Amarin Corporation

New Analysis Shows Icosapent Ethyl (Vascepa®) Is Cost Effective and Offers Rare Finding of Better Outcomes at Lower Healthcare Costs When Used to Treat High-Risk Patients with Cardiovascular Disease or Diabetes and Other Risk Factors

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Projected Lifetime Healthcare Costs of High-Risk Patients on Conventional Medical Therapy, such as Statins, Were Compared with and without the Cardiovascular Risk Reduction Demonstrated with Icosapent Ethyl in the REDUCE IT® Study

Analysis Accounted Patient Treatment Outcomes as Well as U.S. Private Insurance and Medicare Costs

DUBLIN, Ireland and BRIDGEWATER, N.J., Nov. 11, 2019 (GLOBE NEWSWIRE) -- Amarin Corporation plc (NASDAQ: AMRN) announced today a summary of results from a patient-level, cost-effectiveness analysis of icosapent ethyl (*Vascepa*®).[1] This comprehensive analysis evaluated the cost-effectiveness of icosapent ethyl in reducing cardiovascular (CV) risk among high-risk patients as demonstrated in the landmark REDUCE-IT®[2] cardiovascular outcomes study. In this newly reported analysis, use of icosapent ethyl was projected to not only be cost-effective but also to reduce long-term health care costs in a majority of the scenarios analyzed.

The findings were disclosed in an abstract titled, “Cost-Effectiveness of Icosapent Ethyl in REDUCE-IT,” in connection with the 2019 Scientific Sessions of the American Heart Association (AHA), scheduled for November 16 – 18 in Philadelphia, PA. William S. Weintraub, M.D., director of Outcomes Research with MedStar Cardiovascular Research Network, and lead author of the analysis, is scheduled to present the results in more detail at AHA on Saturday, November 16, at 7:30 a.m.

Dr. Weintraub and the MedStar Cardiovascular Research Network, known for conducting thoughtful pharmacoeconomic analysis, used available data for cost information for treatment and rehabilitation of patients from stroke, myocardial infarction, revascularization, hospitalization and cardiovascular death and assessed how such costs decline relative to the cost of patient treatment with icosapent ethyl based on the results of the REDUCE-IT study.

Background: Despite statin therapy and well-controlled LDL-C, many high CV risk patients continue to experience CV events. This “persistent” CV risk was evaluated via REDUCE-IT, which enrolled statin-treated patients with controlled LDL-C (>40 - ≤100 mg/dL) and elevated triglycerides (≥135 - <500 mg/dL), with established CV disease or diabetes combined with other CV risk factors. Over 4.9 years median follow-up, REDUCE-IT showed that icosapent ethyl lowered risk of first and total CV events by 25% and 30%, respectively.

In REDUCE-IT, adverse events occurring with icosapent ethyl use at greater than 5% and greater than placebo were: peripheral edema (6.5% *Vascepa* versus 5.0%), although there was no increase in the rate of heart failure in *Vascepa* patients; constipation (5.4% *Vascepa* versus 3.6%), although mineral oil, as used as placebo, is known to lower constipation; and atrial fibrillation (5.3% *Vascepa* versus 3.9%), although there were reductions in rates of cardiac arrest, sudden death and myocardial infarctions observed in *Vascepa* patients. More information on safety data associated with REDUCE-IT is provided further below.

Methods: The analysis applied treatment effects from REDUCE-IT, health care costs from national sources, including private insurance and Medicare, and conducted a combination cost-effectiveness analysis utilizing both patient-level in-trial cost and clinical outcomes and long-term costs, events and life expectancy derived from Markov simulation models. The model projected lifetime healthcare costs, CV events, survival and quality-adjusted life-years (QALYs) for icosapent ethyl versus placebo in REDUCE-IT eligible patients.

Results: Icosapent ethyl was a dominant strategy (i.e., cost saving) in 70% of simulations, offering the rare finding of better outcomes at lower healthcare costs. In probabilistic sensitivity analysis, >85% of simulations indicated that icosapent ethyl would be cost-effective (i.e., below $50,000 per QALY gained) compared with placebo.

Conclusion: In this combined patient-level and simulation cost-effectiveness analysis, icosapent ethyl in high CV risk patients shows exceptional benefit with CV event reduction as well as cost-savings in-trial and over patients’ lifetime in the majority of simulations.

John Thero, president and chief executive officer of Amarin, developer of *Vascepa*, commented, “This analysis helps to validate something we’ve long believed, and that is central to our mission. It is possible to deliver significant innovation that meaningfully addresses our nation’s most prevalent and costly health epidemic, reduces impacts on patients and families, *and* drives down costs longer term in the health system. We are working to make this therapy broadly available for improved patient care in high risk patients subject to appropriate regulatory review.”

Other Considerations:
MedStar Cardiovascular Research Network (MedStar), which conducted this cost-effectiveness analysis, led by its director of Outcomes Research, Dr. Weintraub, is an organization dedicated to fighting heart disease, stroke and other conditions affecting the heart and blood vessels and is affiliated with MedStar Health Research Institute and Medstar Health. Amarin funded this analysis.

The patient cost and actuarial information used by MedStar in this cost-effective analysis were derived from sources independent of Amarin. Data regarding cardiovascular risk reduction demonstrated by *Vascepa* was sourced from previously published information from the total cohort of the REDUCE-IT study (not from the REDUCE-IT USA cohort published today in *Circulation*[3] which showed even more pronounced results albeit subject to the limitations of subset analysis) with support provided by Amarin in making the data available to MedStar for analysis. Included in this data was outcomes results pertaining to first occurrences of cardiovascular events and recurrent events. As disclosed in the publication of the recurrent events analysis in the *Journal of the American College of Cardiology*[4], the analyses addressed tertiary or exploratory endpoints using a series of statistical models, most of which were prespecified and one of which was post hoc. Each recurrent event statistical model has inherent strengths and weaknesses, with no single model considered definitive or outperforming the other models, as this is an evolving field of science. Nonetheless, results

from the total primary and total key secondary endpoint events analyses are consistent across the various recurrent event statistical models and are also consistent with the original primary and secondary endpoint results.

Furthermore, the cost-effectiveness analysis conducted by MedStar, as is typical of cost-effectiveness analyses, was not prespecified. Amarin funded MedStar because of its expertise to conduct this analysis, as opposed to Amarin conducting it on its own, to mitigate perceptions of potential bias inherent in post hoc analyses.

This press release is timed today pursuant to AHA's release of an abstract for this presentation. It is Amarin's understanding that AHA plans to release abstracts for some but not all (e.g. not any presentation deemed a "late breaker," such as the presentation regarding EVAPORATE) of the seven scientific presentations Amarin listed in its press release dated November 4, 2019. Without potentially jeopardizing presentation at AHA, Amarin looks forward to communications regarding all of these presentations pursuant to their presentation at AHA.

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.

About REDUCE-IT®
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 proportion 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.[5,6]

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.[7]

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.[8,9,10,11]

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 completed its review and made a final determination on a supplemental new drug application related to REDUCE IT. FDA has 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 are expected to 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 time 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 is anticipated to 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. More detailed presentation of such considerations is set forth in the risk factors section of Amarin's Quarterly Report on Form 10-Q filed with the U.S. Securities and Exchange Commission. 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 further 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 and projections related to the cost-effectiveness of *Vascepa*. 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.

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