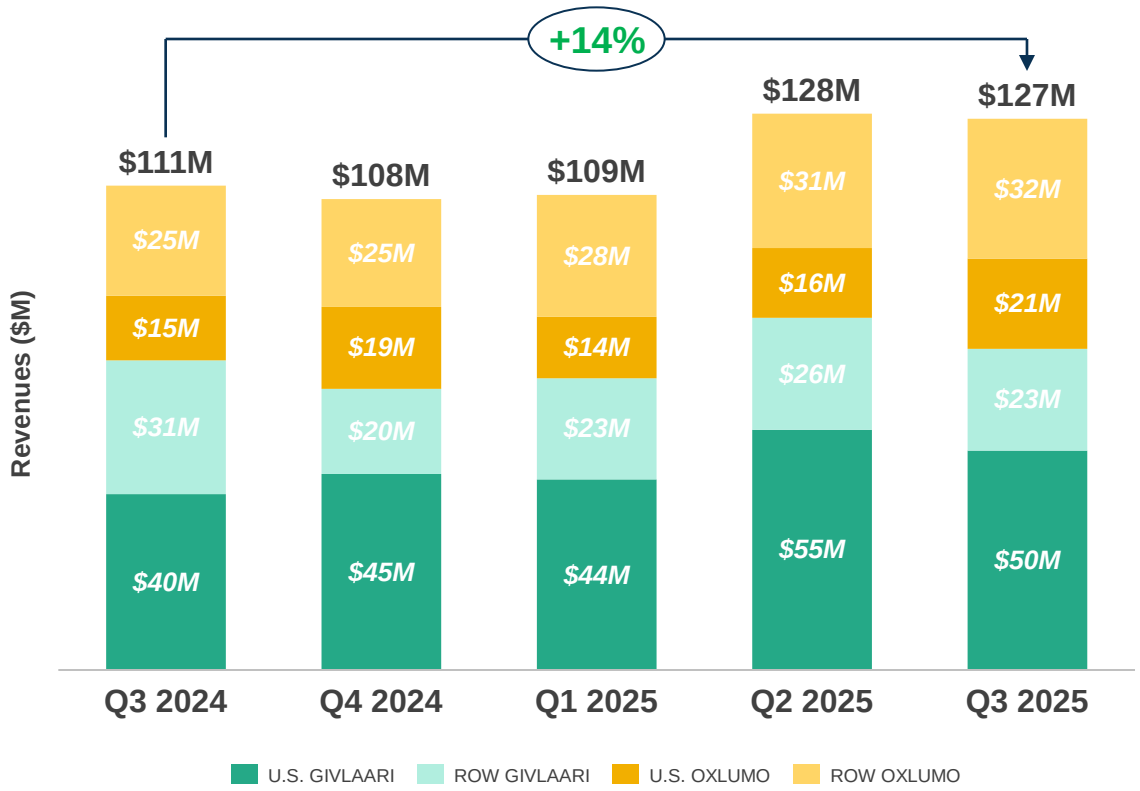
Q3 2025: Sustained Rare Franchise Performance

$127M
Total Rare
Global Q3 2025
Net Product Revenues



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

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

Q3 2025 Rare Franchise Highlights

	QoQ % Growth	YoY % Growth
GIVLAARI	-9%	**4%**
OXLUMO	13%	**31%**
TOTAL Rare	-1%	**14%**

- GIVLAARI YoY +4% growth highlights:
  - ~17% YoY increase in global patients on therapy
  - Reported YoY growth in product sales less than growth in patients primarily due to timing of orders in partner markets
- OXLUMO YoY +31% growth highlights:
  - ~15% YoY increase in global patients on therapy
  - Reported YoY growth in product sales higher than growth in patients primarily due to U.S. inventory build, gross-to-net favorability, and timing of orders in partner markets
- Modest FX tailwind +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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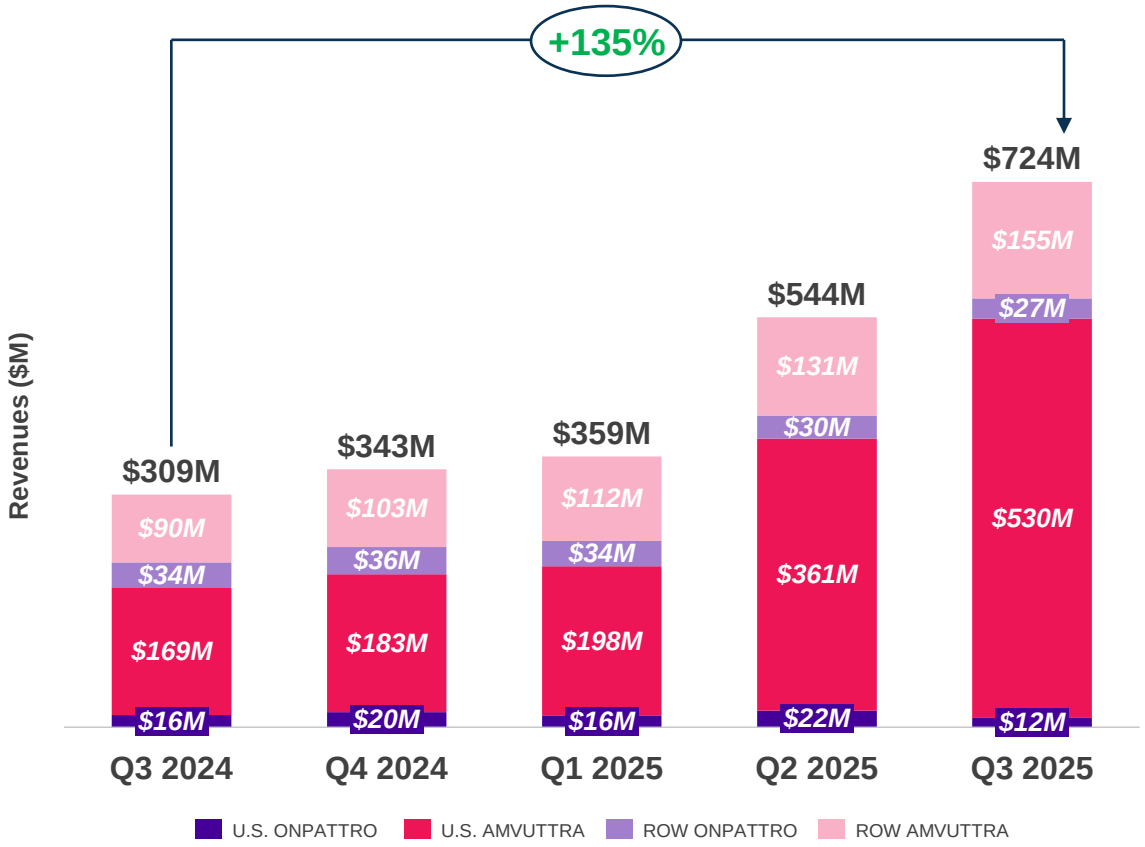
AMVUTTRA ATTR-CM Launch Momentum Continues in Q3 2025

$724M
Total TTR
Global Q3 2025
Net Product Revenues



amvuttra (vutrisiran) injection 25 mg/0.5 mL

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

Q3 2025 TTR Franchise Highlights

	QoQ % Growth	YoY % Growth
U.S.	42%	**194%**
ROW	13%	**46%**
Global	33%	**135%**

- U.S. Q3'25 vs. Q2'25 (QoQ) +42% growth highlights:
  - Continued substantial demand growth (+47%) driven by ATTR-CM launch, estimated ~$300M ATTR-CM Q3 revenue[2]
  - Demand driven inventory channel build more than fully offset by increase in gross-to-net deductions
- U.S. Q3'25 vs. Q3'24 (YoY) +194% growth highlights:
  - ~200% demand growth driven primarily by ATTR-CM launch
  - Partially offset by increase in gross-to-net deductions, in line with our expectations of a mid-single digit decrease in net price YoY
- ROW YoY +46% growth primarily driven by continued ATTR-PN patient growth and initial uptake in ATTR-CM sales in Japan and Germany
- Modest FX tailwind +4% (YoY CER[1] growth = 131%)

[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; [2] See next slide; estimate based on hATTR-PN run-rate

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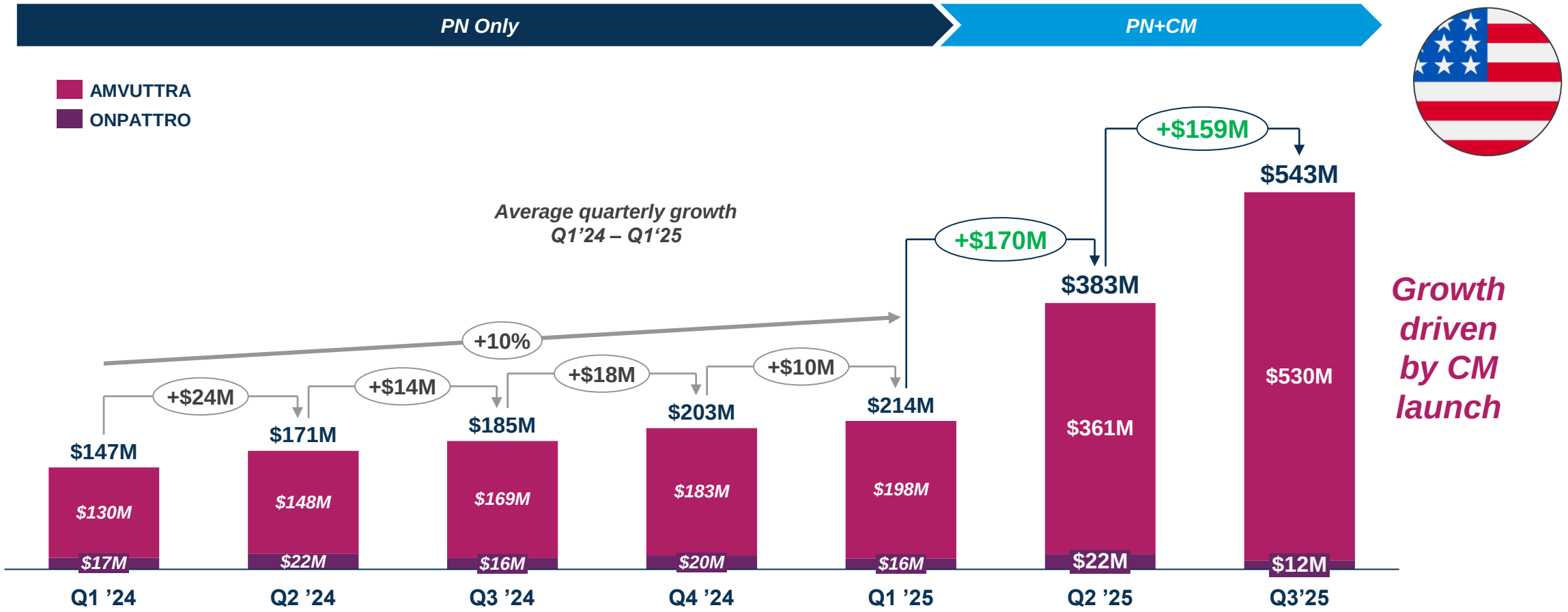
AMVUTTRA ATTR-CM Launch Momentum Continues in Q3 2025

Total TTR Growth in U.S. Driven by Estimated ~$300 Million in ATTR-CM Revenue



	Q1 '24	Q2 '24	Q3 '24	Q4 '24	Q1 '25	Q2 '25	Q3'25
QoQ Growth	3%	16%	8%	10%	5%	80%	42%
YoY Growth	35%	40%	37%	42%	45%	125%	194%

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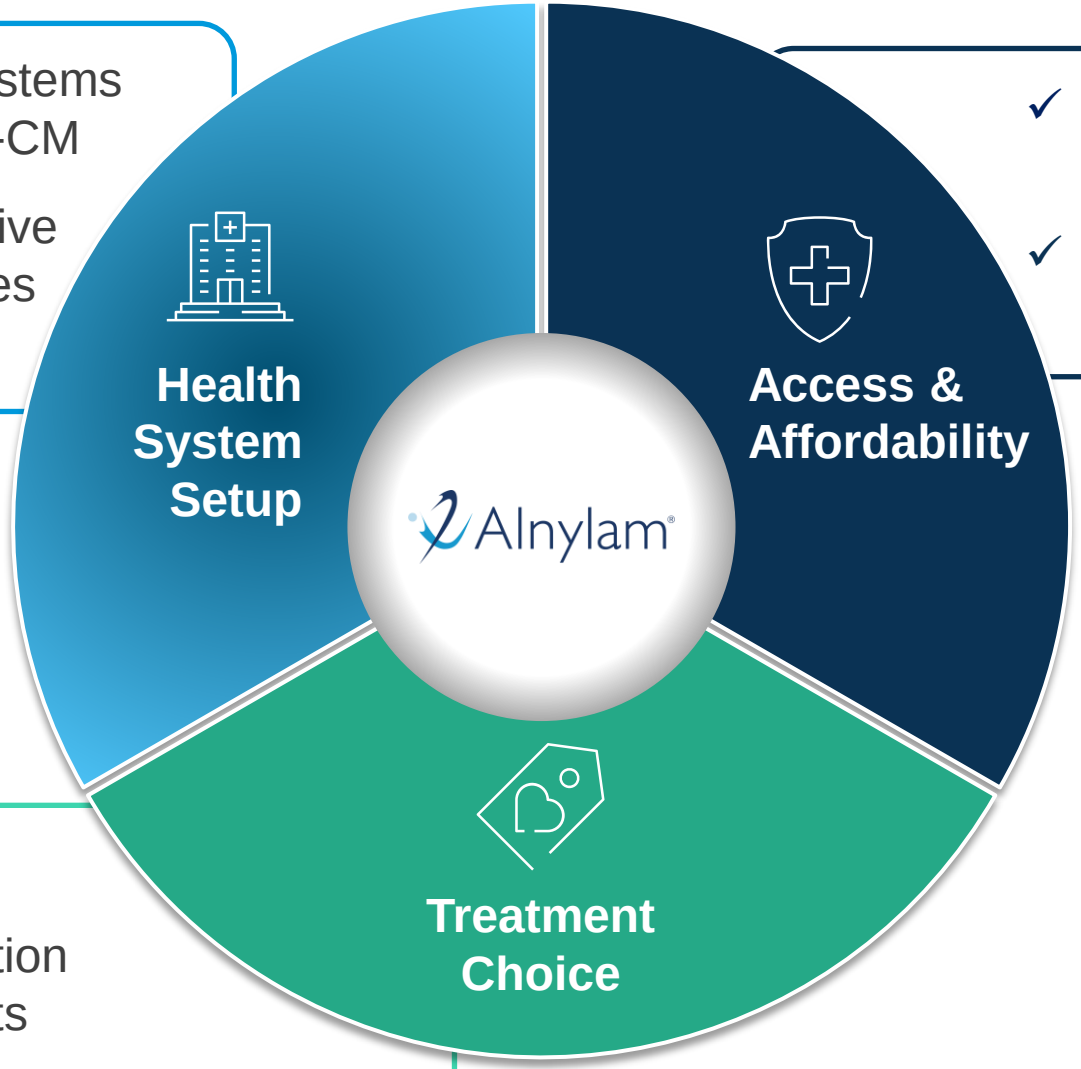
ATTR-CM U.S. Launch Momentum Continues

- ✓ **Nearly all** priority health systems using AMVUTTRA in ATTR-CM
- ✓ **~90% of patients** can receive AMVUTTRA within ~10 miles of home



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

- ✓ **Doubled** demand QoQ
- ✓ **Broad & balanced** utilization across all patient segments
- ✓ **Expanded** prescriber base

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Strong Launch Progress Expected to Drive Sustainable Growth

✓ Well positioned for TTR leadership

✓ Growing & underserved category

✓ Adding global markets in 2026+

Pipeline

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

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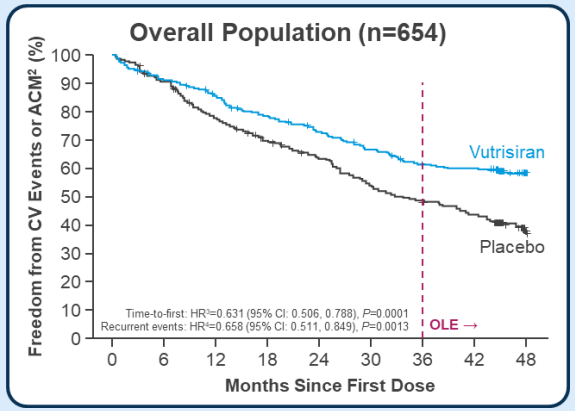
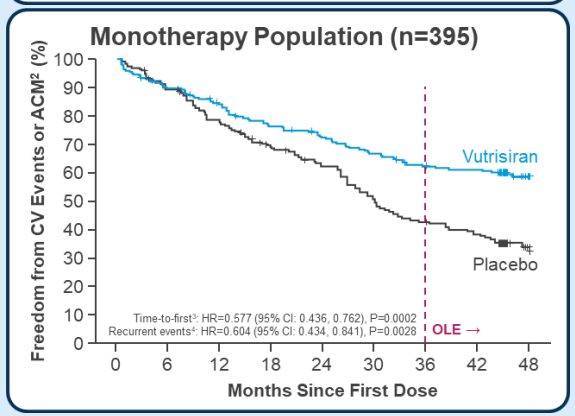
HELIOS-B Data Continue to Support AMVUTTRA's Clinically Differentiated Profile

Long-term vutrisiran treatment significantly reduced the risk of ACM and CV events[1]

Time-to-First Event

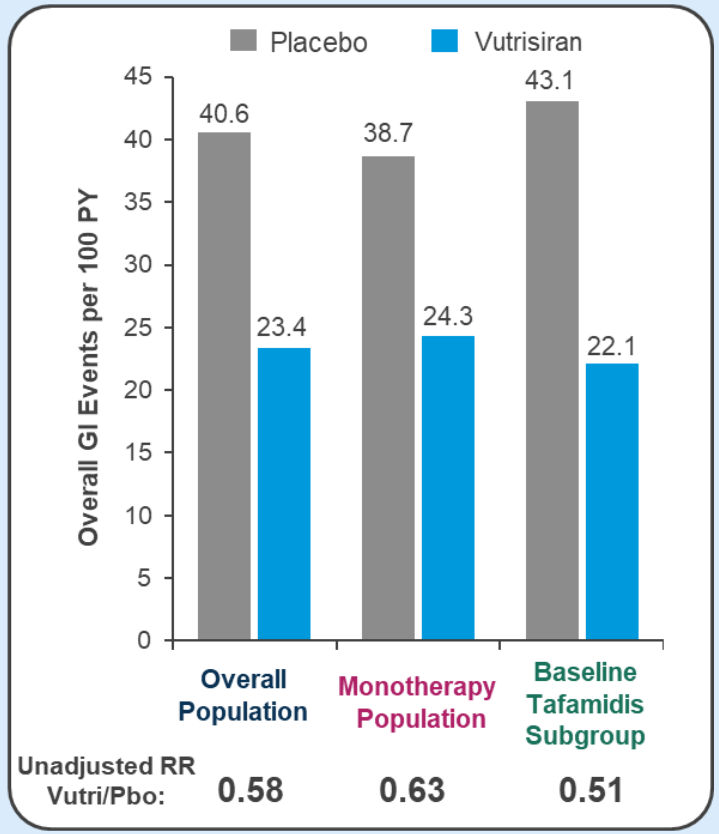


37% Risk Reduction
(nominal p=0.0001)



42% Risk Reduction
(nominal p=0.0002)

Evidence of fewer gastrointestinal events in ATTR-CM patients treated with vutrisiran[5]



[1] Garcia-Pavia, et al. ESC 2025; [2] All-cause mortality includes heart transplantation and left ventricular assist device placement, and CV events include CV-related hospitalizations and urgent heart failure visits; [3] Survival probability based on IPTW-adjusted Kaplan-Meier curves. The HR is derived from Cox proportional hazards model; [4] Recurrent events analysis based on the modified Andersen-Gill model, also known as LWYY; [5] Urey, et al. HFSA 2025 (Adverse Events classified under GI disorders system organ class during the double-blind period of HELIOS-B were compared between the vutrisiran and placebo arms of the overall population, monotherapy population, and baseline tafamidis subgroup)

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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

Targeting Launch ~2030

- Randomized, double-blind, event-driven outcomes study of nucresiran versus placebo (N ~ 1200)
- Primary endpoint of all-cause mortality and recurrent CV events
- **Initiated**

TRITON-PN
hATTR-PN CLINICAL STUDY

Topline results expected in 2028

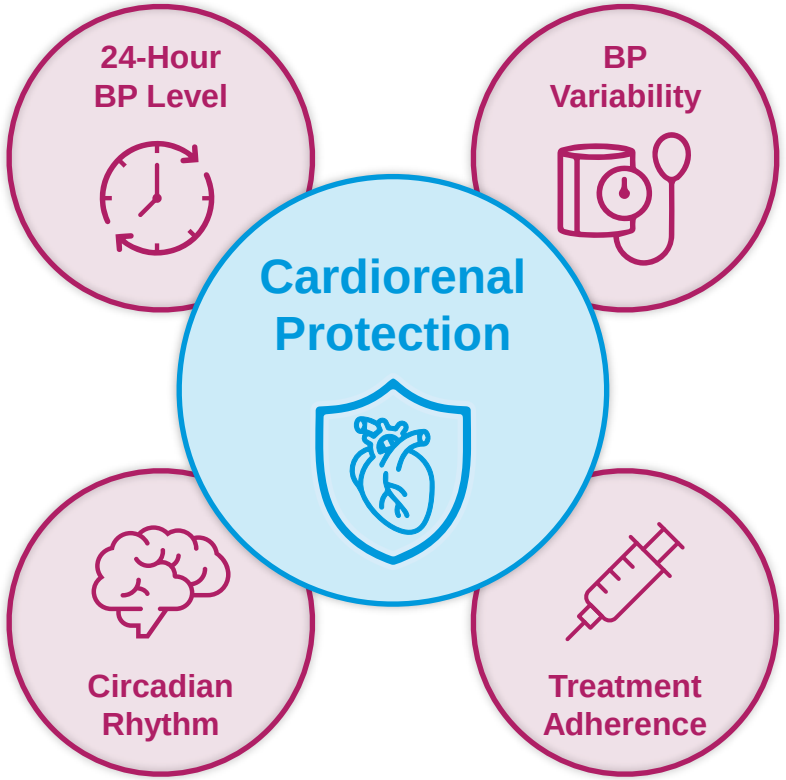
- Randomized, open-label study of nucresiran versus vutrisiran internal reference (N ~ 125)
- Primary endpoint of mNIS+7 at Month 9 in nucresiran versus APOLLO placebo (similar to HELIOS-A); continued data collection through Month 18
- **Initiating Q4 2025**

Nucresiran is an investigational therapeutic in development for the treatment of ATTR amyloidosis. The safety and efficacy of nucresiran have not been established or approved by the FDA, EMA or any other health authority. The safety and efficacy of nucresiran are currently being evaluated by these regulatory authorities.

Zilebesiran: Targeting Continuous Blood Pressure Control to Reduce Cardiovascular & Renal Risk

Reduce SBP throughout the 24-Hour Period

Avoid exaggerated BP variability over 24-Hour and long-term

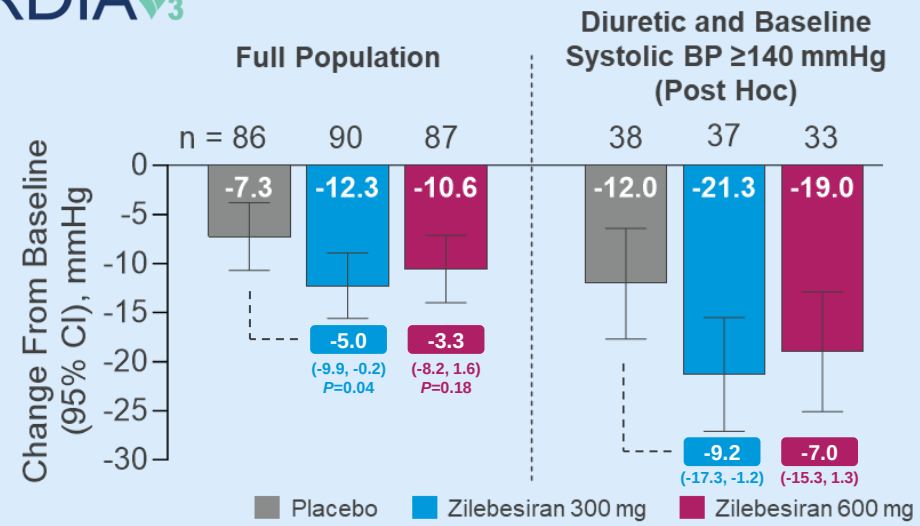


Reduce nighttime SBP/Restore normal nocturnal dipping

Biannual dosing to improve adherence

Placebo-Adjusted Change from Baseline to Month 3 in Office Systolic BP[1]

KARDIA-3



- Clinically meaningful, continuous control of BP over 24h period for up to six months
- Enhanced effect seen in enriched population
- Acceptable safety profile with low rates of hyperkalemia, kidney dysfunction, and hypotension

Zilebesiran is an investigational therapeutic in development for hypertension and improving cardiovascular outcomes. The safety and efficacy of zilebesiran have not been established or approved by the FDA, EMA or any other health authority. The safety and efficacy of zilebesiran are currently being evaluated by these regulatory authorities.

BP, blood pressure; SBP, systolic blood pressure; adapted from Kario K. Prog Cardiovasc Dis. 2016;9:262–81; [1] Pagidipati, et al. ESC 2025.

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zenith Phase 3 Cardiovascular Outcomes Trial Design

Randomized, Double-Blind, Event-Driven Study in High CV Risk Patients with Uncontrolled Hypertension

Study Population

- Adult patients with uncontrolled hypertension and established CV disease or at high risk
- Office systolic BP ≥140 mmHg on stable treatment (≥2 antihypertensive medications, one of which is a diuretic)
- Excluded: eGFR <30 mL/min/1.73m^2, potassium >4.8 mEq/L

Randomize 1:1 (n≈11,000)

Zilebesiran SC 300 mg Q6M + standard of care	Placebo SC Q6M + standard of care

Minimum follow-up: 2 years

Primary Outcome: CV death, nonfatal MI, nonfatal stroke, or HF event

NCT07181109

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ALN-6400: Potential Universal Hemostatic Agent

Therapeutic Hypothesis: Lowering Plasminogen to Reduce Bleeding

Hereditary Hemorrhagic Telangiectasia (HHT):

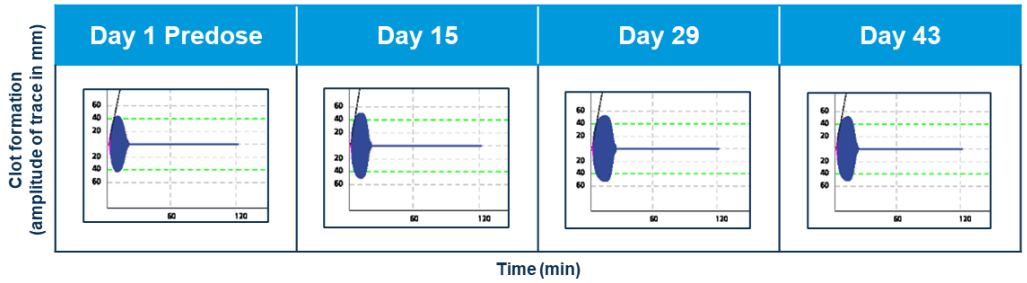
- Second most common inherited bleeding disorder
- 90% live with recurrent nosebleeds
- >50% experience iron deficiency anemia

Targeting plasminogen: genetic validation

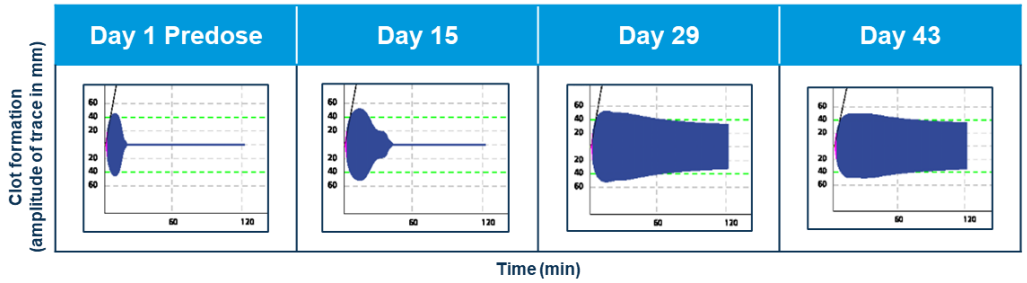
- ↑ **Circulating PLG protein levels**
  - ↑ GI and nose bleeding
  - ↑ Heavy menstrual bleeding
- ↑ **PLG loss of function**
  - ↓ GI and nose bleeding
  - ↓ Heavy menstrual bleeding
  - ↔ No increase in risk of thrombosis

Initial Clinical Proof-of-Mechanism[1]

Healthy Volunteer Dosed with Placebo



Healthy Volunteer Dosed with ALN-6400



Phase 2 HHT Trial Initiated[2]

[1] Initial results, Phase 1, Cohort 1; [2] NCT06659640; ALN-6400 is an investigational therapeutic in development for the treatment of bleeding disorders. The safety and efficacy of ALN-6400 have not been established or approved by the FDA, EMA or any other health authority.

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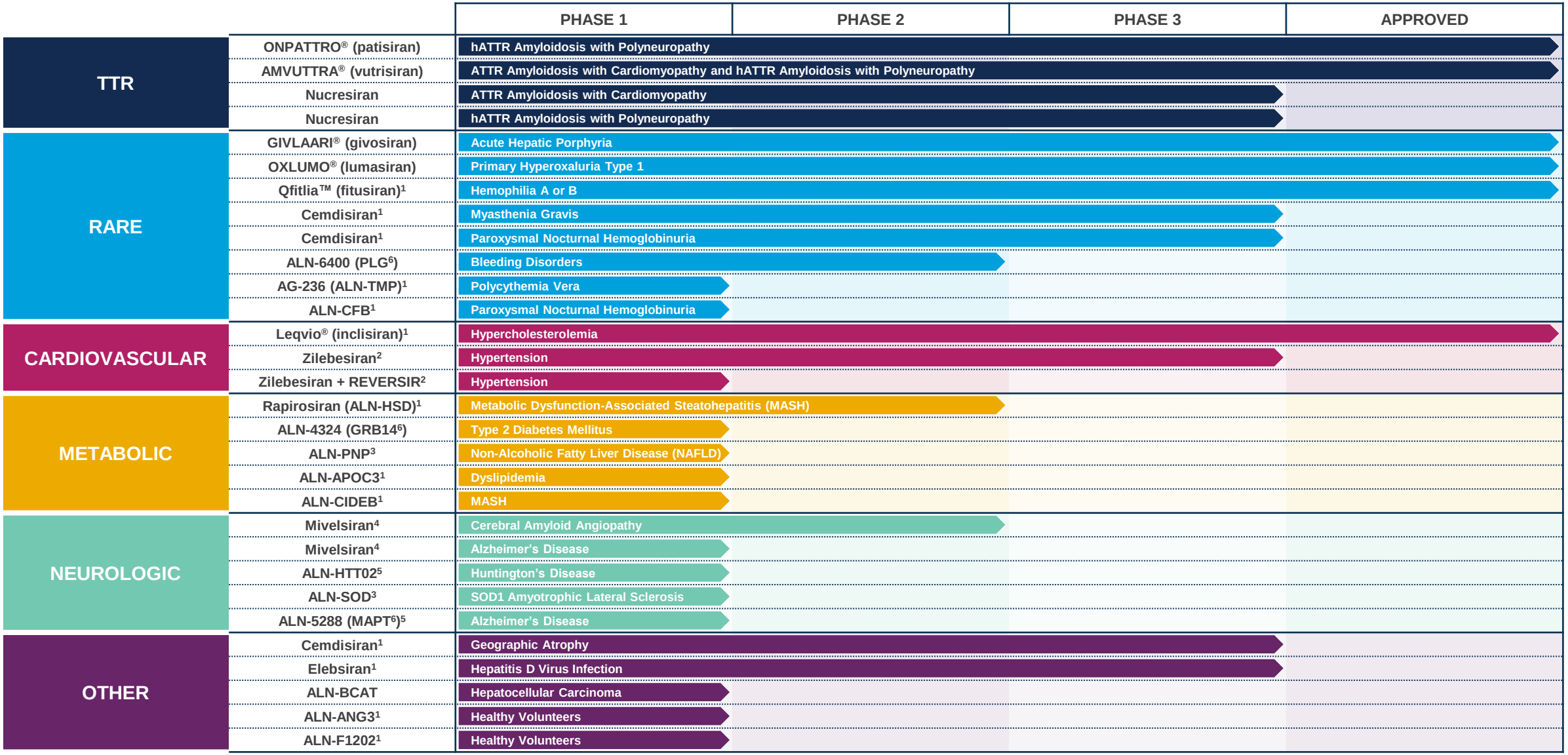
Robust and High-Value Pipeline of RNAi Therapeutics



[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; [6] Gene target

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Financial Summary and Upcoming Milestones

Jeff Poulton
Chief Financial Officer

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Q3 2025 Financial Summary

($ in millions except where noted as percentages)	Q3 2024	Q3 2025	Q3 2025 vs Q3 2024 (Reported)	Q3 2025 vs Q3 2024 (CER[2])
Total Net Product Revenues	$420	**$851**	***103%***	***99%***
Net Revenues from Collaborations & Royalties	81	**398**	***393%***	
Collaboration Revenue	57	352	*513%*	
Royalty Revenue	23	46	*98%*	
Total Revenues	501	**1,249**	***149%***	***147%***
Total Cost of Goods Sold, Collaborations & Royalties	86	**200**		
Gross Margin on Product Revenues	*80%*	*77%*		
Gross Margin on Total Revenues	*83%*	*84%*		
Non-GAAP Combined R&D and SG&A Expenses[1]	446	**573**	***28%***	
R&D	251	310	*23%*	
SG&A	195	263	*35%*	
Non-GAAP Operating Income / (Loss) [1]	(31)	**476**		
Non-GAAP Operating Margin[1]	*(6%)*	***38%***		
Non-GAAP Net Income / (Loss)[1]	(64)	**396**		

($ in millions)	Q4 2024	Q3 2025
Cash, Cash Equivalents & Marketable Securities (period end)	2,695	**2,725**

[1] *Non-GAAP R&D expenses, Non-GAAP SG&A expenses, Non-GAAP operating income / (loss), Non-GAAP Operating Margin, and Non-GAAP Net Income are non-GAAP financial measures that exclude from the corresponding GAAP measures costs related to stock-based compensation expense, loss related to convertible debt, and realized and unrealized gains or losses on marketable equity securities. 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 30, 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 Q3 2025 performance (restated using Q3 2024 exchange rates) to actual Q3 2024 reported performance.*

2025 Full-Year Guidance

Item	Prior FY 2025 Guidance	Updated FY 2025 Guidance
Total Net Product Revenues[1]	**$2,650 to $2,800 million**	**$2,950 to $3,050 million**
• Total Rare Net Product Revenues (GIVLAARI, OXLUMO)	$475 to $525 million	Reiterate FY Guidance
• Total TTR Net Product Revenues (PN & CM) (AMVUTTRA, ONPATTRO)	$2,175 to $2,275 million	$2,475 to $2,525 million
Net Product Revenues Growth vs. 2024 at Reported FX Rates[1]	*61% to 70%*	*79% to 85%*
Net Product Revenues Growth vs. 2024 at constant exchange rates (i.e., operational growth)[2]	*59% to 68%*	*78% to 84%*
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**	**$2,150 to $2,200 million**
Non-GAAP Operating Income[3]	**Achieve profitability**	**Reiterate FY Guidance**

[1] Our 2025 FY Guidance is based upon September 30, 2025 FX rates including 1 EUR = 1.17 USD and 1 USD = 148 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 $345M - $375M in both the Prior FY 2025 Guidance and 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 $2,950M – $3,050M	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

Q3 2025 Financial Results

Alnylam®


Silence disease
Amplify life™
Alnylam®

Appendix

Q3 2025 Financial Results

Alnylam Pharmaceuticals, Inc.

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

	Three Months Ended	
	September 30, 2025	September 30, 2024
Reconciliation of GAAP to Non-GAAP Research and development expenses:		
GAAP Research and development expenses	$ 358,814	$ 270,926
Less: Stock-based compensation expenses	(48,725)	(19,794)
Non-GAAP Research and development expenses	$ 310,089	$ 251,132
Reconciliation of GAAP to Non-GAAP Selling, general and administrative expenses:		
GAAP Selling, general and administrative expenses	$ 322,076	$ 220,993
Less: Stock-based compensation expenses	(59,486)	(26,010)
Non-GAAP Selling, general and administrative expenses	$ 262,590	$ 194,983
Reconciliation of GAAP to Non-GAAP Income (loss) from operations:		
GAAP Income (loss) from operations	$ 367,982	$ (76,905)
Add: Stock-based compensation expenses	108,211	45,804
Non-GAAP Operating income (loss)	$ 476,193	$ (31,101)
Reconciliation of GAAP to Non-GAAP Net income (loss):		
GAAP Net income (loss)	$ 251,084	$ (111,570)
Add: Stock-based compensation expenses	108,211	45,804
Add: Realized and unrealized loss on marketable equity securities	—	1,567
Add: Loss related to convertible debt	39,146	—
Less: Income tax effect of GAAP to non-GAAP reconciling items	(2,261)	—
Non-GAAP Net income (loss)	$ 396,180	$ (64,199)

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

	September 30, 2025 Three Months Ended
Total TTR net product revenue growth, as reported	135 %
Add: Impact of foreign currency translation	(4)
Total TTR net product revenue growth at constant currency	131 %
Total Rare net product revenue growth, as reported	14 %
Add: Impact of foreign currency translation	(3)
Total Rare net product revenue growth at constant currency	11 %
Total net product revenue growth, as reported	103 %
Add: Impact of foreign currency translation	(4)
Total net product revenue growth at constant currency	99 %
Total revenue growth, as reported	149 %
Add: Impact of foreign currency translation	(2)
Total revenue growth at constant currency	147 %

Constant Currency = Constant Exchange Rate, or CER