Amarin Highlights Key REDUCE-IT®-Related Data Presented at American Heart Association 2019 Scientific Sessions

November 18, 2019

REDUCE-IT USA results, in prespecified subgroup analyses, showed cardiovascular risk reductions across all endpoints, including 30% relative risk reduction in all-cause mortality

New analysis determined icosapent ethyl (Vascepa®) is highly cost-effective in patients from the REDUCE-IT study and, as is rarely found, may result in net healthcare cost-savings to patients, payers and society

Data showed prevalence of elevated risk of major cardiovascular events (mean 10-year ASCVD risk score greater than 20%) in more than 20% of patients on statins with triglycerides below 150 mg/dL

Interim EVAPORATE study provides important mechanistic data with relevance to the reduction in cardiovascular events seen in the REDUCE-IT clinical trial; final study results likely in early 2020

DUBLIN, Ireland and BRIDGEWATER, N.J., Nov. 18, 2019 (GLOBE NEWSWIRE) -- Amarin Corporation plc (NASDAQ: AMRN), a pharmaceutical company focused on improving cardiovascular health, hosted a webcast today to discuss important data with study authors who presented at the American Heart Association 2019 Scientific Sessions, November 16-18. The data covered related to *Vascepa*® (icosapent ethyl) capsules, the landmark clinical outcomes study REDUCE-IT®[1] , as well as the cardiovascular risk of patients with elevated triglycerides, a type of fat in the blood.

"The more we study the REDUCE-IT data and the at-risk conditions of the patients studied in this important clinical trial, the better we understand the nature and extent of persistent cardiovascular risk among patients on statins and with elevated triglycerides, and how to address it," said Craig Granowitz, M.D., Ph.D., chief medical officer, Amarin. "At Amarin, we are proud to have played a role in supporting and sharing data with the scientific and medical communities that could make a major difference in cardiovascular care, an area where the need for new and innovative treatment options is urgent and growing."

About Cardiovascular Risk

The number of deaths in the United States attributed to cardiovascular disease continues to rise.[2,][3] 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).[4]

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 high triglycerides. Statin therapy has been shown to control LDL-C, thereby reducing the risk of cardiovascular events by 25-35% – but that still leaves 65-75% risk remaining.[5] People with high triglycerides have 35% more cardiovascular events compared to people with normal (in range) triglycerides taking statins.[6,][7],[8]

Key Data Presented at AHA and Reviewed During Amarin's Webcast

- **"REDUCE-IT USA: Results from the 3,146 Patients Randomized in the United States,"** – presented by Deepak L. Bhatt, M.D., M.P.H., Brigham and Women's Hospital and Harvard Medical School.

  Highlights: This prespecified REDUCE-IT subgroup analysis showed substantial risk reductions in the USA patients treated with icosapent ethyl 4 g/day versus placebo across all prespecified composite and individual primary and secondary endpoints, including 31% relative risk reduction and 6.5% absolute risk reduction in first occurrence of 5-point major adverse cardiovascular events (MACE), corresponding to a number needed to treat of 15 (NNT=15), and a significant 30% relative and 2.6% absolute risk reduction (NNT=39) in all-cause mortality in the USA subgroup.

  Additional prespecified cardiovascular endpoints in which the REDUCE-IT USA subgroup showed significant relative risk reduction included myocardial infarction, cardiovascular death, and stroke, similar to the full cohort in the overall REDUCE-IT global results. These results were incremental to the cardiovascular risk reduction achieved by conventional therapy administered to the high-risk patients studied, including incremental to statin therapy.

  The REDUCE-IT USA subgroup consisted of 3,146 patients (nearly 40%) of the previously reported full trial cohort. REDUCE-IT was not specifically powered to examine individual subgroups. P-values presented for the USA subgroup are nominal and exploratory with no adjustment for multiple comparisons. Differences in efficacy outcomes for the USA

patients are best viewed as qualitative and not quantitative; nevertheless, the data are useful and provide reassurance that the results in the USA are at least as strong as the results seen outside the USA and in the trial overall.

The REDUCE-IT USA study results were also published in *Circulation*, AHA's official scientific journal. [9]

- **"Cost-Effectiveness of Icosapent Ethyl in REDUCE-IT,"** – presented by William S. Weintraub, M.D., MedStar Washington Hospital.

  Highlights: In this combined patient-level and simulation lifetime cost-effectiveness analysis, icosapent ethyl in high cardiovascular risk patients shows exceptional benefit with cardiovascular event reduction as well as cost-savings in-trial and over patients' lifetime in many simulations. Findings of potential cost effectiveness of a medical therapy are rare. This analysis considered the current market cost for *Vascepa* and the potential savings from avoiding major adverse cardiovascular events, such as strokes and heart attacks, the cost of which can be high. This cost-effectiveness analysis was conducted by MedStar. As is typical, the cost-effectiveness analyses were not prespecified as part of the REDUCE-IT clinical trial design but did rely on the results of this landmark outcomes study.

- **"Many Statin Treated Persons with Borderline Triglyceride Levels are at Risk of ASCVD,"** – presented by Nathan D. Wong, Ph.D., M.P.H, University of California, Irvine.

  Highlights: This study showed prevalence of elevated risk of major cardiovascular events (a mean 10-year atherosclerotic cardiovascular disease (ASCVD) risk score greater than 20%) in more than 20% of patients on statins with triglycerides below 150 mg/dL. This suggests the need for greater lifestyle and other therapies to address remaining residual ASCVD risk.

- **"Effect of Icosapent Ethyl on Progression of Coronary Atherosclerosis in Patients with Elevated Triglycerides (200 – 499 mg/dL) on Statin Therapy (EVAPORATE) study,"** – presented by Matthew J. Budoff, M.D., Los Angeles Biomedical Research.

  Highlights: At the prespecified 9-month interim analysis, there was slowing of total non-calcified plaque (sum of LAP, fibrofatty, and fibrous plaque) (35% v. 43%, p=0.010), total plaque (non-calcified + calcified plaque) (p=0.0004), fibrous plaque (15% v. 26%, p=0.011) and calcified plaque (-1% v. 9%, p=0.001), after adjustment by baseline plaque, age, sex, diabetes status, baseline triglyceride levels, and statin use. However, there was no significant change in the primary endpoint of low attenuation plaque between active and placebo groups (74% vs 94%, p=0.469) at this 9-month interim look. This investigator-initiated study is continuing to its designed completion of an 18-month review.

  EVAPORATE is the first study in the United States, which enrolled a total of 80 patients, to use multidetector computed tomography (MDCT) to evaluate the effects of icosapent ethyl as an adjunct to statin therapy on plaque characteristics in a high cardiovascular-risk population with persistent high triglyceride levels. Patients underwent interim scans at 9 months and are currently being followed for an additional 9 months with MDCT. Final results from this study are anticipated in early 2020.

  Arterial plaque and coronary atherosclerosis are key factors leading to significant increases in the probability of acute obstructions and angina or other coronary artery disease signs and symptoms.

All of the analyses highlighted above were funded by Amarin.

A replay of the webcast will be available for two weeks following the webcast. To hear a replay of the webcast, dial 877-481-4010 (inside the United States) or 919-882-2331 (outside the United States). A replay of the webcast is also be available through the company's website, Amarincorp.com, in the Investor section. For both dial-in numbers please use conference ID 55923.

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 cardioprotective effect of icosapent ethyl, a unique prescription therapy, as an add-on to statins in patients with high cardiovascular risk. As defined in the published results of the study, the high cardiovascular risk patients, despite stable statin therapy, had elevated triglyceride levels (lower enrollment target of TG ≥135 mg/dL). As per the study's design, approximately 71% of the enrolled patients had established cardiovascular disease and the other patients were diagnosed, as per trial enrollment requirements, as having diabetes and other cardiovascular risk factors.

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

About *Vascepa*® (icosapent ethyl) Capsules
Vascepa (icosapent ethyl) capsules are a single-molecule prescription product which has been developed and studied for more than a decade and has been prescribed more than 8 million times in the United States. *Vascepa*, known in scientific literature as AMR101, has been designated a new chemical entity by the FDA. Amarin has been issued multiple patents in the United States and 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 or 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. 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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References

[1] Bhatt DL, Steg PG, Miller M, et al. Cardiovascular Risk Reduction with Icosapent Ethyl for Hypertriglyceridemia. N Engl J Med 2019;380:11-22.

[2] American Heart Association. Heart Disease and Stroke Statistics – 2019 Update: A Report from the American Heart Association. Published January 31, 2019.

[3] American Heart Association / American Stroke Association. 2017. Cardiovascular disease: A costly burden for America projections through 2035.

[4] American Heart Association: Heart Disease and Stroke Statistics -- 2019 At-a-Glance.

[5] Ganda OP, Bhatt DL, Mason RP, et al. Unmet need for adjunctive dyslipidemia therapy in hypertriglyceridemia management. J Am Coll Cardiol. 2018;72(3):330-343.

[6] Budoff M. Triglycerides and triglyceride-rich lipoproteins in the causal pathway of cardiovascular disease. Am J Cardiol.

2016;118:138-145.

[7] Toth PP, Granowitz C, Hull M, et al. High triglycerides are associated with increased cardiovascular events, medical costs, and resource use: A real-world administrative claims analysis of statin-treated patients with high residual cardiovascular risk. J Am Heart Assoc. 2018;7(15):e008740.

[8] Nordestgaard BG. Triglyceride-rich lipoproteins and atherosclerotic cardiovascular disease - New insights from epidemiology, genetics, and biology. Circ Res. 2016;118:547-563.

[9] Bhatt DL, Miller M, Brinton EA, et al. REDUCE-IT USA: Results from the 3,146 Patients Randomized in the United States. Circulation 2019. DOI: 10.1161/CIRCULATIONAHA.119.044440.