Amarin Corporation

REDUCE-IT® USA Results, in Prespecified Subgroup Analyses of Landmark REDUCE-IT Global Study, Showed Robust Cardiovascular Risk Reductions Across a Variety of Study Endpoints, Including Cardiovascular Death and All-Cause Mortality

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Prespecified Analysis of 3,146 Patients in the USA Enrolled in REDUCE-IT Showed 31% Relative Risk Reductions for First Occurrence of Both 5-Point MACE and 3-Point MACE

Significant Reductions Shown in All Predefined Composite and Individual Cardiovascular Endpoints, Including Cardiovascular Death and All-Cause Mortality

Tolerability and Safety Findings Consistent with Full Study

Results Published Today in *Circulation* and Scheduled for Presentation at American Heart Association 2019 Scientific Sessions on November 17

DUBLIN, Ireland and BRIDGEWATER, N.J., Nov. 11, 2019 (GLOBE NEWSWIRE) -- Amarin Corporation plc (NASDAQ: AMRN) announced today the results from the subgroup of 3,146 patients randomized in the United States within the global *Vascepa*® (icosapent ethyl) cardiovascular (CV) outcomes trial, REDUCE-IT®. This prespecified REDUCE-IT subgroup analysis showed robust 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=38) 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.[1] 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.

In the REDUCE-IT USA subgroup, 3,146 patients (38.5% of the full trial cohort) were randomized and followed for a median of 4.9 years; 32.3% were women, 9.7% Hispanic. USA placebo patients had a higher primary endpoint event rate compared with the full cohort (67.4 versus 57.4 per 1,000 patient-years, respectively). The primary endpoint (5-point MACE) occurred in 24.7% of placebo versus 18.2% of icosapent ethyl patients (HR 0.69, 95% CI 0.59-0.80, p=0.000001); the key secondary endpoint (3-point MACE) occurred in 16.6% of placebo versus 12.1% of icosapent ethyl patients (HR 0.69, 95% CI 0.57-0.83, p=0.00008). All prespecified hierarchical primary and secondary endpoints were significantly reduced in the USA subgroup, including myocardial infarction (8.8% to 6.7%, HR 0.72, 95% CI 0.56-0.93, p=0.01), cardiovascular death (6.7% to 4.7%, HR 0.66, 95% CI 0.49-0.90, p=0.007), stroke (4.1% to 2.6%, HR 0.63, 95% CI 0.43-0.93, p=0.02), and all-cause mortality (9.8% to 7.2%, HR 0.70, 95% CI 0.55-0.90, p=0.004). In the full study cohort, there was a trend towards a reduction in all-cause mortality, with each of these other primary and secondary endpoints also achieving statistical significance in the full study cohort. Safety and tolerability findings in the USA subgroup were consistent with the full study 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 results are scheduled to be presented on Sunday, November 17 at the 2019 Scientific Sessions of the American Heart Association (AHA) in Philadelphia, PA. The REDUCE-IT USA study results were published today in *Circulation*, AHA's official scientific journal. [2] The global results of REDUCE-IT from the full cohort of the study were previously published in *The New England Journal of Medicine* for the first occurrence of the study's primary and secondary endpoints and results of the study's full cohort with respect to total events were previously published in *The Journal of American College of Cardiology*.[1,3] This newly published data in *Circulation* is the first publication of detailed results from the REDUCE-IT USA cohort.

Scientific presentation: The presentation of the REDUCE-IT USA results at AHA will be delivered by the Global Principal Investigator and Steering Committee Chair of the study, 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. Dr. Bhatt's featured presentation, titled "REDUCE-IT USA: Results from the 3,146 Patients Randomized in the United States," will be delivered on November 17, 4:20 - 4:25 p.m.

Dr. Bhatt stated: "The REDUCE-IT USA results confirm the findings of the global REDUCE-IT trial and further highlight the importance of the prevention of residual, or persistent, risk of cardiovascular events in statin-treated patients with only moderately increased triglycerides. The USA subgroup, which had more risk factors than the overall REDUCE-IT population, experienced particularly robust risk reduction from the use of icosapent ethyl in preventive cardiovascular care, including a statistically significant 30% reduction in death. These findings are also remarkable when you consider that in some multinational cardiovascular trials, patients in the United States experience less benefit."

Amarin perspective
"The results of the REDUCE-IT USA subgroup are further evidence of the robust and consistent nature of this landmark study and its applicability to typical clinical practice in the United States," stated Steven Ketchum, Ph.D., president of research and development and chief scientific officer of Amarin. "We believe that these very impressive results further validate that persistent cardiovascular risk beyond cholesterol management can be

significantly reduced with *Vascepa* in the high-risk patient population studied in REDUCE-IT."

The REDUCE-IT USA subgroup analysis was funded by Amarin. Dr. Bhatt receives research funding from Amarin that goes to Brigham and Women's Hospital.

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 icosapent ethyl (IPE) 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, prior to study enrollment, 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 costs in excess of $500 billion.[4,5]

Multiple primary and secondary prevention trials have shown a significant reduction in the risk of cardiovascular events with statin therapy, leaving significant persistent residual risk despite the achievement of target LDL-C levels.[6]

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.[7,8,9,10]

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. 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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