Amarin Corporation

Amarin Supports Latest Clinical Research Evaluating VASCEPA® (Icosapent Ethyl) in Patients with Persistent Cardiovascular Risk Presented at ESC Congress 2020, the Annual Meeting of the European Society of Cardiology

September 1, 2020

VASCEPA is the first and only agent studied on top of statin therapy reported to exhibit coronary plaque regression in hypertriglyceridemic patients

VASCEPA in REDUCE-IT® cardiovascular outcomes study achieved statistical significance for primary and secondary endpoints at predefined blinded first and second interim analyses that persisted at final analyses

VASCEPA demonstrated significantly greater benefits in total (first and subsequent) cardiovascular events vs. placebo across studied baseline statin types and prespecified baseline levels of triglycerides, LDL-C, and hsCRP and in patients with or without low HDL-C and elevated triglycerides at baseline

DUBLIN, Ireland and BRIDGEWATER, N.J., Sept. 01, 2020 (GLOBE NEWSWIRE) -- Amarin Corporation plc (NASDAQ:AMRN) supported new data, presented at ESC Congress 2020, the annual meeting of the European Society of Cardiology (ESC), held from August 29 - September 1, 2020, adding to the growing body of knowledge on VASCEPA® (icosapent ethyl) in patients at risk for major adverse cardiovascular events.

“Cardiovascular disease continues to impact and challenge us all,” said Craig Granowitz, M.D., Ph.D., Amarin’s senior vice president and chief medical officer. “We see the detrimental effects it has on patients and those who care for them, as well as healthcare systems around the world. Data presented at ESC Congress 2020 provides additional support for potential ways in which VASCEPA can help to alleviate the burden of the worldwide public health crisis that is cardiovascular disease.”

Key data presented at ESC Congress 2020

“Effect of Icosapent Ethyl on Progression of Coronary Atherosclerosis in Patients with Elevated Triglycerides on Statin Therapy: Final results of the EVAPORATE Study” – presented on behalf of all authors by Matthew Budoff, M.D., The Lundquist Institute

Highlights: VASCEPA demonstrated significant, 17% regression of low attenuation plaque (LAP) volume on multidetector computed tomography (MDCT) compared with placebo over 18 months.

A total of 80 patients were enrolled in the randomized, double-blind, placebo-controlled EVAPORATE trial. Patients had to have coronary atherosclerosis as documented by MDCT (1 or more angiographic stenoses with ≥20% narrowing), be on statin therapy, and have persistently elevated triglyceride (TG) levels (mean TG at baseline was 259.1 mg/dL [+/- 78.1]). Patients underwent an interim scan at 9 months and a final scan at 18 months. The prespecified primary endpoint was a comparison of change in LAP volume at 18 months between icosapent ethyl and placebo.

Final results showed a significant reduction in the primary endpoint; icosapent ethyl reduced LAP plaque volume by 17% from baseline to the 18-month scan, whereas there was a progression of LAP plaque volume in the placebo group. There were significant differences between icosapent ethyl and placebo at study end for secondary endpoints of other types of plaque volume changes, including and sequentially total, total non-calcified, fibrofatty, and fibrous plaque volumes. All of these forms of coronary plaque regressed in the icosapent ethyl group and progressed in the placebo group, ($p<0.01$ for all). The only secondary endpoint which did not achieve a significant difference between groups in multivariable modeling was dense calcium ($p=0.053$). VASCEPA is the first and only agent studied on top of statin therapy reported to exhibit coronary plaque regression in hypertriglyceridemic patients.

The presentation is available here and has been published in *European Heart Journal.*

“REDUCE-IT: Accumulation of Data Across Prespecified Interim Analyses to Final Results” – presented on behalf of all authors by Brian Olshansky, M.D., University of Iowa

Highlights: The presentation at ESC Congress 2020 was the first presentation of results from the pre-specified interim analyses for the landmark REDUCE-IT® cardiovascular outcomes study. An independent, unblinded DMC (Data and Safety Monitoring Committee) performed interim analyses of data during the REDUCE-IT cardiovascular outcomes study at approximately 60% and 80% (2.9 and 3.7 years of median primary endpoint follow-up, respectively), with a final analysis at 4.9 years median follow-up. Primary and key secondary endpoints were the reduction in the first occurrence of composite of 5-point (cardiovascular death, myocardial infarction [MI], stroke, coronary revascularization or unstable angina) and 3-point (cardiovascular death, MI, stroke) major adverse cardiovascular events (MACE).

Highly statistically significant outcomes were achieved for both primary and key secondary composite endpoints at the first interim, persisted at the second interim, and fully evolved at the final analysis. Consistent, statistically significant outcome measures demonstrating the robust and early benefit of icosapent ethyl were evident for the primary composite endpoint starting at 21 months, and for the key secondary composite endpoint at 25 months. Allowing the REDUCE-IT dataset to mature fully provided physicians and patients with robust, consistent, and reliable efficacy and safety data upon which to base clinical decisions for icosapent ethyl in cardiovascular risk reduction.

“REDUCE-IT: Total Ischemic Events Reduced Across the Full Range of Baseline LDL-Cholesterol and Other Key Subgroups” – presented on behalf of all authors by Deepak L. Bhatt, M.D., M.P.H., Brigham and Women’s Hospital

Highlights: VASCEPA administered at 4 g/day in the REDUCE-IT cardiovascular outcomes study, as previously reported, significantly reduced total ischemic events in statin-treated patients with elevated triglycerides and other cardiovascular risk factors despite well-controlled LDL-C (<100 mg/dL). Presented at ESC Congress 2020 was that, similar to the results of analyses of first occurrences of MACE, reductions in total (first and subsequent)

occurrences of MACE were observed across a variety of predefined subgroups, including baseline levels of triglycerides and LDL-C, with substantial reductions across already low LDL-C tertiles in both primary (5-point MACE) and key secondary (3-point MACE) endpoints, as well as in the subgroups with or without elevated hsCRP or low HDL and elevated triglycerides at baseline.

"Are the Results of Clinical Trials Relevant in The Real World? The Applicability of REDUCE-IT to the FAST-MI Registry." – presented on behalf of all authors by Jean Ferrières, M.D., M.Sc., FESC, Toulouse Rangueil University Hospital

Highlights: In order to evaluate the applicability of results of the REDUCE-IT cardiovascular outcomes study in a French population, the inclusion and exclusion criteria of this landmark study were applied to French patients who were admitted to coronary or intensive care units within 48 hours of symptom onset during a 1-month period (Registry on Acute ST-elevation and non-ST-elevation Myocardial Infarction (FAST-MI), 2010 and 2015). The results support that, even in this limited registry of patients, many French patients would qualify for the inclusion criteria of REDUCE-IT in which patients treated with VASCEPA experienced significant reductions in major adverse cardiovascular events.

"REDUCE-IT: Outcomes by Baseline Statin Type" – presented on behalf of all authors by Deepak L. Bhatt, M.D., M.P.H., Brigham and Women's Hospital

Highlights: The objectives of this analysis were to explore the impact of baseline and concomitant statin type on atherosclerotic cardiovascular disease (ASCVD) outcomes and on LDL-C and ApoB levels in the results of the REDUCE-IT cardiovascular outcomes study. The exploratory analysis examined the primary and key secondary endpoints of REDUCE-IT by individual statin type: atorvastatin, simvastatin, rosuvastatin, pravastatin, lovastatin, fluvastatin, or pitavastatin; and by statin category: lipophilic (i.e., hydrophobic: atorvastatin, simvastatin) vs. lipophobic (i.e., hydrophilic: rosuvastatin, pravastatin). Icosapent ethyl demonstrated similar benefits vs. placebo across all individual baseline statin types and both lipophilic and lipophobic statin categories. Individual baseline statin type and lipophilic/lipophobic category had no meaningful impact on the modest median LDL-C changes from baseline to 1 year and ApoB changes from baseline to 2 years observed with VASCEPA vs. placebo. Primary and key secondary composite endpoint outcomes and changes in LDL-C and ApoB by concomitant statin use yielded similar results. These data provide clinicians with additional insight regarding concomitant statin therapy considerations when prescribing icosapent ethyl and suggest there are important mechanisms of action for the substantial ASCVD risk reduction observed with VASCEPA that are distinct from the LDL-C receptor pathway.

All analyses highlighted above were funded by Amarin.

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. VASCEPA is not yet approved and available in any other countries. Amarin, on its own or 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.[1] In aggregate, there are more than 2.4 million major adverse cardiovascular events per year from cardiovascular disease or, on average, one 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%.[2] 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.[3,4,5]

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 FDA. The design of the REDUCE-IT study was published in March 2017 in *Clinical Cardiology.*[6] The primary results of REDUCE-IT were published in *The New England Journal of Medicine* in November 2018.[7] The total events results of REDUCE-IT were published in the *Journal of the American College of Cardiology* in March 2019.[8] 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 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 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, 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 FDA in December 2019.

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 statements regarding the potential impact of VASCEPA in various clinical uses. These forward-looking statements are not promises or guarantees and involve substantial risks and uncertainties. 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 and clinical trials such as further clinical evaluations failing to confirm earlier findings. 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.

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[7] 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.

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