Amarin Corporation

Amarin Announced FDA Advisory Committee Voted Unanimously (16-0) to Recommend Approval of Vascepa® (icosapent ethyl) Capsules Label Expansion to Reduce Cardiovascular Risk Based on Landmark REDUCE-IT® Outcomes Trial

November 14, 2019

- ***Cardiovascular disease events like heart attacks, stroke and death affect millions of patients in the United States and are estimated to cost $500 billion annually***
- ***Millions of high-risk patients with cardiovascular disease could benefit from this cost-effective therapy if expanded label receives FDA approval; PDUFA date is December 28***

DUBLIN, Ireland and BRIDGEWATER, N.J., Nov. 14, 2019 (GLOBE NEWSWIRE) -- Amarin Corporation plc (NASDAQ: AMRN) today announced that the Endocrinologic and Metabolic Drugs Advisory Committee (EMDAC) of the U.S. Food and Drug Administration (FDA) has voted unanimously (16-0) to recommend approval of an indication and label expansion for *Vascepa*® (icosapent ethyl) capsules to reduce the risk of cardiovascular events in high-risk patients based on results from the landmark REDUCE-IT®[1] cardiovascular outcomes trial.

The FDA is not bound by the recommendations of an advisory committee. Amarin plans to work with the agency as it completes its review of the company's application seeking an appropriate label expansion for *Vascepa* to reflect REDUCE-IT results.

Cardiovascular disease is the number one cause of death for men and women in the United States and the nation's costliest disease, with direct and indirect expenses in excess of $500 billion each year.[2] An independent drug pricing watchdog group concluded that *Vascepa* is cost effective for cardiovascular risk reduction as demonstrated in REDUCE-IT even under the most stringent standards of that group, a result rarely achieved in its analyses.[3]

"Today we moved an important step closer to potentially helping millions of patients who are at risk for cardiovascular events despite being on standard-of-care statin therapy," said John F. Thero, president and chief executive officer of Amarin. " *Vascepa* is positioned to be the first approved treatment to reduce cardiovascular events in the group of at-risk patients studied in the landmark REDUCE-IT clinical trial. We appreciate both the opportunity to present these results and the committee's strong vote of confidence. We look forward to anticipated labeling discussions with the FDA, and we continue to prepare for the launch of *Vascepa* assuming FDA approval of our sNDA on or before the target PDUFA date of December 28."

Deepak L. Bhatt, M.D., M.P.H., executive director of Interventional Cardiovascular Programs at Brigham and Women's Hospital Heart and Vascular Center, and professor of medicine at Harvard Medical School, said: "The REDUCE-IT results are quite remarkable and illustrate how icosapent ethyl could transform the treatment of cardiovascular disease in the United States and worldwide. From my perspective as not only a researcher but also a practicing physician, icosapent ethyl represents one of the most important developments in the prevention and treatment of cardiovascular disease since statins and, if FDA approved, will be a critical tool for physicians to use to help prevent cardiovascular events such as heart attack and stroke, including fatal ones, in high-risk patients."

"Amarin thanks the patients, advocacy groups, physicians, researchers, and others who expressed overwhelming support for *Vascepa* through their written and in person comments at the advisory committee meeting," Thero said. "We also recognize the contributions of the 8,179 patients who participated in REDUCE-IT, some for over six years. Thousands of patients and professionals contributed to the REDUCE-IT results. We look forward to having their sacrifices and contributions reflected in an expanded indication for *Vascepa* that has the potential to benefit millions of patients."

About REDUCE-IT®

REDUCE-IT was a global cardiovascular outcomes study designed to prospectively 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). The REDUCE-IT®[4] cardiovascular outcomes trial study was conducted over seven years, completed in 2018, and 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*[4] and can be found in the R&D section on the company's website at www.amarincorp.com. The primary results of REDUCE-IT were published in *The New England Journal of Medicine* in November 2018.[5]

About Cardiovascular Risk

The number of deaths in the United States attributed to cardiovascular disease continues to rise.[6,7] 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 similar, accounting for 1 of every 19 U.S. deaths (approximately 1 every 40 seconds).[8]

Controlling bad cholesterol, also known as LDL-C, is one way to reduce a patient's risk for cardiovascular events. 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 high triglycerides, a type of fat in the blood. Statin therapy has been shown to control LDL-C, thereby reducing the risk of cardiovascular events by 25-35% – but that still leaves a 65-75% risk remaining.[9] People with high triglycerides have 35% more cardiovascular events compared to people with normal (in range) triglycerides taking stains.[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 (known as icosapent ethyl or IPE). *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 the information herein or determined whether to approve *Vascepa* for use to reduce the risk of major adverse cardiovascular events as studied in REDUCE-IT.

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.

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.

Forward-Looking Statements

This press release contains forward-looking statements, including statements regarding the use of *Vascepa* to potentially help millions of patients and expectations regarding regulatory review. 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 and the scope of any granted new indication from regulatory

reviews and approvals; 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; 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.

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