Amarin Corporation

National Lipid Association's New Position Statement on Use of Icosapent Ethyl in High and Very-High-Risk Patients Recognizes Importance of Addressing Residual Cardiovascular Risk in Patients on Statins

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Millions of Patients on Statins with Elevated Triglycerides Are at Risk of Cardiovascular Events, Such as Heart Attack, Stroke or Death

Icosapent Ethyl Recognized as Only Non-LDL-Cholesterol Lipid Management Treatment with Cardiovascular Risk Reduction Outcomes Results

DUBLIN, Ireland and BRIDGEWATER, N.J., Sept. 16, 2019 (GLOBE NEWSWIRE) -- Amarin Corporation plc (NASDAQ: AMRN), a pharmaceutical company focused on improving cardiovascular health, today announced that the National Lipid Association (NLA) has issued a position statement recognizing the cardiovascular risk-lowering effects of icosapent ethyl based on the landmark REDUCE-IT™ cardiovascular outcomes study.

The NLA is recommending icosapent ethyl for atherosclerotic cardiovascular disease (ASCVD) risk reduction in high and very-high-risk patients, 45 years of age or older with clinical ASCVD, or 50 years of age or older with type 2 diabetes requiring medication and with ≥ 1 additional risk factor, and fasting triglycerides of 135-499 mg/dL on maximally tolerated statin, with or without ezetimibe. The NLA recommendation was issued as a Class I, Level B-R (STRONG) recommendation, its highest designation, for icosapent ethyl. The NLA is a leading professional society dedicated to enhancing the practice of lipid management in clinical medicine.

Icosapent ethyl – which has been extensively studied in a series of clinical trials, including the REDUCE-IT cardiovascular outcomes study[1,2] – was developed by Amarin and is exclusively marketed by Amarin and its commercial partners in capsule form under the brand name *Vascepa*®. In the United States, *Vascepa* is 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 a label expansion based on the landmark REDUCE-IT results showing reduction of cardiovascular events in high-risk patients. The Prescription Drug User Fee Act (PDUFA) target action date set by the FDA to act on the sNDA is December 28, 2019. Assuming FDA approval, *Vascepa* is positioned to become the first drug indicated to reduce residual cardiovascular risk in statin-managed patients with elevated triglycerides (135 mg/dL or greater) and other risk factors for cardiovascular disease. The approval of such label expansion and the wording of the indication statement is under regulatory review. Based on REDUCE-IT, *Vascepa* use was determined to be cost-effective by an independent third-party organization in the United States that assesses the economic value of drugs.

The NLA does not provide endorsements or any form of certification for brand name commercial products. Accordingly, the NLA position on icosapent ethyl should not be understood as an endorsement or approval by the NLA of *Vascepa*.

Antonio M. Gotto, Jr., M.D., D.Phil., FNLA, president of the National Lipid Association, stated: "The NLA has a long history in the atherosclerotic cardiovascular disease risk and triglyceride space. REDUCE-IT is an important contribution to our understanding of the use of omega-3 fatty acids in ASCVD risk reduction. The NLA has reviewed the existing data between ASCVD, hypertriglyceridemic patients, and high dose omega-3 fatty acids and recommends the use of icosapent ethyl in appropriate high and very-high-risk patients."

Craig B. Granowitz, M.D., Ph.D., senior vice president and chief medical officer of Amarin, said: "The NLA is uniquely focused on improving patient care by reducing atherosclerotic cardiovascular disease. To have this highly credible organization recognize the quality of the REDUCE-IT data and the potential of icosapent ethyl as a new treatment option for potentially millions of people on statins with elevated triglycerides who are at risk of cardiovascular events is tremendous. Icosapent ethyl is the only non-cholesterol lowering agent with demonstrated cardiovascular risk reduction outcomes results recommended for use by NLA."

In issuing its new position statement, the National Lipid Association joins the European Society of Cardiology, European Atherosclerosis Society, American Heart Association, and American Diabetes Association in recognizing the use of icosapent ethyl to reduce cardiovascular risks in appropriate patients on statins with elevated triglycerides.[3,4,5] Together, these organizations represent the world's leading medical bodies in management of cardiology and endocrinology.

In the United States, approximately 15 million people have triglycerides ≥ 135 mg/dL and other cardiovascular risk factors, despite statin treatment.[6] Cardiovascular risks for these patients include heart attack, stroke or death.

The "NLA Position on the Use of Icosapent Ethyl in High and Very-High-Risk Patients" was crafted and approved by the NLA's Board of Directors, comprised of leading experts who specialize in clinical lipidology. The position statement will be submitted for publication in the NLA's *Journal of Clinical Lipidology*.

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.[7,8]

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.[9]

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.[10,11,12,13]

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 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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