Establishing TTR Leadership

Progress in First Year Following Launch

March 24, 2026

amvuttra® (vutrisiran) injection 25 mg/0.5 mL

March 20, 2025

Approved in U.S.

for the treatment of the cardiomyopathy of wild-type or hereditary ATTR amyloidosis (ATTR-CM)

Alnylam

The Future of ATTR Leadership

Accelerate AMVUTTRA Uptake

Scaling global presence and market penetration.

Advance nucresiran

Raising the bar for clinical efficacy and experience.*

Invest in Cutting-Edge Capabilities

Investing in early diagnosis, coordinated care, and long-term outcomes.

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*Assumes positive clinical trial results and regulatory approval. Nucresiran is an investigational medicine. The safety and efficacy of nucresiran have not been established or evaluated by the FDA, EMA, or any other health authority.

Execution is Translating into Results

Over 100% Revenue Growth

TTR franchise revenues more than doubled year-over-year in 2025.

Proven execution

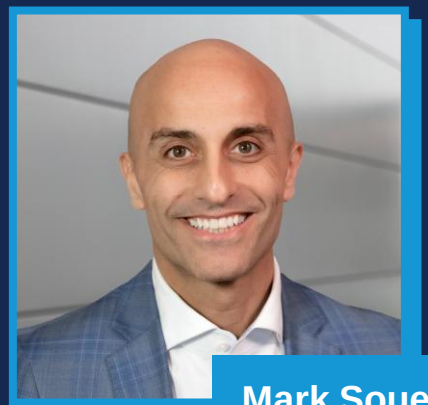
Delivered two consecutive guidance raises in 2025.

Strong 2026 Outlook

Guiding to 83% growth at the mid-point.

Today's Panel

Tolga Tanguler
Chief Commercial Officer



Mark Soued
Senior Vice President,
Head of U.S. & TTR Lead

John P. Kennedy
Senior Vice President, TTR
Franchise Commercialization Lead

Sameer Bansilal,
MD, MS, FACC
Vice President, TTR Disease Area Lead

Christine Akinc
Chief Corporate
Communications Officer

Alnylam®

Agenda

The Opportunity

The AMVUTTRA Value Proposition

Strengthening Leadership

Competing in silencer class
Anticipating stabilizer genericization

Unlocking Category Growth

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Alnylam Forward Looking Statements

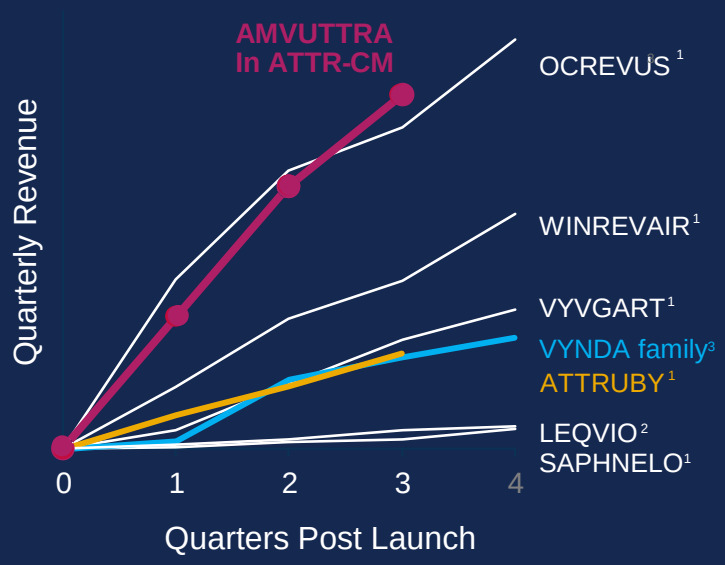
This presentation contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. All statements other than historical statements of fact regarding Alnylam's expectations, beliefs, goals, plans or prospects including, without limitation, statements regarding: Alnylam's ability to be a leader in the treatment of ATTR amyloidosis and to deliver transformative therapies to patients with ATTR amyloidosis; the size of the patient population with ATTR-CM in the U.S. and other jurisdictions; the potential for the ATTR-CM category to continue to increase in size in the future; the potential for diagnosis and treatment rates for ATTR-CM to increase in the future; Alnylam's ability to expander the depth and breadth of physicians who prescribe AMVUTTRA for ATTR-CM; the potential for patients treated with AMVUTTRA to live longer and better lives and to remain on treatment longer; the potential for the market dynamics in hATTR-PN to be transferrable into ATTR-CM; the potential for AMVUTTRA to continue to experience sustained growth, and not to be subject to universal step edits, following the loss of exclusivity of tafamidis; the potential for nucresiran to demonstrate greater knockdown of TTR with two doses per year; the ability of Alnylam to expand diagnosis, increase treatment rates, and strengthen care delivery for ATTR-CM patients across the healthcare system; the ability of Alnylam to achieve regulatory and pricing and reimbursement approvals for AMVUTTRA for the treatment of ATTR-CM in additional jurisdictions; the ability of Alnylam to achieve its *Alnylam 2030* strategy; and Alnylam's projected commercial and financial performance, including the expected range for 2026 of TTR net product revenues, 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 2030* 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; 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; Alnylam's ability to maintain strategic business collaborations; Alnylam's dependence on third parties for the development and commercialization of certain products; the outcome of litigation; the potential risk of government investigations; and unexpected expenditures; as well as those risks more fully discussed in the "Risk Factors" filed with Alnylam's 2025 Annual Report on Form 10-K filed with the Securities and Exchange Commission (SEC), as may be updated from time to time in Alnylam's subsequent Quarterly Reports on Form 10-Q, 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 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.

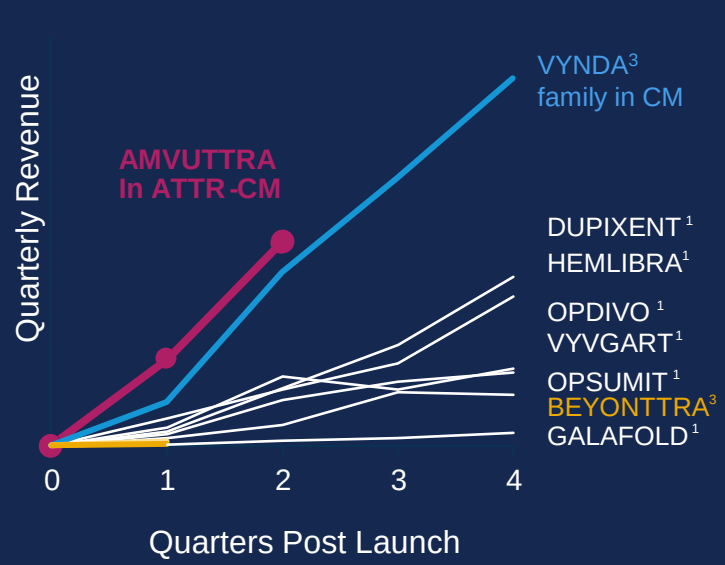
Driving Broad Impact in First Year of Launch

Exceptional Early Launch Momentum

U.S.



Japan



>12K

ATTR Patients on ALNY Treatments Globally
As of March 1, 2026

~1,600

Unique U.S. Prescribers Since ATTR-CM Launch
As of March 1, 2026

$2.1B

Total Global TTR Revenues Since Launch
Revenues through Q4 '25

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Select U.S. analogs are 2nd+ to market with differentiated mechanism of action, specialty/rare, Buy & Bill, or part of direct competitive set. Select Japan analogs are successful launches in the Japanese market across rare, specialty, and prevalent indications or direct competitive set.
1. Evaluate Pharma. 2.ALNY collaboration finance reporting. 3. VYNDA and BEYONTTRA revenues are calculated estimates based on IQVIA data.

We Have Built a Foundation for Durable Growth

Preference & Utilization

Established **1L leadership** among HCPs who have tried AMVUTTRA

Patient Access & Affordability

~90% have first-line access, majority pay $0 OOP

Broader access than in 2025

Provider Network

~90% of patients in the US can receive AMVUTTRA within ~10 miles of home

Robust category growth

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Source: Data on file

Early Launch Momentum and Strong Foundation; Accelerating the Next Phase of Launch

Average Share of New Starts Across First Three Quarters of Launch

~35%

new-to-brand share

despite entering as
the 3rd ATTR-CM therapy

Enablers

- **Experience** Drives Preference
- **Utilization** Drives Depth
- **Most requested** ATTR-CM brand by patients in the U.S.[1]

We are now driving **breadth of prescribers** to unlock the next wave of growth.

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1. Alnylam market research; Q4 2025.

AMVUTTRA Experience Reinforces Physician Confidence & Adoption

Physician Perceptions Prior to AMVUTTRA Experience

Prior authorization challenges

Concerns about buy & bill

All three products are the same

AMVUTTRA Experience Drives Preference

- **85%** of prior authorizations approved on first submission
- **~90%** 1L access; Most pay $0
- **~90%** of patients can receive AMVUTTRA within ~10 miles of home
- **Highly differentiated** clinical profile

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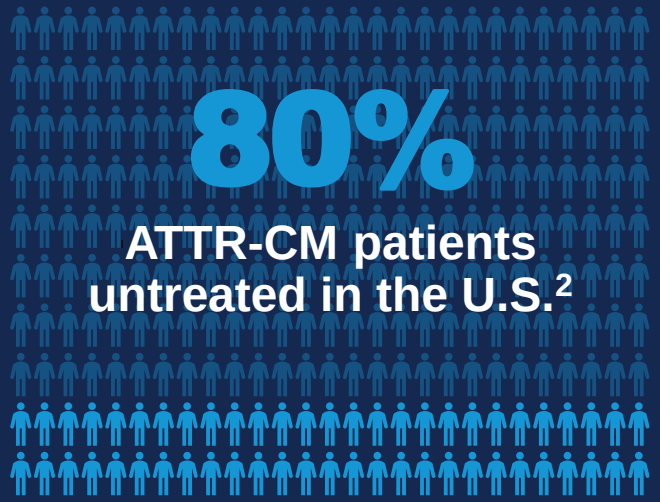
Source: Data on file

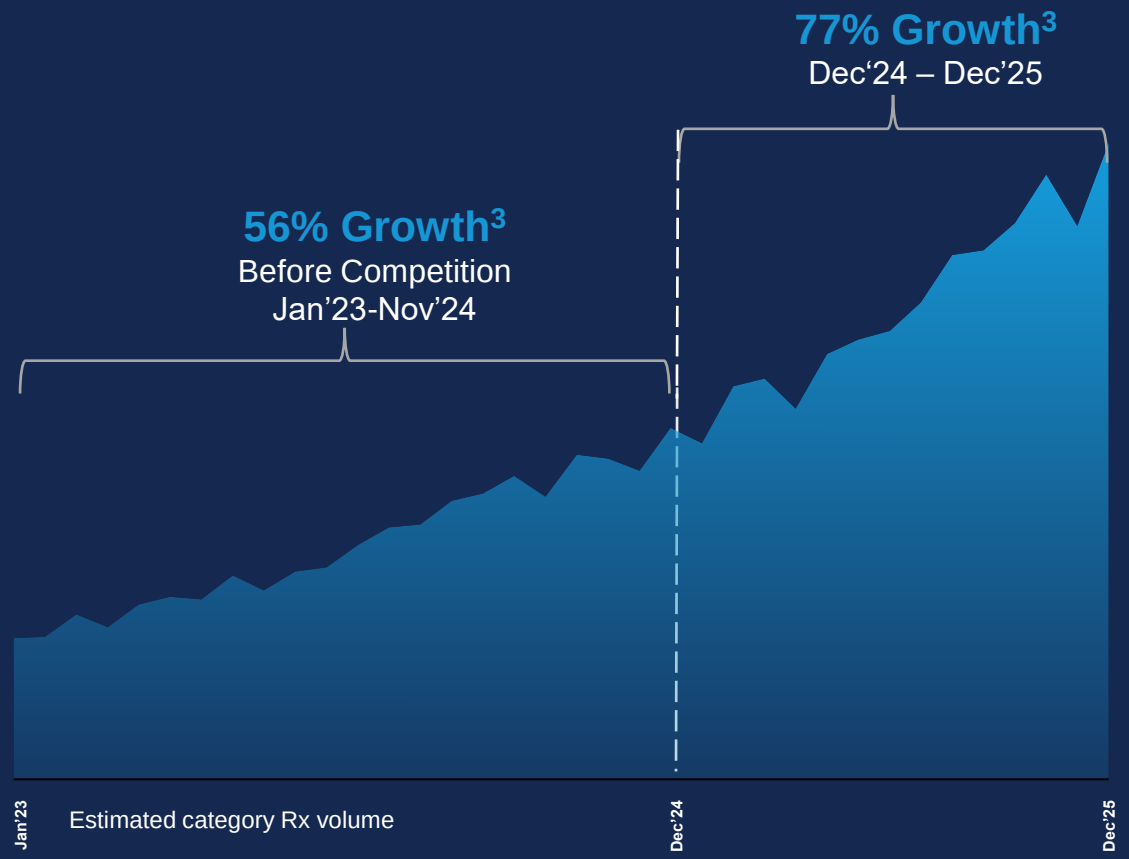
ATTR-CM Category is Large, Underserved and Growing

Significant Unmet Need

~200K U.S. patients[1]



Robust & Sustained Category Growth Accelerating Since Competitor Launches



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Source: Claims data through 12/31/2025; 1. Internal estimate based on claims data projection. 2. Information based on Alnylam modeling data. 3. Growth is based on compound annual growth rate

Agenda

The Opportunity

Mark Soued
Senior Vice President, Head of U.S. & TTR Lead

The AMVUTTRA Value Proposition

Strengthening Leadership

Competing in silencer class
Anticipating stabilizer genericization

Unlocking Category Growth

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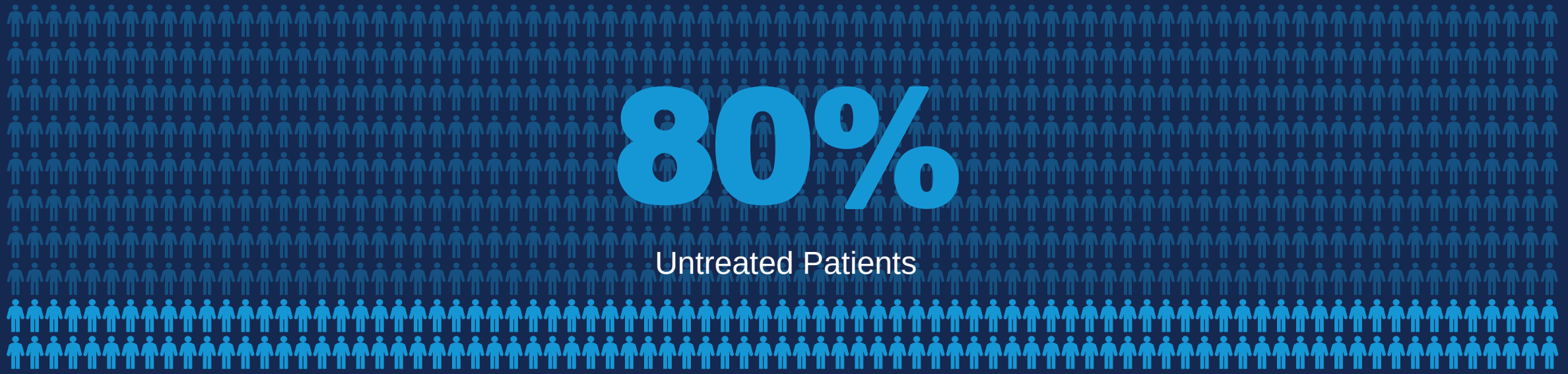
ATTR-CM Category is Large, Underserved and Growing

Significant Unmet Need

Nearly 200K U.S. patients **>500K** Globally



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Source: ATTR-CM, based on Alnylam modeling data

Category Expansion Fuels Sustained Opportunity Across U.S. Patient Segments (First Line + Switch/Add)

80% Untreated Patients[1]

160K Not Actively Treated

New to Treatment

15K+

New to Treatment Patients Annually

Stabilizer Progressors[2]

~15K

Treatment Progressors (50% of actively treating patients on common stabilizer)

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1. Sizing estimates based on claims analyses and internal market research (2026). ~40K patients are being actively treated (globally) 2. Recent literature show a range of estimates for many patients experiencing suboptimal response to Tx. In an analysis of US claims/EHR data (Fontana M, et al. data presented at Heart failure Society of America Annual Scientific Meeting 2024) ~50% experienced cardiac worsening (n >800, over median ~ 1 year)

Increased Competition & New Treatment Guidelines Expected to Accelerate Category Growth Over Time

70%
Diagnosis Rate
Potential Growth
by 2030+

Analogues reach ~70% over time[1]

(e.g., MS, PAH, AFib)

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1. ClearView Analysis

Significant Opportunity Ahead

~200K U.S. patients

More than 80% of ATTR-CM patients remain untreated

Diagnosis and treatment rates accelerating

Growing awareness, improved diagnosis, and expanded treatment options are driving category growth

Multiple pathways to sustained growth

First-line and switch / add-on patients

ATTR-CM represents a major opportunity to expand diagnosis and treatment for an underserved population

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The AMVUTTRA Value Proposition

Sameer Bansilal, MD, MS, FACC
Vice President, TTR Disease Area Lead

Strengthening Leadership

Competing in silencer class
Anticipating stabilizer genericization

Unlocking Category Growth

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Our ambition is that ATTR-CM patients

live longer

and **better lives**

and ensure that patients **adhere to treatment**

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What Matters to Clinicians

Most Important ATTR-CM Product Attributes to HCPs[1]		Physicians Rate AMVUTTRA Highly on These Attributes[2]	
85%	Demonstrated efficacy in **reducing mortality**	**84%**	rate AMVUTTRA highly for **reducing mortality**
100%	Demonstrated efficacy in **reducing CV-related hospitalizations**	**86%**	rate AMVUTTRA highly for **reducing CV hospitalizations**
95%	Positive effect on **quality of life**	**78%**	rate AMVUTTRA highly for **improving quality of life**

1. Alnylam Market Research, Q4'25 (n = 90). Please rate each of the following product characteristics according to how important each is when making a prescribing decision for an ATTR-CM pharmacotherapy. Please use the following scale where 5 = extremely important and 1 = not at all important
2. Alnylam Market Research, Q4;25 (n=81). Product Performance Across Attributes – ATTR-CM. Based on your knowledge of, and/or existing experience with, the following products, please rate how well you believe each product performs for their indication across the listed attributes below on a 0 to 10-point scale.

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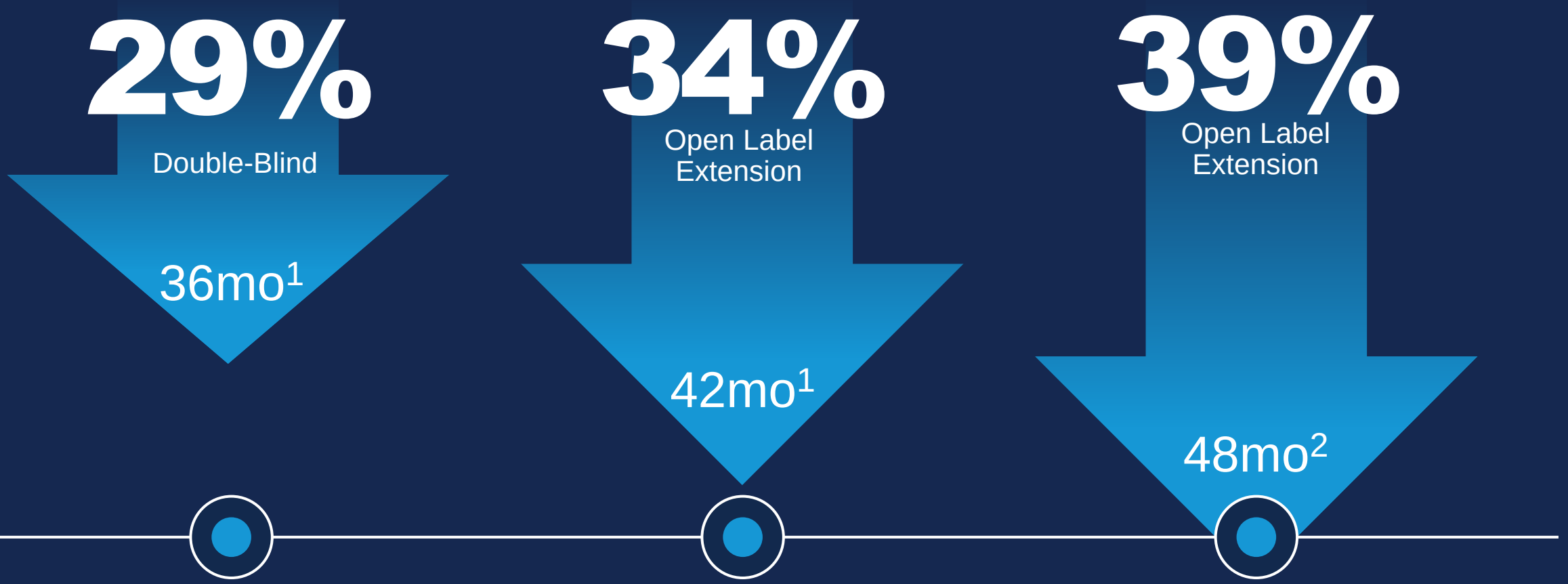
Vutrisiran Demonstrated Profound Impact on Survival

Increasing Mortality Benefit Over Time

Relative reduction in mortality



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1. Fontana M et al. N Engl J Med. 2025;392:33–44. 2. Garcia-Pavia, P. ESC Congress 2025. https://esc365.escardio.org/presentation/303352

Vutrisiran Nearly Halved Extra-Cardiac Adverse Effects

Overall Population

42%

mean reduction in cumulative GI events[1]

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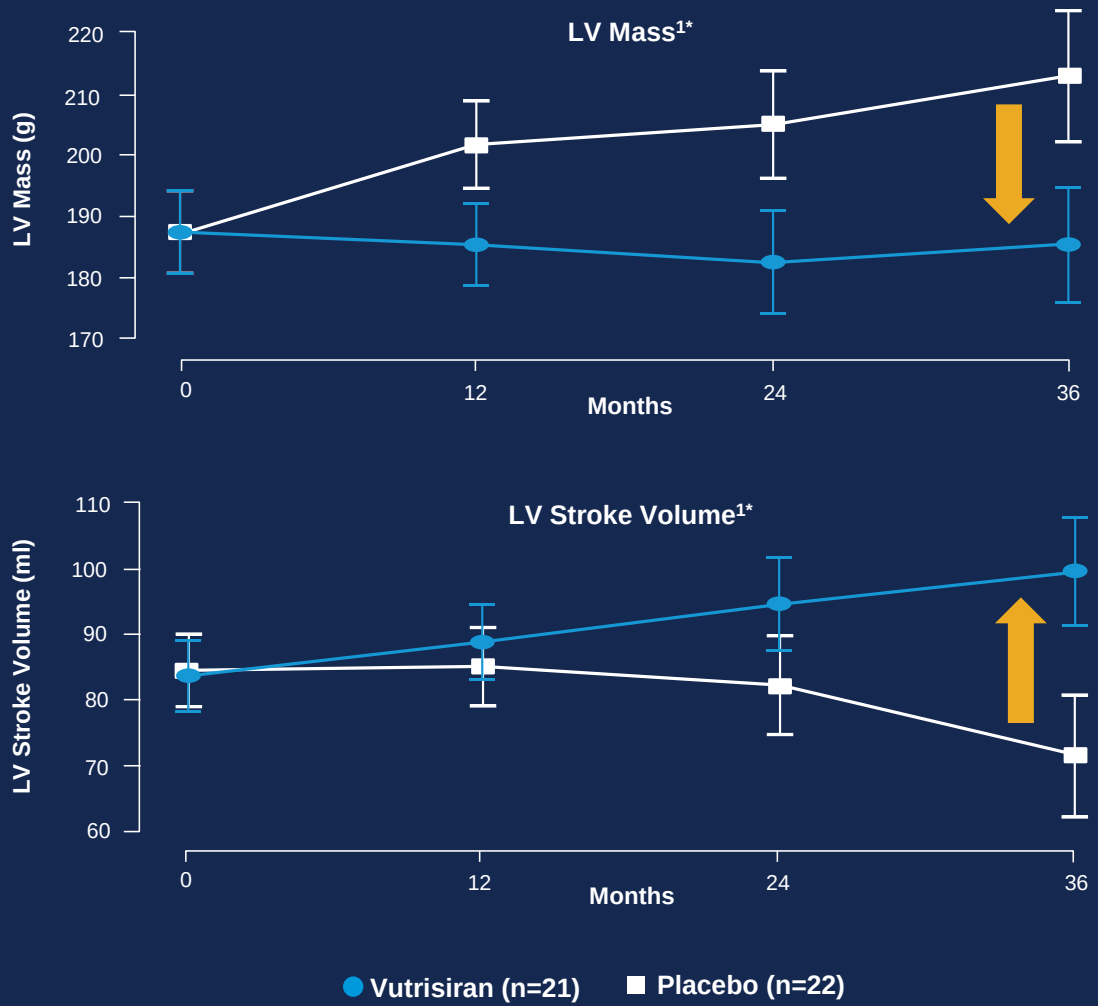
1. Urey MA, et al. Oral presentation at the Heart Failure Society of America (HFSA) Annual Meeting, September 26-29, 2025, Minneapolis, MN.

Vutrisiran Drove Amyloid Regression and Cardiac Structure And Function Improvement

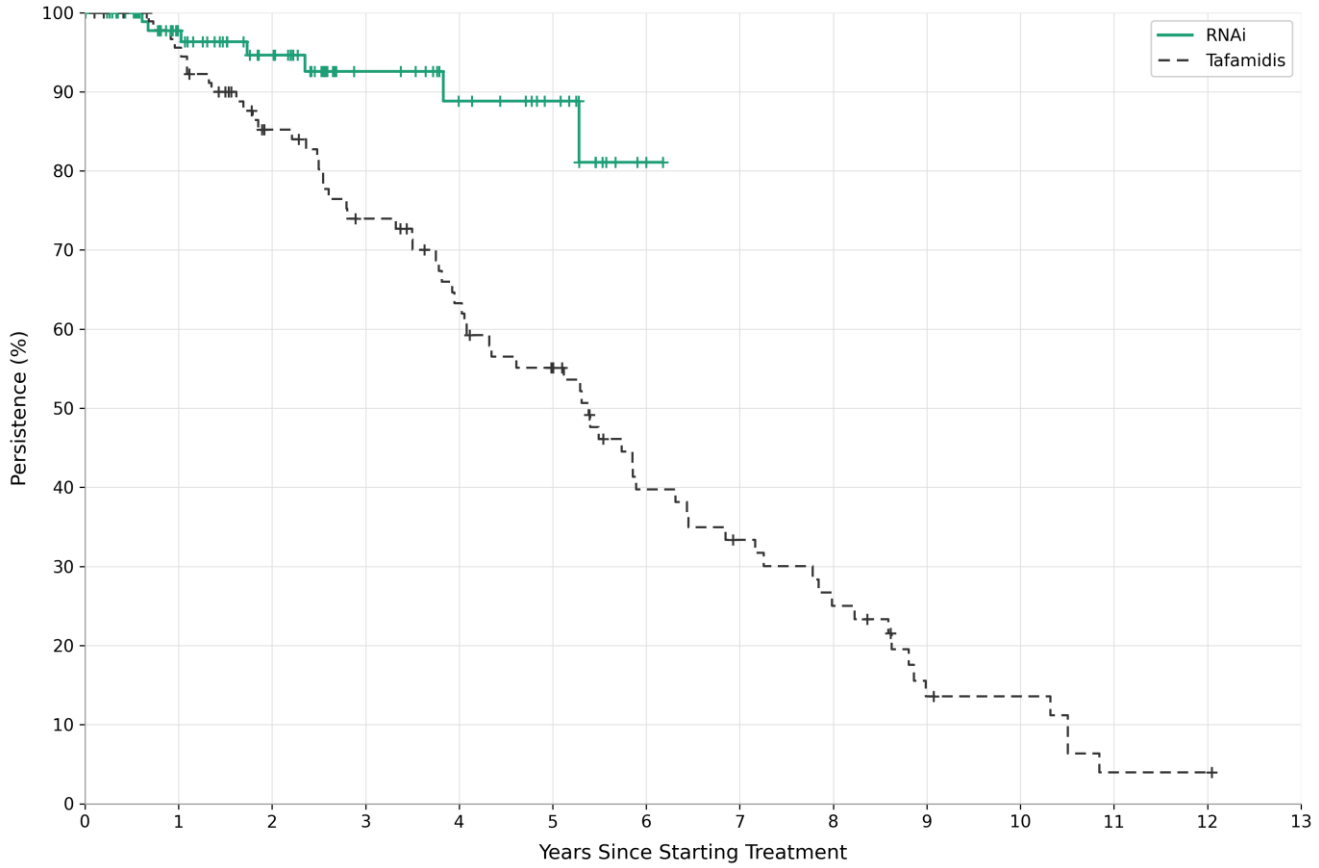


22% amyloid **regression** in patients treated with vutrisiran vs. 63% progressed on placebo[1]

1. Razvi Y, et al. Poster presentation at the American Heart Association (AHA) Scientific Sessions, November 7-10, 2025, New Orleans, LA. * LV Mass p=0.001. *LVSV p=0.001.

Adhere to Treatment | Alnylam RNAi Treatment Persistence; 2x Advantage vs. Once Daily Oral Stabilizer

hATTR-PN Patients



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Peripheral Nerve Society 2025: Conciecao, I, et al.

Continuing to Add to a Robust Body of Evidence

DemonsTTRate

Observational Study

2,000 patients

Real-World Evidence

Capture Range of Patient- & HCP-Function and Outcomes

Enabling Comparative & Combination Treatment Evidence Generation

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Our ambition is that ATTR-CM patients live longer and better lives and ensure that patients adhere to treatment

Live Longer

~40% reduction in mortality over 48 months

Live Better

Lower incidence of self-reported GI adverse effects

22% amyloid regression and improved cardiac structure and function

Adhere to Treatment

Quarterly HCP dosing driving >90% verified adherence rate

Expanding real-world evidence with 2,000 patient observational study

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Agenda

The Opportunity

The AMVUTTRA Value Proposition

Strengthening Leadership

Competing in Silencer Class

> **John P. Kennedy**
> Senior Vice President,
> TTR Franchise Commercialization Lead

Anticipating Stabilizer Genericization

> **Mark Soued**
> Senior Vice President,
> Head of U.S. & TTR Lead

Unlocking Category Growth

Sustaining Leadership in the Silencer Class

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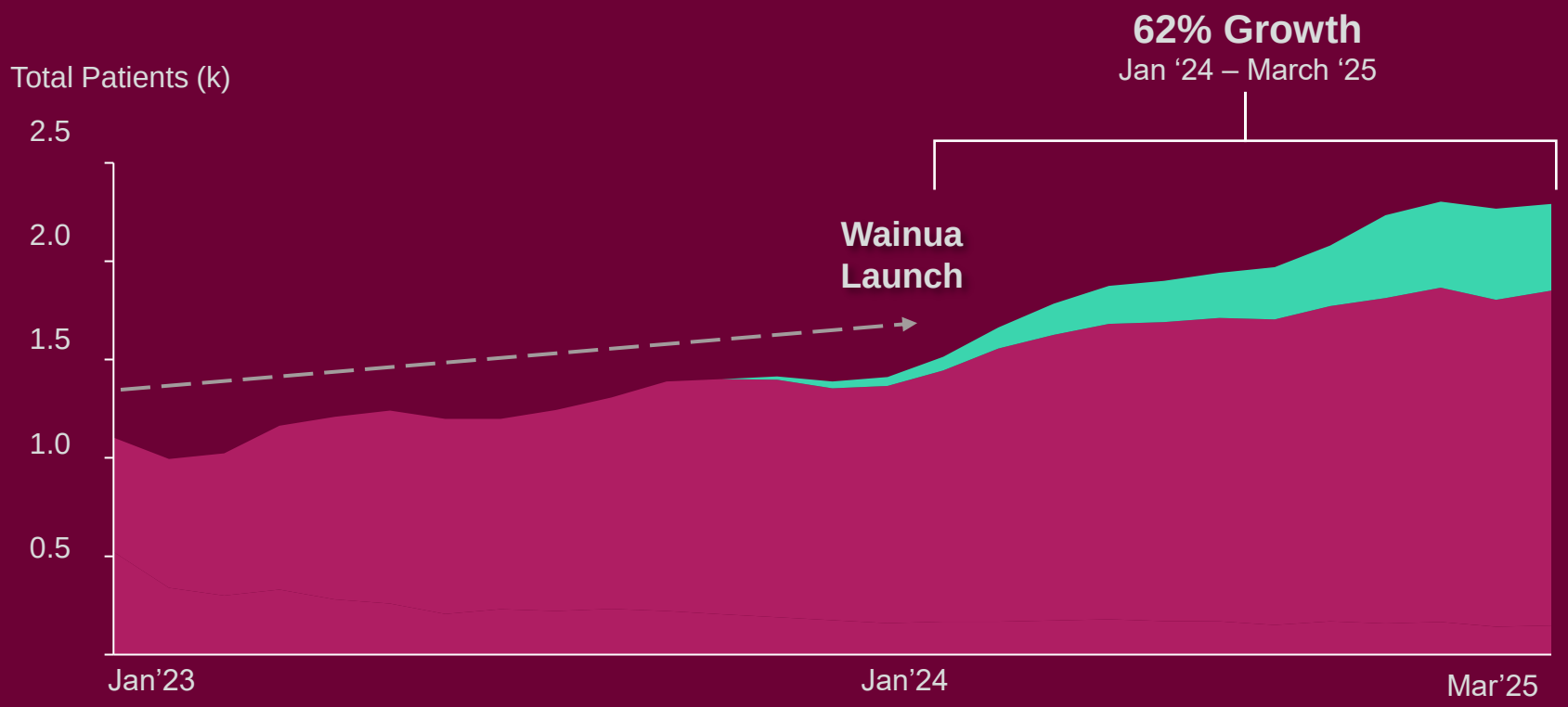
In hATTR-PN, Already Leading in Silencer Competition

In U.S., before CM label expansion

Category Growth Accelerated



AMVUTTRA captured ~80% of all scripts

and >70% of new starts

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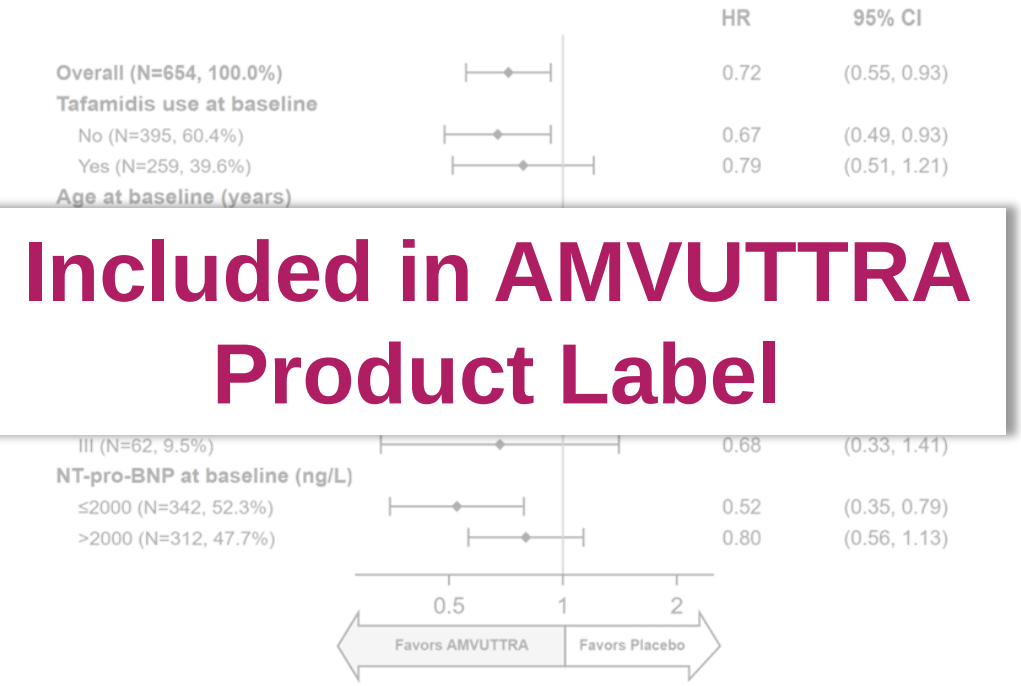
Sources: Claims data analysis, data on file

Treatment Effect of AMVUTTRA on Background Stabilizer Already Established

Results from the subgroup analysis for the primary composite endpoint were consistent across prespecified subgroups in the overall population (Figure 6) and monotherapy population.

Figure 6: Subgroup Analyses of the Primary Composite Endpoint (Overall Population)



Abbreviations: ATTR = transthyretin amyloidosis; CI = confidence interval; hATTR = hereditary transthyretin amyloidosis; HR = hazard ratio; NT-pro-BNP = N-terminal prohormone of B-type natriuretic peptide; NYHA = New York Heart Association; wtATTR = wild-type transthyretin amyloidosis.

HR and 95% CI are based on modified Andersen-Gill model analyses.

Included in AMVUTTRA Product Label

+ Growing Real World Experience

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These highlights do not include all the information needed to use AMVUTTRA safely and effectively. See full prescribing information for AMVUTTRA.

Favorable Read-Through of Corroborating Silencer Data

A Large Majority of Cardiologists

Believe positive combination data from CARDIO-TTRansform will support a class effect[1]

When Choosing a Silencer
Look for Depth, Duration & Consistency of Knockdown Effect

AMVUTTRA for Today

87% mean TTR knockdown with only 4 doses per year

Nucresiran for the Future

>95% mean TTR knockdown with bi-annual dosing*

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*Nucresiran TTR knockdown is based on preliminary Phase 1 data. Assumes positive clinical trial results and regulatory approval. Nucresiran is an investigational medicine. The safety and efficacy of nucresiran have not been established or evaluated by the FDA, EMA, or any other health authority. 1. ALNY market research.

AMVUTTRA Lays Groundwork Across Payer Environments

AMVUTTRA has **broad access as a Medical Benefit Product**

~99%

coverage for AMVUTTRA

~90%

have access to AMVUTTRA as 1L (with no step-through required)

Majority pay **$0** in out-of-pocket costs

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Sustaining Leadership in the Silencer Class

Competition fuels expansion

Robust and sustained category growth + large underserved population

Successfully competing already in hATTR-PN

Maintained clear leadership share after more than a year

More combination data supports class

Corroborates HELIOS-B, already in AMVUTTRA label

Depth, duration & consistency of knockdown profile

AMVUTTRA today, Nucresiran in the future

Competition fuels category growth and we are confident in our ability to compete.

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*Assumes positive clinical trial results and regulatory approval. Nucresiran is an investigational medicine. The safety and efficacy of nucresiran have not been established or evaluated by the FDA, EMA, or any other health authority.

Anticipating Genericization of the Stabilizer Class

Establishing Leadership Demand for AMVUTTRA Silencing MOA Ahead of Stabilizer Genericization

Before tafamidis LOE

Driving Competitive Preference

- Already challenging the 6-year incumbent for leadership share
- Building HCP and patient experience and preference

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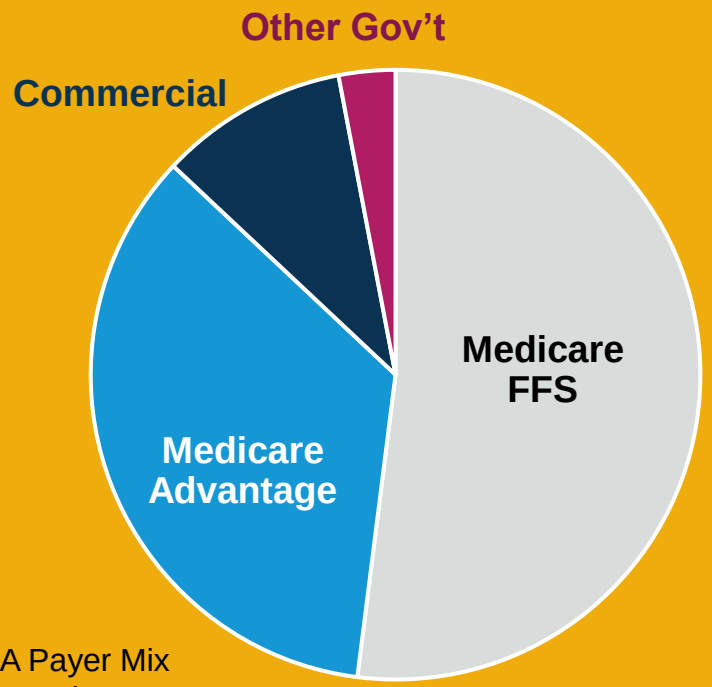
Maintaining Broad & Durable Access

Following tafamidis LOE

1L Access Will Remain For Large Segment of Patients



AMVUTTRA Payer Mix in ATTR-CM Today

Source: Data on file

Alternate MOA for Stabilizer Progressors

as many as

50%

of tafamidis patients may progress

A Catalyst to Unlock Dual-MOA Combination Treatment

Following tafamidis LOE

Unlocking Dual-MOA Treatment Strategies

Cardiology Accustomed

to Dual-MOA Strategies

Corroborating Dual-MOA Data

Anticipated from CARDIO-TTRansform

Generic Stabilizer Availability

Reduces the Cost of Dual-MOA Treatment

Silencer of Choice in a Genericized Stabilizer World

Driving 1L Demand & Preference

Years ahead of anticipated tafamidis LOE

Durable Access & Patient Need

Large segment of market to remain 1L accessible

Need for orthogonal MOA

Unlocking Dual-MOA Treatment

Reduced cost of dual-MOA strategies

Growing body of data supporting dual-MOA

Sustained Opportunity for AMVUTTRA Growth

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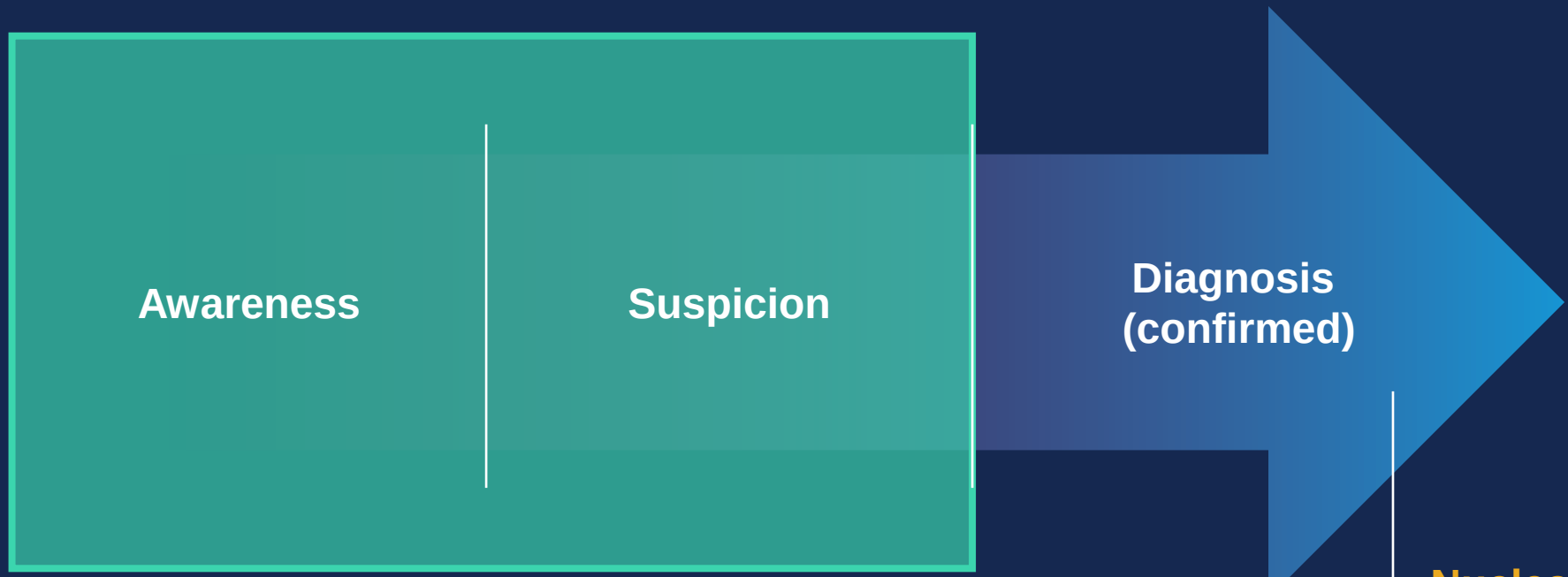
A Strategic Approach to Drive Diagnosis Rate

A Strategic Approach to Drive Diagnosis Rate



Nuclear Scintigraphy
Noninvasive, acceptable accuracy & accessible

Accelerating our Category Growth Investments

A focused, strategic approach

Driving Growth in Patient Awareness & Engagement

Expanding HCP Prescriber Base in ATTR-CM

Enabling End-to-End Health System Engagements

American Heart Association®

Advancing AI-Enabled Diagnostic Technology

iz.ai

Making AMVUTTRA Available Worldwide, Driving Impact & Growth

Commercial Access Unlocked

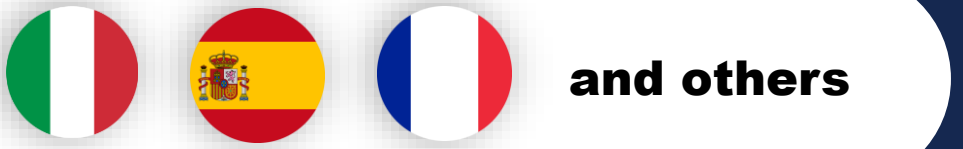
- Launched in Japan, Germany, Austria, UK

APPROVED

Strong Submission Momentum

- Engaging at the public health policy level
- Advancing additional regulatory submissions, and/or pricing and reimbursement negotiations

IN PROCESS



ATTR-CM Category Expansion Creates a Substantial Opportunity

U.S. estimated potential

75K **treated patients in TTR category by 2030**

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Source: Internal estimate

We Have Built a Foundation for Durable Growth

Driving Preference & Utilization

Patient Access & Affordability

Provider Network

Category growth

Strong Foundation Accelerating the Next Phase of Launch

Sustained Category Growth

Breadth of Prescribers

Adherence / Persistence

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Q&A