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): June 14, 2022 (June 13, 2022)

Alnylam Pharmaceuticals, Inc.

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 8.01. Other Events

On June 13, 2022, Alnylam Pharmaceuticals, Inc. (the "Company") issued a press release announcing that the United States Food and Drug Administration has approved the Company's new drug application for AMVUTTRA™ (vutrisiran) an RNAi therapeutic administered via subcutaneous injection once every three months (quarterly) for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults.

The full text of the press release issued in connection with this announcement is attached as Exhibit 99.1 to this Current Report on Form 8-K and incorporated herein by reference.

Item 9.01. Financial Statements and Exhibits

(d) Exhibits

99.1	Press Release dated June 13, 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.

ALNYLAM PHARMACEUTICALS, INC.

Date: June 14, 2022

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

Exhibit 99.1

Contacts:

Alnylam Pharmaceuticals, Inc.

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Alnylam Announces FDA Approval of AMVUTTRA™ (vutrisiran), an RNAi Therapeutic for the Treatment of the Polyneuropathy of Hereditary Transthyretin-Mediated Amyloidosis in Adults

– First and Only FDA-approved Treatment Demonstrating Reversal in Neuropathy Impairment with Subcutaneous Administration Once Every Three Months –

– AMVUTTRA Met Primary and All Secondary Endpoints, with Significant Improvement in Polyneuropathy, Quality of Life and Gait Speed Relative to External Placebo –

– Company Expects to Launch in Early July, with Value-Based Agreements to Accelerate Access –

– Alnylam to Host Conference Call Tomorrow, Tuesday, June 14, 2022 at 8:00 a.m. ET –

CAMBRIDGE, Mass., – June 13, 2022 – Alnylam Pharmaceuticals, Inc. (Nasdaq: ALNY), the leading RNAi therapeutics company, today announced that the U.S. Food and Drug Administration (FDA) approved AMVUTTRA™ (vutrisiran), an RNAi therapeutic administered via subcutaneous injection once every three months (quarterly) for the treatment of the polyneuropathy of hereditary transthyretin-mediated (hATTR) amyloidosis in adults. hATTR amyloidosis is a rare, inherited, rapidly progressive, and fatal disease with debilitating polyneuropathy manifestations, for which there are few treatment options. The FDA approval is based on positive 9-month results from the HELIOS-A Phase 3 study, where AMVUTTRA significantly improved the signs and symptoms of polyneuropathy, with more than 50 percent of patients experiencing halting or reversal of their disease manifestations.

“Twenty years ago, Alnylam was founded with the bold vision for RNA interference to make a meaningful impact on the lives of people around the world in need of new approaches to address serious diseases with significant unmet medical needs, such as hATTR amyloidosis. Today, AMVUTTRA has the potential to change the standard of care for people living with the polyneuropathy of this devastating disease,” said Yvonne Greenstreet, MBChB, Chief Executive Officer of Alnylam Pharmaceuticals. “We are so thankful to the patients, families and investigators involved in making AMVUTTRA a reality for the hATTR amyloidosis community. As the fifth RNAi therapeutic developed by Alnylam to receive regulatory approval in less than four years, we believe AMVUTTRA represents an important milestone that brings us one step closer to achieving our P^{5}x25 goals aimed at Alnylam’s transition to a leading biotech company.”

The FDA approval of AMVUTTRA is based on positive 9-month results from HELIOS-A, a global, randomized, open-label, multicenter, Phase 3 study that evaluated the efficacy and safety of AMVUTTRA across a diverse group of patients with hATTR amyloidosis with polyneuropathy. 164 patients with hATTR amyloidosis were randomized 3:1 to receive either 25 mg of vutrisiran (N=122) via subcutaneous injection once every three months or 0.3 mg/kg of patisiran (N=42) via intravenous infusion once every three weeks (reference group) for 18 months. The efficacy of AMVUTTRA was assessed by comparing the AMVUTTRA group in HELIOS-A with the placebo group (n=77) from the landmark APOLLO Phase 3 study of patisiran, a randomized controlled study in a comparable patient population.

AMVUTTRA met the primary endpoint of the study, the change from baseline in the modified Neuropathy Impairment Score + 7 (mNIS+7) at 9 months. Treatment with AMVUTTRA (N=114) resulted in a 2.2 point mean decrease (improvement) in mNIS+7 from baseline as compared to a 14.8 point mean increase (worsening) reported for the external placebo group (N=67), resulting in a 17.0 point mean difference relative to placebo ($p<0.0001$); by 9 months, 50 percent of patients treated with AMVUTTRA experienced improvement in neuropathy impairment relative to baseline.

AMVUTTRA also met all secondary endpoints in the study at 9 months, with significant improvement in the Norfolk Quality of Life Questionnaire-Diabetic Neuropathy (Norfolk QoL-DN) score and timed 10-meter walk test (10-MWT), and improvements were observed in exploratory endpoints, including change from baseline in modified body mass index (mBMI), all relative to external placebo. Efficacy results at 18 months were consistent with 9-month data, with AMVUTTRA achieving statistically significant improvements compared to external placebo for all secondary endpoints including mNIS+7, Norfolk QoL-DN, 10-MWT and mBMI, and non-inferiority in serum TTR reduction relative to the within-study patisiran reference group.

AMVUTTRA demonstrated an encouraging safety and tolerability profile with 9 months of dosing and there were no drug-related discontinuations or deaths. The most commonly reported adverse events (AEs) in AMVUTTRA-treated patients included arthralgia (11 percent), dyspnea (7 percent) and vitamin A decreased (7 percent). Injection site reactions (ISRs) were reported in 5 patients (4 percent) and were all mild and transient.

“The FDA approval of AMVUTTRA is very encouraging for the hATTR amyloidosis community, who need additional therapies to address the polyneuropathy of this progressive, life-threatening, multisystem disease,” said Michael Polydefkis, M.D., MHS, Professor, Johns Hopkins Neurology and HELIOS-A Study Investigator. “AMVUTTRA is a new therapeutic option that has demonstrated the potential to halt or reverse polyneuropathy progression in patients with an acceptable safety profile, along with an infrequent, subcutaneous dosing regimen that may also help to improve the disease management experience for patients.”

“Today we celebrate the FDA’s approval of vutrisiran, a welcomed treatment option for hATTR amyloidosis patients experiencing the challenges of the polyneuropathy of the disease,” said Isabelle Lousada, Founder and CEO, Amyloidosis Research Consortium. “With this approval, Alnylam has expanded treatment options that may support improvements in quality of life, providing hope for patients and families in the amyloidosis community.”

Alnylam has a strong and proven track record to ensure those who may benefit from RNAi therapeutics will have access to them, as outlined in the Company’s latest Patient Access Philosophy report. Consistent with our Patient Access Philosophy, AMVUTTRA is priced in line with the value delivered. Our existing innovative value-based agreement (VBA) framework is anticipated to help accelerate access to this important therapy for patients. AMVUTTRA is expected to be available for shipment to healthcare providers in the U.S. in early July.

Alnylam offers a patient support services program, Alnylam Assist™, for people in the U.S. prescribed AMVUTTRA and their families to receive help accessing this new therapy. Alnylam Assist includes Case Managers, a team dedicated to helping assist patients with verification of insurance benefits and financial assistance for those who qualify. Patient Education Liaisons are also available to answer patients’ questions about their disease and treatment. Physicians and patients can learn more about Alnylam’s patient support services program by visiting AlnylamAssist.com or calling 1-833-256-2748.

Vutrisiran is under review by the European Medicines Agency (EMA), the Brazilian Health Regulatory Agency (ANVISA) and the Japanese Pharmaceuticals and Medical Devices Agency (PMDA). Vutrisiran was previously granted Orphan Drug Designation in the U.S. and the European Union (EU) for the treatment of ATTR amyloidosis and in Japan for transthyretin type familial amyloidosis with polyneuropathy. A biannual 50mg dosing regimen is under evaluation within the ongoing randomized treatment extension (RTE) period in the HELIOS-A trial. Vutrisiran is also being evaluated in the HELIOS-B Phase 3 study for the treatment of patients with ATTR amyloidosis with cardiomyopathy, including both hATTR and wild-type ATTR (wtATTR) amyloidosis.

Visit AMVUTTRA.com for more information, including full Prescribing Information.

Conference Call Information

Alnylam Management will discuss the FDA approval of AMVUTTRA via conference call on Tuesday, June 14, 2022, at 8:00 am ET. A webcast presentation will also be available on the Investors page of the Company’s website, www.alnylam.com. To access the call, please dial 1-877-312-7507 (domestic) or +1-631-813-4828 (international) five minutes prior to the start time and refer to conference ID 1084157. A replay of the call will be available beginning at 11:00 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 1084157.

IMPORTANT SAFETY INFORMATION

Reduced Serum Vitamin A Levels and Recommended Supplementation

AMVUTTRA treatment leads to a decrease in serum vitamin A levels.

Supplementation at the recommended daily allowance (RDA) of vitamin A is advised for patients taking AMVUTTRA. Higher doses than the RDA should not be given to try to achieve normal serum vitamin A levels during treatment with AMVUTTRA, as serum vitamin A levels do not reflect the total vitamin A in the body.

Patients should be referred to an ophthalmologist if they develop ocular symptoms suggestive of vitamin A deficiency (e.g., night blindness).

Adverse Reactions

The most common adverse reactions that occurred in patients treated with AMVUTTRA were arthralgia (11%), dyspnea (7%), and vitamin A decreased (7%).

For additional information about AMVUTTRA, please see the full Prescribing Information.

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, visit AMVUTTRA.com.

About hATTR Amyloidosis

Hereditary transthyretin-mediated (hATTR) amyloidosis is an inherited, progressively debilitating, and fatal disease caused by variants (i.e., mutations) in the TTR gene. TTR protein is primarily produced in the liver and is normally a carrier of vitamin A. Variants in the TTR gene cause abnormal amyloid proteins to accumulate and damage body organs and tissue, such as the peripheral nerves and heart, resulting in intractable peripheral sensory-motor neuropathy, autonomic neuropathy, and/or cardiomyopathy, as well as other disease manifestations. hATTR amyloidosis, represents a major unmet medical need with significant morbidity and mortality affecting approximately 50,000 people worldwide. The median survival is 4.7 years following diagnosis, with a reduced survival (3.4 years) for patients presenting with cardiomyopathy.

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 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 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 five product candidates that are in late-stage development. Alnylam is executing on its "Alnylam P5x25" 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, 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 future expectations, plans and prospects, including, without limitation, Alnylam's views with respect to the safety and efficacy of AMVUTTRA, a quarterly subcutaneous injection, for the treatment of the polyneuropathy of hATTR amyloidosis in adults, the potential of AMVUTTRA to change the standard of care for people living with the polyneuropathy of hATTR amyloidosis, with demonstrated potential to halt or reverse polyneuropathy progression with an acceptable safety profile and help to improve the disease management experience for patients, the expected timing of the U.S. launch of AMVUTTRA, continued regulatory review of AMVUTTRA in multiple jurisdictions, the continued evaluation of a biannual 50mg dosing regimen in the HELIOS-A trial, the evaluation of vutrisiran in the HELIOS-B Phase 3 study for the treatment of patients with ATTR amyloidosis with cardiomyopathy, and Alnylam's aspiration to become a leading biotech company and the planned achievement of its "Alnylam P5x25" strategy, 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 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; actions or advice of regulatory agencies and Alnylam's ability to obtain and maintain regulatory approval for its product candidates, including vutrisiran, as well as favorable pricing and reimbursement; successfully launching, marketing and selling 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 OXLUMO, ONPATTRO or AMVUTTRA in the future; Alnylam's ability to manage its growth and operating expenses through disciplined investment in operations and its ability to achieve a self-sustainable financial profile in the future without the need for future equity financing; Alnylam's ability to maintain strategic business collaborations; Alnylam's dependence on third parties for the development and commercialization of certain products, including Novartis, Sanofi, Regeneron and Vir; the outcome of litigation; the potential impact of current 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.

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