Amarin Corporation

New 2019 Updates to the European Society of Cardiology's and European Atherosclerosis Society's Guidelines for the Management of Dyslipidaemias Incorporate Findings from the REDUCE-IT™ Cardiovascular Outcomes Study

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Clinical Practice Guidelines address how best to prevent cardiovascular events in high-risk patients with elevated triglycerides on statin treatment, among millions of people globally

BEDMINSTER, N.J., and DUBLIN, Ireland, Sept. 03, 2019 (GLOBE NEWSWIRE) -- Amarin Corporation plc (NASDAQ: AMRN), a pharmaceutical company focused on improving cardiovascular health, today announced that the European Society of Cardiology (ESC) and the European Atherosclerosis Society (EAS) have updated their Clinical Practice Guidelines for the Management of Dyslipidaemias. This 2019 update incorporates findings from the REDUCE-IT™[1,2] cardiovascular outcomes study and includes the recommendation that icosapent ethyl, 2g twice a day, should be considered for patients with cardiovascular disease who have triglyceride levels 135 mg/dL to 499 mg/dL despite statin treatment, which places them at high risk of cardiovascular events, such as heart attack, stroke or death.[3] This new recommendation incorporates icosapent ethyl specifically.

Icosapent ethyl, studied in a series of clinical trials, including the globally conducted REDUCE-IT study, was developed by Amarin and is exclusively marketed by Amarin and its commercial partners in capsule form under the brand name *Vascepa*® (icosapent ethyl). In the United States, *Vascepa* is currently approved as an adjunct to diet to reduce triglyceride levels in adult patients with severe (≥500 mg/dL) hypertriglyceridemia. Amarin has submitted a supplemental new drug application (sNDA) to the U.S. FDA for an expansion of the *Vascepa* U.S. FDA label based on the landmark REDUCE-IT results showing reduction of cardiovascular events in high risk patients. The company plans to submit an application seeking approval for icosapent ethyl in Europe for reducing cardiovascular events before the end of 2019. A similar application has already been submitted and is under priority review by Health Canada.

ESC and EAS do not provide endorsements or any form of certification for brand name commercial products. Accordingly, the inclusion of icosapent ethyl in the Clinical Practice Guidelines for the Management of Dyslipidaemias should not be understood as an endorsement or approval by ESC or EAS of *Vascepa*.

"We are pleased by ESC and EAS's acknowledgement of the significance of the REDUCE-IT results as evidenced by their 2019 updates of the Clinical Practice Guidelines for the Management of Dyslipidaemias," says Craig B. Granowitz, M.D., Ph.D., senior vice president and chief medical officer of Amarin. "Amarin believes strongly in the potential for icosapent ethyl to be an important treatment option for the millions of high-risk patients who are on statin therapy with controlled cholesterol levels, yet have elevated triglycerides and other cardiovascular risk factors. This update comes just weeks after the American Heart Association issued an advisory statement referencing REDUCE-IT and the cardiovascular risk-lowering effects of icosapent ethyl and months after the American Diabetes Association included the REDUCE-IT results as part of its updates to the Standards of Medical Care in Diabetes for 2019.[4, [5]] All of these updates further support the use of icosapent ethyl as an important treatment option for appropriate patients at high risk of cardiovascular events."

Based on the results of REDUCE-IT, the 2019 updates to the Clinical Practice Guidelines for the Management of Dyslipidaemias specifically recommend that:

In high-risk (or above) patients with TG [triglycerides] levels between 1.5 – 5.6 mmol/L (135-499 mg/dL) despite statin treatment, n-3 PUFAs [polyunsaturated fatty acids] (icosapent ethyl 2x2 g/day) should be considered with a statin.[6]

The ESC and EAS recommendation is classified as a IIa recommendation denoting that icosapent ethyl should be considered for treatment of such patients. The classification is a Level B recommendation which reflects a relatively high weight of scientific evidence under ESC and EAS standards. Such recommendations are supported by the results of the REDUCE-IT cardiovascular outcomes study.

In the United States, approximately 15 million people match the criteria of the REDUCE-IT studied population, with triglycerides ≥ 135 mg/dL and other cardiovascular risk factors, despite statin treatment.[7] About 25 percent of a representative sample survey of more than 7,800 patients from 27 European countries with coronary heart disease and controlled cholesterol levels had triglyceride levels of 150 mg/dL or greater, illustrating the potential pervasiveness of high-risk cardiovascular disease in Europe.[8]

"These updated guidelines from such prestigious organizations reaffirm the importance of the REDUCE-IT findings to patients globally, not only in enhancing care, but also in broadening awareness of the need for treatment among patients who may have their cholesterol controlled with a statin, but remain at risk because of elevated triglycerides," says Deepak L. Bhatt, M.D., M.P.H., executive director of Interventional Cardiovascular Programs at Brigham and Women's Hospital, professor of medicine at Harvard Medical School, and principal investigator and steering committee chair for REDUCE-IT. "Based on what we're learning from REDUCE-IT and the related guidance from ESC and EAS, I foresee the beginning of a global change in clinical practice in how best to treat patients with multifactorial risks of cardiovascular events beyond cholesterol management."

Amarin acknowledges the rigor with which the Clinical Practice Guidelines for the Management of Dyslipidaemias are crafted and approved by the ESC's and EAS's task force, which is comprised of more than 15 leading professionals in the European Union who specialize in the care of patients with dyslipidaemias.

The complete 2019 updates to the Clinical Practice Guidelines for the Management of Dyslipidaemias can be accessed online by clicking here.

About Amarin
Amarin Corporation plc. is a rapidly growing, innovative pharmaceutical company focused on developing therapeutics to improve cardiovascular

health. Amarin's product development program leverages its extensive experience in polyunsaturated fatty acids and lipid science. Vascepa (icosapent ethyl) is Amarin's first FDA-approved drug and is available by prescription in the United States, Lebanon and the United Arab Emirates. Amarin's commercial partners are pursuing additional regulatory approvals for Vascepa in Canada, China and the Middle East. For more information about Amarin, visit www.amarincorp.com.

REDUCE-IT™ Study
REDUCE-IT, an 8,179-patient cardiovascular outcomes study, was completed in 2018. REDUCE-IT was the first multinational cardiovascular outcomes study that evaluated the effect of prescription pure EPA therapy as an add-on to statins in patients with high cardiovascular risk who, despite stable statin therapy, had elevated triglyceride levels (at least 135 mg/dL). A large portion of the male and female patients enrolled in this outcomes study were diagnosed with type 2 diabetes.

More information on the REDUCE-IT study results can be found at www.amarincorp.com.

About Cardiovascular Disease
Worldwide, cardiovascular disease (CVD) remains the #1 killer of men and women. In the United States CVD leads to one in every three deaths – one death approximately every 38 seconds – with annual treatment cost in excess of $500 billion.[9,[10]]

Multiple primary and secondary prevention trials have shown a significant reduction of 25% to 35% in the risk of cardiovascular events with statin therapy, leaving significant persistent residual risk despite the achievement of target LDL-C levels.[11]

Beyond the cardiovascular risk associated with LDL-C, genetic, epidemiologic, clinical and real-world data suggest that patients with elevated triglycerides (TG) (fats in the blood), and TG-rich lipoproteins, are at increased risk for cardiovascular disease.[12, 13,[14],[15]]

About Vascepa® (icosapent ethyl) Capsules
Vascepa (icosapent ethyl) capsules are a single-molecule prescription product consisting of the omega-3 acid commonly known as EPA in ethyl-ester form. Vascepa is not fish oil, but is derived from fish through a stringent and complex FDA-regulated manufacturing process designed to effectively eliminate impurities and isolate and protect the single molecule active ingredient from degradation. Vascepa, known in scientific literature as AMR101, has been designated a new chemical entity by the FDA. Amarin has been issued multiple patents internationally based on the unique clinical profile of Vascepa, including the drug's ability to lower triglyceride levels in relevant patient populations without raising LDL-cholesterol levels.

The FDA has not reviewed and opined on a supplemental new drug application related to REDUCE IT. FDA has thus not reviewed the information herein or determined whether to approve Vascepa for use to reduce the risk of major adverse cardiovascular events in the REDUCE-IT patient population

Indication and Usage Based on Current FDA-Approved Label (not including REDUCE-IT results)

- Vascepa (icosapent ethyl) is indicated as an adjunct to diet to reduce triglyceride (TG) levels in adult patients with severe (≥500 mg/dL) hypertriglyceridemia.
- The effect of Vascepa on the risk for pancreatitis and cardiovascular mortality and morbidity in patients with severe hypertriglyceridemia has not been determined.

Important Safety Information for Vascepa Based on Current FDA-Approved Label (not including REDUCE-IT results) (Includes Data from Two 12-Week Studies (n=622) (MARINE and ANCHOR) of Patients with Triglycerides Values of 200 to 2000 mg/dL)

- Vascepa is contraindicated in patients with known hypersensitivity (e.g., anaphylactic reaction) to Vascepa or any of its components.
- In patients with hepatic impairment, monitor ALT and AST levels periodically during therapy.
- Use with caution in patients with known hypersensitivity to fish and/or shellfish.
- The most common reported adverse reaction (incidence >2% and greater than placebo) was arthralgia (2.3% for Vascepa, 1.0% for placebo). There was no reported adverse reaction >3% and greater than placebo.
- Adverse events and product complaints may be reported by calling 1-855-VASCEPA or the FDA at 1-800-FDA-1088. Patients receiving treatment with Vascepa and other drugs affecting coagulation (e.g., anti-platelet agents) should be monitored periodically.
- Patients should be advised to swallow Vascepa capsules whole; not to break open, crush, dissolve, or chew Vascepa.

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

Important Safety Information for Vascepa based on REDUCE-IT, as previously reported in The New England Journal of Medicine publication of the primary results of the REDUCE-IT study:

- Excluding the major adverse cardiovascular events (MACE) results described above, overall adverse event rates in REDUCE-IT were similar across the statin plus Vascepa and the statin plus placebo treatment groups.
- There were no significant differences between treatments in the overall rate of treatment emergent adverse events or serious adverse events leading to withdrawal of study drug.
- There was no serious adverse event (SAE) occurring at a frequency of >2% which occurred at a numerically higher rate in the statin plus Vascepa treatment group than in the statin plus placebo treatment group.
- Adverse events (AEs) occurring in 5% or greater of patients and more frequently with Vascepa than placebo were:
    - peripheral edema (6.5% Vascepa patients versus 5.0% placebo patients), although there was no increase in the

rate of heart failure in Vascepa patients
    - constipation (5.4% Vascepa patients versus 3.6% placebo patients), although mineral oil, as used as placebo, is known to lower constipation, and
    - atrial fibrillation (5.3% Vascepa patients versus 3.9% placebo patients), although there were reductions in rates of cardiac arrest, sudden death and myocardial infarctions observed in Vascepa patients
- There were numerically more SAEs related to bleeding in the statin plus Vascepa treatment group although overall rates were low with no fatal bleeding observed in either group and no significant difference in adjudicated hemorrhagic stroke or serious central nervous system or gastrointestinal bleeding events between treatments.
- In summary, Vascepa was well tolerated with a safety profile generally consistent with clinical experience associated with omega-3 fatty acids and current FDA-approved labeling of such products.

Important Cautionary Information About These Data
Further REDUCE-IT data assessment and data release could yield additional useful information to inform greater understanding of the trial outcome. For example, detailed data assessment by regulatory authorities, such as the FDA and Health Canada, will continue and take several months to complete and announce. The FDA advisory committee process and the final evaluation by regulatory authorities of the totality of efficacy and safety data from REDUCE-IT may include some or all of the following, as well as other considerations: new information or analyses affecting the degree of treatment benefit on studied endpoints; study conduct and data robustness, quality, integrity and consistency; additional safety data considerations and risk/benefit considerations; and consideration of REDUCE-IT results in the context of other clinical studies. Because regulatory reviews are typically fluid and not definitive interactions between sponsor and agency on individual elements of an application and related information, Amarin does not plan to update investors on ongoing communications with regulatory authorities. Amarin plans to announce the final outcome of such regulatory reviews when appropriate.

Forward-Looking Statements
This press release contains forward-looking statements, including statements regarding the use of Vascepa to potentially help millions of patients. 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, clinical trials and related regulatory reviews and approvals; the risk that data interpretations or other information from third parties, the regulatory review process, regulatory authorities and in connection with an advisory committee could be made public that are negative or may delay approval or limit Vascepa's marketability; the risk that special protocol assessment (SPA) agreements with the FDA are not a guarantee that FDA will approve a product candidate; the risk associated with the FDA's rescinding the REDUCE-IT SPA agreement; the risk related to FDA advisory committee meetings; and the risk that the FDA may not complete its review of the REDUCE-IT sNDA within the timing expected. 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.

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
investor.relations@amarincorp.com

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

Media Inquiries:
Gwen Fisher
Corporate Communications
Amarin Corporation plc
In U.S.: +1 (908) 325-0735
pr@amarincorp.com

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