Fourth Quarter and Full Year 2023
Financial Results

February 15, 2024
Agenda

Welcome
• Christine Lindenboom
  Senior Vice President, Investor Relations & Corporate Communications

Overview
• Yvonne Greenstreet, MBChB, MBA
  Chief Executive Officer

Commercial Highlights
• Tolga Tanguler
  Chief Commercial Officer

Alnylam Pipeline
• Pushkal Garg, M.D.
  Chief Medical Officer

Financial Summary and Upcoming Milestones
• Jeff Poulton
  Chief Financial Officer

Q&A Session
Alnylam Forward Looking Statements

This presentation contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. All statements other than historical statements of fact regarding Alnylam’s expectations, beliefs, goals, plans or prospects including, without limitation, statements regarding Alnylam’s aspiration to become a top-tier biotech company, the potential for Alnylam to identify new potential drug development candidates and advance its research and development programs, Alnylam’s ability to obtain approval for new commercial products or additional approved indications for its existing commercial products, and Alnylam’s projected commercial and financial performance, including the expected range of net product revenues and net revenues from collaborations and royalties for 2024, the expected range of aggregate annual GAAP and non-GAAP R&D and SG&A expenses for 2024, the expected timing of topline data from the HELIOS-B Phase 3 clinical study, whether the HELIOS-B Phase 3 clinical study will deliver positive results and the potential of AMVUTTRA to have a market leading profile, including an impactful clinical profile, for the treatment of ATTR cardiomyopathy if approved, and the planned achievement of its “Alnylam P5x25” strategy, 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 P5x25” 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, including vutrisiran, zilebesiran, and ALN-APP; actions or advice of regulatory agencies and Alnylam’s ability to obtain and maintain regulatory approval for its product candidates, including vutrisiran, 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 successfully expand the approved indications for AMVUTTRA in the future; Alnylam’s ability to manage its growth and operating expenses through disciplined investment in operations and its ability to achieve a self-sustainable financial profile in the future without the need for future equity financing; the direct or indirect impact of the COVID-19 global pandemic or any future pandemic on Alnylam’s business, results of operations and financial condition; 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 risk of future government investigations; and unexpected expenditures; as well as those risks more fully discussed in the “Risk Factors” filed with Alnylam’s most recent Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) 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 its 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, are non-GAAP financial measures which are 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.
Overview
2023 Delivered Strong Progress Across the Business

Driving Robust Product Growth

Combined net product revenues of $1,241 million (39% growth YoY)

Over 5,000 patients on Alnylam commercial medicines

Extending RNAi Leadership

Human Proof of Concept for RNAi therapeutics in CNS

Positive zilebesiran Phase 2 results in patients with mild-to-moderate hypertension

Preclinical delivery to new tissue types (adipose and muscle)

55 medical publications, including 14 in high-impact* journals

Building a Sustainable Business

Landmark partnership to maximize global opportunity for zilebesiran in hypertension

Maintained strong financial position $2.4 billion in cash at year-end 2023

* Defined as Impact Factor (IF) > 10.
Patients: Over 0.5 million on Alnylam RNAi therapeutics globally
Products: 6+ marketed products in rare and prevalent diseases
Pipeline: Over 20 clinical programs, with 10+ in late stages and 4+ INDs per year
Performance: ≥40% revenue CAGR through YE 2025
Profitability: Achieve sustainable non-GAAP profitability within period
Tolga Tanguler
Chief Commercial Officer

Commercial Highlights
TTR Franchise Update: Q4 2023

$254M
Total TTR
Global Q4 2023
Net Product Revenues

>4,060
Total TTR patients
worldwide at end of
Q4 2023

• U.S. QoQ growth of +5% driven by:
  - Demand (+7%): continued strong AMVUTTRA demand more than offsetting decrease in ONPATTRO due to cannibalization
  - Inventory (-2%): modest impact from Q4 AMVUTTRA inventory destocking

• ROW QoQ growth +18% driven by:
  - Steady demand growth across key markets, positive price impacts (mainly in Europe), and favorable stocking associated with timing of orders in partner markets

• Modest FX impact (YoY CER\(^1\) growth = 31%)

Q4 TTR Franchise Highlights

<table>
<thead>
<tr>
<th></th>
<th>YoY % Growth</th>
<th>QoQ % Growth</th>
</tr>
</thead>
<tbody>
<tr>
<td>U.S.</td>
<td>38%</td>
<td>5%</td>
</tr>
<tr>
<td>ROW</td>
<td>28%</td>
<td>18%</td>
</tr>
<tr>
<td>Global</td>
<td>33%</td>
<td>10%</td>
</tr>
</tbody>
</table>

\(^1\) 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 2022 – see the Financial Summary slide for more information.
Ultra Rare Franchise Update: Q4 2023

$92M
Total Ultra Rare
Global Q4 2023
Net Product Revenues

>1,080
Total Ultra Rare
patients worldwide
at end of Q4 2023

Q4 Ultra Rare Franchise Highlights

<table>
<thead>
<tr>
<th></th>
<th>YoY % Growth</th>
<th>QoQ % Growth</th>
</tr>
</thead>
<tbody>
<tr>
<td>GIVLAARI</td>
<td>26%</td>
<td>10%</td>
</tr>
<tr>
<td>OXLUMO</td>
<td>37%</td>
<td>14%</td>
</tr>
<tr>
<td>Total Ultra Rare</td>
<td>30%</td>
<td>11%</td>
</tr>
</tbody>
</table>

- GIVLAARI QoQ growth of +10% driven by:
  - U.S. (+7%): favorable gross to net adjustment (release of wastage rebate accrual)
  - ROW (+16%): demand growth and timing of orders in partner markets

- OXLUMO QoQ growth of +14% driven by:
  - U.S. (+9%): increased demand
  - ROW (+16%): increased demand and timing of orders in partner markets

- Modest FX impact (YoY CER\(^1\) growth = 27%)

\(^1\) 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 2022 – see the Financial Summary slide for more information.
Building an Industry-Leading TTR Franchise

Products

Indications

Opportunity

2022 – 2024

Hereditary ATTR amyloidosis with polyneuropathy

~25K – 30K patients globally

2025+

Hereditary ATTR amyloidosis with polyneuropathy (ONPATTRO and AMVUTTRA)

>300K patients globally

LONGER-TERM

Hereditary ATTR amyloidosis with polyneuropathy (ONPATTRO, AMVUTTRA, ALN-TTRsc04)

Hereditary and wild-type ATTR amyloidosis with cardiomyopathy (AMVUTTRA)

>300K patients globally

ALN-TTRsc04

Hereditary and wild-type ATTR amyloidosis with cardiomyopathy (AMVUTTRA and ALN-TTRsc04)

>300K patients globally

Note: The safety and efficacy of AMVUTTRA (vutrisiran) for the treatment of the cardiomyopathy of ATTR have not been established or evaluated by the FDA, EMA or any other health authority. Pending positive HELIOS-B study results and regulatory approval. ALN-TTRsc04 is not approved for any indication and conclusions regarding its safety or effectiveness have not been established.
U.S. ATTR-CM prevalence of ~150K expected to grow ~3% annually as elderly population increases faster than overall population*

First approved therapy and new testing method driving increase in diagnosis rates since 2019

Launch of multiple therapies and modalities ’24–’26 expected to support continued category growth

Source: Internal Market research  * U.S. Census, elderly population defined as 65+

~60% Estimated Dx in ’30
Profile of Vutrisiran Expected to Support First-Line Positioning in ATTR-CM

- **Monotherapy**
  - Cost of combo is prohibitive
  - Payers already restrict combo use for >70% of commercial and Medicare Advantage lives
  - Payer management likely to increase

- **Tafamidis LOE (Q4’28)**
  - Generic tafamidis could allow for combo therapy if data support

- **Monotherapy +/- Combo therapy**

- **AMVUTTRA Pre-Taf LOE**
  - 1st line patients
  - Tafamidis progressors

- **AMVUTTRA Post-Taf LOE**
  - Tafamidis progressors
  - Add-on therapy

- **Continued evidence generation**

Note: The safety and efficacy of AMVUTTRA (vutrisiran) for the treatment of the cardiomyopathy of ATTR have not been established or evaluated by the FDA, EMA or any other health authority. Pending positive HELIOS-B study results and regulatory approval. Sources: Internal Market research, published payer policies. LOE: loss of exclusivity.
Supportive Data from Patisiran in APOLLO-B

Evidence for Disease Stabilization

- Decline in NT-proBNP, Mean Fold Change (95% CI)
  - 1.0, 1.1, 1.2, 1.3, 1.4, 1.5
  - Month: 0, 3, 6, 9, 12

Reduction in Disease Biomarkers

- Reduction in NT-proBNP, Mean Change from Baseline (±SEM)
  - Month: 0, 6, 9, 12, 18, 21, 24

Early Separation of Mortality Curves

- Cumulative All-Cause Mortality (%)
  - Month: 0, 3, 6, 9, 12, 15, 18, 21, 24

Design

- Powered for outcomes; ~2x size and ~3x length as APOLLO-B
- Enriched for patients most likely to benefit, NYHA I and II
- Longest follow-up of any ATTR-CM study (36 months in most patients)
- Analyses planned to demonstrate consistency of effect across key subgroups

Execution

- 10% overenrolled
- 60% monotherapy, 40% baseline tafamidis
- Lower rate of tafamidis drop-ins than expected

No significant difference in mortality was observed in APOLLO-B. The FDA issued a Complete Response Letter to the sNDA for patisiran for treatment of the cardiomyopathy of ATTR amyloidosis. Patisiran has not been approved by the FDA, EMA, or any other regulatory agency for cardiac manifestations of amyloidosis. No conclusions can or should be drawn regarding its safety or effectiveness in this population.
**HELIOS·B** Positioned to Deliver Outcomes Benefit in ATTR-CM

Supportive Data from Patisiran in APOLLO-B

<table>
<thead>
<tr>
<th>Evidence for Disease Stabilization</th>
<th>Design</th>
<th>Execution</th>
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<tbody>
<tr>
<td>Reduction in Disease Biomarkers</td>
<td></td>
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<tr>
<td>Early Separation of Mortality Curves</td>
<td></td>
<td>Double-blind Period Open-label Extension</td>
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Key learnings heading into HELIOS-B:

- Until tafamidis loss of exclusivity, monotherapy likely dominant
- APOLLO-B data demonstrated clear efficacy profile:
  - Evidence of disease stabilization (functional and QOL readouts)
  - Evidence for mortality benefit with separation as early as nine months
  - Greatest effect in monotherapy group

No significant difference in mortality was observed in APOLLO-B. The FDA issued a Complete Response Letter to the sNDA for patisiran for treatment of the cardiomyopathy of ATTR amyloidosis. Patisiran has not been approved by the FDA, EMA, or any other regulatory agency for cardiac manifestations of amyloidosis. No conclusions can or should be drawn regarding its safety or effectiveness in this population.
Enhancing HELIOS-B Statistical Plan

Supports Strong and Competitive Label

Focused on outcomes measures in overall AND monotherapy populations; latter expected to have largest treatment effect

Secondary endpoints honed to support differentiation and potential for disease stabilization

Up to 3 additional months incorporated into double-blind portion of trial to enhance statistical powering
Updated HELIOS-B Statistical Analysis Methodology

Study Duration

**Original**

- Double-blind period up to 36 months
- Primary analysis conducted when last patient reaches Month 30

**Updated**

- Double-blind period up to 36 months
- Primary analysis conducted when last patient reaches **Month 33**

- Three additional months of event collection for patients enrolled later in study, enhancing statistical power
- ~60% of patients remaining on study will have greater follow-up; ~20% more patients will have follow-up to full 36 months
- Longest double-blind follow-up in anyATTR-CM study to date
**Updated HELIOS-B Statistical Analysis Methodology**

**Primary Endpoint**

**Original**

**Primary Endpoint**
- Composite outcome of all-cause mortality and recurrent CV events in overall population

**Updated**

**Primary Endpoint**
- Composite outcome of all-cause mortality and recurrent CV events, analyzed in:
  - Overall population
  - **Monotherapy population** (patients not on tafamidis at baseline)

- Hospitalization and mortality viewed as **most important** outcomes; will be analyzed in:
  - Overall population (100%) to show **broad effect** in largest sample size
  - Monotherapy group (60%) to show vutrisiran’s **greatest impact**

- Primary endpoint tested in parallel; **study positive if**:
  - Both analyses $p \leq 0.05$, OR
  - Either analysis $p \leq 0.025$
Updated HELIOS-B Statistical Analysis Methodology

Secondary Endpoints

<table>
<thead>
<tr>
<th>Original</th>
<th>Updated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Select Secondary Endpoints</td>
<td>Secondary Endpoints</td>
</tr>
<tr>
<td>• 6-MWT distance</td>
<td>• 6-MWT distance</td>
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<tr>
<td>• Kansas City Cardiomyopathy Questionnaire (KCCQ OS) score</td>
<td>• KCCQ-OS</td>
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<tr>
<td>• Echocardiographic parameters</td>
<td>• All-cause mortality</td>
</tr>
<tr>
<td>• All-cause mortality &amp; recurrent all-cause hospitalizations &amp; urgent HF visits</td>
<td>• NYHA Class</td>
</tr>
<tr>
<td>• All-cause mortality</td>
<td>• Secondary endpoints streamlined to clinically relevant endpoints</td>
</tr>
<tr>
<td>• Recurrent CV events</td>
<td>• Prioritized to show potential differentiation and disease stabilization</td>
</tr>
<tr>
<td>• NT-proBNP</td>
<td>• Other prior secondaries will still be analyzed</td>
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</table>
Vutrisiran HELIOS·B Phase 3 Study
Randomized, Double-Blind Outcomes Study in ATTR Amyloidosis Patients with Cardiomyopathy

N = 655
Patient Population
- ATTR amyloidosis; wild-type or any TTR mutation
- Confirmed cardiomyopathy and medical history of symptomatic heart failure
- NYHA ≤ III; minimum walk and NT-proBNP limits at baseline
- 40% of patients on tafamidis at baseline

Vutrisiran SC q3M 25 mg or Placebo SC q3M

Primary Endpoint
- Composite outcome of all-cause mortality and recurrent CV events, assessed when last patient reaches Month 33, in:
  - Overall population
  - Monotherapy population

Secondary Endpoints
- 6-MWT distance
- Kansas City Cardiomyopathy Questionnaire score
- All-cause mortality
- NYHA Class

Topline results expected late June/early July 2024
Assuming positive results, sNDA submission expected late 2024
If Approved, Vutrisiran Expected to Have Market-Leading Profile in ATTR-CM

<table>
<thead>
<tr>
<th>Rapidly growing market with high unmet patient need</th>
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<tr>
<td>HCPs report that ~75% of patients treated with tafamidis have only partial or no response¹</td>
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<tr>
<th>Unique MOA</th>
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<tr>
<td>• Targeted RNAi mechanism enables rapid knockdown</td>
</tr>
<tr>
<td>• Upstream of approved medicines, reduces pathogenic protein</td>
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<table>
<thead>
<tr>
<th>Potential for Impactful Clinical Profile</th>
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<tbody>
<tr>
<td>• Reduction in mortality and CV hospitalizations</td>
</tr>
<tr>
<td>• Stabilization of functional capacity and quality of life</td>
</tr>
<tr>
<td>• Well tolerated safety profile</td>
</tr>
</tbody>
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<table>
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<tr>
<th>Only 4 Doses per Year</th>
</tr>
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<tbody>
<tr>
<td>• Quarterly dosing, strong adherence, aligning with MD visits</td>
</tr>
<tr>
<td>• In-office or at-home administration</td>
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</tbody>
</table>

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<thead>
<tr>
<th>Favorable Payer Dynamics</th>
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<tbody>
<tr>
<td>• Medicare Part B coverage expected to result in majority of patients having $0 out-of-pocket costs</td>
</tr>
<tr>
<td>• Monotherapy favored by payers prior to tafamidis LOE</td>
</tr>
</tbody>
</table>

¹ Alnylam market research with HCPs (n=530).
Note: The safety and efficacy of AMVUTTRA (vutrisiran) for the treatment of the cardiomyopathy of ATTR have not been established or evaluated by the FDA, EMA or any other health authority.
The information is intended to provide an overview of the potential clinical profile of vutrisiran in ATTR-CM.
ALN-APP Achieved Rapid and Durable Reductions in Key Biomarkers
Phase 1 Results* Mark First Demonstration of Gene Silencing by RNAi Therapeutics in Human Brain

- Generally well tolerated
- AEs generally mild to moderate in severity; most unrelated to study drug
- CSF safety biomarkers, routine lab assessments, and preliminary data for exploratory biomarker neurofilament light chain (NfL) all continued to show no concerning trends

Rapid and Durable Reductions in CSF sAPPβ

Marked Reductions in CSF Aβ42 and Aβ40 at Month 2

Dose escalation in Phase 1 Part A ongoing
Multi-dose Part B initiated
Phase 2 CAA study initiation planned for early 2024

* Data presented at 16th Clinical Trials on Alzheimer’s Disease (CTAD) conference, October 2023
ALN-APP Achieved Rapid and Durable Reductions in Key Biomarkers

Phase 1 Results* Mark First Demonstration of Gene Silencing by RNAi Therapeutics in Human Brain

- Generally well tolerated
- AEs generally mild to moderate in severity; most unrelated to study drug
- CSF safety biomarkers, routine lab assessments, and preliminary data for exploratory biomarker neurofilament light chain (NfL) all continued to show no concerning trends

FDA clearance to initiate multi-dosing in Part B of Phase 1 study in U.S.
- In response to partial clinical hold, Alnylam submitted non-clinical data and clinical data from Phase 1
- Multi-dosing cleared to proceed in U.S. at doses up to 180 mg every six months; partial hold for higher or more frequent doses still applies
- Provides clear path forward to explore broad range of doses up to and exceeding levels shown to provide robust and durable target engagement

Dose escalation in Phase 1 Part A ongoing
Multi-dose Part B initiated
Phase 2 CAA study initiation planned for early 2024

* Data presented at 16th Clinical Trials on Alzheimer's Disease (CTAD) conference, October 2023
## Recent Pipeline Progress

### Zilebesiran

*Hypertension*

- Positive results from KARDIA-1 Phase 2 dose-ranging study
- Up to 16.7 mmHg placebo-adjusted reduction of 24-hour mean systolic blood pressure at three months
- Encouraging safety and tolerability profile

### ALN-TTRsc04

*ATTR Amyloidosis*

- Positive Phase 1 study in healthy volunteers
- Rapid knockdown with mean serum TTR reduction up to 97%, durability supporting potential for annual dosing
- Encouraging safety and tolerability profile

### ALN-KHK

*Type 2 Diabetes*

- Positive Phase 1 study in overweight to obese healthy volunteers
- Robust target engagement with single dose; potential for quarterly or less frequent dosing
- Encouraging safety and tolerability profile

### Additional R&D Highlights

- Notable progress in extrahepatic delivery (e.g., muscle and adipose)
- Early advancement of novel targets in areas of high unmet need
- Accelerating pipeline development on track for 15 INDs by end of 2025 (including partner programs)
Multiple Sources of Sustainable Innovation Drive Robust Pipeline
Targeting Nine Alnylam-Led INDs Across Four Tissues by End of 2025

By End of 2025

**Extrahepatic Delivery**
- 5 new liver INDs
  - 10+ including partnered programs

**Platform Designs**
- IKARIA™
- Reversir™
- GEMINI™

**Human Genetics**
- Our Future Health

**Human Genetics**
- 2 new CNS INDs
  - 3+ including partnered programs
- 2 new tissues with INDs
Jeff Poulton
Chief Financial Officer

Financial Summary and Upcoming Milestones
Q4 and Full Year 2023 Financial Summary

<table>
<thead>
<tr>
<th>Financial Results ($ millions)</th>
<th>Q4 2023</th>
<th>Q4 2022</th>
<th>Q4 Reported Growth %</th>
<th>Q4 CER Growth %³</th>
</tr>
</thead>
<tbody>
<tr>
<td>Net Product Revenues</td>
<td>$346</td>
<td>$262</td>
<td>32%</td>
<td>30%</td>
</tr>
<tr>
<td>Net Revenues from Collaborations</td>
<td>$76</td>
<td>$71</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Royalty Revenues</td>
<td>$17</td>
<td>$3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Revenues</td>
<td>$440</td>
<td>$335</td>
<td>31%</td>
<td>29%</td>
</tr>
<tr>
<td>Product Cost of Goods Sold</td>
<td>$72</td>
<td>$46</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cost of Collaborations and Royalties</td>
<td>$14</td>
<td>$5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Cost of Goods Sold</td>
<td>$86</td>
<td>$51</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gross Margin</td>
<td>$354</td>
<td>$284</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Product Sales Gross Margin %¹</td>
<td>79%</td>
<td>82%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-GAAP R&amp;D Expenses²</td>
<td>$253</td>
<td>$245</td>
<td>3%</td>
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<tr>
<td>Non-GAAP SG&amp;A Expenses²</td>
<td>$175</td>
<td>$185</td>
<td>-5%</td>
<td></td>
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<tr>
<td>Non-GAAP Operating Loss ²</td>
<td>($74)</td>
<td>($146)</td>
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<td></td>
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</table>

<table>
<thead>
<tr>
<th>Financial Results ($ millions)</th>
<th>FY 2023</th>
<th>FY 2022</th>
<th>FY23 Reported Growth %</th>
<th>FY23 CER Growth %³</th>
</tr>
</thead>
<tbody>
<tr>
<td>Net Product Revenues</td>
<td>$1,241</td>
<td>$894</td>
<td>39%</td>
<td>39%</td>
</tr>
<tr>
<td>Net Revenues from Collaborations</td>
<td>$546</td>
<td>$135</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Royalty Revenues</td>
<td>$41</td>
<td>$8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Revenues</td>
<td>$1,828</td>
<td>$1,037</td>
<td>76%</td>
<td>76%</td>
</tr>
<tr>
<td>Product Cost of Goods Sold</td>
<td>$268</td>
<td>$140</td>
<td></td>
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<tr>
<td>Cost of Collaborations and Royalties</td>
<td>$42</td>
<td>$29</td>
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<tr>
<td>Total Cost of Goods Sold</td>
<td>$310</td>
<td>$169</td>
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<tr>
<td>Gross Margin</td>
<td>$1,518</td>
<td>$869</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Product Sales Gross Margin %¹</td>
<td>78%</td>
<td>84%</td>
<td></td>
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</tr>
<tr>
<td>Non-GAAP R&amp;D Expenses²</td>
<td>$907</td>
<td>$791</td>
<td>15%</td>
<td></td>
</tr>
<tr>
<td>Non-GAAP SG&amp;A Expenses²</td>
<td>$671</td>
<td>$632</td>
<td>6%</td>
<td></td>
</tr>
<tr>
<td>Non-GAAP Operating Loss ²</td>
<td>($60)</td>
<td>($554)</td>
<td></td>
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</tbody>
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<table>
<thead>
<tr>
<th>Financial Results ($ millions)</th>
<th>Dec 31, 2023</th>
<th>Dec 31, 2022</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cash &amp; Investments</td>
<td>$2,439</td>
<td>$2,192</td>
</tr>
</tbody>
</table>

¹ Product Sales GM % calculation excludes Cost of Collaborations and Royalties associated with Net Revenues from Collaborations and Royalty Revenues.
² Non-GAAP R&D expenses, SG&A expenses and operating income / (loss) are non-GAAP financial measures that exclude from the corresponding GAAP measures costs related to stock-based compensation expense.
³ CER growth rates represent growth at Constant Exchange Rates, a non-GAAP financial measure determined by comparing Q4 2023 performance (restated using Q4 2022 exchange rates) to actual Q4 2022 reported performance and by comparing full-year 2023 performance (restated using 2022 exchange rates) to actual full-year 2022 reported performance. 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 February 15, 2024, which is accessible in the Investors section of our website at www.alnylam.com.
4 Cash, cash equivalents and marketable securities.
# 2024 Full Year Guidance

<table>
<thead>
<tr>
<th>Guidance</th>
<th>Key Assumptions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Net Product Revenue</strong>&lt;sup&gt;1&lt;/sup&gt; ONPATTRO, AMVUTTRA, GIVLAARI, OXLUMO</td>
<td>$1,400M to $1,500M • Uses January 31, 2024 FX rates</td>
</tr>
<tr>
<td><em>Net Product Revenue Growth vs. 2023 at reported Fx rates</em>&lt;sup&gt;1&lt;/sup&gt;</td>
<td>13% to 21% • Uses January 31, 2024 FX rates</td>
</tr>
<tr>
<td><em>Net Product Revenue Growth vs. 2023 at constant exchange rates (i.e., operational growth)</em>&lt;sup&gt;2&lt;/sup&gt;</td>
<td>13% to 21% • Uses 2023 actual FX rates</td>
</tr>
<tr>
<td><strong>Net Revenues from Collaborations &amp; Royalties</strong></td>
<td>$325M to $425M</td>
</tr>
<tr>
<td><strong>Non-GAAP Combined R&amp;D and SG&amp;A Expenses</strong>&lt;sup&gt;3&lt;/sup&gt;</td>
<td>$1,675M to $1,775M</td>
</tr>
</tbody>
</table>

---

1. Our 2024 FY Guidance is based upon January 31, 2024 FX rates including 1 EUR = 1.08 USD and 1 USD = 147 JPY.
2. CER = constant exchange rate, representing growth calculated as if exchange rates had remained unchanged from those used in 2023. CER is a non-GAAP financial measure. Information regarding our use of non-GAAP financial measures is available in our press release dated February 15, 2024, which is accessible in the Investors section of our website at www.alnylam.com.
3. 2024 Non-GAAP Combined R&D and SG&A Expenses guidance are non-GAAP financial measures that exclude the corresponding GAAP measures stock-based compensation expense estimated at $225M - $275M. Information regarding our use of non-GAAP financial measures is available in our press release dated February 15, 2024, which is accessible in the Investors section of our website at www.alnylam.com.
## Alnylam 2024 Goals

<table>
<thead>
<tr>
<th>Program</th>
<th>Indication</th>
<th>Early Milestones</th>
<th>Mid Milestones</th>
<th>Late Milestones</th>
</tr>
</thead>
<tbody>
<tr>
<td>VUTRISIRAN</td>
<td>ATTR Amyloidosis</td>
<td>Combined Net Product Revenue Guidance to be Provided at Q4/YE 2023 Earnings</td>
<td>HELIOS-B Topline Results</td>
<td>●</td>
</tr>
<tr>
<td>ALN-TTRsc04*</td>
<td>ATTR Amyloidosis</td>
<td></td>
<td>sNDA Submission</td>
<td>●</td>
</tr>
<tr>
<td>ZILEBESIRAN*</td>
<td>Hypertension</td>
<td></td>
<td>KARDIA-2 Phase 2 Topline Results</td>
<td>●</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Initiate KARDIA-3 Phase 2 Study</td>
<td>●</td>
</tr>
<tr>
<td>ALN-APP*</td>
<td>Alzheimer’s Disease</td>
<td></td>
<td>Interim Phase 1 Part B Multi-Dose Results</td>
<td>●</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Initiate Phase 2 Study</td>
<td>●</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Initiate Phase 2 Study</td>
<td>●</td>
</tr>
<tr>
<td>ALN-KHK*</td>
<td>Type 2 Diabetes</td>
<td>Initiate Phase 1 Part B</td>
<td></td>
<td>●</td>
</tr>
<tr>
<td>ALN-BCAT*</td>
<td>Hepatocellular Carcinoma</td>
<td>Initiate Phase 1 Study</td>
<td></td>
<td>●</td>
</tr>
</tbody>
</table>

### ADDITIONAL PROGRAMS
- File 3 New INDs

### KEY PARTNER-LED PROGRAM MILESTONES

- **FITUSIRAN* (Sanofi)**
  - Hemophilia
  - Submit NDA Filing
  - 2024

- **ELEBSIRAN* (Vir)**
  - Chronic HBV/HDV Infection
  - Phase 2 Results
  - Q2, Q4

---

*Not approved for any indication and conclusions regarding the safety or effectiveness of these drugs have not been established.

Early is Q1-Q2, Mid is Q2-Q3, and Late is Q3-Q4
Q4 and Full Year 2023 Financial Results

Q&A Session
Thank You!
Q4 and Full Year 2023 Financial Results

Appendix
Alnylam Pharmaceuticals, Inc.
Reconciliation of Selected GAAP Measures to Non-GAAP Measures
(In thousands)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Reconciliation of GAAP to Non-GAAP research and development:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GAAP Research and development</td>
<td>$272,141</td>
<td>$262,039</td>
<td>$1,004,415</td>
<td>$883,015</td>
</tr>
<tr>
<td>Less: Stock-based compensation expenses</td>
<td>(19,085)</td>
<td>(16,944)</td>
<td>(97,273)</td>
<td>(92,161)</td>
</tr>
<tr>
<td>Non-GAAP Research and development</td>
<td>$253,056</td>
<td>$245,095</td>
<td>$907,142</td>
<td>$790,854</td>
</tr>
<tr>
<td><strong>Reconciliation of GAAP to Non-GAAP selling, general and administrative:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GAAP Selling, general and administrative</td>
<td>$198,123</td>
<td>$210,344</td>
<td>$795,646</td>
<td>$770,658</td>
</tr>
<tr>
<td>Non-GAAP Selling, general and administrative</td>
<td>$175,214</td>
<td>$184,521</td>
<td>$671,239</td>
<td>$632,170</td>
</tr>
<tr>
<td><strong>Reconciliation of GAAP to Non-GAAP operating loss:</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GAAP operating loss</td>
<td>$(116,404)</td>
<td>$(188,614)</td>
<td>$(282,175)</td>
<td>$(785,072)</td>
</tr>
<tr>
<td>Add: Stock-based compensation expenses</td>
<td>41,994</td>
<td>42,767</td>
<td>221,680</td>
<td>230,649</td>
</tr>
<tr>
<td>Non-GAAP Operating loss</td>
<td>$(74,410)</td>
<td>$(145,847)</td>
<td>$(60,495)</td>
<td>$(554,423)</td>
</tr>
</tbody>
</table>

Please note that the figures presented may not sum exactly due to rounding.
## Alnylam Pharmaceuticals, Inc.
Reconciliation of Revenue and Growth at Constant Currency

Please note that the figures presented may not sum exactly due to rounding.

Constant Currency = CER

<table>
<thead>
<tr>
<th></th>
<th>December 31, 2023</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Three Months</td>
<td>Twelve Months</td>
</tr>
<tr>
<td>Total TTR net product revenue growth, as reported</td>
<td>33 %</td>
<td>40 %</td>
</tr>
<tr>
<td>Add: Impact of foreign currency translation</td>
<td>(2)</td>
<td>—</td>
</tr>
<tr>
<td>Total TTR net product revenue growth at constant currency</td>
<td>31 %</td>
<td>40 %</td>
</tr>
<tr>
<td>Total Ultra Rare net product revenue growth, as reported</td>
<td>30 %</td>
<td>35 %</td>
</tr>
<tr>
<td>Add: Impact of foreign currency translation</td>
<td>(3)</td>
<td>—</td>
</tr>
<tr>
<td>Total Ultra Rare net product revenue growth at constant currency</td>
<td>27 %</td>
<td>35 %</td>
</tr>
<tr>
<td>Total net product revenue growth, as reported</td>
<td>32 %</td>
<td>39 %</td>
</tr>
<tr>
<td>Add: Impact of foreign currency translation</td>
<td>(2)</td>
<td>—</td>
</tr>
<tr>
<td>Total net product revenue growth at constant currency</td>
<td>30 %</td>
<td>39 %</td>
</tr>
<tr>
<td>Total revenue growth, as reported</td>
<td>31 %</td>
<td>76 %</td>
</tr>
<tr>
<td>Add: Impact of foreign currency translation</td>
<td>(2)</td>
<td>—</td>
</tr>
<tr>
<td>Total revenue growth at constant currency</td>
<td>29 %</td>
<td>76 %</td>
</tr>
</tbody>
</table>