Alnylam Pharma (ALNY)

$135.03 (As of 04/12/21)

Price Target (6-12 Months): **$142.00**

Long Term: 6-12 Months	**Zacks Recommendation:** (Since: 01/01/21) Prior Recommendation: Underperform	**Neutral**
Short Term: 1-3 Months	**Zacks Rank:** (1-5)	**3-Hold**
	Zacks Style Scores:	VGM:D
	Value: D | Growth: C | Momentum: D	

Summary

Alnylam's Onpattro and Givlaari have been witnessing strong uptake since their launch. Oxlumo was approved both in the United States and Europe in November 2020, and Leqvio was approved in Europe in December 2020. The approval of these drugs should boost growth prospects. The company is also making good progress with late-stage candidates. Approval of of the same will be a big boost for the company. However, the company heavily relies on partnerships for supporting operations, which remains a concern. If any of company's partners fails to fund a program or terminate the agreement, Alnylam's prospects would be hampered. Stiff competition remains a woe. Loss estimates looks stable ahead of Q1 results. Alnylam has a mixed record of earnings surprises in recent quarters.

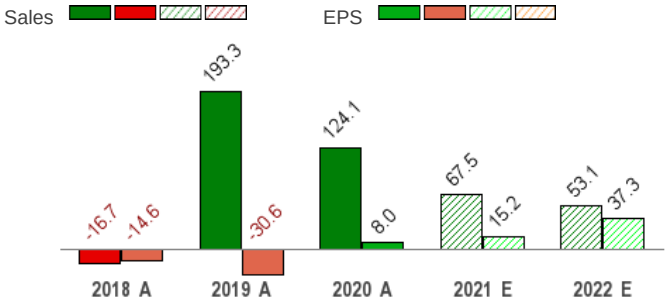
Price, Consensus & Surprise

Source: Zacks Investment Research

Data Overview

52-Week High-Low	**$178.41 - $116.94**
20-Day Average Volume (Shares)	**445,000**
Market Cap	**$16.2 B**
Year-To-Date Price Change	**6.4%**
Beta	**1.27**
Dividend / Dividend Yield	**$0.00 / 0.0%**
Industry	**Medical - Biomedical and Genetics**
Zacks Industry Rank	**Bottom 28% (183 out of 254)**
Last EPS Surprise	**-8.3%**
Last Sales Surprise	**14.8%**
EPS F1 Estimate 4-Week Change	**0.0%**
Expected Report Date	**05/05/2021**
Earnings ESP	**0.0%**
P/E TTM	**NA**
P/E F1	**NA**
PEG F1	**NA**
P/S TTM	**32.9**

Sales and EPS Growth Rates (Y/Y %)



Sales Estimates (millions of $)

	Q1	Q2	Q3	Q4	Annual*
2022	234 E	258 E	286 E	335 E	1,265 E
2021	177 E	198 E	218 E	243 E	827 E
2020	99 A	104 A	126 A	164 A	493 A

EPS Estimates

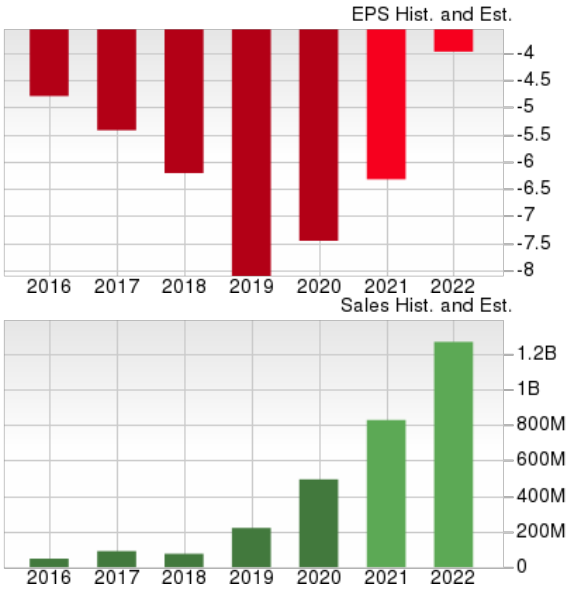
	Q1	Q2	Q3	Q4	Annual*
2022	-$1.84 E	-$1.81 E	-$1.74 E	-$1.56 E	-$3.97 E
2021	-$1.73 E	-$1.62 E	-$1.57 E	-$1.45 E	-$6.33 E
2020	-$1.62 A	-$1.56 A	-$2.18 A	-$2.09 A	-$7.46 A

*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 04/12/2021. The report's text and the analyst-provided price target are as of 04/13/2021.

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 Givlaari (givosiran) for acute hepatic porphyria (AHP).

Moreover, the company is evaluating inclisiran for hypercholesterolemia in partnership with The Medicines Company acquired by Novartis in January 2020. Alnylam also submitted an NDA and an MAA for inclisiran to the FDA and the EMA, respectively in 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. The company reported revenues of $492.9 million in 2020, up 124.3% year over year.

Source: Zacks Investment Research

Reasons To Buy:

> Alnylam expects to bring three products to the market by 2020, including the already approved approved drugs — Givlaari and Onpattro.

- **Onpattro (patisiran) Approval A Significant Boost:** 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 has been strong with more than 1150 patients worldwide on commercial Onpattro treatment since its launch as of Sep 30, 2020. The drug should drive revenues for the company as it will be an important treatment option for people suffering from this often fatal disease.

  In addition, Alnylam is also planning to expand the label of Onpattro. In this regard, the company continued enrolment in the APOLLO-B phase III study in ATTR amyloidosis patients with cardiomyopathy. In February 2020, the company received approval for Onpattro for treating hATTR patients in Brazil. Label expansion of the drug should further boost sales for the company.

- **Givlaari (Givosiran) Approval Encouraging, Oxlumo (Lumasiran) Approved, Leqvio (inclisiran) Gets Approval in Europe:** In November 2019, the FDA approved givosiran injection for subcutaneous use for the treatment of adults with acute hepatic porphyria (AHP). Givosiran injection is marketed by the trade name of Givlaari. This is the second RNAi therapeutic from Alnylam approved by the FDA. This approval further boosts sales for the company. The drug has been performing well.In March 2020, the company received approval for Givlaari for the treatment of AHP in adolescents and adults in the EU.

  In November 2020, the FDA approved Alnylam's RNAi candidate, Oxlumo (lumasiran) injection for subcutaneous use, for the treatment of primary hyperoxaluria type 1 (PH1) to lower urinary oxalate levels in pediatric and adult patients. Oxlumo is the first RNAi therapeutic approved in the United States for use in both children and adults, and the third RNAi medicine to receive FDA approval in less than three years. In the same month, the European Commission (EC) also granted marketing authorization for Oxlumo for the treatment of PH1 in all age groups.

  In December 2020, Alnylam's partner Novartis received marketing authorization for Leqvio(inclisiran)from the European Commission.

  The approval will boost sales of the company.

- **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 (regulatory application accepted for Primary Hyperoxaluria Type 1 (PH1)), vutrisiran (ALN-TTRsc02) a once-quarterly, subcutaneously administered investigational RNAi therapeutic in development for the treatment of ATTR amyloidosis.

  In February 2020, Alnylam completed enrollment in the HELIOS-A phase III study on vutrisiran (ALN-TTRsc02) for the treatment of hATTR amyloidosis with polyneuropathy. In January 2021, Alnylam announced positive top-line results from the phase III -HELIOS-A study. The study met its primary and both secondary endpoints at nine months in patients with hereditary transthyretin (TTR)-mediated amyloidosis with polyneuropathy. The company plans to file a new drug application (NDA) with the FDA in early 2021.The company also initiated the HELIOS-B phase III study in patients with hereditary and wild-type ATTR amyloidosis with cardiomyopathy in November 2019 and enrolment is ongoing in the study.

  The company presented positive interim results from the phase I study of ALN-AGT, in development for the treatment of hypertension.

  The company initiated dosing in the phase I study of ALN-HSD an investigational RNAi therapeutic targeting HSD17B13, in development for the treatment of non-alcoholic steatohepatitis (NASH).

  Alnylam in collaboration with Regeneron, is advancing cemdisiran, an investigational RNAi therapeutic for the treatment of complement-mediated diseases. Enrollmentand dosing in a phase II study of cemdisiran monotherapy in patients with IgA nephropathy is ongoing, with topline results expected in 2021. Alnylam initiated dosing in a phase I study of combination therapy with pozelimab, an anti-C5 monoclonal antibody, in collaboration with Regeneron.

  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. Vir initiated a phase II combination study of VIR-2218 with pegylated interferon-alpha (PEG-IFN-?), with initial clinical data anticipated in 2021.

  Alnylam selected its first CNS-targeted development candidate, ALN-APP, an investigational RNAi therapeutic targeting amyloid precursor protein (APP) for the treatment of hereditary cerebral amyloid angiopathy (hCAA)and autosomal dominant Alzheimer's Disease (ADAD), which remains on track for a CTA filing in mid-2021. The company announced that Regeneron has exercised its co-development/co-commercialization option on the ALN-APP program, which Alnylam will lead.

The 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.

  In April 2019, Alnylam and Regeneron Pharmaceuticals extended their collaboration agreement. Both the companies are working together to discover, develop and commercialize new RNAi therapeutics 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.

  In April 2020, Alnylam and The Blackstone Group entered into a broad strategic collaboration which will support Alnylam's advancement of innovative RNAi medicines with up to $2 billion investment from Blackstone. Alnylam believes that the deal with Blackstone will make the company self-sustainable. The Blackstone investment will also likely accelerate the commercial potential of Alnylam's rapidly advancing product portfolio and support the development and delivery of promising medicines.

  In April 2020, the company entered into an agreement with Dicerna to develop and commercialize investigational RNAi therapeutics for the treatment of alpha-1 antitrypsin (A1AT) deficiency-associated liver disease, and completed a non-exclusive cross-licensing agreement with Dicerna regarding the companies' respective intellectual property for Alnylam's lumasiran and Dicerna'snedosiran investigational programs for the treatment of primary hyperoxaluria.

  In July 2020, Alnylam and taiba Middle East, a leading rare disease company based in the United Arab Emirates and covering the Middle East region, announced that they have formed a Distribution Agreement for both Onpattro and Givlaari. The Agreement between Alnylam and taiba will initially cover the Gulf states, including the Kingdom of Saudi Arabia, Kuwait, Bahrain, Qatar, Oman and the United Arab Emirates. It includes Onpattro, approved in the European Union (EU) for the treatment of hATTRamyloidosis in adults with stage 1 or stage 2 polyneuropathy; Givlaari, approved in the EU for the treatment of acute hepatic porphyria (AHP); and lumasiran, a late-stage investigational RNAi therapeutic for the treatment of PH1.

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.

  Alnylam's partner Novartis received a Complete Response Letter for Leqvio from the FDA in December 2020, due to unresolved facility inspection-related conditions at a third-party manufacturing facility in Europe. Novartis is working closely with the third-party manufacturer and the FDA to obtain approval as soon as possible, and has guided for a resubmission of its NDA in the second or third quarter of 2021.

  In October 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).

- **High Reliance on Partnerships & High Competition:** Alnylam derives a substantial amount of revenues from strategic partnerships with companies like Sanofi, Takeda, Monsanto and Novartis. 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. The cholesterol management market represents huge commercial potential and with companies like 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 Q4 Loss Wider Than Expected, Revenues Beat

Quarter Ending	12/2020
Report Date	Feb 11, 2021
Sales Surprise	14.79%
EPS Surprise	-8.29%
Quarterly EPS	-2.09
Annual EPS (TTM)	-7.45

Alnylamincurred a loss of $2.09 per share in the fourth quarter of 2020, wider than the Zacks Consensus Estimate of a loss of $1.93. The loss includes stock-based compensation expenses, costs associated with the strategic financing collaboration, change in estimates of contingent liabilities and unrealized loss on equity securities. Excluding these items, adjusted loss was $1.60 per share, narrower than the adjusted loss of $1.98 in the year-ago quarter.

The company recorded revenues of $163.6 million, which beat the Zacks Consensus Estimate of $142 million. In the year-ago quarter, revenues were $71.6 million. Net product revenues were $112.8 million, up 102% year over year, driven by the addition of new patients on therapy led by growth in established markets and the global expansion of Onpattro (patisiran) and Givlaari (givosiran)as well as initial net product revenues from Oxlumo following regulatory approval in the fourth quarter of 2020.

Net revenues from collaborators were $50.7 million, up from $15.7 million in the year-ago quarter, primarily due to the achievement of a $15-million milestone related to the Leqvio approval in Europe under the Novartis collaboration agreement, as well as an increase in revenues recognized in connection with the collaboration agreement with Regeneron.

Quarter in Detail

Onpattro was approved for the treatment of polyneuropathy of hereditary transthyretin-mediated (hATTR) amyloidosis in 2018. The injection recorded sales of $90 million in the fourth quarter, up 61.9% year over year, driven by new patient demand.

Givlaari (givosiran) is Alnylam's second product and was approved for the treatment of acute hepatic porphyria (AHP) in the United States in November 2019 and Europe in March 2020. In the fourth quarter, it recorded sales of $22 million.

For the period following the EMA and FDA approvals of Oxlumo in late November 2020, it recorded global net product revenues for the fourth quarter of about $0.3 million representing initial patient demand in Europe.

Adjusted research and development expenses (R&D) increased to $153.5 million from $166.5 million in the year-ago quarter. The decrease was primarily due to decreases in manufacturing activity for clinical drugs.

Adjusted selling, general and administrative expenses (SG&A) rose to $136.7 million from $124.9 million in the year-ago quarter. The increase was due to higher investments in commercial and medical affair activities to support the ongoing launches of Onpattro,Givlaari and Oxlumo.

Full-Year 2020 Results

The company reported revenues of $492.9 million, up 124.3% year over year. It surpassed the Zacks Consensus Estimate of $471.09 million.

Adjusted loss was $6.38 per share in 2020, narrower than $6.70 in 2019.

2021 Guidance

Alnylam expectsnet product revenues for Onpattro, Givlaari and Oxlumoin the range of $610-$660 million.

Net revenues from collaborations and royalties are expected in the range of $150-$200 million.

Pipeline & Collaboration Updates

The company is developing Leqvio (inclisiran) for hypercholesterolemia in partnership with Novartis.Novartis received marketing authorization for Leqvio from the European Commission in December 2020.

Novartis received a complete response letter from the FDA in December 2020, due to unresolved facility inspection-related conditions at a third-party manufacturing facility in Europe. The company is working closely with the third-party manufacturer and the FDA to obtain approval as soon as possible and has guided for a resubmission of its new drug application (NDA) in the second or third quarter of 2021.

Alnylam is developing fitusiran in partnership with Sanofi for the treatment of hemophilia A or B with and without inhibitors. Sanofi resumed dosing and enrollment in the ATLAS phase III program.

Recent News

Launches “Alnylam P5x25” Strategy-Jan 10

Alnylam launched P5x25 strategy which is aimed at fulfilling Alnylam's aspirations and potential of becoming one of the most successful biotech companies ever with transformative medicines in both rare and common diseases for patients around the world, supported by additional growth through label expansion, a robust and high yielding pipeline of first and/or best-in-class product candidates from organic product engine and exceptional financial performance with over 40% revenue CAGR to year-end 2025 and sustainable profitability achieved within the period.

Alnylam’s P5x25” is focused on the company’s planned transition to a top-5 biotech (measured by market capitalization) in the next 5 years through: sustainable innovation yielding transformative medicines for rare and common diseases for patients around the world and delivery of exceptional financial performance.

Alnylam Posts Positive Top-Line Data From Vutrisiran Study-Jan 7

Alnylam announced positive top-line results from the phase III -HELIOS-A study of vutrisiran, an investigational RNAi therapeutic in development for the treatment of transthyretin-mediated (ATTR) amyloidosis with polyneuropathy. The study met its primary and both secondary endpoints at nine months in patients with hereditary transthyretin (TTR)-mediated amyloidosis with polyneuropathy.

hATTR is an inherited, often fatal disease caused by mutations in the TTR gene.

In the study, patients were randomized 3:1 to receive either 25mg 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 (as a reference comparator) for 18 months. Vutrisiran met primary and all secondary endpoints, demonstrating statistically significant improvements in the progression of neuropathy, quality of life (QOL) and gait speed relative to placebo, after nine months. The primary endpoint of the phase III HELIOS-A study was the change from baseline in the modified Neuropathy Impairment Score (mNIS+7) at nine months as compared to historical placebo data from the APOLLO phase III study of patisiran.

Additionally, a majority of patients in the phase III HELIOS-A study showed reversal of disease manifestations with improvements in neuropathy impairment and QOL, relative to baseline.

In addition, vutrisiran treatment showed improvement compared to placebo on the exploratory cardiac biomarker endpoint, NT-proBNP (nominal p less than 0.05).

Based on the results from the HELIOS-A study, Alnylam intends to submit a new drug application (NDA) for vutrisiran this year in the United States and follow that up with regulatory filings in other countries. The company will seek approval in the European Union after an 18-month analysis, which is expected in late 2021.

Provides Program Updates-Dec 15

Alnylam announced 2021 product and pipeline goals and provided program updates at R&D day.

The company aims to deliver performance on four commercial brands-Onpattro, Givlaari, Oxlumo and Vutrisiran, file one new drug application (NDA), and report topline results on two phase III programs, amongst other objectives.

The company expects to file an NDA for Vutrisiran, an investigational RNAi therapeutic in development for the treatment of ATTR amyloidosis.

Alnylam will discuss the opportunity for its ATTR franchise programs with patisiran and vutrisiran in wild-type ATTR amyloidosis.

The company will present new clinical data from the ongoing Phase 1 study of ALN-AGT, an investigational RNAi therapeutic targeting angiotensinogen in development for the treatment of hypertension. New clinical data presented from phase I monotherapy study of ALN-AGT showed mean reduction in 24-hour systolic blood pressure of over 15 mm Hg.

New highlighted programs include investigational Rnai therapeutics for recurrent renal stones, non-alcoholic steatohepatitis (NASH), gout, metabolic syndrome, and Type II diabetes, expanding Rnai opportunities into specialty and prevalent disease markets.

Alnylam Ends Enrollment in Advanced Hyperoxaluria Study-Dec 3

Alnylam announced that it achieved full patient enrollment in its ILLUMINATE-C phase III study of its RNAi candidate, Oxlumo (lumasiran), targeting the hydroxyacid oxidase 1 (HAO1) the gene encoding glycolate oxidase (GO) — for the treatment of adults and children with advanced primary hyperoxaluria type 1 (PH1). The ultra-rare disease causes a progressive decline in kidney function and can lead to end-stage renal disease.

ILLUMINATE-C (NCT04152200) is a single arm, open-label, multinational phase III study to evaluate the safety and efficacy of lumasiran in PH1 patients of all ages and advanced PH1 including those experiencing systemic oxalosis and undergoing hemodialysis. The primary endpoint of the study is the percent change in plasma oxalate from baseline to month 6. Key secondary endpoints are designed to evaluate additional measures of plasma oxalate and changes in urinary oxalate, and quality of life assessments. The company expects to report top-line results from the study in mid-2021.

The company believes that lumasiran has the potential to address the full spectrum of PH1 disease severity.

Alnylam Gets FDA Nod for Oxlumo to Treat Renal Disease-Nov 24

Alnylam announced that the FDA approved Oxlumo (lumasiran) injection for subcutaneous use, for the treatment of primary hyperoxaluria type 1 (PH1) to lower urinary oxalate levels in pediatric and adult patients. The ultra-rare disease causes a progressive decline in kidney function and can lead to end-stage renal disease.

Oxlumo is the first RNAi therapeutic approved in the United States for use in both children and adults, and the third RNAi medicine to receive FDA approval in less than three years.

The FDA approval was primarily based on positive results from ILLUMINATE-A, the largest controlled phase III study ever conducted in PH1 — where Oxlumo significantly reduced levels of urinary oxalate relative to placebo, with the majority of patients achieving normal or near-normal levels. The FDA also took into consideration positive interim results from the single-arm, open-label ILLUMINATE-B phase III pediatric study.

With the approval of Oxlumo, the FDA granted Alnylam a pediatric rare disease priority review voucher that entitles the company to designate a single new drug application to qualify for a priority review in the future.

The company also announced a new framework for value-based agreements (VBAs) designed to help people with PH1 gain access to Oxlumo. The VBA framework includes an innovative patient need adjustment that offers payers increased cost predictability across the entire spectrum of PH1 patient ages, from infant to adult.

Alnylam Gets EU Nod for Oxlumo to Treat Renal Disease-Nov 19

Alnylam announced that the European Commission (EC) has granted marketing authorization for Oxlumo (lumasiran), an RNAi therapeutic, for the treatment of primary hyperoxaluria type 1 (PH1) in all age groups. The ultra-rare disease causes a progressive decline in kidney function and can lead to end-stage renal disease.

Oxlumo is the first therapeutic approved for the treatment of PH1 and the only therapy proven to lower harmful oxalate levels that drive the progression of the PH1 disease.

The approval is supported by the efficacy and safety findings of Oxlumo in PH1 patients, including data from both ILLUMINATE-A and ILLUMINATE-B phase III studies. Key primary and secondary endpoints included the reduction of urinary and plasma oxalate and the proportion of patients achieving normalization or near-normalization of urinary oxalate in response to Oxlumo compared to placebo. This approval in the European Union follows the positive opinion from the Committee for Medicinal Products for Human Use (CHMP) in October 2020.

Reports Positive Interim Results from Ongoing Phase 1 Study of ALN-AGT-Nov 13

Alnylam announced positive interim data from the ongoing phase I study of ALN-AGT, a subcutaneous investigational RNAi therapeutic targeting liver-expressed angiotensinogen (AGT) for the treatment of hypertension. The study was a placebo-controlled, single ascending dose (SAD) study, and evaluated the safety, tolerability and preliminary pharmacokinetic and pharmacodynamic activity of ALN-AGT in patients with mild or moderate hypertension, who were either treatment naive or had discontinued other anti-hypertensive medications. Patients had a mean age of 52 years (range 35 – 65) and a mean baseline 24-hour systolic blood pressure (SBP) and diastolic blood pressure (DBP) of 139 millimeters of mercury (mm Hg) and 86 mm Hg, respectively. Patients were enrolled in ascending dose cohorts of 10 mg, 25 mg, 50 mg, 100 mg or 200 mg ALN-AGT.

Compared to placebo, patients treated with ALN-AGT experienced dose-dependent reductions in serum AGT — the sole precursor of all angiotensin peptides, including the potent vasoconstrictor angiotensin (Ang) II. In the 200 mg dose cohort, the mean reduction of AGT at 8 weeks was 94.9 +/- 1.6%. Reductions of more than 90% persisting through 12 weeks after single doses of 100 or 200 mg were observed, with up to 97.6% AGT knockdown at 200 mg. The durability of AGT knockdown supports the potential for once quarterly dosing and possibly even less frequent dosing.

Durable AGT knockdown through 12 Weeks supported a once quarterly or potentially less frequent dosing regimen.

ALN-AGT was shown to be generally well tolerated with an acceptable safety profile for continued development.

Alnylam Gets Positive CHMP Opinion for Lumasiran-Oct 22

Alnylam announced that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) adopted a positive opinion recommending the approval of its RNAi candidate, lumasiran, targeting the hydroxyacid oxidase 1 (HAO1) mRNA — encoding glycolate oxidase (GO) — in development for the treatment of primary hyperoxaluria type 1 (PH1). The ultra-rare disease causes a progressive decline in kidney function and can lead to end-stage renal disease. Lumasiran will be marketed in Europe under the brand name Oxlumo. A decision by the European Commission is expected in the fourth quarter of 2020.

The positive opinion is supported by the efficacy and safety findings of Oxlumo in PH1 patients, including data from both ILLUMINATE-A and ILLUMINATE-B phase III studies.

Valuation

Alnylam's shares are up 3.9% in the year-to-date period and 11.9% over the trailing 12-month period. Stocks in the Zacks sub-industry are down 6.8% while the stocks in the Zacks sector are down 3%, in the year-to-date period. Over the past year, stocks in the sub-industry and the sector

are down 0.1% and up 6.8%, respectively.

The S&P 500 Index is up 10.6% in the year-to-date period and up 48.1% in the past year.

The stock is currently trading at 15.55X trailing 12-month book value, which compares to 2.96X for the Zacks sub-industry, 3.85X for the Zacks sector and 7.01X for the S&P 500 Index.

Over the past five years, the stock has traded as high as 20.09X and as low as 2.65X, with a 5-year median of 6.39X. Our Neutral recommendation indicates that the stock will perform in-line with the market. Our $142.00 price target reflects 16.35X 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	15.55	2.96	3.85	7.01
	5-Year High	20.09	5.09	5.12	7.01
	5-Year Low	2.65	2.01	3.03	3.83
	5-Year Median	6.39	3.74	4.36	4.98
P/S TTM	Current	31.86	2.73	3.14	5.32
	5-Year High	224.15	3.82	3.69	5.32
	5-Year Low	29.92	2.36	2.42	2.83
	5-Year Median	89.05	3.21	3.27	3.91

As of 04/12/2021 *Source: Zacks Investment Research*

Industry Analysis **Zacks Industry Rank:** Bottom 28% (183 out of 254)

Source: Zacks Investment Research

Top Peers

Company (Ticker)	Rec	Rank
Acorda Therapeutics, Inc. **(ACOR)**	Outperform	2
Blueprint Medicines Corporation **(BPMC)**	Neutral	3
Halozyme Therapeutics, Inc. **(HALO)**	Neutral	4
OSMOTICA PHARM **(OSMT)**	Neutral	4
Pfizer Inc. **(PFE)**	Neutral	3
Vanda Pharmaceuticals Inc. **(VNDA)**	Neutral	3
ANI Pharmaceuticals, Inc. **(ANIP)**	Underperform	5
Bayer Aktiengesellschaft **(BAYRY)**	Underperform	5

The positions listed should not be deemed a recommendation to buy, hold or sell.

Industry Comparison Industry: Medical - Biomedical And Genetics

Industry Peers

	ALNY	X Industry	S&P 500	ACOR	HALO	OSMT
Zacks Recommendation (Long Term)	Neutral	-	-	Outperform	Neutral	Neutral
Zacks Rank (Short Term)	3	-	-	2	4	4
VGM Score	D	-	-	D	C	C
Market Cap	16.22 B	379.09 M	29.81 B	39.76 M	6.13 B	207.16 M
# of Analysts	10	3	12	1	4	1
Dividend Yield	0.00%	0.00%	1.33%	0.00%	0.00%	0.00%
Value Score	D	-	-	F	C	B
Cash/Price	0.12	0.22	0.06	2.12	0.06	0.55
EV/EBITDA	-20.32	-5.53	16.97	-8.22	34.46	12.84
PEG F1	NA	1.52	2.38	NA	NA	NA
P/B	15.80	4.14	4.01	0.14	38.28	2.21
P/CF	NA	21.98	17.10	NA	39.40	2.75
P/E F1	NA	25.62	22.05	NA	28.00	NA
P/S TTM	32.90	24.29	3.42	0.26	22.90	1.16
Earnings Yield	-4.58%	-11.16%	4.47%	-179.95%	3.58%	-26.89%
Debt/Equity	0.19	0.00	0.66	0.70	0.00	2.34
Cash Flow ($/share)	-6.75	-1.01	6.78	-4.65	1.09	1.13
Growth Score	C	-	-	C	B	D
Historical EPS Growth (3-5 Years)	NA%	18.08%	9.34%	NA	NA	NA
Projected EPS Growth (F1/F0)	15.21%	6.85%	15.26%	16.41%	67.86%	32.06%
Current Cash Flow Growth	-5.76%	14.70%	0.61%	-116.03%	-316.18%	-80.02%
Historical Cash Flow Growth (3-5 Years)	NA%	6.02%	7.37%	NA	46.82%	NA
Current Ratio	4.47	6.20	1.39	1.61	1.32	3.10
Debt/Capital	15.84%	0.00%	41.26%	41.12%	0.00%	70.05%
Net Margin	-174.15%	-179.15%	10.59%	43.47%	48.24%	-44.74%
Return on Equity	-68.93%	-57.22%	14.86%	23.15%	124.82%	-28.69%
Sales/Assets	0.16	0.17	0.51	0.22	0.50	0.41
Projected Sales Growth (F1/F0)	67.70%	13.66%	7.37%	-37.42%	49.14%	-19.95%
Momentum Score	D	-	-	A	D	B
Daily Price Change	-2.32%	-2.39%	0.24%	-2.63%	0.42%	-6.34%
1-Week Price Change	-2.52%	-3.73%	1.54%	-12.34%	0.80%	-2.65%
4-Week Price Change	-7.59%	-14.04%	2.84%	-30.49%	-1.42%	-15.53%
12-Week Price Change	-18.83%	-9.80%	10.11%	-39.10%	-9.45%	-28.74%
52-Week Price Change	13.46%	35.88%	55.81%	-37.02%	138.35%	-19.48%
20-Day Average Volume (Shares)	445,000	342,044	1,992,726	161,974	1,141,949	349,166
EPS F1 Estimate 1-Week Change	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%
EPS F1 Estimate 4-Week Change	0.00%	0.00%	0.00%	0.00%	0.00%	-17.88%
EPS F1 Estimate 12-Week Change	-1.51%	-2.13%	2.05%	33.26%	-0.16%	-19.46%
EPS Q1 Estimate Monthly Change	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%

Source: Zacks Investment Research

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 maintain a 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

Value Score	D
Growth Score	C
Momentum Score	D
VGM Score	D

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.

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.

Disclosures

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ZIR uses the following rating system for the securities it covers. **Outperform-** ZIR expects that the subject company will outperform the broader U.S. equities markets over the next six to twelve months. **Neutral-** ZIR expects that the company will perform in line with the broader U.S. equities markets over the next six to twelve months. **Underperform-** ZIR expects the company will underperform the broader U.S. equities markets over the next six to twelve months.

Additional Disclosure

This material represents an assessment of the market and economic environment at a specific point in time and is not intended to be a forecast of future events, or a guarantee of future results. Forward-looking statements are subject to certain risks and uncertainties. Any statements that refer to expectations, projections or characterizations of future events or circumstances, including any underlying assumptions, are forwardlooking statements. Actual results, performance, or achievements may differ materially from those expressed or implied.

Returns quoted represent past performance which is no guarantee of future results. Investment returns and principal value will fluctuate so that when shares are redeemed, they may be worth more or less than their original cost. Current performance may be higher or lower than the performance shown.

Investing involves risk; principal loss is possible. There is no guarantee that companies that can issue dividends will declare, continue to pay or increase dividends.

Glossary of Terms and Definitions

52-Week High-Low: The range of the highest and lowest prices at which a stock has traded during the past year. This range is determined based on the stock's daily closing price which may differ from the intra-day high or low. Many investors use it as a technical indicator to determine a stock's current value and future price movement. The idea here is that if price breaks out from the 52-week range, in either direction, the momentum may continue in the same direction.

20-Day Average Volume (Shares): The average number of shares of a company traded in a day over the last 20 days. It is a direct indication of a security's overall liquidity. The higher the average daily trading volume, the easier it is to enter or exit the stock at a desired price with more buyers and sellers being available.

Daily Price Change: This is the percentage difference between a trading day's closing price and the prior trading day's closing price. This item is updated at 9 p.m. EST each day.

1-Week Price Change: This is the percentage change in a stock's closing price over the last 5 trading days. This change reflects the collective buying and selling sentiment over the 1-week period.

A strong weekly price increase for the stock, especially when accompanied by increased volume, is an indication of it gaining momentum.

4-Week Price Change: This is the percentage change in a stock's closing price over the last 20 trading days or past 4 weeks. This is a mediumterm price change metric and an indication of the stock gaining momentum.

12-Week Price Change: This is the percentage change of a stock's closing price over the last 60 trading days or past 12 weeks. Similar to 4-week price change, this is a medium-term price change metric. It shows whether a stock has been enjoying strong investor demand, or if it has been in consolidation, or distress over this period.

52-Week Price Change: This is the percentage change in a stock's closing price over the last 260 trading days or past 52 weeks. This long-term price change metric is a good reference point for investors. Some investors seek stocks with the best percentage price change over the last 52 weeks, expecting the momentum to continue.

Market Cap: The number of outstanding common shares of a company times its latest price per share. This figure represents a company's size, which indicates various characteristics, including price stability and risk, in which investors could be interested.

Year-To-Date Price Change: Change in a stock's daily closing price in the period of time beginning the first day of the current calendar year through to the previous trading day.

# of Analysts: Number of EPS estimates used in calculating the current-quarter consensus. These estimates come from the brokerage analysts tracking this stock. However, the number of such analysts tracking this stock may not match the number of estimates, as all brokerage analysts may not come up with an estimate or provide it to us.

Beta: A measure of risk commonly used to compare the volatility of a stock to the overall market. The S&P 500 Index is the base for calculating beta and carries a value of 1. A stock with beta below 1 is less risky than the market as a whole. And a stock with beta above 1 is riskier.

Dividend: The portion of earnings a company is expected to distribute to its common shareholders in the next 12 months for each share they own. Dividends are usually paid quarterly. Dividend payments reflect positively on a company and help maintain investors' trust. Investors typically find dividend-paying stocks appealing because the dividend adds to any market price appreciation to result in higher return on investment (ROI). Moreover, a steady or increasing dividend payment provides investors a cushion in a down market.

Dividend Yield: The ratio of a company's annual dividend to its share price. The annual dividend used in the ratio is calculated based on the mostrecent dividend paid by the company. Dividend yield is an estimate of the dividend-only return from a stock in the next 12 months. Since dividend itself doesn't change frequently, dividend yield usually changes with a stock's price movement. As a result, often an unusually high dividend yield is a result of weak stock price.

S&P 500 Index: The Standard & Poor's 500 (S&P 500) Index is an unmanaged group of securities considered to be representative of the stock market in general. It is a market-capitalization-weighted index of stocks of the 500 largest U.S. companies. Each stock's weight in the index is proportionate to its market value.

Industry: One of the 250+ groups that Zacks classifies all stocks into based on the nature of business. These groups are termed as expanded (aka "X") industries and map to their respective (economic) sectors; Zacks has 16 sectors.

Zacks Industry Rank: The Zacks Industry Rank is determined by calculating the average Zacks Rank for all stocks in the industry and then assigning an ordinal rank to it. For example, an industry with an average Zacks Rank of 1.6 is better than an industry with an average Zacks Rank of 2.3. So, the industry with the better average Zacks Rank would get a better Zacks Industry Rank. If an industry has the best average Zacks Rank, it would be considered the top industry (1 out of 250+), which would place it at the top 1% of Zacks-ranked industries. Studies have shown that roughly half of a stock's price movement can be attributed to the industry group it belongs to. In fact, the top 50% of Zacks-ranked industries outperforms the bottom 50% by a factor of more than 2 to 1.

Last EPS Surprise: The percentage deviation of a company's last reported earnings per share from the Zacks Consensus Estimate. Companies with a positive earnings surprise are more likely to surprise again in the future (or miss again if they recently missed).

Last Sales Surprise: The percentage deviation of a company's last reported sales from the Zacks Consensus Estimate.

Expected Report Date: This is an estimated date of a company's next earnings release. The information originated or gathered by Zacks Investment Research from its information providers or publicly available sources is the basis of this estimate.

Earnings ESP: The Zacks Earnings ESP compares the Most Accurate Estimate to the Zacks Consensus Estimate for the yet-to-be reported quarter. The Most Accurate Estimate is the most recent version of the Zacks Consensus EPS Estimate. The idea here is that analysts revising their estimates closer to an earnings release have the latest information, which could potentially be more accurate than what they and others contributing to the consensus had predicted earlier. Thus, a positive or negative Earnings ESP reading theoretically indicates the likely deviation of the actual earnings from the consensus estimate. However, the model's predictive power is significant for positive ESP readings only. A positive Earnings ESP is a strong predictor of an earnings beat, particularly when combined with a Zacks Rank #1 (Strong Buy), #2 (Buy) or #3 (Hold). Our research shows that stocks with this combination produce a positive surprise nearly 70% of the time.

Periods:

TTM: Trailing 12 months. Using TTM figures is an effective way of analyzing the most-recent financial data in an annualized format that helps neutralize the effects of seasonality and other quarter-to-quarter variation.

F1: Current fiscal year. This period is used to analyze the estimates for the ongoing full fiscal year.

F2: Next fiscal year. This period is used to analyze the estimates for the next full fiscal year.

F12M: Forward 12 months. Using F12M figures is an effective way of analyzing the near-term (the following four unreported quarters) estimates in an annualized manner. Instead of typically representing estimates for the full fiscal year, which may not represent the nitty-gritty of each quarter, F12M figures suggest an all-inclusive annualized estimate for the following four quarters. The annualization helps neutralize the potential effects of seasonality and other quarter-to-quarter variations.

P/E Ratio: The price-to-earnings ratio measures a company's current market price per share relative to its earnings per share (EPS). Usually, the trailing-12-month (TTM) EPS, current-fiscal-year (F1) EPS estimate, or forward-12-month (F12M) EPS estimate is used as the denominator. In essence, this ratio shows what the market is willing to pay today for each dollar of EPS. In other words, this ratio gives a sense of what the relative value of the company is at the already reported level of earnings or at a future level of earnings.

It is one of the most widely-used multiples for determining the value of a company and helps comparing its valuation with that of a competitor, the industry group or a benchmark.

PEG Ratio: The price/earnings to growth ratio is a stock's P/E ratio using current fiscal year (F1) EPS estimate divided by its expected EPS growth rate over the coming 3 to 5 years. This ratio essentially determines a stock's value by factoring in the company's expected earnings growth and is thus believed to provide a more complete picture than just the P/E ratio, particularly for faster-growing companies.

P/S Ratio: The price-to-sales ratio is calculated as a company's current price per share divided by trailing 12 months (TTM) sales or revenues per share. This ratio shows what the market is willing to pay today for each dollar of TTM sales per share. The P/S ratio is at times the only valuation metric when the company has yet to become profitable.

Cash/Price Ratio: The cash-to-price ratio or Cash Yield is calculated as cash and marketable securities per share divided by the company's current share price. Like the earnings yield, which shows the anticipated yield (or return) on a stock from earnings for each dollar invested, the cash yield does the same, with cash being the source of return instead of earnings. For example, a cash/price ratio of 0.08 suggests a return of 8% or 8 cents for every $1 investment.

EV/EBITDA Ratio: The EV/EBITDA ratio, also known as Enterprise Multiple, is calculated as a company's enterprise value (market capitalization + value of total long-term debt + book value of preferred shares - cash and marketable securities) divided by EBITDA (earnings before interest, taxes, depreciation and amortization). Usually, trailing-12-month (TTM) or forward-12-month (F12M) EBITDA is used as the denominator.

EV/Sales Ratio: The enterprise value-to-sales ratio is calculated as a company's enterprise value (market capitalization + value of total long-term debt + book value of preferred shares - cash and marketable securities) divided by annual sales. It is an expansion of the P/S valuation, which uses market value instead of enterprise value. The EV/Sales ratio is perceived as more accurate than P/S, in part, because the market capitalization does not take a company's debt into account when valuing it.

EV/CF Ratio: The enterprise value-to-cash flow ratio is calculated as a company's enterprise value (market capitalization + value of total long-term debt + book value of preferred shares - cash and marketable securities) divided by the trailing-12-month (TTM) operating cash flow. It's a measure of how long it would take to buy the entire business if you were able to use all the company's operating cash flow.

The EV/CF ratio is perceived as more accurate than the P/CF ratio, in part, because the market price does not take a company's debt into account when valuing it.

EV/FCF Ratio: The enterprise value-to-free cash flow metric compares a company's enterprise value to its trailing-12-month (TTM) free cash flow (FCF). This metric is very similar to the EV/CF ratio, but is considered a more exact measure owing to the fact that it uses free cash flow, which subtracts capital expenditures (CAPEX) from a company's total operating cash flow, thereby reflecting the actual cash flow available for funding growth activities and payments to shareholders.

P/EBITDA Ratio: The P/EBITDA ratio is calculated as a company's per share market value divided by EBITDA (earnings before interest, taxes, depreciation, and amortization). This metric is very similar to the EV/EBITDA ratio, but is considered a little less exact measure as it uses market price, which does not take a company's debt into account. However, since EBITDA is often considered a proxy for cash income, the metric is used as a measure of what the market is willing to pay today for each dollar of the company's cash profitability in the trailing 12 months (TTM) or forward 12 months (F12M).

P/B Ratio: The price-to-book ratio is calculated as a company's current price per share divided by its book value (total assets – liabilities – preferred stocks) per share. In short, the book value is how much a company is worth. In other words, it reflects the total value of a company's assets that its common shareholders would receive if it were to be liquidated. So, the P/B ratio indicates whether you're paying higher or lower than what would remain if the company went bankrupt immediately. Investors typically use this metric to determine how a company's stock price stacks up to its intrinsic value.

P/TB Ratio: The price-to-tangible-book value ratio is calculated as a the per share market value of a company divided by the value of its tangible assets (total assets – liabilities – preferred stocks – intangible assets) per share. Tangible book value is the same thing as book value except it excludes the value of intangible assets to get a step closer to the baseline value of the company.

P/CF Ratio: The price-to-cash flow ratio measures a company's per share market price relative to its trailing-12-month (TTM) operating cash flow per share. This metric is used to determine whether a company is undervalued or overvalued relative to another stock, industry or sector. And like the P/E ratio, a lower number is typically considered better from the value perspective.

One of the reasons why P/CF ratio is often preferred over P/E ratio is the fact that operating cash flow adds back non-cash expenses such as depreciation and amortization to net income. This feature helps valuing stocks that have positive cash flow but are not profitable because of large noncash charges.

P/FCF Ratio: The price-to-free cash flow ratio is an extension of P/CF ratio, which uses trailing-12-month (TTM) free cash flow per share instead of operating cash flow per share. This metric is considered a more exact measure than P/CF ratio, as free cash flow subtracts capital expenditures (CAPEX) from a company's total operating cash flow, thereby reflecting the actual cash flow available for funding activities that generate additional revenues.

Earnings Yield: The earnings yield is calculated as current fiscal year (F1) EPS estimate divided by the company's current share price. The ratio, which is the inverse of the P/E ratio, measures the anticipated yield (or return) from earnings for each dollar invested in a stock today.

For example, earnings yield for a stock, which is trading at $35 and expected to earn $3 per share in the current fiscal year (F1), would be 0.0857 (3/35 = 0.0857) or 8.57%. In other words, for $1 invested in the stock today, the yield from earnings is anticipated to be 8.57 cents.

Investors most commonly compare the earnings yield of a stock to that of a broad market index (such as the S&P 500) and prevailing interest rates, such as the current 10-year Treasury yield. Since bonds and stocks compete for investors' dollars, stock investors typically demand a higher yield for the extra risk they assume compared to investors of U.S. Treasury-backed securities that offer virtually risk-free returns. This additional return is referred to as the risk premium.

Debt/Equity Ratio: The debt-to-equity ratio is calculated as a company's total liabilities divided by its shareholder equity. This metric is used to gauge a company's financial leverage. In other words, it is a measure of the degree to which a company is financing its operations through debt versus its own funds. The higher the ratio, the higher the risk for shareholders.

However, this ratio is difficult to compare across industry groups where ideal amounts of debt vary. Some businesses are more capital intensive than others and typically require higher debt to finance their operations. So, a company's debt-to-equity ratio should be compared with other companies in the same industry.

Cash Flow ($/share): Cash flow per share is calculated as operating cash flow (after-tax earnings + depreciation + other non-cash charges) divided by common shares outstanding. It is used by many investors as a measure of a company's financial strength. Since cash flow per share takes into consideration a company's ability to generate cash by adding back non-cash expenses, it is regarded by some as a more accurate measure of a company's financial situation than earnings per share, which could be artificially deflated.

Current Ratio: The current ratio or liquidity ratio is a company's current assets divided by its current liabilities. It measures a company's ability to pay short-term obligations. A current ratio that is in line with the industry average or slightly higher is generally considered acceptable. A current ratio that is lower than the industry average would indicate a higher risk of distress or default. A higher number is usually better. However, a very high current ratio compared to the industry average could be an indication of inefficient use of assets by management.

Debt/Capital Ratio: Debt-to-capital ratio is a company's total debt (interest-bearing debt + both short- and long-term liabilities) divided its total capital (interest-bearing debt + shareholders' equity). It is a measure of a company's financial leverage. All else being equal, the higher the debt-to-capital ratio, the riskier the stock.

However, this ratio can vary widely from industry to industry, the ideal amount of required debt being different. Some businesses are more capital intensive than others and typically require higher debt to finance their operations. So, a company's debt-to-capital ratio should be compared with the same for its industry.

Net Margin: Net margin is calculated as net income divided by sales. It shows how much of each dollar in sales generated by a company translates into profit. For example, if a company's net margin is 15%, its net income is 15 cents for every $1 of sales it makes.

A change in margin can reflect either a change in business conditions, or a company's cost controls, or both. If a company's expenses are growing faster than sales, its net margin will decline. However, different net margin rates are considered good for different industries, so it's better to compare net margin rates of companies in the same industry group.

Return on Equity: Return on equity (ROE) is calculated as trailing-12-month net income divided by trailing-12-month average shareholder equity (including reinvested earnings). This metric is considered a measure of how effectively management is using a company's assets to generate profits. For example, if a company's ROE is 10%, it creates 10 cents profits for every $1 shareholder equity, which is basically the company's assets minus debt. A company's ROE deemed good or bad depends on what's normal for its peers or industry group.

Sales/Assets Ratio: The sales-to-assets ratio or asset utilization ratio or asset turnover ratio is calculated as a company's annual sales divided by average assets (average of assets at the beginning of the year and at the year's end). This metric helps investors understand how effectively a company is using its assets to generate sales. For example, a sales-to-assets ratio of 2.5 indicates that the company generated $2.50 in sales for every $1 of assets on its books.

The higher the sales-to-assets ratio, the better the company is performing. However, similar to many other ratios, the asset turnover ratio tends to be higher for companies in certain industries/sectors than in others. So, a company's sales-to-assets ratio should be compared with the same for its industry/sector.

Historical EPS Growth (3-5 Years): This is the average annual (trailing-12-month) EPS growth rate over the last 3-5 years. This metric helps investors see how a company's EPS has grown from a long-term perspective.

Note: There are many factors that can influence short-term numbers — a recession will reduce this number, while a recovery will inflate it. The longterm perspective helps smooth out short-term events.

Projected EPS Growth (F1/F0): This is the estimated EPS growth rate for the current financial year. It is calculated as the consensus estimate for the current fiscal year (F1) divided by the reported EPS for the last completed fiscal year (F0).

Current Cash Flow Growth: It measures the latest year-over-year change in operating cash flow. Cash flow growth tells an investor how quickly a company is generating inflows of cash from operations. A positive change in the cash flow is desired and shows that more 'cash' is coming in than going out.

Historical Cash Flow Growth (3-5 Years): This is the annualized change in cash flow over the last 3-5 years. The change in a longer period helps put the current reading into proper perspective. By looking at the rate, rather than the actual dollar value, the comparison across the industry and peers becomes easier.

Projected Sales Growth (F1/F0): This metric looks at the estimated sales growth for the current year. It is calculated as sales estimate for the current fiscal year (F1) divided by the reported sales for the last completed fiscal year (F0).

Like EPS growth, a higher rate is better for sales growth. A look at a company's projected sales growth instantly tells you what the outlook is for their products and services. However, different sales growth rates are considered good for different industries, so it's better to compare sales growth rates of companies in the same industry group.

EPS F1 Estimate 1-Week Change: The percentage change in the Zacks Consensus EPS estimate for the current fiscal year over the past week. The change in a company's consensus EPS estimate (or earnings estimate revision) has proven to be strongly correlated with the near-term price movement of its shares. It is an integral part of the Zacks Rank.

If a stock's consensus EPS estimate is $1.10 now versus $1.00 a week ago, that will be reflected as a 10% upward revision. If, on the other hand, it went from $1.00 to 90 cents, that would be a 10% downward revision.

EPS F1 Estimate 4-Week Change: The percentage change in the Zacks Consensus EPS estimate for the current fiscal year over the past four weeks.

A stock's earnings estimate revision in a 1-week period is important. But it's more meaningful to look at the longer-term revision. And, of course, the 4-week change helps put the 1-week change into proper perspective.

EPS F1 Estimate 12-Week Change: The percentage change in the Zacks Consensus EPS estimate for the current fiscal year over the past 12 weeks.

This metric essentially shows how the consensus EPS estimate has changed over a period longer than 1 week or 4 weeks.

EPS Q1 Estimate Monthly Change: The percentage change in the Zacks Consensus EPS estimate for the current fiscal quarter over the past four weeks.

While the revision in consensus EPS estimate for the current fiscal year is strongly correlated with the near-term price movement of its shares, the estimate revision for the current fiscal quarter is an important metric as well, especially over the short term, and particularly as a stock approaches its earnings date. If a stock's Q1 EPS estimate decreases ahead of its earnings release, it's usually a negative sign, whereas an increase is a positive sign.