Alnylam Pharmaceuticals Reports Third Quarter 2017 Financial Results and Highlights Recent Period Activity

November 7, 2017

– Reported Positive APOLLO Phase 3 Results for Patisiran, with Plans for First New Drug Application (NDA) Filing by Year-End –

– Advanced Four RNAi Therapeutics in Late-Stage Development, Including Initiation of ENVISION Phase 3 Study for Givosiran in Acute Hepatic Porphyrias –

– Maintained Strong Balance Sheet with $1.15 Billion in Cash and Plans to End 2017 with Greater than $1 Billion in Cash –

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Nov. 7, 2017-- Alnylam Pharmaceuticals, Inc. (Nasdaq: ALNY), the leading RNAi therapeutics company, today reported its consolidated financial results for the third quarter 2017, and highlighted recent progress in advancing its pipeline.

"In our view, 2017 has proven to be a remarkable year for RNAi therapeutics, for Alnylam, and, most importantly, for the patients that we serve. With patisiran, our recent APOLLO Phase 3 study results demonstrate what we believe to be the transformative potential for RNAi therapeutics as a new class of innovative medicines. With these data, we expect to submit our first regulatory filings in the coming months, and are planning for the possibility of having regulatory approval for patisiran in mid-2018," said John Maraganore, Ph.D., Chief Executive Officer of Alnylam. "We have also made significant progress across our other programs, including the initiation of our ENVISION Phase 3 program for givosiran in acute hepatic porphyrias and, with our partners at The Medicines Company, the ORION Phase 3 program in hypercholesterolemia. Additionally, we aim to resume dosing in all fitusiran studies, including the ATLAS Phase 3 program, as soon as possible. These milestones position Alnylam with multiple late-stage clinical assets, while we concurrently transition into a fully integrated commercial company with the goal of delivering innovative medicines to patients around the world."

Third Quarter 2017 and Recent Significant Corporate Highlights

- Advanced patisiran, an investigational RNAi therapeutic in development for the treatment of patients with hereditary ATTR (hATTR) amyloidosis, with positive results from the APOLLO Phase 3 study (N=225).
  - Patisiran met its primary endpoint ($p = 9.26 \times 10^{-24}$) with a 34.0 point mean difference relative to placebo and a negative 6.0 point mean change (improvement) relative to baseline in the modified neuropathy impairment score (mNIS+7) at 18 months, as well as all secondary endpoints (p less than 0.001), including a 21.1 point mean difference relative to placebo and a negative 6.7 point mean change (improvement) relative to baseline in the NORFOLK Quality of Life-Diabetic Neuropathy score (NORFOLK QOL-DN) ($p = 1.10 \times 10^{-10}$), at 18 months.
  - Patisiran also demonstrated a favorable safety and tolerability profile relative to placebo. The most commonly reported adverse events (AEs) for patisiran were generally mild to moderate and included peripheral edema (29.7 percent) and infusion-related reactions (IRRs) (18.9 percent), and the frequency of deaths and serious adverse events (SAEs) was similar in the patisiran and placebo groups. No deaths were considered drug-related.
  - Specifically, the Company believes that these data support a potentially "best-in-class" product profile, with significant benefit relative to placebo, negative mean and median values (improvement) for mNIS+7 and QOL measures relative to baseline, and encouraging safety and tolerability.
  - In addition, patisiran achieved significant effects in the study's cardiac subpopulation, including on disease biomarker, echocardiographic, and functional parameters.
  - The Company believes the totality of the APOLLO data are consistent with a clinically meaningful impact for patisiran on hATTR amyloidosis, and plans to submit an NDA for patisiran by the end of 2017 and a Marketing Authorisation Application (MAA) shortly thereafter.
- Advanced ALN-TTRsc02, a subcutaneously administered investigational RNAi therapeutic in development for the treatment of ATTR amyloidosis.
  - Presented updated Phase 1 data showing up to 95% transthyretin (TTR) knockdown with a single 50 mg dose, with durability supportive of a once quarterly and, possibly, bi-annual subcutaneous dose regimen.
  - Reaffirmed guidance to initiate a Phase 3 program for ALN-TTRsc02 in 2018.
- Advanced givosiran, an investigational RNAi therapeutic in development for the treatment of acute hepatic porphyrias (AHPs), with initiation of the ENVISION Phase 3 study.
  - The Company reached alignment with the U.S. Food and Drug Administration (FDA) on the design of ENVISION, including an interim analysis based on reduction of urinary aminolevulinic acid (ALA), a biomarker that the FDA considers to be reasonably likely to predict clinical benefit.
  - The Company has also reached alignment on the ENVISION Phase 3 study design with the European Medicines Agency (EMA).
  - The Company is guiding that it expects interim analysis results in mid-2018 and, pending FDA review of the program at the time of interim analysis and assuming positive results, it expects to submit an NDA at or around

year-end 2018.

- Advanced fitusiran, an investigational RNAi therapeutic in development for the treatment of hemophilia A and B with or without inhibitors, with new positive datafrom the Phase 2 open-label extension (OLE) study presented at the International Society on Thrombosis and Haemostasis 2017 Congress.
    - Results from the Phase 1 study were published in *The New England Journal of Medicine*in a paper titled, “Targeting of Antithrombin in Hemophilia A or B with RNAi Therapy.”
    - Announced the initiation of the ATLAS Phase 3 program, a global, multicenter clinical program designed to evaluate the safety and efficacy of fitusiran in patients with hemophilia A and B with or without inhibitors.
    - The Company temporarily suspended dosing in all ongoing studies of fitusiran following the observation of a fatal thrombotic SAE that occurred in a patient with hemophilia A without inhibitors who was receiving fitusiran in the Phase 2 OLE study. Alnylam and fitusiran study investigators have aligned on a risk management plan for further advancement of fitusiran and are now conferring with global regulators with the goal of resuming dosing as soon as possible, potentially by the end of 2017.

- Alnylam and The Medicines Company announced initiation of the ORION-11 Phase 3 study of inclisiran, an investigational RNAi therapeutic targeting PCSK9 in development for the treatment of hypercholesterolemia, in patients with atherosclerotic cardiovascular disease (ASCVD).
    - The companies announced new positive datafrom the ORION-1 Phase 2 study of inclisiran at the European Society of Cardiology Congress 2017.
- Advanced cemdisiran (formerly known as ALN-CC5), a subcutaneously administered investigational RNAi therapeutic targeting complement component C5 for the treatment of complement-mediated diseases, with the initiation of a Phase 2 clinical study in patients with atypical hemolytic-uremic syndrome (aHUS).
- Advanced lumasiran (formerly known as ALN-GO1), an investigational RNAi therapeutic in development for the treatment of primary hyperoxaluria type 1 (PH1), with new positive datafrom the Phase 1/2 study presented at the American Society of Nephrology Kidney Week 2017 Annual Meeting.
- Alnylam announced a licensing agreement with Vir Biotechnology for the development and commercialization of RNAi therapeutics for infectious diseases, including hepatitis B.
- Advanced RNAi platform technology with new pre-clinical dataon Alnylam’s next generation “Enhanced Stabilization Chemistry Plus” (ESC+) GalNAc-siRNA conjugate platform presented at the 13th Annual Meeting of the Oligonucleotide Therapeutics Society.

Upcoming Events

- Alnylam announces today that Alnylam scientists and collaborators will present new results from multiple pipeline programs at the 59thAmerican Society of Hematology (ASH) Annual Meeting, being held December 9 – 12, 2017 in Atlanta, Georgia. Presentations include:
    - Explore: A Prospective, Multinational History Study of Patients with Acute Hepatic Porphyrias (AHP) with Recurrent Attacks
      Session: 102. Regulation of Iron Metabolism: Poster II
      Date/Time: Sunday, December 10, 6:00 – 8:00 p.m. ET
    - Perioperative Management in Patients with Hemophilia Receiving Fitusiran, an Investigational RNAi Therapeutic Targeting Antithrombin for the Treatment of Hemophilia
      Session: 322. Disorders of Coagulation or Fibrinolysis: Poster II
      Date/Time: Sunday, December 10, 6:00 – 8:00 p.m. ET
    - In Silico Modeling of the Impact of Antithrombin Lowering on Thrombin Generation in Rare Bleeding Disorders
      Session: 321. Blood Coagulation and Fibrinolytic Factors: Poster III
      Date/Time: Monday, December 11, 6:00 – 8:00 p.m. ET
- Alnylam plans to file its first NDA for patisiran with the FDA by the end of 2017, followed by an MAA in the EU in early 2018.
- Alnylam plans to meet with global regulatory authorities with the goal of reaching agreement on a risk mitigation plan and resumption of dosing in fitusiran clinical studies.

Financial results for the quarter ended September 30, 2017

“Alnylam’s strong balance sheet and overall financial position allow us to build our commercial capabilities in preparation for anticipated product launches in the U.S. and Western Europe during 2018, assuming regulatory approvals in the U.S. and EU,” said Manmeet Soni, Chief Financial Officer of Alnylam. “Additionally, we continue to invest in our broad pipeline of investigational RNAi therapeutics, advancing our four late-stage programs as well as the early-stage pipeline programs.”

Cash and Investments
At September 30, 2017, Alnylam had cash, cash equivalents and fixed income marketable securities, and restricted investments of $1.15 billion, as compared to $1.09 billion at December 31, 2016.

GAAP and Non-GAAP Net Loss
The net loss according to accounting principles generally accepted in the U.S. (GAAP) for the third quarter of 2017 was $122.9 million, or $1.34 per share on both a basic and diluted basis, as compared to a net loss of $104.1 million, or $1.21 per share on both a basic and diluted basis, for the same period in the previous year.

The non-GAAP net loss for the third quarter of 2017 was $97.0 million, or $1.06 per share on both a basic and diluted basis, as compared to a non-GAAP net loss of $88.5 million, or $1.03 per share on both a basic and diluted basis for the same period in the previous year.

The non-GAAP net loss excludes stock-based compensation expense. See “Use of Non-GAAP Financial Measures” below for a description of non-GAAP financial measures and a reconciliation between GAAP and non-GAAP net loss appearing later in this press release.

Revenues
Revenues were $17.1 million in the third quarter of 2017, as compared to $13.7 million in the third quarter of 2016. Revenues for the third quarter of 2017 included $14.6 million from the Company’s alliance with Sanofi Genzyme, $2.3 million from the Company’s alliance with The Medicines Company and $0.2 million from other sources.

GAAP and Non-GAAP Research and Development Expenses
GAAP research and development (R&D) expenses were $95.3 million in the third quarter of 2017 as compared to $97.9 million in the third quarter of 2016.

Non-GAAP R&D expenses were $80.2 million in the third quarter of 2017 as compared to $88.6 million in the third quarter of 2016. Non-GAAP R&D expenses exclude stock-based compensation expense. A reconciliation between GAAP and non-GAAP R&D expenses appears later in this press release.

GAAP and Non-GAAP General and Administrative Expenses
GAAP general and administrative (G&A) expenses were $47.6 million in the third quarter of 2017 as compared to $22.4 million in the third quarter of 2016.

Non-GAAP G&A expenses were $36.8 million in the third quarter of 2017 as compared to $16.2 million in the third quarter of 2016. Non-GAAP G&A expenses exclude stock-based compensation expense. A reconciliation between GAAP and non-GAAP G&A expenses appears later in this press release.

Financial Guidance
Alnylam remains on track to end 2017 with greater than $1.0 billion in cash, cash equivalents and fixed income marketable securities including $150.0 million in restricted investments.

Conference Call Information
Management will provide an update on the Company and discuss third quarter 2017 results as well as expectations for the future via conference call on Tuesday, November 7, 2017 at 4:30 p.m. ET. To access the call, please dial 877-312-7507 (domestic) or 631-813-4828 (international) five minutes prior to the start time and refer to conference ID 2432127. A replay of the call will be available beginning at 7:30 p.m. ET on the day of the call. To access the replay, please dial 855-859-2056 (domestic) or 404-537-3406 (international), and refer to conference ID 2432127.

Alnylam – Sanofi Genzyme Alliance
In January 2014, Alnylam and Sanofi Genzyme, the specialty care global business unit of Sanofi, formed an alliance to accelerate the advancement of RNAi therapeutics as a potential new class of innovative medicines for patients around the world with rare genetic diseases. The alliance enables Sanofi Genzyme to expand its rare disease pipeline with Alnylam’s novel RNAi technology and provides access to Alnylam’s R&D engine, while Alnylam benefits from Sanofi Genzyme’s proven global capabilities to advance late-stage development and, upon commercialization, accelerate market access for these promising genetic medicine products.

In the case of patisiran, Alnylam will advance the product in the United States, Canada and Western Europe, while Sanofi Genzyme will advance the product in the rest of the world. In November 2016, Sanofi Genzyme elected to co-develop (through Sanofi R&D) and co-commercialize fitusiran in the United States, Canada and Western Europe, in addition to commercializing fitusiran in its rest of world territories. Sanofi Genzyme has the right to opt in to develop and commercialize lumasiran in territories outside of the United States, Canada and Western Europe and could elect to exercise its one right to a global license for lumasiran. In the case of ALN-TTRsc02, Sanofi Genzyme has the right to opt into the program with co-development/co-commercialization rights.

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 major new class of medicines, known as RNAi therapeutics, is on the horizon. 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 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 LNP Technology
Alnylam has licenses to Arbutus LNP intellectual property for use in RNAi therapeutic products using LNP technology.

About Alnylam Pharmaceuticals
Alnylam (Nasdaq: ALNY) is leading 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 genetic, cardio-metabolic, and hepatic infectious diseases. Based on Nobel Prize-winning science, RNAi therapeutics represent a powerful, clinically validated approach for the treatment of a wide range of severe and debilitating diseases. Founded in 2002, Alnylam is delivering on a bold vision to turn scientific possibility into reality, with a robust discovery platform and deep pipeline of investigational medicines, including four product candidates that are in late-stage development. Looking forward, Alnylam will continue to execute on its "Alnylam 2020" strategy of building a multi-product, commercial-stage biopharmaceutical company with a sustainable pipeline of RNAi-based medicines to

address the needs of patients who have limited or inadequate treatment options. Alnylam employs over 600 people in the U.S. and Europe and 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 or on LinkedIn.

Use of Non-GAAP Financial Measures
This press release contains non-GAAP financial measures, including expenses adjusted to exclude certain non-cash expenses. 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 item included in GAAP presentations but excluded for purposes of determining non-GAAP financial measures for the periods presented in the press release is stock-based compensation expense. 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 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. 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.

Alnylam Forward Looking Statements
Various statements in this release concerning Alnylam's future expectations, plans and prospects, including without limitation, Alnylam's views with respect to the potential for RNAi therapeutics, including patisiran, fitusiran, givosiran, inclisiran, cemdisiran and lumasiran, its expectations regarding the timing of clinical studies and the presentation of clinical data, including for studies for fitusiran, givosiran, inclisiran, cemdisiran and lumasiran, its expectations regarding the potential of its ESC+ GalNAc-siRNA conjugate platform, its expectations regarding the potential filing of an NDA for patisiran by the end of 2017 and an MAA shortly thereafter, its expected transition to commercial operations in mid-2018 if patisiran is approved, its plans for the development and commercialization of RNAi therapeutics for infectious diseases with Vir Biotechnology, its expected cash, cash equivalents, fixed income marketable securities and restricted investments position as of December 31, 2017, and its "Alnylam 2020" guidance for the advancement and commercialization of RNAi therapeutics, 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, Alnylam's ability to discover and develop novel drug candidates and delivery approaches, successfully demonstrate the efficacy and safety of its product candidates, the pre-clinical and clinical results for its product candidates, which may not be replicated or continue to occur in other subjects or in additional studies or otherwise support further development of product candidates for a specified indication or at all, actions or advice of regulatory agencies, which may affect the design, initiation, timing, continuation and/or progress of clinical trials or result in the need for additional pre-clinical and/or clinical testing, delays, interruptions or failures in the manufacture and supply of our product candidates, obtaining, maintaining and protecting intellectual property, Alnylam's ability to enforce its intellectual property rights against third parties and defend its patent portfolio against challenges from third parties, obtaining and maintaining regulatory approval, pricing and reimbursement for products, progress in establishing a commercial and ex-United States infrastructure, competition from others using technology similar to Alnylam's and others developing products for similar uses, Alnylam's ability to manage its growth and operating expenses, obtain additional funding to support its business activities, and establish and maintain strategic business alliances and new business initiatives, Alnylam's dependence on third parties for development, manufacture and distribution of products, the outcome of litigation, the risk of 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.

The scientific information referenced in this news release relating to Alnylam's investigational therapeutics is preliminary and investigative. None of Alnylam's investigational therapeutics, including inclisiran, which is partnered with The Medicines Company, have been approved by the U.S. Food and Drug Administration, European Medicines Agency, or any other regulatory authority and no conclusions can or should be drawn regarding the safety or effectiveness of these therapeutics.

ALNYLAM PHARMACEUTICALS, INC.
UNAUDITED CONDENSED CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS
(In thousands, except per share amounts)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2017	2016	2017	2016
Net revenues from collaborators	$ 17,096	$ 13,651	$ 51,988	$ 29,705
Operating expenses:				
Research and development	95,252	97,936	272,863	277,381
General and administrative	47,644	22,391	131,910	61,478

Total operating expenses	142,896	120,327	404,773	338,859
Loss from operations	(125,800)	(106,676)	(352,785)	(309,154)
Other income (expense):				
Interest income	3,296	2,204	8,001	6,109
Other (expense) income	(433)	401	(3,863)	5,871
Total other income	2,863	2,605	4,138	11,980
Net loss	$ (122,937)	$ (104,071)	$ (348,647)	$ (297,174)
Net loss per common share - basic and diluted	$ (1.34)	$ (1.21)	$ (3.93)	$ (3.48)
Weighted-average common shares used to compute basic and diluted net loss per common share	91,828	85,716	88,672	85,513
Comprehensive loss:				
Net loss	$ (122,937)	$ (104,071)	$ (348,647)	$ (297,174)
Unrealized gain (loss) on marketable securities, net of tax	218	1,224	(2,194)	(25,331)
Reclassification adjustment for realized loss (gain) on marketable securities included in net loss	—	(706)	1,894	(6,816)
Comprehensive loss	$ (122,719)	$ (103,553)	$ (348,947)	$ (329,321)

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2017	**2016**	**2017**	**2016**
Reconciliation of GAAP to Non-GAAP Research and development:				
GAAP Research and development	$ 95,252	$ 97,936	$ 272,863	$ 277,381
Less: Stock-based compensation expenses	(15,090)	(9,341)	(37,035)	(32,974)
Non-GAAP Research and development	$ 80,162	$ 88,595	$ 235,828	$ 244,407
Reconciliation of GAAP to Non-GAAP General and administrative:				
GAAP General and administrative	$ 47,644	$ 22,391	$ 131,910	$ 61,478
Less: Stock-based compensation expenses	(10,865)	(6,240)	(28,667)	(21,903)
Non-GAAP General and administrative	$ 36,779	$ 16,151	$ 103,243	$ 39,575
Reconciliation of GAAP to Non-GAAP Operating expenses:				
GAAP Operating expenses	$ 142,896	$ 120,327	$ 404,773	$ 338,859
Less: Stock-based compensation expenses	(25,955)	(15,581)	(65,702)	(54,877)
Non-GAAP Operating expenses	$ 116,941	$ 104,746	$ 339,071	$ 283,982
Reconciliation of GAAP to Non-GAAP Net loss:				
GAAP Net loss	$ (122,937)	$ (104,071)	$ (348,647)	$ (297,174)
Add: Stock-based compensation expenses	25,955	15,581	65,702	54,877
Non-GAAP Net loss	$ (96,982)	$ (88,490)	$ (282,945)	$ (242,297)
Reconciliation of GAAP to Non-GAAP Net loss per common share-basic and diluted:				
GAAP Net loss per common share - basic and diluted	$ (1.34)	$ (1.21)	$ (3.93)	$ (3.48)
Add: Stock-based compensation expenses	0.28	0.18	0.74	0.65
Non-GAAP Net loss per common share - basic and diluted	$ (1.06)	$ (1.03)	$ (3.19)	$ (2.83)

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

	September 30, 2017	December 31, 2016
Cash, cash equivalents and fixed income marketable securities	$ 999,837	$ 942,601
Restricted investments	150,000	150,000
Billed and unbilled collaboration receivables	14,644	23,334
Prepaid expenses and other assets	31,901	32,303
Property, plant and equipment, net	161,899	114,572
Total assets	$ 1,358,281	$ 1,262,810
Accounts payable, accrued expenses and other liabilities	$ 63,341	$ 99,650
Total deferred revenue	76,888	82,932
Total deferred rent	9,217	10,007
Long-term debt	150,000	150,000
Total stockholders' equity (92.4 million and 85.9 million common shares issued an outstanding at September 30, 2017 and December 31, 2016, respectively)	1,058,835	920,221
Total liabilities and stockholders' equity	$ 1,358,281	$ 1,262,810

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, 2016.

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