Alnylam Pharma (ALNY)

$115.97 (As of 01/06/20)

Price Target (6-12 Months): **$122.00**

Long Term: 6-12 Months	**Zacks Recommendation:** (Since: 08/02/19) Prior Recommendation: Outperform	**Neutral**
Short Term: 1-3 Months	**Zacks Rank:** (1-5)	**3-Hold**
	Zacks Style Scores:	VGM:F
	Value: F | Growth: F | Momentum: C	

Summary

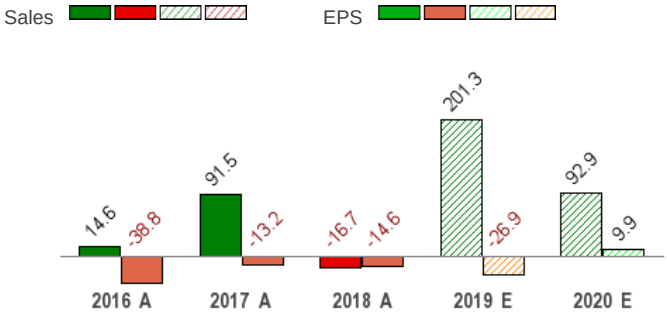
Alnylam's new drug Onpattro is witnessing strong uptake since its launch. In November, the FDA approved its Givlaree (givosiran) for acute hepatic porphyria (AHP), its second FDA approval in less than two years. Meanwhile, the company also expects to submit an NDA for inclisiran in 2019. Alnylam expects to bring three products to the market by 2020, including the already-approved drugs — Givlaree and Onpattro. It has a landmark ocular and CNS disease alliance with Regeneron. The company also aims to expand the label of Onpattro into cardiomyopathy. A potential label expansion should boost sales. Although we are pleased with Alnylam's broad and promising pipeline, heavy dependence on the drug for growth is a concern. Moreover, the company heavily relies on partnerships for supporting operations. Shares have outperformed the industry

Price, Consensus & Surprise

Data Overview

52 Week High-Low	**$125.72 - $65.81**
20 Day Average Volume (sh)	**547,040**
Market Cap	**$12.9 B**
YTD Price Change	**0.7%**
Beta	**2.44**
Dividend / Div Yld	**$0.00 / 0.0%**
Industry	**Medical - Biomedical and Genetics**
Zacks Industry Rank	**Top 19% (49 out of 254)**
Last EPS Surprise	**11.5%**
Last Sales Surprise	**14.2%**
EPS F1 Est- 4 week change	**-1.1%**
Expected Report Date	**02/06/2020**
Earnings ESP	**-8.2%**
P/E TTM	**NA**
P/E F1	**NA**
PEG F1	**NA**
P/S TTM	**76.5**

Sales and EPS Growth Rates (Y/Y %)



Sales Estimates (millions of $)

	Q1	Q2	Q3	Q4	Annual*
2020	85 E	99 E	111 E	141 E	436 E
2019	33 A	45 A	70 A	71 E	226 E
2018	22 A	30 A	2 A	21 A	75 A

EPS Estimates

	Q1	Q2	Q3	Q4	Annual*
2020	-$1.87 E	-$1.85 E	-$1.82 E	-$1.70 E	-$7.10 E
2019	-$1.42 A	-$1.83 A	-$1.92 A	-$2.22 E	-$7.88 E
2018	-$1.22 A	-$1.61 A	-$1.56 A	-$1.82 A	-$6.21 A

*Quarterly figures may not add up to annual.

The data in the charts and tables, including the Zacks Consensus EPS and Sales estimates, is as of 01/06/2020. The reports text is as of 01/07/2020.

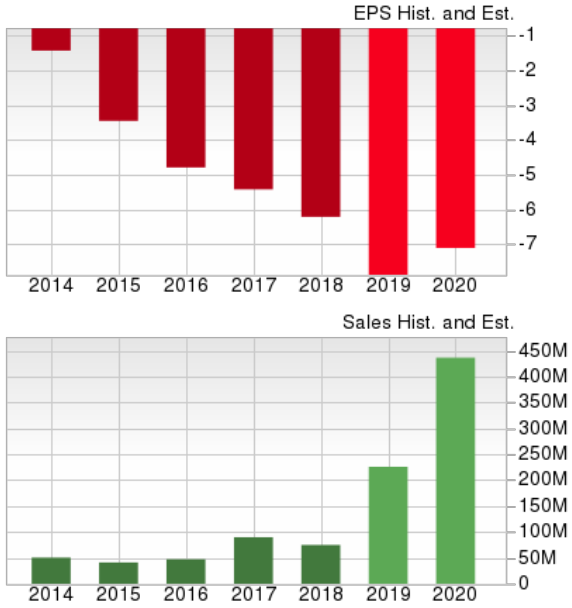
Overview

Cambridge, MA-based Alnylam Pharmaceuticals Inc. is a development-stage biopharmaceutical company focused on the development of novel therapeutics based on RNA interference (RNAi). The company's pipeline of experimental RNAi therapeutics is focused across three strategic therapeutic areas (STArs) – genetic medicines, cardio-metabolic disease and hepatic infectious disease.

In August 2018, the company's lead drug-Onpattro (patisiran) received regulatory approvals in the United States and Europe for the treatment of hereditary transthyretin-mediated (hATTR) amyloidosis in adults. Onpattro is the first and only FDA-approved treatment for this indication. In November 2019, the FDA approved Givlaree (givosiran) for acute hepatic porphyria(AHP). Alnylam expects to submit an NDA for inclisiran for the treatment of hypercholesterolemiain 2019.

Alnylam's expertise in RNAi therapeutics and broad intellectual property estate has allowed the company to enter into collaborations with leading pharmaceutical and life sciences companies including Ionis Pharmaceuticals, Novartis, Roche, Takeda, Merck, Monsanto, The Medicines Company and Sanofi's specialty care global business unit, Genzyme among others.

Alnylam generates revenues from research collaborations, grants, and licensing of the RNAi technology outside its core focus area. In 2018, Alnylam recorded sales of $74.9 million, down 16.7% year over year



Reasons To Buy:

- **Onpattro (patisiran) Receives Approval in the United States and Europe:** In August 2018, the FDA approved Onpattro (patisiran) lipid complex injection- a first-of-its-kind RNA interference (RNAi) therapeutic, for the treatment of the polyneuropathy of hereditary transthyretin-mediated (hATTR) amyloidosis in adults. Onpattro is the first and only FDA-approved treatment for this indication. The uptake of the drug have been strong with more than 600 patients worldwide on commercial Onpattro treatment since its launch as of Sep 30, 2019. The drug should drive revenues for the company as it will be an important treatment option for people suffering from this often fatal disease.

> Alnylam expects to bring three products to the market by 2020, including the already approved approved drugs — Givlaree and Onpattro. It expects to submit an NDA for inclisiran in 2019.

Pending regulatory approvals, Alnylam will commercialize Onpattro in Western Europe, with Sanofi Genzyme commercializing the product in the rest of the world.

Alnylam is also planning to expand the label of Onpattro. In this regard, the company initiated APOLLO-B, a placebo-controlled phase III study of Onpattro in hereditary and wild-type ATTR amyloidosis patients with cardiomyopathy, in September 2019. In October 2019, the company filed a marketing authorization application in Brazil seeking approval for Onpattro for treating hATTR patients. The application has been granted priority review and a decision from the regulatory authorities in Brazil is expected in the mid 2020. Label expansion of the drug should further boost sales for the company.

- **Givosiran Approval Comes Earlier Than Expected, Inclisiran to be Filed Soon**: In November, the FDA approved givosiran injection for subcutaneous use for the treatment of adults with acute hepatic porphyria (AHP). The approval came three months before the PDUFA date of Feb 20, 2020. Gvosiran injection will be marketed by the trade name of Givlaari. This is the second RNAi therapeutic from Alnylam approved by the FDA in the last sixteen months. Givlaari is expected to be available in the United States by the end of 2019. The drug's approval was based on positive results from the phase III ENVISION study, which showed that AHP patients treated with the same experienced 70% lesser porphyria attacks compared to placebo. This approval should further boost sales for the company.

The company plans to achieve regulatory approval from the European Medicines Agency (EMA) for Givlaari (givosiran), in early 2020 for the treatment of acute hepatic porphyria (AHP). It also plans to execute on U.S. and EU commercial launches throughout 2020.

Moreover, the company is evaluating inclisiran phase III ORION studies for hypercholesterolemia in partnership with The Medicines Company . The companies reported positive initial top-line results from the ORION-9, 10 and 11 phase III studies of inclisiran and expects to file an NDA in the end of 2019.

- **RNAi Technology Holds Promise:** Alnylam makes use of a potentially radical RNAi technology. This technology is a naturally occurring biological pathway within cells for selectively silencing and regulating the expression of specific genes. Since many diseases are caused by the inappropriate activity of specific genes, the ability to make the genes silent selectively through RNAi hold the potential to change the way diseases are treated.

Alnylam's pipeline of experimental RNAi therapeutics is focused across three STArs: genetic medicines – for the treatment of rare diseases; cardio-metabolic disease – cardiovascular and metabolic diseases such as dyslipidemia, non-alcoholic steatohepatitis, type II diabetes, hypertension and other major diseases; as well as hepatic infectious disease – hepatic infectious diseases, beginning with hepatitis B and hepatitis D viral infections.

- **Broad & Promising Pipeline:** The company is also evaluating several other candidates. Interesting ones include ALN-CC5 (phase I/II; complement-mediated diseases), cemdisiran (phase II, complement-mediated diseases) and lumasiran (formerly known as ALN-GO1, Phase I/II , Primary Hyperoxaluria Type 1 (PH1), vutrisiran (ALN-TTRsc02) a once-quarterly, subcutaneously administered investigational RNAi therapeutic in development for the treatment of ATTR amyloidosis.

Vutrisiran (ALN-AAT02) is the first investigational RNA interference (RNAi) therapeutic targeting AAT with Alnylam's enhanced stabilization chemistry plus (ESC+) GalNAc-conjugate technology. During the third quarter of 2019, Alnylam continued enrollment in the HELIOS-A phase III study on vutrisiran (ALN-TTRsc02) for the treatment of hATTR amyloidosis with polyneuropathy. It expects to complete enrollment in the HELIOS-A phase III study in early 2020.

The company also obtained regulatory alignment from the FDA on the design of another phase III study, HELIOS-B, for the candidate to treat hereditary and wild-type ATTR amyloidosis cardiomyopathy, and expects to start the study in shortly. In November 2019, Alnylam initiated the HELIOS-B phase III study of vutrisiran. The company plans to continue enrollment in the HELIOS-B study throughout 2020.

In June 2018, the company received orphan drug designation for ALN-TTRsc02 by the FDA.

In August 2019, Alnylam and Ironwood Pharmaceuticals, Inc., a GI healthcare company, announced a U.S. GI disease education and promotional agreement for givosiran. Per the agreement, Ironwood will provide AHP disease education to gastroenterologists and other healthcare practitioners that Ironwood currently calls on for LINZESS (linaclotide). If approved by the U.S. FDA, Ironwood clinical sales specialists will then begin givosiran promotional efforts, augmenting Alnylam's broader commercialization activities. The company also completed submission of a Marketing Authorization Application (MAA) under an Accelerated Assessment to the European Medicines Agency (EMA) for givosiran.

Givosiran received Priority Review designation and Breakthrough Therapy Designation from the FDA, as well as Orphan Drug Designation in the United States and PRIME designation by the EMA. In May 2017, Alnylam announced that it has received Breakthrough Therapy designation from the FDA for givosiran for the prophylaxis of attacks in patients with AHP.

Alnylam advanced lumasiran, an investigational RNAi therapeutic in development for the treatment of primary hyperoxaluria type I (PH1). Alnylam continues enrollment in theILLUMINATE-A, a global phase III pivotal study of lumasiran in children and adult PH1 patients with

preserved renal function. The company reported positive top-line results from ILLUMINATE-A in December 2019 and it met its primary efficacy endpoint and all tested secondary endpoints. Based on these results, the company expects to file a new drug application (NDA) and a marketing authorisation application (MAA) with the FDA and EMA, respectively, in early 2020. In April 2019, the company initiated ILLUMINATE-B, a phase III pediatric study of lumasiran in PH1 patients under six years of age. It expects to report topline results from the ILLUMINATE-B pediatric phase III study in mid-2020. It plans to achieve FDA and EMA regulatory approvals in late 2020.

Lumasiran has been granted Breakthrough Therapy designation (BTD) by the FDA, representing the third BTD received by the company to date. It initiated the ILLUMINATE-C phase III study of the drug in PH1 patients with severe renal impairment in October 2019. In March 2018, the European Medicines Agency (EMA) granted access to its Priority Medicines (PRIME) scheme for lumasiran.

Moreover, the company is evaluating inclisiran (formerly known as PCSK9si or ALN-PCSsc) in phase III ORION studies for hypercholesterolemia. The company's partner The Medicines Company reported positive results for inclisiran, an investigational RNAi therapeutic, in developing the treatment of hypercholesterolemia. The company reported initial top-line results from the ORION-9, 10 and 11 phase III studies of inclisiran and expects to file an NDA in the end of 2019. It expects to file for regulatory approval with the EMA in early 2020.

A phase II study of cemdisiran, an investigational RNAi therapeutic targeting complement C5 for the treatment of complement-mediated diseases in IgA nephropathy is ongoing.

ALN-HBV02 (also known as VIR-2218), partnered with Vir and in development for the treatment of chronic hepatitis B virus (HBV) infection, which is currently in a Phase I/II study.

ALN-AGT, an investigational RNAi therapeutic targeting angiotensinogen (AGT) for the treatment of hypertension in high unmet need populations, including patients with resistant or refractory hypertension, chronic kidney disease or heart failure is currently in a phase I study.

Alnylam submitted a Clinical Trial Authorization (CTA) application for ALN-AAT02, an investigational RNAi therapeutic for the treatment of alpha-1 antitrypsin deficiency-associated liver disease (alpha-1 liver disease). Itis currently in a phase I/II study.

Alnylam selected its first CNS-targeted development candidate, ALN-APP, an investigational RNAi therapeutic targeting amyloid precursor protein (APP) for the treatment of cerebral amyloid angiopathy (CAA).

Successful development and subsequent approval of these candidates will be a huge boost for the company**.**

- **Encouraging Collaborations:** Alnylam has entered into several collaborations for the development and commercialization of its broad pipeline of RNAi therapeutic candidates across three STArs. Particularly, with respect to Alnylam's genetic medicine pipeline, the company formed a broad strategic alliance with Sanofi's Genzyme in 2014, following which Sanofi became a major Alnylam shareholder with an investment of $700 million. In January 2018, Alnylam and Sanofi announced a strategic restructuring of their RNAi therapeutics rare genetic diseases alliance. The companies entered into the agreement to optimize the development and commercialization of certain products for the treatment of rare genetic diseases. Per the agreement, Alnylam will fund all the development and commercialization costs for — Onpattro and its investigational RNAi therapeutics candidate ALN-TTRsc02 — that are being evaluated for the treatment of ATTR amyloidosis..

  In April 2018, Alnylam and Sanofi agreed to close the research and option phase of the companies' 2014 RNAi therapeutics alliance in rare genetic diseases. The material collaboration terms for Onpattro, vutrisiran and fitusiran will remain unchanged. Per the agreement, Alnylam will advance a selected investigational asset in an undisclosed rare genetic disease through the end of the IND-enabling studies. Sanofi will be responsible for any potential further development or commercialization of the asset. If this product is approved, Alnylam will be eligible to receive tiered double-digit royalties on its global net sales.

  Following the restructuring initiative, Sanofi will undertake full responsibility for the development and commercialization of fitusiran, including costs. Sanofi will retain the right to opt for other Alnylam rare genetic disease programs for development and commercialization in territories outside the United States, Canada, and Western Europe as well as right to a global license. Sanofi continues enrollment in the fitusiran phase III ATLAS program in patients with hemophilia A or B with and without inhibitors.

  In April 2019, Alnylam and Regeneron Pharmaceuticals extended their collaboration agreement. Both the companies will work together to discover, develop and commercialize new RNAitherapeutics for a broad range of diseases by addressing disease targets expressed in the eye and central nervous system (CNS), in addition to a select number of targets expressed in the liver. The companies plan to advance programs directed to 30 targets. Other candidates also might be introduced into clinical development during the initial five-year discovery period, which may extend.

Reasons To Sell:

Alnylam relies highly on collaborators for funding. Any development/regulatory setback would be a negative for the company. Stiff competition remains a threat as well.

- **Pipeline Setbacks:** Although we are pleased with Alnylam's broad and promising pipeline, we note that most candidates are in their early or mid stages of development. These candidates still have a long way to go before hitting the market. Currently, Alnylam depends heavily on Onpattro for growth. We also note that gaining approval for pipeline candidates has become more difficult now. With several data read-outs expected over the next few quarters, an unfavorable outcome will be a huge setback for the company and hamper its prospects.

  We note that Alnylam is no stranger to pipeline setbacks. In Sep 2012, the company suffered a pipeline setback for its candidate ALN-RSV01 (respiratory syncytial virus). Moreover, in Oct 2016, Alnylam discontinued the phase III ENDEAVOUR study on revusiran for the treatment of hereditary ATTR amyloidosis with cardiomyopathy (hATTR-CM). The decision followed the recommendation of a Data Monitoring Committee which suggested that the benefit-risk profile of the candidate did not support continued dosing in patients.

  During the third quarter of 2018, the company announced that due to recruitment challenges, it has discontinued a phase II study of cemdisiran in atypical hemolytic uremic syndrome (aHUS). Alnylam will now focus its cemdisiran clinical efforts on a phase II study in IgA nephropathy.

- **High Reliance on Partnerships & High Competition:** With only one approved product in its portfolio, Alnylam derives a substantial amount of revenues from strategic partnerships with companies like Sanofi, Takeda, Monsanto and The Medicines Co. Therefore, Alnylam is heavily dependent on its partnerships for supporting operations and pipeline development activities. The company expects to continue deriving revenues from the existing and new strategic alliances, which may include license and other fees, funded R&D and milestone payments over the next several years. If any of the company's partners fails to fund a program or terminate collaboration agreement, Alnylam's prospects would be hampered.

  Moreover, Alnylam is not the only company working on the development of RNAi-based therapeutics. Companies like Ionis, Sarepta Therapeutics and Roche Innovation Center are involved in the development of RNA-based drugs. Some of the companies including Takeda, Wave Life Sciences and Dicerna Pharmaceuticals are even looking to develop chemically synthesized siRNAs as drugs. While Alnylam's candidates that are currently under development target lucrative markets, they will face intense competition too, if approved. The hemophilia and bleeding disorders market has several players like Bayer, Pfizer, Biogen, CSL Behring and Shire. Meanwhile, the market for complement-mediated diseases has players like Alexion Pharmaceuticals and Achillion Pharmaceuticals. The cholesterol management market represents huge commercial potential and with companies like Aegerion Pharmaceuticals and Ionis operating in it. Competition in this space intensified with the introduction of PCSK9 inhibitors – Amgen's Repatha and Regeneron/Sanofi's Praluent. Also, Ionis is developing IONIS-TTRRx, to treat all forms of ATTR amyloidosis, FAP, FAC, and wild-type TTR amyloidosis.

Last Earnings Report

Alnylam's Q3 Earnings and Revenues Beat Estimates

Quarter Ending	09/2019
Report Date	**Oct 31, 2019**
Sales Surprise	**14.15%**
EPS Surprise	**11.52%**
Quarterly EPS	**-1.92**
Annual EPS (TTM)	**-6.99**

Alnylam incurred loss of $1.92 per share in the third quarter of 2019, narrower than the year-ago quarter's loss of $2.43 and the Zacks Consensus Estimate of a loss of $2.17. Adjusted loss, which excluded stock-based compensation expenses, was $1.50 per share compared with adjusted loss of $1.56 per share in the year-ago quarter.

The company recorded revenues of $70.1 million, which beat the Zacks Consensus Estimate of $61.38 million. In the year-ago quarter, revenues were $2.1 million. The top line in the quarter included net product revenues of $46.1 million from sales of Onpattro (patisiran), which was approved by the FDA in August 2018. Net revenues from collaborators were $24 million, including $15.3 million from the recently inked collaboration with Regeneron Pharmaceuticals, Inc. compared with $1.6 million in the year-ago quarter.

Quarter in Detail

Alnylam received marketing authorization approvals for Onpattro in Switzerland and launched the drug in Japan and Canada. These approvals, launches and multiple reimbursement approvals enabling commercial sales in more than several countries across the Canada, Europe, Middle East and Africa (CEMEA) region expanded the company's global footprint.

Adjusted research and development (R&D) expenses increased 46.6% from the year-ago period to $138.1 million. Adjusted selling, general and administrative (SG&A) expenses rose 30.5% from the year-ago quarter to $97.1 million.

2019 Guidance

Alnylam maintained its guidance for adjusted operating expenses in 2019. The company expects adjusted SG&A expenses to be $390-$400 million and adjusted R&D expenses in the range of $550-$575 million. The company also expects its current liquid resources to fund its operations for multiple years at the current pace of cash burn.

Pipeline Updates

The company initiated the APOLLO-B phase III study for Onpattro in ATTR amyloidosis patients with cardiomyopathy during the third quarter.

During the quarter, Alnylam continued enrollment in the HELIOS-A phase III study on vutrisiran (ALN-TTRsc02), a subcutaneously-administered, investigational RNAi therapeutic, for the treatment of hATTR amyloidosis with polyneuropathy. The company expects to start another phase III study, HELIOS-B, on the candidate in hereditary and wild-type ATTR amyloidosis cardiomyopathy by the end of 2019.

Alnylam announced that the FDA has granted priority review to the new drug application ("NDA"), seeking approval for RNAi therapeutic candidate, givosiran, for the treatment of acute hepatic porphyrias (AHPs). The regulatory authority has set an action date of Feb 4, 2020 for the NDA. The company has also submitted a regulatory application for givosiran in Europe. The company is planning to initiate launch activities for givosiran, assuming potential approvals.

Alnylam continued enrollment in the ILLUMINATE-A, a global phase III study of lumasiran in children and adults with primary hyperoxaluria type 1 (PH1). The company expects to report top-line results from the study by the end of 2019. The company also continued enrollment in ILLUMINATE-B, a phase III pediatric study of lumasiran in PH1 patients under six years of age. It expects to initiate the ILLUMINATE-C phase III study of the drug in PH1 patients with severe renal impairment in late 2019.

Alnylam's partner, The Medicines Company, reported successful completion of three pivotal studies evaluating inclisiran for the treatment of hypercholesterolemia. The company intends to file regulatory applications in the United States and Europe seeking approval for inclisiran by the end of 2019 and early 2020.

The company is also developing another candidate, fitusiran, in partnership with Sanofi for the treatment of hemophilia.

Recent News

Reports Positive Topline Results from ILLUMINATE-A Study of Lumasiran- Dec 17

Alnylam announced that the ILLUMINATE-A phase III study of lumasiran, an investigational RNAi therapeutic targeting glycolate oxidase (GO) in development for the treatment of primary hyperoxaluria type 1 (PH1), met its primary efficacy endpoint and all tested secondary endpoints.

Lumasiran met the primary efficacy endpoint of percent change from baseline, relative to placebo, in 24-hour urinary oxalate excretion averaged across months 3 to 6. The study also achieved statistically significant results for all six tested secondary endpoints. Lumasiran also demonstrated an encouraging safety and tolerability profile. Based on these results, the company plans to submit a new drug application (NDA) and file a Marketing Authorisation Application (MAA) for lumasiran in early 2020.

Provides 2020 Product and Pipeline Goals-Nov 22

Alnylam provided updates and 2020 goals at it R&D day. The company expects to exceed Alnylam 2020 Goals with four marketed products, 14 organic clinical stage programs, including 6 in late-stage development, across 4 strategic therapeutic areas (STArs), by end of 2020.

The company expects to receive approval of Onpattro in Brazil in mid-2020, with planned launches in additional countries throughout 2020. It also expects to complete enrollment in the APOLLO-B study in late 2020.

The company plans to achieve regulatory approval from the European Medicines Agency (EMA) for Givlaari (givosiran), in early 2020 for the treatment of acute hepatic porphyria (AHP). It also plans to execute on U.S. and EU commercial launches throughout 2020.

Alnylam is initiated the HELIOS-B phase III study of vutrisiran in patients with hereditary and wild-type ATTR amyloidosis patients with cardiomyopathy. HELIOS-B will evaluate the efficacy of vutrisiran versus placebo toward the composite outcome of all-cause mortality and recurrent cardiovascular hospitalizations at 30 months, the primary study endpoint. The company plans to continue enrollment in the HELIOS-B study throughout 2020. It also expects to complete enrollment in the HELIOS-A phase III study in early 2020.

The company expects to file a New Drug Application (NDA) and a Marketing Authorisation Application (MAA) for lumasiran with the FDA and EMA, respectively, in early 2020, assuming positive results from the ILLUMINATE-A phase III study. It expects to report topline results from the ILLUMINATE-B pediatric phase III study in mid-2020. It plans to achieve FDA and EMA regulatory approvals in late 2020.

In addition, the company reported initial positive data with ALN-AAT02, ALN-HBV02 (VIR-2218), and ALN-AGT, representing the first human proof of concept for Alnylam's ESC+ GalNAc conjugate delivery technology – having the potential to enable greater target selectivity and a wider therapeutic index – and expansion of the Alnylam pipeline in highly prevalent chronic disease opportunities. The company is also reporting progress in its efforts with CNS and ocular delivery of RNAi therapeutics, including an update on the status of its collaborative work with Regeneron, and announced a new investigational CNS program, ALN-HTT, in development for the treatment of Huntington's disease.

Alnylam's Givosiran Gets FDA Nod for Acute Hepatic Porphyria

Alnylam Pannounced that the FDA approved its givosiran injection for subcutaneous use for the treatment of adults with acute hepatic porphyria (AHP). The approval came in three months before the PDUFA date of Feb 20, 2020. Gvosiran injection will be marketed by the trade name of Givlaari. This is the second RNAi therapeutic from Alnylam to have received an FDA approval in the last 16 months and the first-ever galnac-conjugate RNA therapeutic to get an approval, marking a significant advancement of precision genetic medicines. Givlaari is expected to be available in the United States by the end of 2019. Reportedly, the drug is priced considerably high at $575,000 per annum.

Givlaari's approval was based on the positive results from the phase III ENVISION study, which showed that AHP patients treated with this drugexperienced 70% lesser porphyria attacks compared to placebo. Givlaarialso led to a similar reduction in intravenous hemin use, as well as reductions in urinary aminolevulinic acid (ALA) and urinary porphobilinogen (PBG) compared to placebo.

Givlaari was reviewed by the FDA on a priority review basis and had previously been granted Breakthrough Therapy and Orphan Drug designations in the United States. The drugis currently being reviewed under accelerated assessment by the European Medicines Agency (EMA).

The company also announced that it reached value-based agreements (VBAs) in principle with Harvard Pilgrim Healthcare to cover the drug. The framework is designed to accelerate patient and provider access to Givlaari. Under this agreement, Alnylam would be paid the drug's full price based on the ability of the same to deliver outcomes in the real world setting compared to those seen in clinical trials.

Currently, the population of AHP patients diagnosed with active disease in the United States and Europe is estimated to be about 3,000.

Initiates ILLUMINATE-C Phase III Study of Lumasiran-Nov 9

Alnylam announced that the company has initiated ILLUMINATE-C, a new global phase III study of lumasiran, an investigational, subcutaneously administered RNAi therapeutic in development for the treatment of primary hyperoxaluria type 1 (PH1). The study will enroll patients of all ages with advanced renal disease, and the primary study endpoint is the percent reduction in plasma oxalate from baseline to six months. Alnylam expects to report initial ILLUMINATE-C results in late 2020.

The company also announced new positive efficacy results from the ongoing phase II open-label extension (OLE) study of lumasiran, which were

presented at the American Society of Nephrology (ASN) 2019 Annual Meeting.

The OLE study results were reported as of the data cut-off date of Sep 12, 2019 and demonstrated a 76% mean maximal reduction (range: 43%-91%) in urinary oxalate excretion relative to phase I/II baseline values in all cohorts (N=19). In the study, all patients achieved a urinary oxalate level at or below 1.5 times the upper limit of normal and 68% of patients achieved a urinary oxalate level within the normal range. Patients also experienced an 82% mean maximal reduction in urinary oxalate:creatinine ratio after lumasiran dosing across all cohorts (N=20).

The OLE safety results were based on a median study duration of 10.4 months since the first dose administered in the OLE study. As of the data cut-off date, there were no discontinuations from treatment.

Seeks Approval for Onpattro in Brazil – Oct 10

Alnylam announced that it has filed a marketing authorization application in Brazil seeking approval for Onpattro for treating hATTR patients. The application has been granted priority review and a decision from the regulatory authorities in Brazil is expected in the first half of 2020.

Begins Phase III Study on Onpattro for New Indication – Sep 16

Alnylam announced that it has initiated a phase III APOLLO-B study on its lead drug Onpattro for the treatment of ATTR amyloidosis with cardiomyopathy. The primary endpoint of this global placebo-controlled study is to see the change from baseline in the 6-minute walk test (6MWT) at month 12.

Presents New Clinical Results for Givosiran at the 2019 International Congress-Sep 10

Alnylam and its collaborators presented new clinical results at the 2019 International Congress on Porphyrins and Porphyrias (ICPP), held September 8-11, 2019 in Milan, Italy. Presentations included additional results from the ENVISION phase III study and the phase I/II open-label extension (OLE) study of givosiran, an investigational RNAi therapeutic targeting aminolevulinic acid synthase 1 (ALAS1) in development for the treatment of acute hepatic porphyria (AHP).

As of the data cut-off date of January 31, 2019, all eligible patients (N=93) from the ENVISION study of givosiran rolled over into the OLE phase of the study. Reduction in the composite porphyria attack rate with givosiran treatment, which had been observed in the ENVISION study as early as one month after dosing, was shown to be sustained with continued dosing in the OLE phase of the study.

As of the data cut-off date of Apr 19, 2019, a robust treatment effect was maintained in givosiran-treated patients with continued dosing in the phase I/II OLE study (N=16), with a mean time on treatment of 22.8 months and total time on treatment across the phase I and OLE studies of up to 35 months. Substantial mean reductions in annualized attack rate (AAR) and in annualized hemin use of greater than 90% were observed, with evidence for sustained or potentially enhanced clinical activity with continued dosing.

The overall safety profile of givosiran in the Phase 1/2 OLE as of the data cut-off date remains consistent with that previously reported.

Presents New Clinical Research Findings-Sep 3

Alnylam and its collaborators presented results from a proteome-wide biomarker analysis of samples from the APOLLO phase III study of Onpattro (patisiran), an RNAi therapeutic for the treatment of the polyneuropathy of hereditary ATTR (hATTR) amyloidosis in adults. In addition, results were presented from an analysis of the UK Biobank – a prospective cohort study with genetic, physical, and health data on approximately 500,000 individuals across the United Kingdom – on clinical outcomes and medical history of individuals with the non-pathogenic transthyretin (TTR) “stabilizing” T119M variant.

These new clinical research findings provide important insights on a potential biomarker for monitoring polyneuropathy and response to treatment, and highlight human genetic data showing no evidence for protection against vascular disease or life-extending advantages of a ‘stabilizing’ T119M gene variant associated with elevated TTR plasma levels.

Valuation

Alnylam's shares are up 35.9% over the trailing 12-month period. Over the past year, the Zacks sub-industry is down 1.7% and the sector is up 5.4%.

The S&P 500 index is up 25.1% in the past year.

The stock is currently trading at 8.05X trailing 12-month book value, which compares to 3.86X for the Zacks sub-industry, 4.48X for the Zacks sector and 4.43X for the S&P 500 index.

Over the past five years, the stock has traded as high as 12.13X and as low as 2.65X, with a 5-year median of 5.87X. Our Neutral recommendation indicates that the stock will perform in-line with the market. Our $122.00 price target reflects 9.09X trailing 12-month book value.

The table below shows summary valuation data for ALNY

Valuation Multiples - ALNY

		Stock	Sub-Industry	Sector	S&P 500
P/B TTM	Current	8.05	3.86	4.48	4.43
	5-Year High	12.13	5.68	5.01	4.45
	5-Year Low	2.65	2.41	3.42	2.85
	5-Year Median	5.87	3.24	4.27	3.6

	Current	29.2	2.81	2.81	3.48
P/S F12M	5-Year High	227.88	2.92	3.8	3.48
	5-Year Low	22.12	1.99	2.42	2.54
	5-Year Median	79.42	2.52	2.93	3

As of 01/06/2020

Industry Analysis **Zacks Industry Rank:** Top 19% (49 out of 254)

Top Peers

Alexion Pharmaceuticals, Inc. **(ALXN)**	Outperform
Amgen Inc. **(AMGN)**	Neutral
Bayer Aktiengesellschaft **(BAYRY)**	Neutral
Ionis Pharmaceuticals, Inc. **(IONS)**	Neutral
Regeneron Pharmaceuticals, Inc. **(REGN)**	Neutral
Roche Holding AG **(RHHBY)**	Neutral
Sanofi **(SNY)**	Neutral
WAVE Life Sciences Ltd. **(WVE)**	Neutral

Industry Comparison Industry: Medical - Biomedical And Genetics

Industry Peers

	ALNY Neutral	X Industry	S&P 500	ALXN Outperform	AMGN Neutral	REGN Neutral
VGM Score	F	-	-	A	B	A
Market Cap	12.93 B	187.11 M	23.72 B	23.59 B	142.78 B	40.81 B
# of Analysts	8	3	13	14	14	12
Dividend Yield	0.00%	0.00%	1.79%	0.00%	2.41%	0.00%
Value Score	F	-	-	B	B	B
Cash/Price	0.13	0.24	0.04	0.09	0.15	0.07
EV/EBITDA	-15.23	-3.51	13.90	32.11	11.62	14.16
PEG Ratio	NA	1.67	2.00	0.67	2.08	0.86
Price/Book (P/B)	8.05	3.70	3.34	2.28	13.07	3.89
Price/Cash Flow (P/CF)	NA	11.82	13.67	11.79	13.29	16.74
P/E (F1)	NA	25.55	18.72	9.42	15.05	13.89
Price/Sales (P/S)	76.46	12.61	2.66	4.98	6.10	5.36
Earnings Yield	-6.12%	-15.96%	5.31%	10.62%	6.65%	7.20%
Debt/Equity	0.17	0.02	0.72	0.25	2.54	0.07
Cash Flow ($/share)	-7.46	-1.07	6.94	9.04	18.08	22.21
Growth Score	F	-	-	A	D	B
Hist. EPS Growth (3-5 yrs)	NA%	17.09%	10.56%	17.67%	11.35%	28.23%
Proj. EPS Growth (F1/F0)	9.79%	7.31%	7.42%	9.30%	9.37%	12.59%
Curr. Cash Flow Growth	58.12%	19.64%	14.83%	20.32%	2.84%	41.83%
Hist. Cash Flow Growth (3-5 yrs)	NA%	8.23%	9.00%	26.87%	10.23%	23.06%
Current Ratio	5.38	5.15	1.23	3.98	2.89	4.03
Debt/Capital	14.68%	3.95%	42.92%	19.89%	71.74%	6.35%
Net Margin	-485.73%	-196.01%	11.08%	31.05%	34.48%	28.13%
Return on Equity	-52.88%	-63.46%	17.16%	21.21%	80.26%	24.85%
Sales/Assets	0.08	0.21	0.55	0.33	0.38	0.59
Proj. Sales Growth (F1/F0)	93.33%	17.10%	4.15%	13.31%	8.27%	9.24%
Momentum Score	C	-	-	A	A	A
Daily Price Chg	0.25%	0.18%	0.10%	0.16%	0.77%	0.70%
1 Week Price Chg	-1.58%	-0.87%	-0.30%	-1.97%	-1.27%	-1.11%
4 Week Price Chg	-3.93%	2.33%	2.33%	-5.25%	3.21%	1.67%
12 Week Price Chg	46.54%	14.69%	7.02%	5.17%	18.44%	21.71%
52 Week Price Chg	41.81%	-6.46%	24.61%	-1.26%	21.32%	-6.28%
20 Day Average Volume	547,040	225,533	1,589,897	1,476,666	1,809,848	629,783
(F1) EPS Est 1 week change	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%
(F1) EPS Est 4 week change	-1.09%	0.00%	0.00%	0.05%	0.75%	7.35%
(F1) EPS Est 12 week change	6.08%	0.63%	-0.56%	5.59%	3.47%	10.87%
(Q1) EPS Est Mthly Chg	0.00%	0.00%	0.00%	0.08%	-0.21%	NA

Zacks Stock Rating System

We offer two rating systems that take into account investors' holding horizons: Zacks Rank and Zacks Recommendation. Each provides valuable insights into the future profitability of the stock and can be used separately or in combination with each other depending on your investment style.

Zacks Recommendation

The Zacks Recommendation aims to predict performance over the next 6 to 12 months. The foundation for the quantitatively determined Zacks Recommendation is trends in the company's estimate revisions and earnings outlook. The Zacks Recommendation is broken down into 3 Levels; Outperform, Neutral and Underperform. Unlike many Wall Street firms, we have an excellent balance between the number of Outperform and Neutral recommendations. Our team of 70 analysts are fully versed in the benefits of earnings estimate revisions and how that is harnessed through the Zacks quantitative rating system. But we have given our analysts the ability to override the Zacks Recommendation for the 1200 stocks that they follow. The reason for the analyst over-rides is that there are often factors such as valuation, industry conditions and management effectiveness that a trained investment professional can spot better than a quantitative model.

Zacks Rank

The Zacks Rank is our short-term rating system that is most effective over the one- to three-month holding horizon. The underlying driver for the quantitatively-determined Zacks Rank is the same as the Zacks Recommendation, and reflects trends in earnings estimate revisions.

Zacks Style Scores

The Zacks Style Score is as a complementary indicator to the Zacks rating system, giving investors a way to focus on the highest rated stocks that best fit their own stock picking preferences.

Academic research has proven that stocks with the best Value, Growth and Momentum characteristics outperform the market. The Zacks Style Scores rate stocks on each of these individual styles and assigns a rating of A, B, C, D and F. We also produce the VGM Score (V for Value, G for Growth and M for Momentum), which combines the weighted average of the individual Style Scores into one score. This is perfectly suited for those who want their stocks to have the best scores across the board.

Value Score	F
Growth Score	F
Momentum Score	C
VGM Score	F

As an investor, you want to buy stocks with the highest probability of success. That means buying stocks with a Zacks Recommendation of Outperform, which also has a Style Score of an A or a B.

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