UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): October 27, 2022

Alnylam Pharmaceuticals, Inc.
(Exact Name of Registrant as Specified in Charter)

Delaware	001-36407	77-0602661
(State or Other Jurisdiction of Incorporation)	(Commission File Number)	(IRS Employer Identification No.)

675 West Kendall Street, Henri A. Termeer Square Cambridge, Massachusetts	02142
(Address of Principal Executive Offices)	(Zip Code)

Registrant's telephone number, including area code: (617) 551-8200

Not applicable
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (*see* General Instruction A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of Each Class	**Trading Symbol(s)**	**Name of Each Exchange on Which Registered**
Common Stock, $0.01 par value per share	ALNY	The Nasdaq Stock Market LLC

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934(§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 2.02. Results of Operations and Financial Condition

On October 27, 2022, Alnylam Pharmaceuticals, Inc. (the "Company") announced its financial results for the quarter ended September 30, 2022. The full text of the press release issued in connection with the announcement is furnished as Exhibit 99.1 to this Current Report on Form 8-K.

The information in Item 2.02 of this Form 8-K (including Exhibit 99.1) shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such a filing.

Item 9.01. Financial Statements and Exhibits

(d) Exhibits

The following exhibit relating to Item 2.02 shall be deemed to be furnished, and not filed:

99.1	Press Release dated October 27, 2022.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: October 27, 2022

ALNYLAM PHARMACEUTICALS, INC.

By: /s/ Jeffrey V. Poulton
Jeffrey V. Poulton
Executive Vice President, Chief Financial Officer

Exhibit 99.1

Alnylam Pharmaceuticals Reports Third Quarter 2022 Financial Results and Highlights Recent Period Activity

– Achieved Third Quarter 2022 Global Net Product Revenues of $232 Million for ONPATTRO®, AMVUTTRA®, GIVLAARI®, and OXLUMO® –

– Strong First Full Quarter of AMVUTTRA in U.S.: Achieving $25 Million in Net Product Revenues and Driving 30% U.S. Total TTR Growth Compared with Q2 2022 –

– Reported Positive Results from the APOLLO-B Phase 3 Study of Patisiran, and Remains on Track for a Supplemental New Drug Application (sNDA) Submission in Late 2022 –

– Reiterated 2022 Combined Net Product Revenue Guidance of $870-$930 Million –

CAMBRIDGE, Mass.--(BUSINESS WIRE)--October 27, 2022--Alnylam Pharmaceuticals, Inc. (Nasdaq: ALNY), the leading RNAi therapeutics company, today reported its consolidated financial results for the third quarter ended September 30, 2022 and reviewed recent business highlights.

“The third quarter of 2022 was one of strong execution across our commercial and clinical development operations. AMVUTTRA has completed its first full quarter on the market since its U.S. approval and launch in June and is off to a great start, demonstrating the potential of our RNAi therapeutics portfolio in patients with hATTR amyloidosis with polyneuropathy which achieved 30% U.S. growth compared to Q2. We’re also looking forward to potentially expanding the opportunity for this franchise and are encouraged by the positive APOLLO-B Phase 3 results for patisiran in patients with ATTR amyloidosis with cardiomyopathy presented recently. We are on track to submit an sNDA for ONPATTRO by year-end and hope to bring this treatment option to patients in 2023 assuming successful regulatory review and approval,” said Yvonne Greenstreet, MBChB, Chief Executive Officer of Alnylam. “The rest of our pipeline continues to progress well, and we are excited for several important upcoming milestones, including results for a potential biannual dose regimen for vutrisiran, preliminary Phase 1 results for ALN-XDH in patients with gout, completion of enrollment in the KARDIA-2 Phase 2 study of zilebesiran, and initiation of a Phase 1 study of ALN-TTRsc04 in healthy volunteers. We are encouraged by our steady and continuous execution on all fronts, and believe we are on track to achieve our *Alnylam P^{5}x25* goals and become a top-tier biotech company.”

Third Quarter 2022 and Recent Significant Corporate Highlights

Commercial Performance

Total TTR: ONPATTRO® (patisiran) & AMVUTTRA® (vutrisiran)

- Achieved global net product revenues for ONPATTRO and AMVUTTRA for the third quarter of 2022 of $145 million and $25 million, respectively, representing a total TTR increase of 11% compared to Q2 2022, with the U.S. market contributing 30% total TTR growth underpinned by the strength of the AMVUTTRA launch.
- Attained over 2,580 hATTR amyloidosis patients with polyneuropathy worldwide on commercial treatment with ONPATTRO or AMVUTTRA as of September 30, 2022, up from over 2,400 on commercial ONPATTRO as of June 30, 2022, representing 8% total TTR quarterly growth.
- Received 475 Start Forms in the U.S. for AMVUTTRA from launch through September 30, 2022, with 46% representing new patients and 54% representing patients switching from ONPATTRO.

GIVLAARI® (givosiran)

- Achieved global net product revenues for the third quarter of 2022 of $46 million, representing a 1% increase compared to Q2 2022.
- Attained over 460 patients worldwide on commercial GIVLAARI treatment as of September 30, 2022, up from over 420 commercial patients as of June 30, 2022, representing 10% quarterly growth.

OXLUMO® (lumasiran)

- Achieved global net product revenues for the third quarter of 2022 of $16 million, representing a 10% increase compared to Q2 2022.
- Attained over 230 patients worldwide on commercial OXLUMO treatment as of September 30, 2022, up from over 200 commercial patients as of June 30, 2022, representing 15% quarterly growth.

Leqvio® (inclisiran)

- Launch in the U.S. and other markets is ongoing, with focus on patient onboarding, removing access hurdles and enhancing medical education.

R&D Highlights

Patisiran (the non-proprietary name for ONPATTRO), in development for the treatment of ATTR amyloidosis.

- Reported positive results from the APOLLO-B Phase 3 study in patients with ATTR amyloidosis with cardiomyopathy. The Company remains on track to submit an sNDA for review by the United States Food and Drug Administration (FDA) by year-end.

Vutrisiran (the non-proprietary name for AMVUTTRA), in development for the treatment of ATTR amyloidosis.

- Received marketing authorization for AMVUTTRA for the treatment of hereditary transthyretin-mediated (hATTR) amyloidosis in adults with stage 1 or stage 2 polyneuropathy in Europe and the UK, as well as approval for transthyretin (TTR) type familial amyloidosis with polyneuropathy in Japan.
- Alnylam announces today that it does not plan to conduct the optional interim analysis for the HELIOS-B Phase 3 study in patients with ATTR amyloidosis with cardiomyopathy. The study remains on track for topline results in early 2024.
- The Company also announces today that it is considering options for the best path toward advancing an RNAi therapeutic for the treatment of Stargardt Disease. At this time, it will not initiate a Phase 3 study of vutrisiran in Stargardt Disease in late 2022, as previously guided, as it continues to evaluate the impact of the Inflation Reduction Act.

Lumasiran (the non-proprietary name for OXLUMO), for the treatment of primary hyperoxaluria type 1 (PH1), and in development for the treatment of recurrent kidney stone disease.

- Based on the successful outcome of the ILLUMINATE-C study in children and adults with advanced PH1, received approval from the U.S. FDA of an sNDA for OXLUMO, expanding the indication for the treatment of PH1 to lower urinary oxalate and plasma oxalate levels in pediatric and adult patients, and received approval from the European Medicines Agency (EMA) of a Type II variation to include the ILLUMINATE-C data in the label.

Cemdisiran, in development for the treatment of complement-mediated diseases, in collaboration with Regeneron.

- Reported positive results from the Phase 2 study in patients with immunoglobulin A nephropathy (IgAN).
- Alnylam is working with Regeneron to finalize plans for the Phase 3 clinical development of cemdisiran in IgAN.

Early- and mid-stage investigational RNAi therapeutic pipeline programs and RNAi platform

- Published preclinical results in *Nature Biotechnology* based on novel conjugate technology facilitating delivery of siRNA to the CNS and other extrahepatic tissues.
- Vir Biotechnology announced that the first patient has been dosed in the Phase 2 SOLSTICE clinical trial evaluating **ALN-HBV02 (VIR-2218)** and VIR-3434 as monotherapy and in combination for the treatment of people living with chronic hepatitis D virus (HDV), which occurs as a simultaneous co-infection or super-infection alongside hepatitis B virus (HBV).
- Published research findings in *Nature Communications* identifying mutations in the *INHBE* gene associated with protection against abdominal obesity and metabolic syndrome.
- Reported preliminary data from the ongoing Phase 1 study of **ALN-HSD**, in development for the treatment of nonalcoholic steatohepatitis (NASH).
- Alnylam announces today that enrollment and dose escalation continue in the Phase 1 study of **ALN-APP** in patients with early onset Alzheimer's Disease, in collaboration with Regeneron, and initial results are now expected in early 2023.
- Filed a Clinical Trial Application (CTA) for **ALN-TTRsc04**, the first clinical program from the Company's IKARIA™ platform, aimed at achieving an annual dosing regimen with highly potent and reversible effects of TTR lowering.

Additional Business Updates

- Appointed Piyush Sharma as Chief Ethics and Compliance Officer and Evan Lippman as Chief Corporate Development and Strategy Officer.
- Issued $1,035 million convertible senior notes with proceeds primarily used to pay down Blackstone $700 million credit facility and approximately $200 million in prepayment premiums under the credit facility, the purchase of capped call transactions, and underwriter fees.
- Ranked #1 on *Fast Company*'s fourth annual list of **Best Workplaces for Innovators**.
- Named a **Top Place to Work for Women** by *Fortune* magazine.

Upcoming Events

In late 2022, Alnylam intends to:

- Present a review of its pipeline and platform activities at its upcoming R&D Day being held virtually on Thursday, December 15, 2022.
- Submit an sNDA to the FDA for review for **ONPATTRO** for the treatment of patients with ATTR amyloidosis with cardiomyopathy.
- Report results on a biannual dose regimen for **vutrisiran**.
- Initiate a Phase 1 study for **ALN-TTRsc04** in healthy volunteers.
- Complete enrollment in the Phase 2 study of **lumasiran** in patients with recurrent renal stones.
- Complete enrollment in the KARDIA-2 Phase 2 study of **zilebesiran** (at or around year-end).
- Report preliminary results from the Phase 1 study of **ALN-XDH** in patients with gout.
- Submit CTA filings for **ALN-KHK** for the treatment of metabolic liver disease, including diabetes, and in collaboration with its partner Regeneron, submit an IND for **ALN-PNP** for the treatment of NASH.

Financial Results for the Quarter Ended September 30, 2022

Financial Highlights

	Three Months Ended September 30,	
(in thousands, except per share amounts)	**2022**	**2021**
Net product revenues	$ 232,267	$ 167,044
Net revenue from collaborations	$ 29,297	$ 20,136
Royalty revenue	$ 2,742	$ 453
GAAP Operating loss	$ (258,040)	$ (181,677)
Non-GAAP Operating loss	$ (129,922)	$ (148,310)
GAAP Other expense, net	$ (147,903)	$ (22,559)
Non-GAAP Other expense, net	$ (63,467)	$ (41,250)
GAAP Net loss	$ (405,920)	$ (204,514)
Non-GAAP Net loss	$ (193,366)	$ (189,838)
GAAP Net loss per common share – basic and diluted	$ (3.32)	$ (1.72)
Non-GAAP Net loss per common share – basic and diluted	$ (1.58)	$ (1.59)

Net Product Revenues

	Three Months Ended September 30,		Year over Year % Growth	
(in thousands, except percentages)	**2022**	**2021**	**As Reported**	**At CER***
ONPATTRO net product revenues	$ 144,950	$ 120,317	20%	31%
AMVUTTRA net product revenues	25,229	----	N/A	N/A
Total TTR net product revenues	170,179	120,317	41%	52%
GIVLAARI net product revenues	45,659	31,833	43%	50%
OXLUMO net product revenues	16,429	14,894	10%	20%
Total net product revenues	$ 232,267	$ 167,044	39%	49%

* CER = Constant Exchange Rate, representing growth calculated as if the exchange rates had remained unchanged from those used in the third quarter 2021. CER is a Non-GAAP measure.

- Net product revenues increased 39% at actual currency during the third quarter of 2022, as compared to the prior year, and 49% at CER. The increase is primarily due to increased patients on ONPATTRO, AMVUTTRA, GIVLAARI, and OXLUMO.

Net Revenues from Collaborations

- Net revenues from collaborations increased 45% during the third quarter 2022, as compared to the prior year, primarily due to an increase in revenue from our collaboration with Regeneron resulting from the timing of reimbursable activities.

Operating Expenses

	Three Months Ended September 30,	
(in thousands)	**2022**	**2021**
GAAP research and development expenses	$ 245,371	$ 194,572
Non-GAAP research and development expenses	$ 192,409	$ 182,155
GAAP selling, general and administrative expenses	$ 235,859	$ 142,075
Non-GAAP selling, general and administrative expenses	$ 160,703	$ 121,125

Research & Development (R&D) Expenses

- GAAP and non-GAAP R&D expenses increased during the third quarter 2022, as compared to the prior year, primarily due to increases in headcount to support our R&D pipeline and development expenses associated with the KARDIA-1 and KARDIA-2 zilebesiran Phase 2 studies, offset by a decrease in the cost of clinical batches manufactured during the quarter. GAAP R&D expenses further increased due to increased stock-based compensation expense related to the accounting for certain performance-based awards that vested during the period.

Selling, General & Administrative (SG&A) Expenses

- GAAP and non-GAAP SG&A expenses increased during the third quarter 2022, as compared to the prior year, primarily due to increased headcount and other strategic investments in support of the U.S. AMVUTTRA launch and other corporate purposes. GAAP SG&A expenses further increased due to stock-based compensation expense related to the accounting for certain performance-based awards that vested during the period.

Other Financial Highlights

- GAAP Other expense, net, increased during the third quarter 2022 as compared to the prior year, primarily due to a $77 million loss on the extinguishment of the Blackstone credit agreement and a $25 million loss from the fair value adjustment on the development derivative liability.
- Cash, cash equivalents and marketable securities were $2.27 billion as of September 30, 2022 compared to $2.44 billion as of December 31, 2021 with the decrease primarily due to our year-to-date operating loss in 2022. This decrease was largely offset by approximately $200 million received from employee option award exercises and approximately $135 million received from the issuance of convertible debt, net of repayment of borrowings, inclusive of prepayment premiums under the credit facility, the purchase of capped call transactions, and underwriter fees.

A reconciliation of our GAAP to non-GAAP results for the current quarter is included in the tables of this press release.

2022 Updated Financial Guidance
Full year 2022 financial guidance has been updated as follows:

	Provided 4/28/2022[1]	Updated 10/27/2022[2]
Combined net product revenues for ONPATTRO, GIVLAARI, OXLUMO and AMVUTTRA	$870 million - $930 million	Unchanged
Net revenues from collaborations and royalties	$175 million - $225 million	$100 million - $150 million
GAAP R&D and SG&A expenses	$1,620 million - $1,700 million	Unchanged
Non-GAAP R&D and SG&A expenses[3]	$1,390 million - $1,450 million	Unchanged

[1] Prior FY 2022 guidance utilized April 18, 2022 FX rates of: 1 EUR = 1.08 USD; 1 GBP = 1.31 USD; 1 CHF = 1.06 USD; 1 CAD = 0.79 USD, 1 USD = 126 JPY
[2] Updated FY 2022 guidance utilizes September 27, 2022 FX rates of: 1 EUR = 0.96 USD; 1 GBP = 1.08 USD; 1 CHF = 1.01 USD; 1 CAD = 0.73 USD, 1 USD = 145 JPY
[3] Primarily excludes $230-$250 million of stock-based compensation expense from estimated GAAP R&D and SG&A expenses.

Use of Non-GAAP Financial Measures
This press release contains non-GAAP financial measures, including expenses adjusted to exclude certain non-cash expenses and non-recurring gains outside the ordinary course of the Company's business. 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.

The items included in GAAP presentations but excluded for purposes of determining non-GAAP financial measures for the periods presented in this press release are stock-based compensation expenses, realized and unrealized (gains) losses on marketable equity securities and loss on the extinguishment of debt. The Company has excluded the impact of stock-based compensation expense, which may fluctuate from period to period based on factors including the variability associated with performance-based grants for stock options and restricted stock units and changes in the Company's stock price, which impacts the fair value of these awards. The Company has excluded the impact of the realized and unrealized (gains) losses on marketable equity securities because the Company does not believe these adjustments accurately reflect the performance of the Company's ongoing operations for the period in which such gains or losses are reported, as their sole purpose is to adjust amounts on the balance sheet. The Company has excluded the loss on the extinguishment of debt because the Company believes the item is a non-recurring transaction outside the ordinary course of the Company's business.

Percentage changes in revenue growth at CER are presented excluding the impact of changes in foreign currency exchange rates for investors to understand the underlying business performance. The current period's foreign currency revenue values are converted into U.S. dollars using the average exchange rates from the prior period.

The Company believes the presentation of non-GAAP financial measures provides useful information to management and investors regarding the Company's financial condition and results of operations. When GAAP financial measures are viewed in conjunction with non-GAAP financial measures, investors are provided with a more meaningful understanding of the Company's ongoing operating performance and are better able to compare the Company's performance between periods. In addition, these non-GAAP financial measures are among those indicators the Company uses as a basis for evaluating performance, allocating resources and planning and forecasting future periods. Non-GAAP financial measures are not intended to be considered in isolation or as a substitute for GAAP financial measures. A reconciliation between GAAP and non-GAAP measures is provided later in this press release.

Conference Call Information
Management will provide an update on the Company and discuss third quarter 2022 results as well as expectations for the future via conference call on Thursday, October 27, 2022 at 8:30 am ET. To access the call, please register online at https://register.vevent.com/register/BI1581caadac4f4c80820e2eb8a001b2c3. Participants are requested to register at a minimum 15 minutes before the start of the call. A replay of the call will be available two hours after the call and archived on the same web page for six months.

A live audio webcast of the call will be available on the Investors section of the Company's website at www.alnylam.com/events. An archived webcast will be available on the Alnylam website approximately two hours after the event.

About ONPATTRO® (patisiran)
ONPATTRO is an RNAi therapeutic that is approved in the United States and Canada for the treatment of the polyneuropathy of hATTR amyloidosis in adults. ONPATTRO is also approved in the European Union, Switzerland and Brazil for the treatment of hATTR amyloidosis in adults with Stage 1 or Stage 2 polyneuropathy, and in Japan for the treatment of hATTR amyloidosis with polyneuropathy. ONPATTRO is an intravenously administered RNAi therapeutic targeting transthyretin (TTR). It is designed to target and silence TTR messenger RNA, thereby reducing the production of TTR protein before it is made. Reducing the pathogenic protein leads to a reduction in amyloid deposits in tissues. For more information about ONPATTRO, including full Prescribing Information, visit ONPATTRO.com.

About GIVLAARI® (givosiran)
GIVLAARI is an RNAi therapeutic targeting aminolevulinic acid synthase 1 (ALAS1) approved in the United States and Brazil for the treatment of adults with acute hepatic porphyria (AHP). GIVLAARI is also approved in the European Union for the treatment of AHP in adults and adolescents aged 12 years and older. In the pivotal study, givosiran was shown to significantly reduce the rate of porphyria attacks that required hospitalizations, urgent healthcare visits or intravenous hemin administration at home compared to placebo. GIVLAARI is Alnylam's first commercially available therapeutic based on its Enhanced Stabilization Chemistry ESC-GalNAc conjugate technology to increase potency and durability. GIVLAARI is administered via subcutaneous injection once monthly at a dose based on actual body weight and should be administered by a healthcare professional. GIVLAARI works by specifically reducing elevated levels of ALAS1 messenger RNA (mRNA), leading to reduction of toxins associated with attacks and other disease manifestations of AHP. For more information about GIVLAARI, including the full U.S. Prescribing Information, visit GIVLAARI.com.

About OXLUMO® (lumasiran)
OXLUMO (lumasiran) is an RNAi therapeutic targeting hydroxyacid oxidase 1 (HAO1). HAO1 encodes glycolate oxidase (GO). Thus, by silencing HAO1 and depleting the GO enzyme, OXLUMO inhibits production of oxalate – the metabolite that directly contributes to the pathophysiology of PH1. OXLUMO utilizes Alnylam's Enhanced Stabilization Chemistry (ESC)-GalNAc-conjugate technology, which enables subcutaneous dosing with increased potency and durability and a wide therapeutic index. OXLUMO has received regulatory approvals from the U.S. Food and Drug Administration (FDA) for the treatment of primary hyperoxaluria type 1 (PH1) to lower urinary and plasma oxalate levels in pediatric and adult patients and from the European Medicines Agency (EMA) for the treatment of PH1 in all age groups. In the pivotal ILLUMINATE-A study, OXLUMO was shown to significantly reduce levels of urinary oxalate relative to placebo, with the majority of patients reaching normal or near-normal levels. In the ILLUMINATE-B pediatric Phase 3 study, OXLUMO demonstrated an efficacy and safety profile consistent to that observed in ILLUMINATE-A. In the ILLUMINATE-C study, OXLUMO resulted in substantial reductions in plasma oxalate in patients with advanced PH1. Across all three studies, injection site reactions (ISRs) were the most common drug-related adverse reaction. OXLUMO is administered via subcutaneous injection once monthly for three months, then once quarterly beginning one month after the last loading dose at a dose based on actual body weight. For patients who weigh less than 10 kg, ongoing dosing remains monthly. OXLUMO should be administered by a healthcare professional. For more information about OXLUMO, including the full U.S. Prescribing Information, visit OXLUMO.com.

About AMVUTTRA® (vutrisiran)
AMVUTTRA® (vutrisiran) is an RNAi therapeutic approved in the United States for the treatment of the polyneuropathy of hereditary transthyretin-mediated (hATTR) amyloidosis in adults. It is a double-stranded small interfering RNA (siRNA) that targets mutant and wild-type transthyretin (TTR) messenger RNA (mRNA). Using Alnylam's Enhanced Stabilization Chemistry (ESC)-GalNAc-conjugate delivery platform, AMVUTTRA is designed for increased potency and high metabolic stability to allow for subcutaneous injection once every three months (quarterly). Results from the pivotal HELIOS-A Phase 3 study demonstrate AMVUTTRA rapidly reduces serum TTR levels, has the potential to reverse neuropathy impairment relative to baseline and improves other key measures of disease burden relative to external placebo in patients with the polyneuropathy of hATTR amyloidosis. For more information about AMVUTTRA, including the full U.S. Prescribing Information, visit AMVUTTRA.com.

About LNP Technology
Alnylam has licenses to Arbutus Biopharma LNP intellectual property for use in RNAi therapeutic products using LNP technology.

About RNAi
RNAi (RNA interference) is a natural cellular process of gene silencing that represents one of the most promising and rapidly advancing frontiers in biology and drug development today. Its discovery has been heralded as "a major scientific breakthrough that happens once every decade or so," and was recognized with the award of the 2006 Nobel Prize for Physiology or Medicine. By harnessing the natural biological process of RNAi occurring in our cells, a new class of medicines known as RNAi therapeutics is now a reality. Small interfering RNA (siRNA), the molecules that mediate RNAi and comprise Alnylam's RNAi therapeutic platform, function upstream of today's medicines by potently silencing messenger RNA (mRNA) – the genetic precursors – that encode for disease-causing or disease pathway proteins, thus preventing them from being made. This is a revolutionary approach with the potential to transform the care of patients with genetic and other diseases.

About Alnylam Pharmaceuticals
Alnylam (Nasdaq: ALNY) has led the translation of RNA interference (RNAi) into a whole new class of innovative medicines with the potential to transform the lives of people afflicted with rare and prevalent diseases with unmet need. Based on Nobel Prize-winning science, RNAi therapeutics represent a powerful, clinically validated approach yielding transformative medicines. Since its founding 20 years ago, Alnylam has led the RNAi Revolution and continues to deliver on a bold vision to turn scientific possibility into reality. Alnylam's commercial RNAi therapeutic products are ONPATTRO® (patisiran), GIVLAARI® (givosiran), OXLUMO® (lumasiran), AMVUTTRA® (vutrisiran) and Leqvio® (inclisiran) being developed and commercialized by Alnylam's partner, Novartis. Alnylam has a deep pipeline of investigational medicines, including multiple product candidates that are in late-stage development. Alnylam is executing on its "Alnylam P^5x25" strategy to deliver transformative medicines in both rare and common diseases benefiting patients around the world through sustainable innovation and exceptional financial performance, resulting in a leading biotech profile. Alnylam is headquartered in Cambridge, MA. For more information about our people, science and pipeline, please visit www.alnylam.com and engage with us on Twitter at @Alnylam, on LinkedIn, or on Instagram.

Alnylam Forward Looking Statements

Various statements in this release concerning Alnylam's expectations, plans, aspirations and goals, including, without limitation, our aspiration to become a leading biotech company and the planned achievement of our "*Alnylam P5x25*" strategy, the potential submission of a sNDA for ONPATTRO for patients with ATTR amyloidosis with cardiomyopathy by year-end for FDA review, the potential expansion of Alnylam's TTR franchise, assuming successful review and approval of the ONPATTRO sNDA, the achievement of additional pipeline milestones and data, including relating to ongoing clinical studies of vutrisiran, zilebesiran, lumasiran, cemdisiran, ALN-HBV02 (Vir 2218), ALN-APP and ALN-XDH, the filing of an IND for ALN-TTRsc04 and a CTA for ALN-PNP and ALN-KHK, the expected range of net product revenues for 2022, the updated expected range of net revenues from collaborations and royalties for 2022, and the expected range of aggregate annual GAAP and non-GAAP R&D and SG&A expenses for 2022, constitute forward-looking statements for the purposes of the safe harbor provisions under The Private Securities Litigation Reform Act of 1995. 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: 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 and the effectiveness or timeliness of Alnylam's efforts to mitigate the impact of the pandemic; the potential impact of the January 2022 leadership transition on Alnylam's ability to attract and retain talent and 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 its product candidates, including patisiran and vutrisiran; actions or advice of regulatory agencies and Alnylam's ability to obtain and maintain regulatory approval for its product candidates, including patisiran, as well as favorable pricing and reimbursement; successfully launching, marketing and selling its approved products globally; delays, interruptions or failures in the manufacture and supply of its product candidates or its marketed products; obtaining, maintaining and protecting intellectual property; Alnylam's ability to successfully expand the indication for ONPATTRO, AMVUTTRA or OXLUMO 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; Alnylam's ability to maintain strategic business collaborations; Alnylam's dependence on third parties for the development and commercialization of certain products, including Novartis, Regeneron and Vir; the outcome of litigation; the potential impact of a current government investigation and 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 its other SEC filings. 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 release discusses investigational RNAi therapeutics and uses of previously approved RNAi therapeutics in development and is not intended to convey conclusions about efficacy or safety as to those investigational therapeutics or uses. There is no guarantee that any investigational therapeutics or expanded uses of commercial products will successfully complete clinical development or gain health authority approval.

ALNYLAM PHARMACEUTICALS, INC.
CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS
(In thousands, except per share amounts)
(Unaudited)

	Three Months Ended		Nine Months Ended	
	September 30, 2022	**September 30, 2021**	**September 30, 2022**	**September 30, 2021**
Statements of Operations				
Revenues:				
Net product revenues	$ 232,267	$ 167,044	$ 632,654	$ 463,624
Net revenues from collaborations	29,297	20,136	64,267	121,328
Royalty revenue	2,742	453	5,462	800
Total revenues	264,306	187,633	702,383	585,752
Operating costs and expenses:				
Cost of goods sold	36,507	28,091	94,002	81,370
Cost of collaborations and royalties	4,609	4,572	23,549	21,110
Research and development	245,371	194,572	620,976	563,106
Selling, general and administrative	235,859	142,075	560,314	434,257
Total operating costs and expenses	522,346	369,310	1,298,841	1,099,843
Loss from operations	(258,040)	(181,677)	(596,458)	(514,091)
Other (expense) income:				
Interest expense	(41,084)	(40,274)	(126,055)	(106,205)
Other (expense) income, net	(30,233)	17,715	(120,873)	28,454
Loss on the extinguishment of debt	(76,586)	—	(76,586)	—
Total other expense, net	(147,903)	(22,559)	(323,514)	(77,751)
Loss before income taxes	(405,943)	(204,236)	(919,972)	(591,842)
Provision for income taxes	23	(278)	(3,691)	(2,522)
Net loss	$ (405,920)	$ (204,514)	$ (923,663)	$ (594,364)
Net loss per common share - basic and diluted	$ (3.32)	$ (1.72)	$ (7.62)	$ (5.04)
Weighted-average common shares used to compute basic and diluted net loss per common share	122,166	119,141	121,158	118,005

ALNYLAM PHARMACEUTICALS, INC.
RECONCILIATION OF SELECTED GAAP MEASURES TO NON-GAAP MEASURES
(In thousands, except per share amounts)
(Unaudited)

	Three Months Ended		Nine Months Ended	
	September 30, 2022	September 30, 2021[1]	September 30, 2022	September 30, 2021[1]
Reconciliation of GAAP to Non-GAAP research and development:				
GAAP Research and development	$ 245,371	$ 194,572	$ 620,976	$ 563,106
Less: Stock-based compensation expenses	(52,962)	(12,417)	(75,217)	(49,878)
Non-GAAP Research and development	$ 192,409	$ 182,155	$ 545,759	$ 513,228
Reconciliation of GAAP to Non-GAAP selling, general and administrative:				
GAAP Selling, general and administrative	$ 235,859	$ 142,075	$ 560,314	$ 434,257
Less: Stock-based compensation expenses	(75,156)	(20,950)	(112,665)	(71,257)
Non-GAAP Selling, general and administrative	$ 160,703	$ 121,125	$ 447,649	$ 363,000
Reconciliation of GAAP to Non-GAAP operating loss:				
GAAP Operating loss	$ (258,040)	$ (181,677)	$ (596,458)	$ (514,091)
Add: Stock-based compensation expenses	128,118	33,367	187,882	121,135
Non-GAAP Operating loss	$ (129,922)	$ (148,310)	$ (408,576)	$ (392,956)
Reconciliation of GAAP to Non-GAAP Other (expense) income:				
GAAP Total other expense, net	$ (147,903)	$ (22,559)	$ (323,514)	$ (77,751)
Add (Less): Realized and unrealized loss (gain) on marketable equity securities	7,850	(18,691)	40,108	(61,273)
Add: Loss on the extinguishment of debt	76,586	—	76,586	—
Non-GAAP Other expense, net	$ (63,467)	$ (41,250)	$ (206,820)	$ (139,024)
Reconciliation of GAAP to Non-GAAP net loss:				
GAAP Net loss	$ (405,920)	$ (204,514)	$ (923,663)	$ (594,364)
Add: Stock-based compensation expenses	128,118	33,367	187,882	121,135
Add (Less): Realized and unrealized loss (gain) on marketable equity securities	7,850	(18,691)	40,108	(61,273)
Add: Loss on the extinguishment of debt	76,586	—	76,586	—
Non-GAAP Net loss	$ (193,366)	$ (189,838)	$ (619,087)	$ (534,502)
Reconciliation of GAAP to Non-GAAP net loss per common share-basic and diluted:				
GAAP Net loss per common share - basic and diluted	$ (3.32)	$ (1.72)	$ (7.62)	$ (5.04)
Add: Stock-based compensation expenses	1.05	0.28	1.55	1.03
Add (Less): Realized and unrealized loss (gain) on marketable equity securities	0.06	(0.16)	0.33	(0.52)
Add: Loss on the extinguishment of debt	0.63	—	0.63	—
Non-GAAP Net loss per common share - basic and diluted	$ (1.58)	$ (1.59)	$ (5.11)	$ (4.53)

[1] Beginning in 2022, presentations of non-GAAP financial measures will not include adjustments for upfront payment on license and collaboration agreement. Non-GAAP financial measures for three- and nine-months ended September 30, 2021 have been adjusted to reflect this updated presentation.

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

ALNYLAM PHARMACEUTICALS, INC.
RECONCILIATION OF GAAP TO NON-GAAP
PRODUCT REVENUE GROWTH AT CONSTANT CURRENCY
(Unaudited)

	September 30, 2022	
	Three Months Ended	**Nine Months Ended**
ONPATTRO net product revenue growth, as reported	20%	30%
Add: Impact of foreign currency translation	11	8
ONPATTRO net product revenue growth at constant currency	31%	38%
AMVUTTRA net product revenue growth, as reported	N/A	N/A
Add: Impact of foreign currency translation	N/A	N/A
AMVUTTRA net product revenue growth at constant currency	—%	—%
GIVLAARI net product revenue growth, as reported	43%	45%
Add: Impact of foreign currency translation	7	5
GIVLAARI net product revenue growth at constant currency	50%	50%
OXLUMO net product revenue growth, as reported	10%	14%
Add: Impact of foreign currency translation	10	7
OXLUMO net product revenue growth at constant currency	20%	21%
Total net product revenue growth, as reported	39%	36%
Add: Impact of foreign currency translation	10	8
Total net product revenue growth at constant currency	49%	44%

ALNYLAM PHARMACEUTICALS, INC.
CONDENSED CONSOLIDATED BALANCE SHEETS
(In thousands, except per share amounts)
(Unaudited)

	September 30, 2022	December 31, 2021
ASSETS		
Current assets:		
Cash and cash equivalents	$ 1,073,228	$ 819,975
Marketable debt securities	1,169,050	1,548,617
Marketable equity securities	23,051	66,972
Accounts receivable, net	184,513	198,571
Inventory	115,489	86,363
Prepaid expenses and other current assets	125,516	88,078
Total current assets	2,690,847	2,808,576
Property, plant and equipment, net	514,821	501,958
Operating lease right-of-use assets	218,802	231,675
Restricted investments	49,389	40,891
Other assets	61,396	60,204
Total assets	$ 3,535,255	$ 3,643,304
LIABILITIES AND STOCKHOLDERS' (DEFICIT) EQUITY		
Current liabilities:		
Accounts payable	$ 40,572	$ 73,426
Accrued expenses	510,579	395,174
Operating lease liability	41,581	40,548
Deferred revenue	144,208	149,483
Liability related to the sale of future royalties	35,851	37,079
Total current liabilities	772,791	695,710
Operating lease liability, net of current portion	266,323	281,347
Deferred revenue, net of current portion	132,930	152,360
Convertible debt	1,015,975	—
Long-term debt	—	675,697
Liability related to the sale of future royalties, net of current portion	1,231,873	1,151,024
Other liabilities	183,001	98,963
Total liabilities	3,602,893	3,055,101
Commitments and contingencies (Note 14)		
Stockholders' (deficit) equity:		
Preferred stock, $0.01 par value per share, 5,000 shares authorized and no shares issued and outstanding as of September 30, 2022 and December 31, 2021	—	—
Common stock, $0.01 par value per share, 250,000 shares authorized; 122,991 shares issued and outstanding as of September 30, 2022; 120,182 shares issued and outstanding as of December 31, 2021	1,230	1,202
Additional paid-in capital	6,336,771	6,058,453
Accumulated other comprehensive loss	(43,783)	(33,259)
Accumulated deficit	(6,361,856)	(5,438,193)
Total stockholders' (deficit) equity	(67,638)	588,203
Total liabilities and stockholders' (deficit) equity	$ 3,535,255	$ 3,643,304

This selected financial information should be read in conjunction with the consolidated financial statements and notes thereto included in Alnylam's Annual Report on Form 10-K which includes the audited financial statements for the year ended December 31, 2021.

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