



Accelerating Innovation and Scaling Impact to Transform Human Health

44th Annual J.P. Morgan Healthcare Conference

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Chief Executive Officer

January 12, 2026



Alnylam Forward Looking Statements

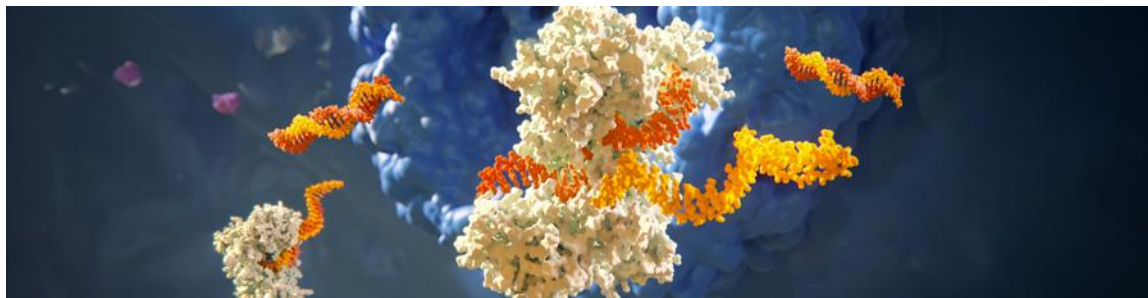
This presentation contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934, including, without limitation, statements regarding our 2026 financial guidance, our aspirational five-year objectives, our ability to continue to innovate, our ability to achieve durable growth, and market value projections. Such statements incorporate the additional forward-looking statements about potential timing and success of (1) clinical and regulatory advancement of product candidates and (2) potential commercialization and financial contribution from those candidates. Each forward-looking statement contained in this deck is subject to risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such statement. Applicable risks and uncertainties include our potential inability to grow revenue from currently marketed products and to successfully advance, and generate revenue from, product candidates, each of which may be negatively impacted by competition from products marketed by other companies and product candidates developed by other companies that successfully reach the market; negative decisions by regulatory authorities, including adverse regulatory actions or dosing and labeling determinations; challenges enrolling clinical trials rapidly and successfully; healthcare providers, patients, and regulators not assessing our products to have a positive benefit-risk profile; the sizes of patient populations we seek to address being smaller than stated or implied by forward-looking statements; our inability and the inability of our third party contractors to supply and manufacture products and product candidates, which can be impacted by shortages of inputs or regulatory or physical constraints encountered at production facilities; potential negative consequences of actions by governments, including healthcare reform measures, actions impacting trade, and actions impacting pricing; and possible negative consequences of litigation or government actions. Additional factors that could cause actual results to differ materially from those projected or suggested in any forward-looking statements are contained in our periodic filings with the Securities and Exchange Commission, or SEC, including those factors discussed under the caption "Risk Factors" in such filings; these filings are available at www.sec.gov and in the Investors section of our website at www.alnylam.com. We caution investors and potential investors not to place substantial reliance on the forward-looking statements contained in this presentation and to consider the risks and uncertainties noted above or contained in our SEC filings. The forward-looking statements in this presentation speak only as of the date of this document, and we undertake no obligation to update or revise any of these statements.

This presentation also includes forward-looking financial measures, non-GAAP operating margin and non-GAAP R&D, that were not prepared in accordance with U.S. generally accepted accounting principles (GAAP). We do not provide a reconciliation of these forward-looking non-GAAP financial measures to the most directly comparable financial measures calculated and presented in accordance with GAAP on a forward-looking basis because such reconciliation is not accessible with reasonable effort, due to the uncertainty and inherent difficulty of predicting the occurrence and the financial impact of adjustments, such as stock-based compensation expense; such adjustments could be material. We use these non-GAAP measures as indicators of financial performance for the purpose of internal evaluation of progress toward financial objectives. We also believe that these non-GAAP measures provide investors with useful information with respect to our operational goals. A non-GAAP financial measure is not, and should not be viewed as, a substitute for financial measures required by GAAP, has no standardized meaning prescribed by GAAP, and may not be comparable to the calculation of the measure by other companies.



Anylam: A Unique Profile in the Biotech Industry

Established, Sustainable Innovation Engine and Commercial Excellence to Drive Durable Growth



Leadership in RNAi, with a Proven, Organic Product Engine



High-Yielding Pipeline with >25 Active Clinical Programs



6 Medicines Collectively Generating Multi-Billion-Dollar Revenues



Consistent Record of Setting and Exceeding Ambitious Long-Term Goals

2011 – 2015

5  15TM
Aylam

✓ **7** clinical programs

2016 – 2020

 Aylam[®]
PHARMACEUTICALS
2020

✓ **4** approved products

2021 – 2025

 Aylam
P5  25

✓ **6** approved products

✓ **~500k** patients

✓ **>25** clinical programs

✓ **~50%** revenue CAGR*

✓ On track to achieve non-GAAP profitability

* Assumes the midpoint of collaboration and royalty revenue guidance for 2025. Preliminary selected financial results are unaudited, subject to adjustment, and provided as estimates in advance of the Company's announcement of complete financial results in February 2026.



2025: A Transformational Year for Alnylam

Landmark Approval, Commercial Excellence Drove Outstanding Financial Performance



Global launch of
AMVUTTRA for ATTR-CM



Combined net product revenues:
\$2,987 million* (+81% YoY)



On track to achieve
Non-GAAP profitability

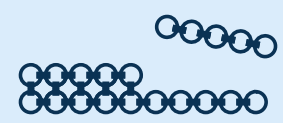
Advanced Innovative RNAi Pipeline and Platform Capabilities



Initiated
3 Phase 3 Studies



Expanded clinical pipeline with
4 proprietary CTAs
and 5 CTAs filed by partners



Developed and launched siRELIS™
enzymatic ligation-based
RNAi manufacturing platform

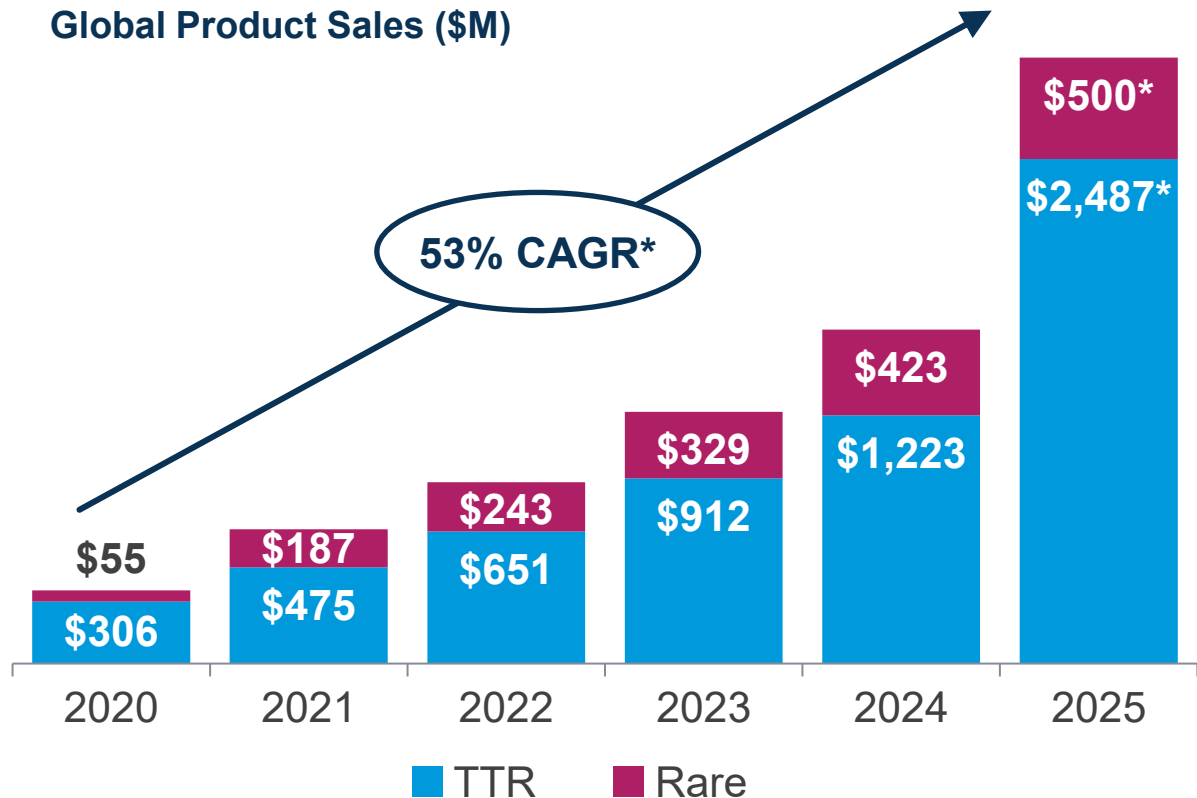
* Preliminary selected financial results are unaudited, subject to adjustment, and provided as estimates in advance of the Company's announcement of complete financial results in February 2026.



2025: Outstanding Commercial Performance

Doubled TTR Franchise Revenues in One Year

Robust 81% 2025 YoY Growth* in Total Net Product Revenues



Total TTR

103%*

YoY growth in Total TTR revenues

Total Rare

18%*

YoY growth in Total Rare revenues

* Preliminary selected financial results are unaudited, subject to adjustment, and provided as estimates in advance of the Company's announcement of complete financial results in February 2026.

Anylam 2030

Accelerating Innovation. Scaling Impact.



2030



Achieve Global TTR Leadership

BUILD A DURABLE TTR FRANCHISE

- Lead TTR market in revenue by 2030 and cumulatively across 5-year period
- Launch best-in-class, next-gen silencer, nucresiran, in PN by 2028 and CM by 2030



Grow Through Sustainable Innovation

DELIVER THERAPIES THAT PREVENT, HALT, OR REVERSE DISEASE

- Deliver 2+ new transformative medicines beyond TTR with blockbuster potential
- Expand to 10 tissue types and > 40 clinical programs
- Invest ~30% of revenues in non-GAAP R&D, including select external innovation



Scale with Discipline & Agility

DRIVE SUSTAINED, PROFITABLE GROWTH

- Achieve 25%+ total revenue CAGR through YE 2030
- Deliver ~30% non-GAAP operating margin



Achieve Global TTR Leadership

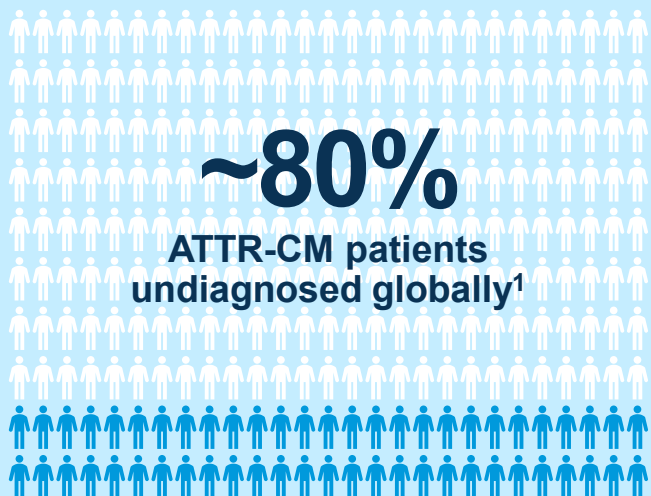
BUILD A DURABLE TTR FRANCHISE



Building Leadership in Large, Growing ATTR-CM Market

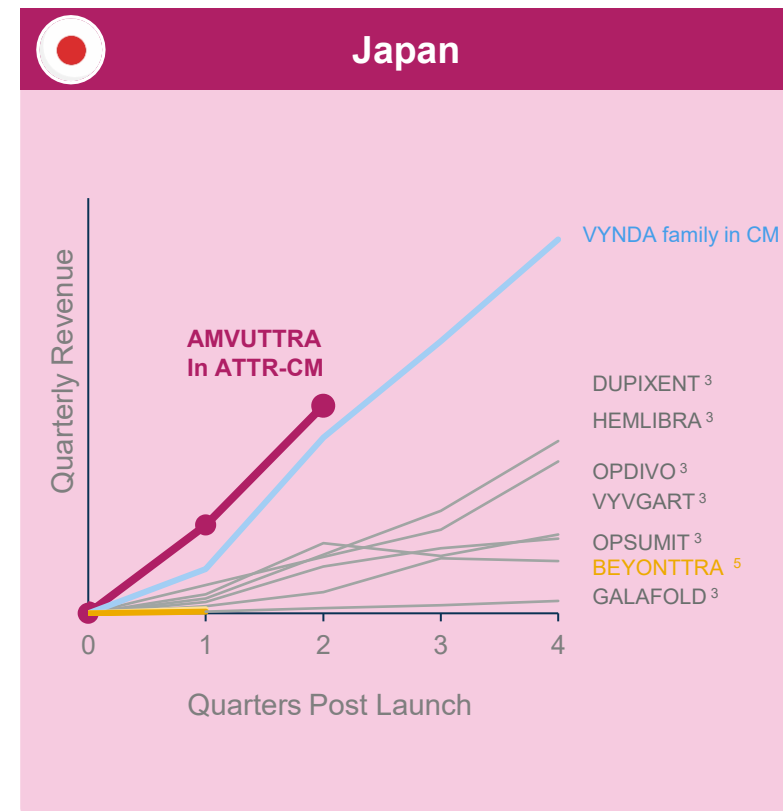
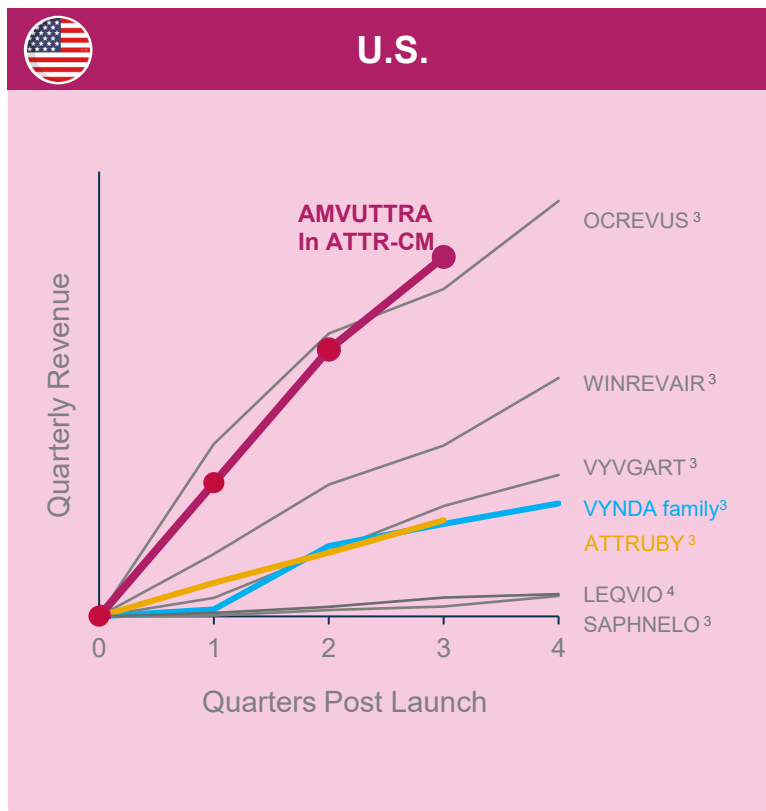
Significant Unmet Need

>300K patients globally¹



40%+ Average Annual Category Volume Growth Since 2019²

Exceptional Early Launch Momentum



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. Internal estimate based on U.S. + EU5 + Japan. 2. Internal Estimates of commercial volume based on claims data. 3. Evaluate Pharma. 4. ALNY collaboration finance reporting. 5. VYNDA and BEYONTTTRA revenues are calculated estimates based on IQVIA data.



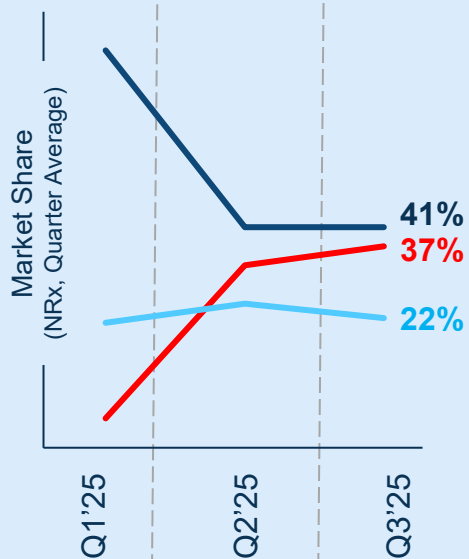
Establishing Preference Across Lines of Therapy



ATTR-CM: Building Leadership in Growing Category

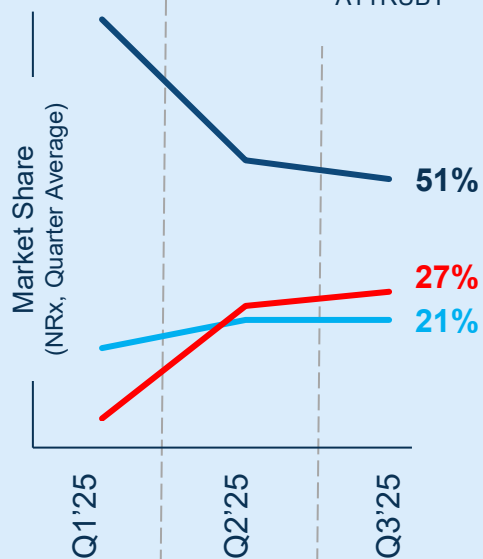
Competitive in New Starts

ALL new starts
(both first- and second-line)

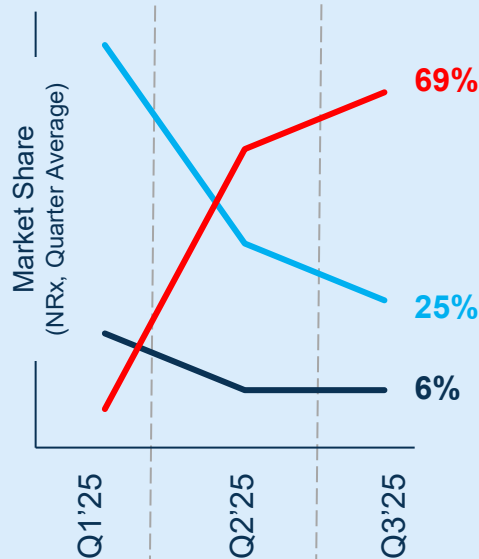


Building First-Line Preference

Legend:
 — AMVUTTRA (Red)
 — VYNDAMAX (Dark Blue)
 — ATTRUBY (Light Blue)



Clear Second-Line Leadership



Maintaining Broad Access and Patient Affordability

- **First-line access** (i.e., no step edit required) for large majority of U.S. covered lives
- **\$0 in out-of-pocket costs** for majority of patients
- **~90% of patients** can receive AMVUTTRA treatment within ~10 miles of where they live

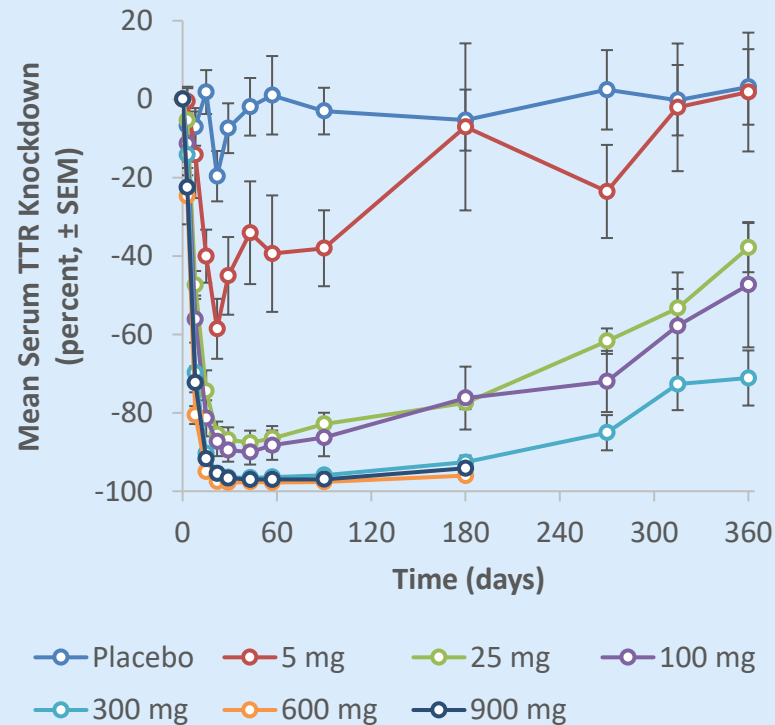
Reinvesting to Sustain Growth and Solidify Leadership

>\$1B Planned in TTR Research and Education Investments Over Next Five Years

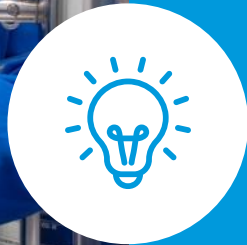
Enabling Diagnosis and Enhancing Patient Care

- Broad disease education & awareness initiatives
- 60+ studies and research collaborations
- Advancing novel diagnostic methods (e.g., AI-assisted, blood-based)

Advancing Nucesiran, with Category Leader Potential



- ~ 95% TTR knockdown
- Biannual dosing
- Potential for best-in-class efficacy as monotherapy or on top of stabilizers
- PN launch expected 2028; CM launch expected 2030*



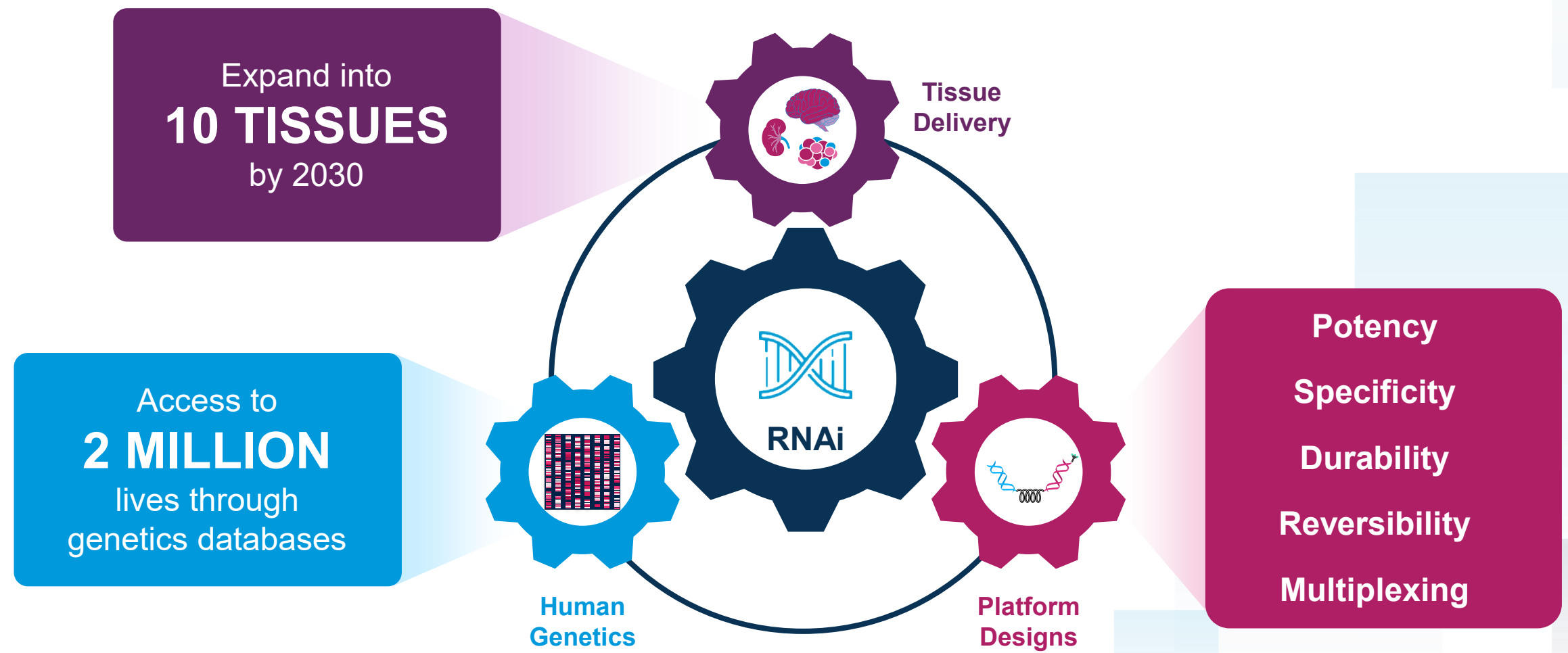
Grow Through Sustainable Innovation

DELIVER THERAPIES THAT PREVENT, HALT, OR REVERSE DISEASE



The Engine Driving Sustainable Innovation

Modular Drug Discovery Platform to Catalyze Long-Term Growth





Industry Leading Pipeline of RNAi Therapeutics

		PHASE 1	PHASE 2	PHASE 3
TTR	Nucresiran	ATTR Amyloidosis with Cardiomyopathy		
	Nucresiran	hATTR Amyloidosis with Polyneuropathy		
CARDIOVASCULAR	Zilebesiran ²	Hypertension		
	Zilebesiran + REVERSIR ²	Hypertension		
METABOLIC	Raprosiran (ALN-HSD) ¹	Metabolic Dysfunction-Associated Steatohepatitis (MASH)		
	ALN-ANG3 ¹	Diabetic Kidney Disease		
	ALN-4324 (GRB14)	Type 2 Diabetes Mellitus		
	ALN-2232 (ACVR1C)	Obesity & Weight Management		
	ALN-PNP ³	Non-Alcoholic Fatty Liver Disease (NAFLD)		
	ALN-APOC3 ¹	Dyslipidemia		
	ALN-CIDEB ¹	MASH		
NEUROSCIENCE	Cemdisiran ¹	Myasthenia Gravis		
	Mivelsiran	Cerebral Amyloid Angiopathy		
	Mivelsiran	Alzheimer's Disease		
	ALN-HTT02 ⁴	Huntington's Disease		
	ALN-5288 (MAPT) ⁴	Alzheimer's Disease		
	ALN-SOD ³	SOD1 Amyotrophic Lateral Sclerosis		
	ALN-SNCA ³	Parkinson's Disease		
HEMATOLOGY	Cemdisiran ¹	Paroxysmal Nocturnal Hemoglobinuria		
	ALN-6400 (PLG)	Bleeding Disorders		
	AG-236 (ALN-TMP) ¹	Polycythemia Vera		
	ALN-CFB ¹	Paroxysmal Nocturnal Hemoglobinuria		
OTHER	Cemdisiran ¹	Geographic Atrophy		
	Elebsiran ¹	Hepatitis D Virus Infection		
	ALN-BCAT	Hepatocellular Carcinoma		
	ALN-F1202 ¹	Healthy Volunteers		

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 Partnered, Alnylam-led with profit split

Next Wave of Transformative Medicines

Investigational Therapies with Multi-Billion-Dollar Potential



CARDIOVASCULAR + METABOLIC

ZILEBESIRAN

Hypertension

ALN-4324

Type 2 Diabetes Mellitus

ALN-2232

Obesity & Weight Management



NEUROSCIENCE

MIVELSIRAN

*Cerebral Amyloid Angiopathy
and Alzheimer's Disease*

ALN-HTT02

Huntington's Disease



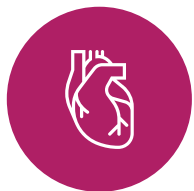
HEMATOLOGY

ALN-6400

Bleeding Disorders



Next Wave of Transformative Medicines



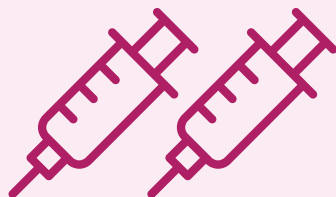
CARDIOVASCULAR
+ METABOLIC

ZILEBESIRAN

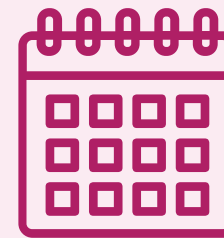
Targeting Angiotensinogen to Achieve Continuous Control of Blood Pressure



>60M patients
in 7 major markets
with uncontrolled hypertension
and high CV risk¹



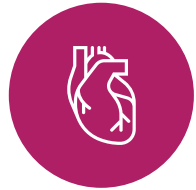
2 doses
per year



Continuing enrollment in
ZENITH Phase 3 CVOT;
Launch expected ~2030*

The safety and efficacy of zilebesiran have not been established or evaluated by the FDA, EMA, or any other health authority. * Launch assumes positive clinical trial results and regulatory approval. Zilebesiran is being co-developed and co-commercialized by Alnylam and Roche. 1. Internal estimate based on NCD-RisC, 2021; Nguyen T & Chow C, Lancet (2021); Muntner P et al., Hypertension (2020).

Next Wave of Transformative Medicines



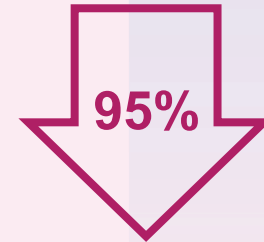
CARDIOVASCULAR
+ METABOLIC

ALN-4324 (GRB14)

ALN-2232 (ACVR1C)

Novel Insulin Sensitizer for Type 2 Diabetes Mellitus

Adipose Target for Durable, Fat-Specific Weight Loss



>500M adults
globally living with T2DM¹

GRB14
Knockdown*

1 in 2 people
expected to be living with
overweight or obesity by 2030²

ACVR1C
Knockdown*

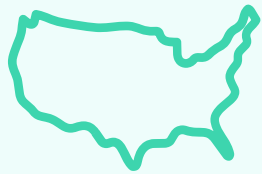
Next Wave of Transformative Medicines



NEUROSCIENCE

MIVELSIRAN

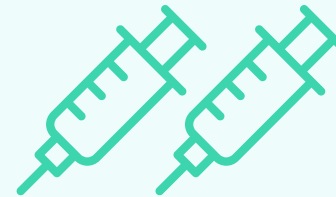
Targeting Amyloid Precursor Protein for Cerebral Amyloid Angiopathy and Alzheimer's Disease



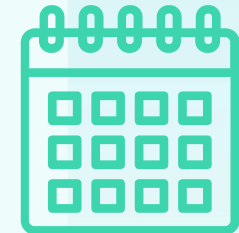
~80K annual U.S. cases
of intracerebral hemorrhage,
of which CAA is the
2nd leading cause¹



~100M people
with mild cognitive impairment
or dementia associated with
Alzheimer's Disease globally²



2 doses
per year



cAPPricorn-1 Phase 2
enrolling CAA patients;
Phase 2 AD study to
initiate in 1H26

Next Wave of Transformative Medicines



ALN-HTT02

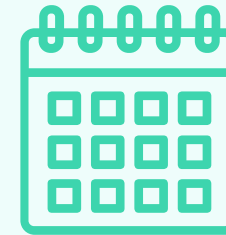
Targeting Exon 1 of Huntingtin Gene to Reduce Progression of Huntington's Disease



>100K
symptomatic HD
patients globally¹



Reductions in
HTT*



Initial Phase 1 data
expected 2H26

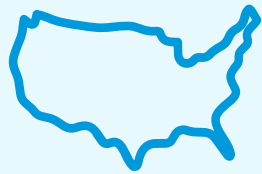
Next Wave of Transformative Medicines



HEMATOLOGY

ALN-6400

Targeting Plasminogen to Address Wide Range of Bleeding Disorders



>3M people in U.S. estimated to have inherited bleeding disorders¹



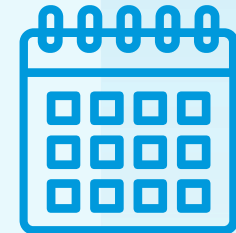
Hereditary Hemorrhagic Telangiectasia (HHT)

2nd most common inherited bleeding disorder²

70K estimated HHT patients in the U.S.³



Reductions in circulating PLG* and clinical Proof of Mechanism



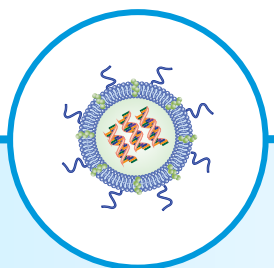
Phase 2 HHT trial underway; Phase 2 trial in 2nd bleeding disorder to initiate in 2H26



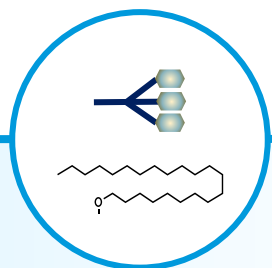
Accelerating Innovation in RNAi Therapeutics

2002 to Today

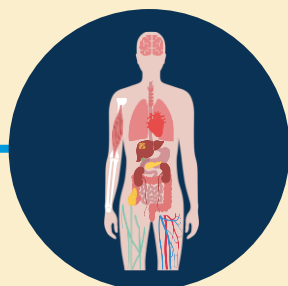
Solved hepatic delivery, proved the platform, with six approved medicines



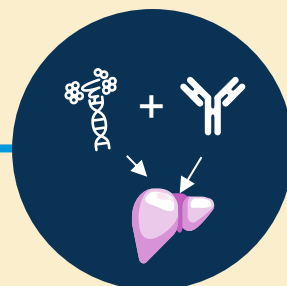
LIPID NANOPARTICLES



SMALL MOLECULE LIGANDS



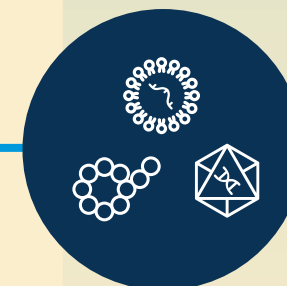
NEW TISSUES



COMBINATIONS & POLYGENIC APPROACHES



CONTINUED PLATFORM ENHANCEMENTS



SELECT EXTERNAL INNOVATION

Today to 2030+

Sustain growth and differentiation



2026 Guidance and Goals



2026 Net Product Revenue Guidance Reflects Robust Growth and Strong Commercial Execution

	2026 Guidance	YoY Growth at Midpoint
Total TTR Net Product Sales (AMVUTTRA, ONPATTRO)	\$4,400 to \$4,700 million	83%
Total Rare Net Product Sales (GIVLAARI, OXLUMO)	\$500 to \$600 million	10%
Total Combined Net Product Sales	\$4,900 to \$5,300 million	71%

Note: Additional financial guidance, including collaboration and royalty revenue and GAAP and non-GAAP combined R&D and SG&A expenses, will be provided on Alnylam's year-end earnings call in February 2026.

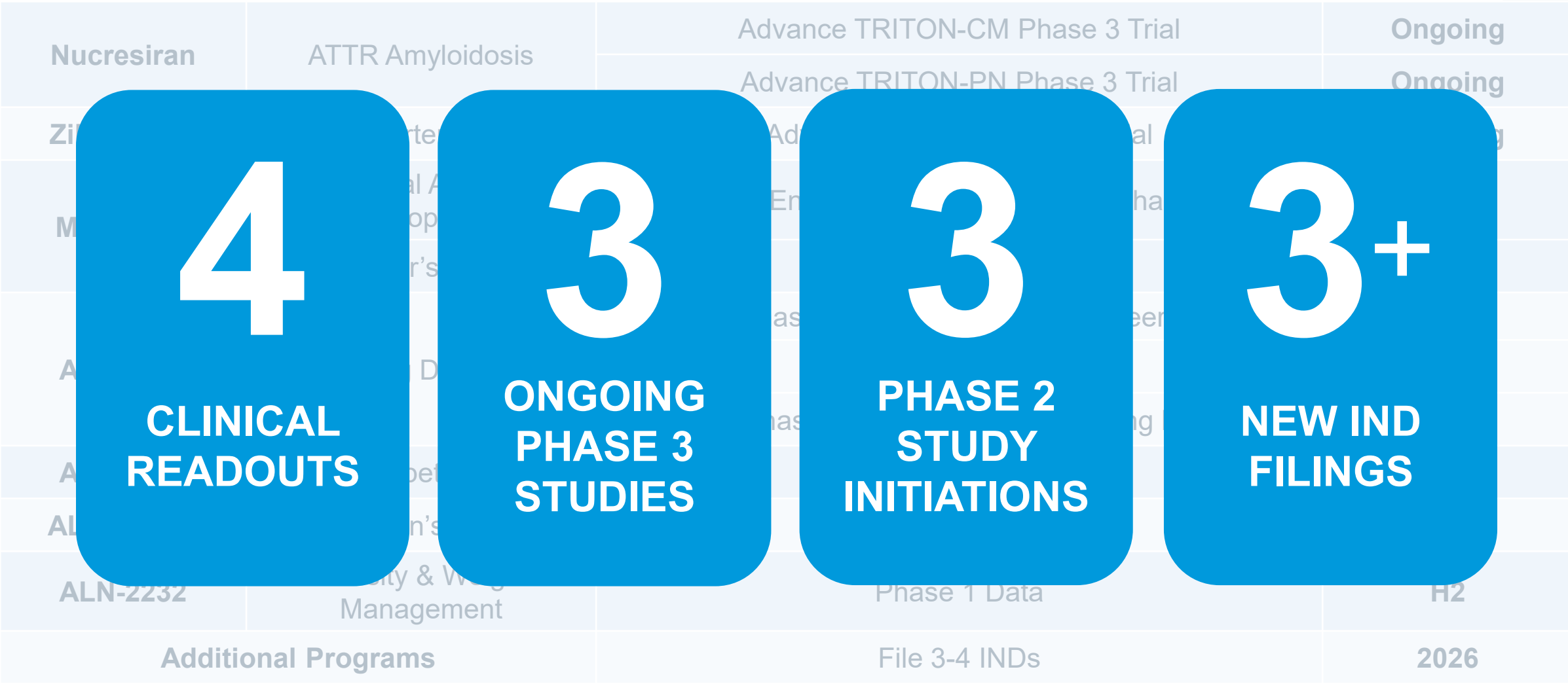


2026 Pipeline Goals to Drive Our Next Phase of Growth

Nucresiran	ATTR Amyloidosis	Advance TRITON-CM Phase 3 Trial	Ongoing
		Advance TRITON-PN Phase 3 Trial	Ongoing
Zilebesiran	Hypertension	Advance ZENITH Phase 3 Trial	Ongoing
Mivelsiran	Cerebral Amyloid Angiopathy	Complete Enrollment of cAPPricorn-1 Phase 2 Trial	H1
	Alzheimer's Disease	Initiate Phase 2 Trial	H1
ALN-6400	Bleeding Disorders	Phase 1 Data in Healthy Volunteers	H2
		Phase 2 Data in HHT	H2
		Initiate Phase 2 Trial in Second Bleeding Disorder	H1
ALN-4324	Type 2 Diabetes Mellitus	Initiate Phase 2 Trial	H1
ALN-HTT02	Huntington's Disease	Phase 1 Data	H2
ALN-2232	Obesity & Weight Management	Phase 1 Data	H2
Additional Programs		File 3-4 INDs	2026



2026 Pipeline Goals to Drive Our Next Phase of Growth



4
CLINICAL READOUTS

3
ONGOING PHASE 3 STUDIES

3
PHASE 2 STUDY INITIATIONS

3+
NEW IND FILINGS

Products mentioned above are not approved for any indication and conclusions regarding the safety or effectiveness of these drugs have not been established.



Anylam 2030: Accelerating Innovation. Scaling Impact.

GLOBAL HUMAN HEALTH IMPACT

>\$10B IN ANNUAL REVENUES

INDUSTRY LEADING PIPELINE

SCALABLE MANUFACTURING



SOCIAL RESPONSIBILITY

SUBSTANTIAL SHAREHOLDER VALUE CREATION



Silence disease

Amplify life™

 Alylam®