Alnylam Pharmaceuticals Reports First Quarter 2018 Financial Results and Highlights Recent Period Activity

May 3, 2018

– Presented Positive New Clinical Results from APOLLO Phase 3 Study of Patisiran, and Phase 1 and Phase 1/2 Open-Label Extension (OLE) Studies of Givosiran –

– Advanced Two Additional RNAi Therapeutics in Phase 3 Development: Inclisiran in ORION-9, -10, and -11 Studies, and Fitusiran in the ATLAS Program –

– Company Provides Positive New Development Updates on Phase 3 Programs for Givosiran and Lumasiran –

– Maintained Strong Balance Sheet with $1.6 Billion in Cash and Plans to End 2018 with Approximately $1.0 Billion in Cash –

CAMBRIDGE, Mass.--(BUSINESS WIRE)--May 3, 2018-- Alnylam Pharmaceuticals, Inc. (Nasdaq: ALNY), the leading RNAi therapeutics company, today reported its consolidated financial results for the first quarter 2018 and highlighted recent progress in advancing its pipeline.

"We had a very productive first quarter of 2018 and recent period. We're working in close coordination with global regulatory authorities on bringing investigational patisiran to patients around the world. In parallel, we are actively preparing for our U.S. launch of patisiran, following an anticipated mid-2018 FDA approval. With our U.S. field team on-boarded, we believe we are 'launch ready' and prepared to get patisiran to patients as soon as it is approved," said John Maraganore, Ph.D., Chief Executive Officer of Alnylam. "Beyond patisiran, we were very pleased to announce that we've completed enrollment of the first 30 patients in our ENVISION Phase 3 study with givosiran, putting us on track to complete an interim analysis in the September timeframe. We are also excited to announce that we've reached alignment with the U.S. FDA on a pivotal study design on our lumasiran program, significantly accelerating our development efforts for this investigational RNAi therapeutic. In sum, we believe our efforts position the Company to achieve its *Alnylam 2020* goals of building a multi-product, commercial-stage company with a deep clinical-stage pipeline and robust product engine by the end of 2020, a profile rarely achieved in the biotech industry."

First Quarter 2018 and Recent Significant Corporate Highlights

- Advanced patisiran, an investigational RNAi therapeutic for the treatment of patients with hereditary ATTR amyloidosis.
  - Presented new data from the APOLLO Phase 3 study, including:
    - Data at the International Symposium on Amyloidosis (ISA), including results on the effects of patisiran on cardiomyopathy manifestations; and,
    - New data from a post-hoc analysis presented at the American Academy of Neurology (AAN) meeting on the effects of patisiran on the composite rate of all-cause hospitalization and mortality.
  - Received acceptance from the United States Food and Drug Administration (FDA) and the European Medicines Agency (EMA) of patisiran's New Drug Application (NDA) and Marketing Authorisation Application (MAA), respectively.
  - The Company is continuing to fulfill requests from treating physicians for early access or compassionate use of patisiran, and to date, more than 150 eligible patients have begun treatment with patisiran under these programs in the U.S. and EU.

- Advanced ALN-TTRsc02, a subcutaneously administered investigational RNAi therapeutic in development for the treatment of ATTR amyloidosis, with updated data from the Phase 1 study presented at ISA, and receipt of a positive opinion from the EMA Committee for Orphan Medicinal Products (COMP) for Orphan Drug Designation in the European Union for ALN-TTRsc02 for the treatment of ATTR amyloidosis.
- Advanced givosiran, an investigational RNAi therapeutic in development for the treatment of acute hepatic porphyrias (AHPs).
  - Presented new positive Phase 1 and Phase 1/2 open-label extension (OLE) study results at the European Association for the Study of the Liver (EASL) meeting.
  - The Company announces today that it has completed enrollment of the first 30 patients in the ENVISION Phase 3 study, which comprise the interim analysis cohort for a potential accelerated approval by the FDA. This positions the Company to report interim analysis results in the September timeframe and, pending FDA review of the program at the time of interim analysis and assuming positive results, the Company expects to submit an NDA at or around year-end 2018.
  - The Company also announces today that notwithstanding productive conversations with the EMA on a potential accelerated approval pathway for givosiran, the Company has decided to file an MAA on the full dataset from ENVISION, expected in 2019, to optimize market access in Europe.
  - Expanded the Alnylam Act™ program to include no-charge, third-party genetic testing and counseling requested by enrolled physicians for individuals who may carry a gene mutation known to be associated with AHPs. The

Company announces that out of approximately 50 samples submitted to date by physicians with patients with symptoms consistent with AHPs, eight have tested positive for known mutations associated with AHPs.

- Advanced lumasiran, an investigational RNAi therapeutic in development for the treatment of primary hyperoxaluria type 1 (PH1).
  - Retained global rights to the program following the decision by Sanofi Genzyme to decline its opt-in for lumasiran's development and commercialization.
  - As announced earlier today, the Company has reached alignment with the FDA on a pivotal study design for lumasiran with reduction at six months in urinary oxalate as the primary endpoint. In addition, the pivotal study will comprise approximately 25 patients with PH1. Alnylam is now guiding that it expects to initiate the lumasiran Phase 3 trial in mid-2018 with results expected in 2019. If positive, Alnylam expects to file an NDA in early 2020.
  - Lumasiran was recently granted Breakthrough Therapy Designation by the FDA as well as access to the EMA's Priority Medicines (PRIME) scheme.
- With partner Sanofi, advanced fitusiran – an investigational RNAi therapeutic in development for the treatment of hemophilia A and B with or without inhibitors – with the initiation of dosing in the ATLAS Phase 3 program. The Company expects to fully transition development and commercialization leadership of the fitusiran program to Sanofi in mid-2018.
- Alnylam's partner, The Medicines Company, completed enrollment in the ORION-9, -10, and -11 Phase 3 studies of inclisiran in 3,660 patients with atherosclerotic cardiovascular disease (ASCVD) or heterozygous familial hypercholesterolemia (HeFH).
- Announced a strategic restructuring of the Company's rare disease alliance with Sanofi, originally formed in 2014, with Alnylam obtaining global rights to its ATTR amyloidosis programs – patisiran and ALN-TTRsc02 – and Sanofi obtaining global rights to fitusiran.
- Announced plans to collaborate with Regeneron to identify RNAi therapeutics targeting the genetically validated target HSD17B13 for nonalcoholic steatohepatitis (NASH) and potentially other related diseases.
- Joined a research consortium with the UK Biobank, Regeneron, and four major pharmaceutical companies aimed at generating 500,000 human exome sequences linked to medical records by the end of 2019.
- Announced a settlement of all pending litigation between the Company and Dicerna, in which Dicerna agreed to pay $25 million in cash and equity to Alnylam and also agreed to restrictions on its development and other activities relating to oligonucleotide-based therapeutics directed toward certain Alnylam targets, for periods ranging from eighteen months up to four years. The settlement does not include any licenses of Alnylam's GalNAc technology platform patent rights or licenses of any other intellectual property.

Upcoming Events in Mid-2018

- Alnylam expects to gain regulatory approval for patisiran from the FDA in mid-2018. The FDA has set an action date of August 11, 2018, under the Prescription Drug User Fee Act (PDUFA). The Company expects to launch patisiran in the U.S. shortly after FDA approval.
- Alnylam plans to file for regulatory approval for patisiran in Japan and other global markets, including a Japanese NDA filing with the Pharmaceuticals and Medical Device Agency (PMDA) in mid-2018.
- Alnylam intends to report topline interim results from the ENVISION Phase 3 trial for givosiran in the September timeframe.
  - The interim analysis is based on lowering of urinary aminolevulinic acid (ALA) levels at 3 months of treatment as a surrogate marker that is reasonably likely to predict clinical benefit.
  - In addition, a blinded assessment of attack rate results will be conducted at the time of the interim analysis, which the Company expects will likely result in an increase in ENVISION study sample size to approximately 95 patients.
- Alnylam intends to initiate the lumasiran Phase 3 study in mid-2018.
- The Medicines Company has guided its intention to initiate enrollment in the ORION-4 cardiovascular outcomes (CVOT) study in mid-2018.
- Alnylam and Sanofi expect to enroll patients in the ATLAS Phase 3 program of fitusiran in patients with hemophilia A and B with or without inhibitors throughout the year.

Financial results for the quarter ended March 31, 2018

"Alnylam's strong balance sheet with approximately $1.6 billion in cash and investments allows us to execute on preparations for our anticipated product launches for patisiran in 2018 and givosiran in 2019, assuming regulatory approvals," said Manmeet Soni, Chief Financial Officer of Alnylam. "We are pleased to have retained global commercial rights to lumasiran, and remain committed to investing in the advancement of our many promising pipeline programs across all stages of clinical development."

Cash and Investments

At March 31, 2018, Alnylam had cash, cash equivalents and fixed income marketable securities, and restricted investments of $1.60 billion, as compared to $1.73 billion at December 31, 2017.

GAAP and Non-GAAP Net Loss

The net loss according to accounting principles generally accepted in the U.S. (GAAP) for the first quarter of 2018 was $141.2 million, or $1.41 per share on both a basic and diluted basis, as compared to a net loss of $107.3 million, or $1.25 per share on both a basic and diluted basis, for the same

period in the previous year.

The non-GAAP net loss for the first quarter of 2018 was $121.6 million, or $1.22 per share on both a basic and diluted basis, as compared to a non-GAAP net loss of $91.6 million, or $1.06 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 $21.9 million in the first quarter of 2018, as compared to $19.0 million in the first quarter of 2017. Revenues for the first quarter of 2018 included $18.9 million from the Company’s alliance with Sanofi Genzyme, $1.3 million from the Company's alliance with The Medicines Company and $1.7 million from other sources.

GAAP and Non-GAAP Research and Development Expenses
GAAP research and development (R&D) expenses were $96.9 million in the first quarter of 2018 as compared to $87.0 million in the first quarter of 2017.

Non-GAAP R&D expenses were $86.7 million in the first quarter of 2018 as compared to $78.3 million in the first quarter of 2017. 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 $72.4 million in the first quarter of 2018 as compared to $38.5 million in the first quarter of 2017.

Non-GAAP G&A expenses were $63.0 million in the first quarter of 2018 as compared to $31.5 million in the first quarter of 2017. 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.

2018 Updated Financial Guidance
Alnylam remains on track to end 2018 with approximately $1.0 billion of cash, cash equivalents and fixed income marketable securities, restricted cash and restricted investments.

The Company now expects its 2018 annual non-GAAP R&D expenses to be in the range of $420 million to $460 million and non-GAAP selling, general and administrative (SG&A) expenses to remain in the range of $280 million to $320 million. Both non-GAAP R&D and SG&A expenses exclude stock-based compensation expenses.

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.

Conference Call Information
Management will provide an update on the Company and discuss first quarter 2018 results as well as expectations for the future via conference call on Thursday, May 3, 2018 at 4:30 pm 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 3294608. A replay of the call will be available beginning at 7:30 pm 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 3294608.

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 January 2018, Alnylam and Sanofi Genzyme restructured their alliance, providing Alnylam with global rights to develop and commercialize products for the treatment of ATTR amyloidosis, including patisiran and ALN-TTRsc02, and Sanofi Genzyme with global rights to develop and commercialize fitusiran for the treatment of hemophilia and other rare bleeding disorders. Sanofi Genzyme continues to have the right to opt into other Alnylam rare genetic disease programs for development and commercialization in territories outside of the United States, Canada and Western Europe, as well as one right to a global license.

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 Biopharma 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 800 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.

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, givosiran, fitusiran, inclisiran, ALN-TTRsc02 and lumasiran, its expectations regarding the review, potential regulatory approval and commercial launch of patisiran in the United States and Europe, its expectations regarding the timing of clinical studies and the presentation of clinical data, its expectations regarding the timing for the interim analysis in the ENVISION Phase 3 clinical trial of givosiran and the potential timing for an NDA filing for givosiran, if such interim analysis is positive, as well as a likely increase in the ENVISION study sample size to approximately 95 patients, its plans to file an MAA on the full dataset from ENVISION, expected in 2019, to optimize market access in Europe, its expectations regarding the pivotal study design for lumasiran, the initiation of the planned Phase 3 study, the potential timing of Phase 3 study results for lumasiran in 2019 and a possible filing of an NDA in early 2020 if such results are positive, its expected cash, cash equivalents and fixed income marketable securities, restricted cash and restricted investments position as of December 31, 2018, its expected range of 2018 annual non-GAAP R&D expenses and non-GAAP SG&A expenses, expectations regarding the receipt of consideration from Dicerna in connection with the settlement of ongoing litigation, and expectations regarding 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 its 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 Annual Report on Form 10-K 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.

None of Alnylam's investigational therapeutics 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 such investigational therapeutics.

ALNYLAM PHARMACEUTICALS, INC.

UNAUDITED CONDENSED CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS

(In thousands, except per share amounts)

	Three Months Ended March 31,	
	2018	**2017**
Net revenues from collaborators	$ 21,899	$ 18,960
Operating expenses:		
Research and development	96,857	86,984
General and administrative	72,447	38,487

Total operating expenses	169,304	125,471
Loss from operations	(147,405)	(106,511)
Other income (expense):		
Interest income	5,794	2,128
Other income (expense)	335	(2,907)
Total other income (expense)	6,129	(779)
Loss before income taxes	(141,276)	(107,290)
Benefit from income taxes	62	—
Net loss	$ (141,214)	$ (107,290)
Net loss per common share - basic and diluted	$ (1.41)	$ (1.25)
Weighted-average common shares used to compute basic and diluted net loss per common share	99,979	86,027
Comprehensive loss:		
Net loss	$ (141,214)	$ (107,290)
Unrealized loss on marketable securities, net of tax	(420)	(1,936)
Reclassification adjustment for realized loss on marketable securities included in net loss	—	1,549
Comprehensive loss	$ (141,634)	$ (107,677)

ALNYLAM PHARMACEUTICALS, INC.

RECONCILIATION OF SELECTED GAAP MEASURES TO NON-GAAP MEASURES

(In thousands, except per share amounts)

	Three Months Ended March 31,	
	2018	**2017**
Reconciliation of GAAP to Non-GAAP Research and development:		
GAAP Research and development	$ 96,857	$ 86,984
Less: Stock-based compensation expenses	(10,137)	(8,691)
Non-GAAP Research and development	$ 86,720	$ 78,293
Reconciliation of GAAP to Non-GAAP General and administrative:		
GAAP General and administrative	$ 72,447	$ 38,487
Less: Stock-based compensation expenses	(9,447)	(7,026)
Non-GAAP General and administrative	$ 63,000	$ 31,461
Reconciliation of GAAP to Non-GAAP Operating expenses:		
GAAP Operating expenses	$ 169,304	$ 125,471
Less: Stock-based compensation expenses	(19,584)	(15,717)
Non-GAAP Operating expenses	$ 149,720	$ 109,754
Reconciliation of GAAP to Non-GAAP Net loss:		
GAAP Net loss	$ (141,214)	$ (107,290)
Add: Stock-based compensation expenses	19,584	15,717
Non-GAAP Net loss	$ (121,630)	$ (91,573)
Reconciliation of GAAP to Non-GAAP Net loss per common share-basic and diluted:		
GAAP Net loss per common share - basic and diluted	$ (1.41)	$ (1.25)
Add: Stock-based compensation expenses	0.19	0.19
Non-GAAP Net loss per common share - basic and diluted	$ (1.22)	$ (1.06)

ALNYLAM PHARMACEUTICALS, INC.

UNAUDITED CONDENSED CONSOLIDATED BALANCE SHEETS

(In thousands, except share amounts)

	March 31, 2018	December 31, 2017
Cash, cash equivalents and fixed income marketable securities	$ 1,568,512	$ 1,704,537
Restricted investments	30,000	30,000
Billed and unbilled collaboration receivables	50,768	34,002
Prepaid expenses and other assets	71,880	44,291
Property, plant and equipment, net	201,979	181,900
Total assets	$ 1,923,139	$ 1,994,730
Accounts payable, accrued expenses and other liabilities	$ 81,488	$ 104,905
Total deferred revenue	43,531	84,780
Total deferred rent	13,315	8,614
Long-term debt	30,000	30,000
Total stockholders' equity (100.5 million and 99.7 million common shares issued and outstanding at March 31, 2018 and December 31, 2017, respectively)	1,754,805	1,766,431
Total liabilities and stockholders' equity	$ 1,923,139	$ 1,994,730

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, 2017.

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Source: Alnylam Pharmaceuticals, Inc.

Alnylam Pharmaceuticals, Inc.
Christine Regan Lindenboom, 617-682-4340
(Investors and Media)
or
Josh Brodsky, 617-551-8276
(Investors)