Amarin Corporation

Amarin Announces Plans to Maximize Blockbuster Potential of VASCEPA® (icosapent ethyl) in Europe

August 4, 2020

Amarin to Build Dedicated Organization to Retain Substantial Value of One of the Most Anticipated Cardiovascular Drug Products in Decades

Veteran Cardiovascular Commercial Executive Hired to Lead Focused Launch

DUBLIN, Ireland and BRIDGEWATER, N.J., Aug. 04, 2020 (GLOBE NEWSWIRE) -- Amarin Corporation plc (NASDAQ:AMRN), today announced the company's plans to undertake its own focused commercial launch of VASCEPA® (icosapent ethyl) in Europe. Amarin's plan is subject to review and approval of its Marketing Authorization Application (MAA) by the European Medicines Agency and the European Commission, respectively. The application is in the late stages of review for the reduction of cardiovascular (CV) risk in high-risk patients based on the REDUCE-IT® cardiovascular outcomes study.

"With more than 80 million people in Europe with cardiovascular disease [1], there is a significant and untapped market opportunity for a safe and effective treatment beyond conventional therapies for cardiovascular risk reduction for appropriate patients based on the REDUCE-IT study," said John Thero, president and chief executive officer, Amarin. "In anticipation of approval, we conducted an extensive evaluation of the commercial options for VASCEPA in Europe. Based on that analysis, we determined that a commercialization team within Amarin and dedicated to VASCEPA is the best choice to maximize the blockbuster potential of the drug in Europe. Amarin's plan will allow the company to retain substantially all of the economic benefits of this sizeable market opportunity in key regions within Europe and is expected to result in select partnering transactions in certain smaller countries. Amarin has the passion, commitment and in-depth understanding of the product and its unique cardiovascular benefits necessary for a commercial launch. We look forward to advancing VASCEPA through the regulatory process and maximizing the blockbuster potential of VASCEPA in Europe to help millions of patients in need."

Ten to eleven years of market protection is anticipated from regulatory exclusivity in connection with VASCEPA approval based on REDUCE-IT in Europe. Amarin has filed for additional patent protection, which has the potential to extend exclusivity into 2039.

Over the past year, Amarin has made considerable progress laying the foundation for a successful commercial launch in Europe. While not yet approved for sale in Europe, VASCEPA is already included in the medical treatment guidelines of the European Society of Cardiology (ESC) and the European Atherosclerosis Society. Amarin is also looking forward to supporting a series of robust clinical data presentations highlighting the role of VASCEPA in CV risk reduction at the ESC annual meeting later this month. In addition, Amarin has been conducting market analysis and payor access research in order to size the market opportunity and prepare for the reimbursement negotiations in the various countries.

To enable Amarin to deliver on its vision in Europe, the company announces its recent hiring of Karim Mikhail as senior vice president, commercial head Europe. Mr. Mikhail joins Amarin from THEODON, a global commercial strategy consultancy that he founded in 2018 and where he served as chief executive officer. Prior to that, he was with Merck for 22 years, in a career spanning seven different countries across three continents. His most recent role was global commercial leader for Merck's $4 billion lipid franchise, where he led the global launch of ezetimibe with the IMPROVE-IT study indication. Prior to that Mr. Mikhail was also chief marketing officer for Europe, Middle East and Africa and chief operating officer for emerging markets. While at Merck, Mr. Mikhail led the successful commercial launch of dozens of products, including ezetimibe and various molecules in diabetes, hypertension, immunology, and oncology.

At Amarin, Karim plans on selecting a team of highly talented professionals to fill key positions while leveraging third-party relationships to focus further on product reimbursement and launch plans. Reimbursement, which needs to be sought for VASCEPA on a country-by-country basis, should be supported by the drug' s demonstrated effectiveness and support from leaders in the medical community.

Based on its current plans and expectations, Amarin believes that its current capital resources are sufficient to achieve sustained positive cash flows from VASCEPA, including commercial launch of VASCEPA in Europe. Physician targets to be educated about VASCEPA in Europe tend to be more concentrated than in the United States. In addition, the efficiency of launching a product and educating physicians in Europe should be aided by innovations in digital communication and other forms of education and promotion.

"We are delighted to welcome Karim to the Amarin team," continued Mr. Thero. "He is an accomplished professional with a successful track record in building organizations and commercializing numerous products in Europe and internationally. Karim brings to Amarin extensive European regulatory experience, market access expertise and the commercial innovation needed to successfully launch VASCEPA in Europe. Importantly, Karim shares our vision and excitement for VASCEPA and its potential multi-billion-dollar market opportunity in Europe."

"Assuming market authorization is granted in early 2021, we look forward to the successful launch of VASCEPA as the first and only non-LDL lowering agent approved in Europe with a cardiovascular disease risk reduction indication as an adjunct to statin therapy in dyslipidemic patients," concluded Mr. Thero.

About Amarin

Amarin Corporation plc is a rapidly growing, innovative pharmaceutical company focused on developing and commercializing therapeutics to cost-effectively improve cardiovascular health. Amarin's lead product, VASCEPA (icosapent ethyl), is available by prescription in the United States, Canada, Lebanon, and the United Arab Emirates. Amarin, together with its commercial partners in select geographies, is pursuing additional regulatory approvals for VASCEPA in China, Europe, and the Middle East. For more information about Amarin, visit www.amarincorp.com.

About Cardiovascular Risk

The number of deaths in the United States attributed to cardiovascular disease continues to rise. There are 605,000 new and 200,000 recurrent heart attacks per year (approximately 1 every 40 seconds), in the United States. Stroke rates are 795,000 per year (approximately 1 every 40 seconds), accounting for 1 of every 19 U.S. deaths. Cardiovascular disease results in 859,000 deaths per year in the United States.[2] In aggregate, this is more than 2.4 million major adverse cardiovascular events per year from cardiovascular disease or, on average, 1 every 13 seconds in the United States alone.

Controlling bad cholesterol, also known as LDL-C, is one way to reduce a patient's risk for cardiovascular events, such as heart attack, stroke, or death. However, even with the achievement of target LDL-C levels, millions of patients still have significant and persistent risk of cardiovascular events, especially those patients with elevated triglycerides. Statin therapy has been shown to control LDL-C, thereby reducing the risk of cardiovascular events by 25-35%.[3] Significant cardiovascular risk remains after statin therapy. People with elevated triglycerides have 35% more cardiovascular events compared to people with normal (in range) triglycerides taking statins.[4,5,6]

About REDUCE-IT®

REDUCE-IT was a global cardiovascular outcomes study designed to evaluate the effect of VASCEPA in adult patients with LDL-C controlled to between 41-100 mg/dL (median baseline 75 mg/dL) by statin therapy and various cardiovascular risk factors including persistent elevated triglycerides between 135-499 mg/dL (median baseline 216 mg/dL) and either established cardiovascular disease (secondary prevention cohort) or diabetes mellitus and at least one other cardiovascular risk factor (primary prevention cohort).

REDUCE-IT, conducted over seven years and completed in 2018, followed 8,179 patients at over 400 clinical sites in 11 countries with the largest number of sites located within the United States. REDUCE-IT was conducted based on a special protocol assessment agreement with U.S. FDA. The design of the REDUCE-IT study was published in March 2017 in *Clinical Cardiology.*[7] The primary results of REDUCE-IT were published in *The New England Journal of Medicine* in November 2018.[8] The total events results of REDUCE-IT were published in the *Journal of the American College of Cardiology* in March 2019.[9] These and other publications can be found in the R&D section on the company's website at www.amarincorp.com.

About VASCEPA (icosapent ethyl) Capsules

VASCEPA (icosapent ethyl) capsules are the first-and-only prescription treatment approved by the U.S. FDA comprised solely of the active ingredient, icosapent ethyl (IPE), a unique form of eicosapentaenoic acid. VASCEPA was initially launched in the United States in 2013 based on the drug's initial U.S. FDA approved indication for use as an adjunct therapy to diet to reduce triglyceride levels in adult patients with severe (≥500 mg/dL) hypertriglyceridemia. Since launch in the U.S., VASCEPA has been prescribed over eight million times. VASCEPA is covered by most major medical insurance plans. The new, cardiovascular risk indication for VASCEPA was approved by the U.S. FDA in December 2019.

U.S. FDA Indications and Limitation of Use

VASCEPA is indicated:

- As an adjunct to maximally tolerated statin therapy to reduce the risk of myocardial infarction, stroke, coronary revascularization and unstable angina requiring hospitalization in adult patients with elevated triglyceride (TG) levels (≥ 150 mg/dL) and
  -- established cardiovascular disease or
  -- diabetes mellitus and two or more additional risk factors for cardiovascular disease.
- As an adjunct to diet to reduce TG levels in adult patients with severe (≥ 500 mg/dL) hypertriglyceridemia.

The effect of VASCEPA on the risk for pancreatitis in patients with severe hypertriglyceridemia has not been determined.

Important Safety Information

- VASCEPA is contraindicated in patients with known hypersensitivity (e.g., anaphylactic reaction) to VASCEPA or any of its components.
- VASCEPA was associated with an increased risk (3% vs 2%) of atrial fibrillation or atrial flutter requiring hospitalization in a double-blind, placebo-controlled trial. The incidence of atrial fibrillation was greater in patients with a previous history of atrial fibrillation or atrial flutter.
- It is not known whether patients with allergies to fish and/or shellfish are at an increased risk of an allergic reaction to VASCEPA. Patients with such allergies should discontinue VASCEPA if any reactions occur.
- VASCEPA was associated with an increased risk (12% vs 10%) of bleeding in a double-blind, placebo-controlled trial. The incidence of bleeding was greater in patients receiving concomitant antithrombotic medications, such as aspirin, clopidogrel or warfarin.
- Common adverse reactions in the cardiovascular outcomes trial (incidence ≥3% and ≥1% more frequent than placebo): musculoskeletal pain (4% vs 3%), peripheral edema (7% vs 5%), constipation (5% vs 4%), gout (4% vs 3%), and atrial fibrillation (5% vs 4%).
- Common adverse reactions in the hypertriglyceridemia trials (incidence ≥1% more frequent than placebo): arthralgia (2% vs 1%) and oropharyngeal pain (1% vs 0.3%).
- Adverse events may be reported by calling 1-855-VASCEPA or the FDA at 1-800-FDA-1088.
- Patients receiving VASCEPA and concomitant anticoagulants and/or anti-platelet agents should be monitored for bleeding.

Key clinical effects of VASCEPA on major adverse cardiovascular events are included in the Clinical Studies section of the prescribing information for VASCEPA, as set forth below:

Effect of VASCEPA on Time to First Occurrence of Cardiovascular Events in Patients with Elevated Triglyceride levels and Other Risk Factors for Cardiovascular Disease in REDUCE-IT

	VASCEPA		Placebo		VASCEPA vs Placebo
	N = 4089 n (%)	Incidence Rate (per 100 patient years)	N = 4090 n (%)	Incidence Rate (per 100 patient years)	Hazard Ratio (95% CI)
Primary composite endpoint					
Cardiovascular death, myocardial infarction, stroke, coronary revascularization, hospitalization for unstable angina (5-point MACE)	705 (17.2)	4.3	901 (22.0)	5.7	0.75 (0.68, 0.83)
Key secondary composite endpoint					
Cardiovascular death, myocardial infarction, stroke (3-point MACE)	459 (11.2)	2.7	606 (14.8)	3.7	0.74 (0.65, 0.83)
Other secondary endpoints					
Fatal or non-fatal myocardial infarction	250 (6.1)	1.5	355 (8.7)	2.1	0.69 (0.58, 0.81)
Emergent or urgent coronary revascularization	216 (5.3)	1.3	321 (7.8)	1.9	0.65 (0.55, 0.78)
Cardiovascular death [1]	174 (4.3)	1.0	213 (5.2)	1.2	0.80 (0.66, 0.98)
Hospitalization for unstable angina [2]	108 (2.6)	0.6	157 (3.8)	0.9	0.68 (0.53, 0.87)
Fatal or non-fatal stroke	98 (2.4)	0.6	134 (3.3)	0.8	0.72 (0.55, 0.93)

[1] Includes adjudicated cardiovascular deaths and deaths of undetermined causality.

[2] Determined to be caused by myocardial ischemia by invasive/non-invasive testing and requiring emergent hospitalization.

FULL VASCEPA PRESCRIBING INFORMATION CAN BE FOUND AT WWW.VASCEPA.COM.

Forward-Looking Statements

This press release contains forward-looking statements, including expectations regarding commercialization plans and anticipated regulatory approvals and pricing determinations in Europe and expectations related to exclusivity in various jurisdictions and associated business plans in various scenarios. These forward-looking statements are not promises or guarantees and involve substantial risks and uncertainties. Amarin's ability to effectively commercialize VASCEPA will depend in part on its ability to continue to effectively finance its business, efforts of third parties, its ability to create market demand for VASCEPA through education, marketing and sales activities, to achieve broad market acceptance of VASCEPA, to receive adequate levels of reimbursement from relevant third-parties, to develop and maintain a consistent source of commercial supply at a competitive price, to comply with legal and regulatory requirements in connection with the sale and promotion of VASCEPA and to secure and maintain exclusivity and patent protection for VASCEPA. Among the factors that could cause actual results to differ materially from those described or projected herein include the following: uncertainties associated generally with research and development, clinical trials and related regulatory approvals; the risk that sales may not meet expectations and related cost may increase beyond expectations; the risk that patents may be determined to not be infringed or not be valid in patent litigation and applications may not result in issued patents sufficient to protect the VASCEPA franchise. A further list and description of these risks, uncertainties and other risks associated with an investment in Amarin can be found in Amarin's filings with the U.S. Securities and Exchange Commission, including its most recent quarterly report on Form 10-Q. Existing and prospective investors are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. Amarin undertakes no obligation to update or revise the information contained in this press release, whether as a result of new information, future events or circumstances or otherwise. Amarin's forward-looking statements do not reflect the potential impact of significant transactions the company may enter into, such as mergers, acquisitions, dispositions, joint ventures or any material agreements that Amarin may enter into, amend or terminate.

Availability of Other Information About Amarin

Investors and others should note that Amarin communicates with its investors and the public using the company website (www.amarincorp.com), the investor relations website (investor.amarincorp.com), including but not limited to investor presentations and investor FAQs, Securities and Exchange Commission filings, press releases, public conference calls and webcasts. The information that Amarin posts on these channels and websites could be deemed to be material information. As a result, Amarin encourages investors, the media, and others interested in Amarin to review the information that is posted on these channels, including the investor relations website, on a regular basis. This list of channels may be updated from time to time on Amarin's investor relations website and may include social media channels. The contents of Amarin's website or these channels, or any other website that may be accessed from its website or these channels, shall not be deemed incorporated by reference in any filing under the Securities Act of 1933.

Amarin Contact Information

Investor Inquiries:
Elisabeth Schwartz
Investor Relations
Amarin Corporation plc
In U.S.: +1 (908) 719-1315
IR@amarincorp.com (Investor inquiries)

Lee M. Stern
Solebury Trout
In U.S.: +1 (646) 378-2992
lstern@soleburytrout.com

Media Inquiries:
Alina Kolomeyer
Communications
Amarin Corporation plc
In U.S.: +1 (908) 892-2028
PR@amarincorp.com (media inquiries)

References

[1] http://www.ehnheart.org/cvd-statistics.html

[2] American Heart Association. Heart Disease and Stroke Statistics—2020 Update: A Report From the American Heart Association. Circulation. 2020;141:e139–e596.

[3] Ganda OP, Bhatt DL, Mason RP, et al. Unmet need for adjunctive dyslipidemia therapy in hypertriglyceridemia management. J Am Coll Cardiol. 2018;72(3):330-343.

[4] Budoff M. Triglycerides and triglyceride-rich lipoproteins in the causal pathway of cardiovascular disease. *Am J Cardiol*. 2016;118:138-145.

[5] Toth PP, Granowitz C, Hull M, et al. High triglycerides are associated with increased cardiovascular events, medical costs, and resource use: A real-world administrative claims analysis of statin-treated patients with high residual cardiovascular risk. *J Am Heart Assoc*. 2018;7(15):e008740.

[6] Nordestgaard BG. Triglyceride-rich lipoproteins and atherosclerotic cardiovascular disease - New insights from epidemiology, genetics, and biology. *Circ Res*. 2016;118:547-563.

[7] Bhatt DL, Steg PG, Brinton E, et al., on behalf of the REDUCE-IT Investigators. Rationale and Design of REDUCE-IT: Reduction of Cardiovascular Events with Icosapent Ethyl–Intervention Trial. *Clin Cardiol*. 2017;40:138-148.

[8] Bhatt DL, Steg PG, Miller M, et al., on behalf of the REDUCE-IT Investigators. Cardiovascular Risk Reduction with Icosapent Ethyl for Hypertriglyceridemia. *N Engl J Med*. 2019;380:11-22.

[9] Bhatt DL, Steg PG, Miller M, et al., on behalf of the REDUCE-IT Investigators. Reduction in first and total ischemic events with icosapent ethyl across baseline triglyceride tertiles. *J Am Coll Cardiol*. 2019;74:1159-1161.