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

Apr 28, 2022

– Achieved First Quarter 2022 Global Net Product Revenues of $187 Million for ONPATTRO®, GIVLAARI®, and OXLUMO® –

– Reported Positive 18-Month Results from HELIOS-A Phase 3 Study of Vutrisiran in hATTR Amyloidosis Patients with Polyneuropathy –

– Announced 3-Month Extension of Review Period for New Drug Application for Vutrisiran due to Amendment to Address Pending Inspection Classification at Third-Party Secondary Packaging and Labeling Facility –

– Decreased 2022 Guidance Range for Combined Net Product Revenues from $900 Million – $1 Billion to $870 – $930 Million –

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Apr. 28, 2022--

Alnylam Pharmaceuticals, Inc. (https://cts.businesswire.com/ct/CT?id=smartlink&url=https%3A%2F%2Fwww.alnylam.com&esheet=52699593&newsitemid=20220428005131&lan=en-US&anchor=Alnylam+Pharmaceuticals%2C+Inc.&index=1&md5=a2e0af777dfefdd3e29bd9537376d303) (Nasdaq: ALNY), the leading RNAi therapeutics company, today reported its consolidated financial results for the first quarter ended March 31, 2022 and reviewed recent business highlights.

“The first quarter of 2022 saw a steady increase in patients on therapy across all products in our commercial portfolio, despite combined product revenues that were down compared to Q4 2021, as anticipated, given several non-recurring revenue benefits in the fourth quarter of 2021, as well as some pandemic-related impact experienced early in the quarter. We continue to make progress with our pipeline programs, including our TTR franchise, for which we reported positive 18-month results from the HELIOS-A study of vutrisiran, and we remain on track for topline results from the APOLLO-B study of patisiran in the middle of this year,” said Yvonne Greenstreet, MBChB, MBA, Chief Executive Officer of Alnylam. “With our earlier stage programs, we’re excited to have initiated our first clinical study of an Alnylam investigational RNAi therapeutic targeting a CNS disorder with the start of our Phase 1 study for ALN-APP in patients with early-onset Alzheimer’s disease, and are announcing today that the Phase 1 study of ALN-XDH in patients with gout also has been initiated. These programs underscore our commitment to advancing innovative new medicines into the clinic, and we anticipate data from both programs later this year. We look forward to continuing our steady execution across our commercial products and advancement of our clinical development pipeline, with many key upcoming milestones to mark our progress toward achieving our *Alnylam P^{5}x25* strategy.”

First Quarter 2022 and Recent Significant Corporate Highlights

Commercial Performance

ONPATTRO® (patisiran)

- Achieved global net product revenues for the first quarter of 2022 of $137 million, representing a 1% decrease compared to Q4 2021.
- Attained over 2,200 hATTR amyloidosis patients with polyneuropathy worldwide on commercial ONPATTRO treatment as of March 31, 2022, up from over 2,050 commercial patients at year end 2021, representing 7% quarterly growth.

GIVLAARI® (givosiran)

- Achieved global net product revenues for the first quarter of 2022 of $35 million, representing a 13% decrease compared to Q4 2021.
- Attained over 400 patients worldwide on commercial GIVLAARI treatment as of March 31, 2022, up from over 350 commercial patients at year end 2021, representing 14% quarterly growth.

OXLUMO® (lumasiran)

- Achieved global net product revenues for the first quarter of 2022 of $15 million, representing a 24% decrease compared to Q4 2021.
- Attained over 160 patients worldwide on commercial OXLUMO treatment as of March 31, 2022, up from over 140 commercial patients at year end 2021, representing 14% quarterly growth.

Leqvio® (inclisiran)

- Launch in the U.S. and in other markets is ongoing, with focus on patient on-boarding, removing access hurdles and driving urgency to treat. *Leqvio* is now approved in more than 55 countries, with most awaiting reimbursement.

R&D Highlights

Vutrisiran, a subcutaneously administered investigational RNAi therapeutic in development for the treatment of ATTR amyloidosis and Stargardt disease

- Reported positive results (https://cts.businesswire.com/ct/CT?id=smartlink&url=https%3A%2F%2Fwww.alnylam.com%2F2022%2F01%2F21%2Fvutri-sfnp-2022%2F&esheet=52699593&newsitemid=20220428005131&lan=en-US&anchor=positive+results&index=2&md5=10eae4a929d329e0da669da0a7fe81bc) for 18-month endpoints and safety from the HELIOS-A Phase 3 study in hATTR amyloidosis patients with polyneuropathy.
  - Vutrisiran met all 18-month secondary endpoints, including statistically significant improvements in neuropathy impairment, quality of life (QoL), gait speed, nutritional status and overall disability, relative to external placebo.
    - Vutrisiran continued to demonstrate halting or reversal of polyneuropathy, with improvements in neuropathy impairment and QoL, relative to baseline.
  - Additionally, vutrisiran continued to demonstrate an encouraging safety and tolerability profile.
  - At month 18, vutrisiran also showed improvements in exploratory cardiac endpoints, including NT-proBNP, a measure of cardiac stress; certain echocardiographic parameters, relative to placebo; and technetium uptake in the heart, providing potential evidence for reduced cardiac amyloid burden.
- Announced that the U.S. Food and Drug Administration (FDA) has extended the review timeline of the New Drug Application (NDA) for vutrisiran to allow for review of newly

added information related to the new secondary packaging and labeling facility.
    - The updated Prescription Drug User Fee Act (PDUFA) goal date to allow for this review is July 14, 2022. No additional clinical data have been requested by the FDA.
    - Vutrisiran is also under review by the European Medicines Agency (EMA), the Brazilian Health Regulatory Agency (ANVISA) and the Japanese Pharmaceuticals and Medical Devices Agency (PMDA).

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

- Announced U.S. FDA acceptance of the Company's supplemental NDA for OXLUMO for the treatment of advanced PH1.
    - The FDA has set a PDUFA goal date of October 6, 2022.
- Additionally, a Type II variation for lumasiran to amend the label to further inform on the use of lumasiran in patients with advanced PH1 was submitted in December 2021 and is undergoing review by the Committee for Medicinal Products for Human Use (CHMP) with a decision expected by year-end.

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

- Initiated a Phase 1 study of **ALN-APP** in patients with early-onset Alzheimer's disease (EOAD).
- The Company announces today that it has initiated a Phase 1 study of **ALN-XDH** in patients with gout.
- The Company announces today that, due in part to impacts related to COVID-19 as well as the ongoing situation in Ukraine, it now expects to complete enrollment in the KARDIA-1 Phase 2 monotherapy study of **zilebesiran** in patients with mild-to-moderate hypertension in early 2023, with topline results now expected in mid-2023.
- Vir Biotechnology reported encouraging results from its Phase 2 trial evaluating **ALN-HBV02 (VIR-2218)**, an investigational RNAi therapeutic in development for the treatment of chronic hepatitis B virus (HBV) infection, in combination with its investigational monoclonal antibody VIR-3434.

Additional Business Updates

- Appointed Akshay Vaishnaw, M.D., Ph.D., formerly President, Research and Development, as President effective January 1, 2022.
- Appointed Indrani Franchini as Chief Legal Officer effective January 31, 2022.
- Entered into a collaboration with Novartis to explore a targeted therapy designed to promote the regrowth of functional liver cells and to provide an alternative to transplantation for patients with liver failure.
- Launched a partnership with Our Future Health, the UK's largest ever health research program that aims to genotype samples from up to 5 million participants.

- Published 2021 Corporate Responsibility Report (https://cts.businesswire.com/ct/CT?id=smartlink&url=https%3A%2F%2Fwww.alnylam.com%2Fsites%2Fdefault%2Ffiles%2Fpdfs%2FAlnylam-Corporate-Responsibility-Summary.pdf&esheet=52699593&newsitemid=20220428005131&lan=en-US&anchor=Corporate+Responsibility+Report&index=3&md5=287579b408aab423a899c45a1038baac).
- Filed separate patent infringement suits against Pfizer, Inc. and Moderna, Inc., seeking damages for infringement of U.S. Patent No. 11,246,933 in the parties' manufacture and sale of their messenger RNA (mRNA) COVID-19 vaccines. The patent relates to Alnylam's biodegradable cationic lipids that are foundational to the success of the mRNA COVID-19 vaccines.

Upcoming Events

In early and mid-2022, Alnylam intends to:

- Launch **vutrisiran** in the U.S., assuming successful review and approval from the FDA, for the treatment of hATTR amyloidosis patients with polyneuropathy.
- Report topline results from the APOLLO-B Phase 3 study of **patisiran** in ATTR amyloidosis patients with cardiomyopathy.
- Report results from the Phase 2 monotherapy study of **cemdisiran** in patients with IgA nephropathy.
- Novartis plans to report results from its ORION-3 Phase 2 study of **inclisiran** in patients with heterozygous familial hypercholesterolemia or pre-existing atherosclerotic cardiovascular disease on background statin +/- ezetimibe therapy.
- Report topline results from Part B of the Phase 1 study of **ALN-HSD** in patients with NASH.

Financial Results for the Quarter Ended March 31, 2022

Financial Highlights
(in thousands, except per share amounts)

	Three Months Ended March 31,	
	2022	2021
ONPATTRO net product revenues	$ 137,009	$ 101,951
GIVLAARI net product revenues	35,277	24,673
OXLUMO net product revenues	14,586	9,145
Total net product revenues	$ 186,872	$ 135,769
Net revenue from collaborations	$ 25,945	$ 41,797

Royalty revenue	$ 442	$ —
GAAP operating loss	$ (146,732)	$ (186,254)
Non-GAAP operating loss	$ (117,439)	$ (130,564)
GAAP other expense	$ (92,624)	$ (13,021)
Non-GAAP other expense	$ (61,463)	$ (60,037)
GAAP net loss	$ (240,341)	$ (200,291)
Non-GAAP net loss	$ (179,887)	$ (191,617)
GAAP net loss per common share - basic and diluted	$ (2.00)	$ (1.71)
Non-GAAP net loss per common share - basic and diluted	$ (1.49)	$ (1.64)

Net Product Revenues

- Net product revenues increased 38% compared to the first quarter of 2021, primarily due to increased patients on ONPATTRO, GIVLAARI, and OXLUMO therapies, offset by an unfavorable impact from foreign exchange rates on our international revenue.

Net Revenues from Collaborations

- Net revenues from collaborations decreased 38% compared to the first quarter of 2021, primarily due to a decrease in revenue from our collaboration with Regeneron.

First Quarter 2022 Expenses

	Three Months Ended March 31,	
	2022	**2021**
GAAP research and development expenses	$ 169,893	$ 185,899
Non-GAAP research and development expenses	$ 158,276	$ 161,524
GAAP selling, general and administrative expenses	$ 154,471	$ 146,859
Non-GAAP selling, general and administrative expenses	$ 136,795	$ 115,544

Research & Development (R&D) Expenses

- GAAP R&D expenses decreased compared to the first quarter of 2021, primarily due to decreased stock-based compensation expense primarily due to the accounting for certain performance-based awards.

Selling, General & Administrative (SG&A) Expenses

- GAAP and Non-GAAP SG&A expenses increased compared to the first quarter of 2021, primarily due to increased legal expenses, charitable contributions, and other expenses to support our strategic growth. On a GAAP basis, these increases were offset by decreased stock-based compensation expense primarily due to the accounting for certain performance-based awards.

Other Financial Highlights

- GAAP other expense increased compared to the first quarter of 2021, primarily due to approximately $80 million of realized and unrealized losses on our marketable equity securities holdings and an increase in interest expenses of approximately $10 million due to additional draws on our term loan facility.
- Cash, cash equivalents and marketable securities were $2.24 billion as of March 31, 2022 compared to $2.44 billion as of December 31, 2021 with the decrease primarily due to our operating loss in the first quarter of 2022.

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 2/10/2022 ($ millions)[1]	**Updated 4/28/2022 ($ millions)[2]**
Combined net product revenues for ONPATTRO, GIVLAARI, OXLUMO and vutrisiran[3]	$900 – $1,000	$870 – $930
Net revenues from collaborations and royalties	$175 – $225	Unchanged
GAAP R&D and SG&A expenses	$1,630 – $1,750	$1,620 – $1,700
Non-GAAP R&D and SG&A expenses[4]	$1,400 – $1,500	$1,390 – $1,450

[1] Prior FY 2022 Guidance utilized January 31, 2022 FX rates of: 1 EUR = 1.12 USD; 1 GBP = 1.34 USD; 1 CHF = 1.08 USD; 1 CAD = 0.79 USD, 1 USD = 115 JPY

[2] Updated FY 2022 Guidance utilizes 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

[3] Assuming FDA approval of vutrisiran by the July 14, 2022 PDUFA goal date

[4] 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 and realized and unrealized (gains) losses on marketable equity securities. 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 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 first quarter 2022 results as well as expectations for the future via conference call on Thursday, April 28, 2022 at 8:30 am ET. To access the call, please dial 877-312-7507 (domestic) or +1-631-813-4828 (international) five minutes prior to the start time and refer to conference ID 2758447. A replay of the call will be available beginning at 11:30 am ET on the day of the call. To access the replay, please dial 855-859-2056 (domestic) or +1-404-537-3406 (international) and refer to conference ID 2758447.

A live audio webcast of the call will be available on the Investors section of the Company's website at www.alnylam.com/events (https://cts.businesswire.com/ct/CT?id=smartlink&url=https%3A%2F%2Finvestors.alnylam.com%2Fevents&esheet=52699593&newsitemid=20220428005131&lan=en-

US&anchor=www.alnylam.com%2Fevents&index=4&md5=671b0fc7cc03bb8c492d763a7d52a4f3). 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 was 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) and should be administered via a healthcare professional. It is designed to target and silence TTR messenger RNA, thereby blocking the production of TTR protein before it is made. ONPATTRO blocks the production of TTR in the liver, reducing its accumulation in the body's tissues in order to halt or slow down the progression of the polyneuropathy associated with the disease. For more information about ONPATTRO, including please see the full U.S. Prescribing Information (https://cts.businesswire.com/ct/CT?id=smartlink&url=https%3A%2F%2Fwww.alnylam.com%2Fwp-content%2Fuploads%2Fpdfs%2FONPATTRO-Prescribing-Information.pdf&esheet=52699593&newsitemid=20220428005131&lan=en-US&anchor=Prescribing+Information&index=5&md5=2bd6882859cc0b085148cfc65ebfc553), visit ONPATTRO.com (https://cts.businesswire.com/ct/CT?id=smartlink&url=http%3A%2F%2Fwww.onpattro.com%2F&esheet=52699593&newsitemid=20220428005131&lan=en-US&anchor=ONPATTRO.com&index=6&md5=4273a7dd5b88a21b82029cce7be6d8c2).

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 (https://cts.businesswire.com/ct/CT?id=smartlink&url=https%3A%2F%2Fwww.alnylam.com%2FGIVLAARI-Prescribing-

Information&esheet=52699593&newsitemid=20220428005131&lan=en-US&anchor=Prescribing+Information&index=7&md5=3b41337c270afb1b85f250d5d7a585d3), visit GIVLAARI.com (https://cts.businesswire.com/ct/CT?id=smartlink&url=http%3A%2F%2Fwww.givlaari.com%2F&esheet=52699593&newsitemid=20220428005131&lan=en-US&anchor=GIVLAARI.com&index=8&md5=c2a44e600b8c2a5ceb9adff3f098fbff).

About OXLUMO® (lumasiran)

OXLUMO is an RNAi therapeutic targeting hydroxyacid oxidase 1 (HAO1) for the treatment of primary hyperoxaluria type 1 (PH1) to lower urinary oxalate levels in pediatric and adult patients. HAO1 encodes glycolate oxidase (GO), an enzyme upstream of the disease-causing defect in PH1. OXLUMO works by degrading HAO1 messenger RNA and reducing the synthesis of GO, which inhibits hepatic production of oxalate – the toxic metabolite responsible for the clinical manifestations of PH1. 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. Injection site reactions (ISRs) were the most common drug-related adverse reaction. In the ILLUMINATE-B pediatric Phase 3 study, OXLUMO demonstrated an efficacy and safety profile consistent to that observed in ILLUMINATE-A. OXLUMO utilizes Alnylam's Enhanced Stabilization Chemistry (ESC)-GalNAc conjugate technology designed to increase potency and durability. OXLUMO is administered via subcutaneous injection once monthly for three months, then once quarterly thereafter 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. (https://cts.businesswire.com/ct/CT?id=smartlink&url=http%3A%2F%2Fwww.alnylam.com%2Foxlumo-us-prescribing-information&esheet=52699593&newsitemid=20220428005131&lan=en-US&anchor=Prescribing+Information.&index=9&md5=b3c316423bc53d151ca796725ef93d13) visit OXLUMO.com (https://cts.businesswire.com/ct/CT?id=smartlink&url=https%3A%2F%2Fwww.oxlumo.com&esheet=52699593&newsitemid=20220428005131&lan=en-US&anchor=OXLUMO.com&index=10&md5=b46a81504309ed789c4bd5d27dc8a82b).

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) and Leqvio® (inclisiran) being developed and commercialized by Alnylam's partner, Novartis. Alnylam has a deep pipeline of investigational medicines, including five product candidates that are in late-stage development. Alnylam is executing on its "*Alnylam P^{5}x25*" 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 (https://cts.businesswire.com/ct/CT?id=smartlink&url=http%3A%2F%2Fwww.alnylam.com&esheet=52699593&newsitemid=20220428005131&lan=en-US&anchor=www.alnylam.com&index=11&md5=abe86343125a66eb55ddb29f9120eef8) and engage with us on Twitter at @Alnylam (https://cts.businesswire.com/ct/CT?id=smartlink&url=https%3A%2F%2Ftwitter.com%2FAlnylam&esheet=52699593&newsitemid=20220428005131&lan=en-US&anchor=%40Alnylam&index=12&md5=f6d0a89993e04760ce3f09ca358dcf2a), on LinkedIn (https://cts.businesswire.com/ct/CT?id=smartlink&url=https%3A%2F%2Fwww.linkedin.com%2Fcompany%2F48171%2F&esheet=52699593&newsitemid=20220428005131&lan=en-US&anchor=LinkedIn&index=13&md5=a271403c46d88216946bdf2ec50404bf), or on Instagram (https://cts.businesswire.com/ct/CT?

id=smartlink&url=https%3A%2F%2Fwww.instagram.com%2Falnylampharma%2F&esheet=52699593&newsitemid=20220428005131&lan=en-US&anchor=Instagram&index=14&md5=e117236c90dfa9024cad7f136e85a37b).

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 P^{5}x25*" strategy, the potential launch of vutrisiran for the treatment of hATTR amyloidosis patients with polyneuropathy, if approved by the FDA, and the ongoing review of vutrisiran by other regulatory authorities, FDA review of a supplemental NDA for OXLUMO and CHMP review of a Type II variation for lumasiran to amend the label, the achievement of additional pipeline milestones and data, including relating to ongoing clinical studies of patisiran, zilebesiran, cemdisiran, ALN-HBV02 (Vir 2218), and ALN-HSD, the initiation of clinical studies for ALN-APP and ALN-XDH, the expected impact of the conflict in Ukraine and the ongoing pandemic on enrollment in the zilebesiran KARDIA-1 Phase 2 study and timing for topline data, the expected range of net product revenues, as updated, and 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, as updated, 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 recent leadership transition on Alnylam's ability to attract and retain talent and to successfully execute on its "*Alnylam P^{5}x25*" 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, including vutrisiran and patisiran; the pre-clinical and clinical results for its product candidates; actions or advice of regulatory agencies and Alnylam's ability to obtain and maintain regulatory approval for its product candidates, including vutrisiran and lumasiran, 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, including vutrisiran; obtaining, maintaining and protecting intellectual property; Alnylam's ability to successfully expand the indication for OXLUMO and ONPATTRO (and vutrisiran, if approved) 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	
	March 31, 2022	March 31, 2021
Statements of Operations		
Revenues:		
Net product revenues	$ 186,872	$ 135,769
Net revenues from collaborations	25,945	41,797
Royalty revenue	442	—
Total revenues	213,259	177,566
Operating costs and expenses:		
Cost of goods sold	23,457	23,023
Cost of collaborations and royalties	12,170	8,039
Research and development	169,893	185,899
Selling, general and administrative	154,471	146,859

Total operating costs and expenses	359,991	363,820
Loss from operations	(146,732)	(186,254)
Other (expense) income:		
Interest expense	(42,362)	(32,515)
Interest income	1,012	450
Other (expense) income, net	(51,274)	19,044
Total other (expense) income, net	(92,624)	(13,021)
Loss before income taxes	(239,356)	(199,275)
Provision for income taxes	(985)	(1,016)
Net loss	$ (240,341)	$ (200,291)
Net loss per common share - basic and diluted	$ (2.00)	$ (1.71)
Weighted-average common shares used to compute basic and diluted net loss per common share	120,393	117,080

ALNYLAM PHARMACEUTICALS, INC.

RECONCILIATION OF SELECTED GAAP MEASURES TO NON-GAAP MEASURES

(In thousands, except per share amounts)

	Three Months Ended March 31, 2022	March 31, 2021
Reconciliation of GAAP to Non-GAAP research and development:		
GAAP Research and development	$ 169,893	$ 185,899
Less: Stock-based compensation expenses	(11,617)	(24,375)
Non-GAAP Research and development	$ 158,276	$ 161,524
Reconciliation of GAAP to Non-GAAP selling, general and administrative:		
GAAP Selling, general and administrative	$ 154,471	$ 146,859
Less: Stock-based compensation expenses	(17,676)	(31,315)
Non-GAAP Selling, general and administrative	$ 136,795	$ 115,544

Reconciliation of GAAP to Non-GAAP operating loss:

GAAP operating loss	$(146,732)	$(186,254)
Add: Stock-based compensation expenses	29,293	55,690
Non-GAAP operating loss	$(117,439)	$(130,564)

Reconciliation of GAAP to Non-GAAP net loss:

GAAP net loss	$(240,341)	$(200,291)
Add: Stock-based compensation expenses	29,293	55,690
Add (Less): Realized and unrealized loss (gain) on marketable equity securities	31,161	(47,016)
Non-GAAP net loss	$(179,887)	$(191,617)

Reconciliation of GAAP to Non-GAAP net loss per common share-basic and diluted:

GAAP net loss per common share - basic and diluted	$(2.00)	$(1.71)
Add: Stock-based compensation expenses	0.24	0.48
Add (Less): Realized and unrealized loss (gain) on marketable equity securities	0.26	(0.40)
Non-GAAP net loss per common share - basic and diluted	$(1.49)	$(1.64)

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

ALNYLAM PHARMACEUTICALS, INC.

CONDENSED CONSOLIDATED BALANCE SHEETS

(In thousands, except share amounts)

(Unaudited)

	March 31, 2022	December 31, 2021
ASSETS		
Current assets:		
Cash and cash equivalents	$534,081	$ 819,975
Marketable debt securities	1,673,485	1,548,617
Marketable equity securities	31,997	66,972
Accounts receivable, net	156,533	198,571

Inventory	78,516	86,363
Prepaid expenses and other current assets	115,065	88,078
Total current assets	2,589,677	2,808,576
Property, plant and equipment, net	504,389	501,958
Operating lease right-of-use assets	228,769	231,675
Restricted investments	40,889	40,891
Other assets	69,821	60,204
Total assets	$3,433,545	$ 3,643,304
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$54,916	$ 73,426
Accrued expenses	355,936	395,174
Operating lease liability	41,290	40,548
Deferred revenue	131,838	149,483
Liability related to the sale of future royalties	21,983	37,079
Total current liabilities	605,963	695,710
Operating lease liability, net of current portion	277,388	281,347
Deferred revenue, net of current portion	157,668	152,360
Long-term debt	676,710	675,697
Liability related to the sale of future royalties, net of current portion	1,193,822	1,151,024
Other liabilities	120,828	98,963
Total liabilities	3,032,379	3,055,101
Commitments and contingencies (Note 13)		
Stockholders' equity:		
Preferred stock, $0.01 par value per share, 5,000 shares authorized and no shares issued and outstanding as of March 31, 2022 and December 31, 2021	—	—
Common stock, $0.01 par value per share, 250,000 shares authorized; 120,729 shares issued and outstanding as of March 31, 2022; 120,182 shares issued and outstanding as of December 31, 2021	1,207	1,202
Additional paid-in capital	6,116,558	6,058,453
Accumulated other comprehensive loss	(38,065)	(33,259)
Accumulated deficit	(5,678,534)	(5,438,193)
Total stockholders' equity	401,166	588,203
Total liabilities and stockholders' equity	$3,433,545	$ 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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