REDUCE-IT™ Cardiovascular Outcomes Study of Vascepa® (icosapent ethyl) Capsules Met Primary Endpoint

September 24, 2018

REDUCE-IT Is First Outcomes Study to Assess Treatment of Patients with LDL-C Controlled by Statin Therapy, Persistent Elevated Triglycerides and Other Cardiovascular Risk Factors

Results Specific to Pure EPA Vascepa at 4 Grams Daily

Conference Call Scheduled for Today, Monday, September 24, 2018 at 8:00 am ET

BEDMINSTER, N.J. and DUBLIN, Ireland, Sept. 24, 2018 (GLOBE NEWSWIRE) -- Amarin Corporation plc (NASDAQ:AMRN), announced today topline results from the Vascepa® cardiovascular (CV) outcomes trial, REDUCE-IT™, a global study of 8,179 statin-treated adults with elevated CV risk. REDUCE-IT met its primary endpoint demonstrating an approximately 25% relative risk reduction, to a high degree of statistical significance ($p<0.001$), in major adverse CV events (MACE) in the intent-to-treat patient population with use of Vascepa 4 grams/day as compared to placebo.

Patients enrolled in REDUCE-IT had LDL-C between 41-100 mg/dL (median baseline LDL-C 75 mg/dL) controlled by statin therapy and various cardiovascular risk factors including persistent elevated triglycerides (TGs) between 150-499 mg/dL (median baseline 216 mg/dL) and either established cardiovascular disease (secondary prevention cohort) or diabetes mellitus and at least one other CV risk factor (primary prevention cohort).

Key topline results include:

- Efficacy: Approximately 25% relative risk reduction, demonstrated to a high degree of statistical significance ($p<0.001$), in the primary endpoint composite of the first occurrence of MACE, including cardiovascular death, nonfatal myocardial infarction (MI), nonfatal stroke, coronary revascularization, or unstable angina requiring hospitalization. This result was supported by robust demonstrations of efficacy across multiple secondary endpoints.

- Safety: Vascepa was well tolerated with a safety profile consistent with clinical experience associated with omega-3 fatty acids and current FDA-approved labeling. The proportions of patients experiencing adverse events and serious adverse events in REDUCE-IT were similar between the active and placebo treatment groups. Median follow-up time in REDUCE-IT was 4.9 years.

Amarin is eager to share REDUCE-IT data in greater detail with both the medical community and regulatory authorities. REDUCE-IT results have been accepted for presentation at the 2018 Scientific Sessions of the American Heart Association (AHA) on November 10, 2018 in Chicago, Illinois. The presentation, classified as late breaking clinical trial results, is scheduled to commence at 2:16 pm Central Time and listed as Main Event 1 for the time frame. This acceptance as a presentation of late-breaking clinical trial results was granted based on the ability of REDUCE-IT to address a critical question in cardiovascular prevention.

“I look forward to the publication of these detailed REDUCE-IT results in a major peer-reviewed journal and to presenting them at the AHA in November,” stated Deepak L. Bhatt, MD, MPH, Professor of Medicine at Harvard Medical School, Executive Director of Interventional Cardiovascular Programs in the Heart and Vascular Center at Brigham and Women's Hospital, and the Principal Investigator and Steering Committee Chair for REDUCE-IT.

“Amarin expresses its great appreciation for all the people that brought REDUCE-IT to completion, especially the patients and investigators and their colleagues at clinical sites that participated in this study for many years,” stated Steven Ketchum, PhD, president of research and development and chief scientific officer of Amarin. “Amarin is also grateful to the U.S. Food and Drug Administration (FDA) for its continued encouragement and support toward study design and completion. REDUCE-IT was conducted under a special protocol assessment agreement with FDA that was re-affirmed in 2016.”

“We are delighted with these topline study results,” said John F. Thero, president and CEO of Amarin. “Given Vascepa is affordably priced, orally administered and has a favorable safety profile, REDUCE-IT results could lead to a new paradigm in treatment to further reduce the significant cardiovascular risk that remains in millions of patients with LDL-C controlled by statin therapy, as studied in REDUCE-IT.”

“Considered against the backdrop of multiple unsuccessful cardiovascular outcomes studies of earlier generation drug therapies, including multiple recent failed cardiovascular studies of omega-3 mixture products that contain the omega-3 acid DHA, REDUCE-IT topline results stand alone as positive and confirm our hypothesis that pure EPA Vascepa at 4 grams/day can provide additional cardiovascular risk reduction benefit on top of LDL-C control with standard of care statin therapy in studied patients,”

added Craig Granowitz, MD, PhD, senior vice president and chief medical officer of Amarin. “REDUCE-IT results cannot be generalized to fenofibrate, fish oil or omega-3 mixture products that contain DHA. The most relevant comparator study to REDUCE-IT is the Japan EPA lipid intervention study (JELIS), the 18,645 patient, open label, blinded endpoint outcomes study of EPA added to low-dose statin therapy, which showed cardiovascular event reduction in Japanese hypercholesterolemic patients of 19% in the overall population and 53% in a subgroup of patients with elevated TG levels and low HDL-C.”[1, 2, 3]

Commercial Expansion and Next Steps

As previously described, given the successful topline results of REDUCE-IT, Amarin is in the process of increasing the number of company sales representatives promoting Vascepa to over 400 people in the United States. This will provide a greater concentration of coverage in current sales territories and provide new coverage where Amarin currently does not have sales representatives.

In addition to sales force expansion in the United States, Amarin plans to work with its international partners to support regulatory efforts outside the United States based on REDUCE-IT results. As previously described in the months leading up to REDUCE-IT results, Amarin increased its Vascepa inventory levels in preparation for positive results.

Overall managed care insurance coverage for Vascepa has been broad. Amarin looks forward to working with insurance carriers to increase understanding of REDUCE-IT results and the potential benefits Vascepa could bring to many millions of patients.

REDUCE-IT Study Background

The REDUCE-IT cardiovascular outcomes study commenced in 2011, enrolled and followed 8,179 randomized patients, and was conducted based on a special protocol assessment agreement with FDA.

REDUCE-IT is the first global cardiovascular outcomes study to prospectively evaluate the effect of Vascepa, or any therapy, 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 TGs between 150-499 mg/dL (median baseline 216 mg/dL) and either established cardiovascular disease (secondary prevention cohort) or diabetes mellitus and at least one other CV risk factor (primary prevention cohort). The design of the REDUCE-IT cardiovascular outcomes 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 REDUCE-IT hypothesis tested whether additional cardiovascular risk reduction beyond LDL-C controlled with statin therapy could be achieved in high risk patients with the putative cardioprotective effects of Vascepa 4 grams/day. Independent of REDUCE-IT, Amarin has worked to further support the REDUCE-IT hypothesis with published scientific findings based on various degrees of evidence that show EPA may interrupt the atherosclerotic process (e.g., plaque formation and instability) by beneficially affecting cellular functions thought to contribute to atherosclerosis and cardiovascular events and by beneficially affecting lipid, lipoprotein and inflammation biomarkers.[5, 6, 7, 8, 9]

Financial Disclosure

Funding from Amarin was provided to Brigham and Women’s Hospital for Dr. Deepak L. Bhatt’s work as the REDUCE-IT study chair and international principal investigator.

Conference Call and Webcast Information

Amarin will host a conference call at 8:00 a.m. ET, September 24, 2018 to discuss this information. The call will be accessible through the investor relations section of the company’s website at www.amarincorp.com. The call can also be heard via telephone by dialing 877-407-8033. A replay of the call will be made available for a period of two weeks following the conference call. To hear a replay of the call, dial 877-481-4010 (inside the United States) or 919-882-2331 (outside the United States). A replay of the call will also be available through the company's website shortly after the call. For both dial-in numbers please use conference ID 37638.

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 lipid science and the potential therapeutic benefits of polyunsaturated fatty acids. 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 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.[10, 11]

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.[5]

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. [12, 13, 14, 15]

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. 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.

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.

Vascepa has been approved for use by the United States Food and Drug Administration (FDA) as an adjunct to diet to reduce triglyceride levels in adult patients with severe (≥500 mg/dL) hypertriglyceridemia. Nothing in this press release should be construed as promoting the use of Vascepa in any indication that has not been approved by the FDA.

Important Cautionary Information About Topline Results

Existing and prospective investors are cautioned not to place undue reliance on topline results. As with any topline cardiovascular outcomes study result, further REDUCE-IT data assessment and data release will yield additional useful information to inform greater understanding of the study outcome. Aspects that could change and impact the final evaluation of the totality of the efficacy/safety data from REDUCE-IT may include: the magnitude of the treatment benefit on the primary composite endpoint, its components, secondary endpoints and the primary and secondary risk prevention cohorts; consideration of which components of the composite or secondary endpoints have the most clinical significance; the consistency of the primary and secondary endpoints; the consistency of findings across cohorts and subgroups; tolerability and safety considerations and risk/benefit considerations; consideration of REDUCE-IT results in the context of other clinical studies; and study conduct and data quality, integrity and consistency.

Forward-Looking Statements

This press release contains forward-looking statements, including expectations regarding planned publication, scientific presentation, regulatory review and related timing thereof; expectations that REDUCE-IT results could lead to a new treatment paradigm in the patient population studied; plans for sales force, international and insurance coverage expansion. These forward-looking statements are not promises or guarantees and involve substantial risks and uncertainties. In addition, Amarin's ability to effectively commercialize Vascepa will depend in part on its ability to continue to effectively finance its business, efforts of third parties, its ability to create market demand for Vascepa through education, marketing and sales activities, to achieve market acceptance of Vascepa, to receive adequate levels of reimbursement from third-party payers, to develop and maintain a consistent source of commercial supply at a competitive price, to comply with legal and regulatory requirements in connection with the sale and promotion of Vascepa and to maintain patent protection for Vascepa. 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 approvals; the risk that sales may not meet expectations and related cost may increase beyond expectations; the risk that patents may not be upheld in patent litigation and applications may not result in

issued patents sufficient to protect the Vascepa franchise. 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 http://www.amarincorp.com/), the investor relations website (http://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.

References

[1] Yokoyama M, Origasa H, Matsuzaki M, et al. Effects of eicosapentaenoic acid on major coronary events in hypercholesterolaemic patients (JELIS): a randomised open-label, blinded endpoint analysis. *Lancet*. 2007;369(9567):1090-1098.

[2] Saito Y, Yokoyama M, Origasa H, et al. Effects of EPA on coronary artery disease in hypercholesterolemic patients with multiple risk factors: sub-analysis of primary prevention cases from the Japan EPA Lipid Intervention Study (JELIS). *Atherosclerosis*. 2008;200(1):135-140.

[3] Matsuzaki M, Yokoyama M, Saito Y, et al. Incremental effects of eicosapentaenoic acid on cardiovascular events in statin-treated patients with coronary artery disease. *Circ J.* 2009;73(7):1283-1290.

[4] Bhatt DL, Steg G, Brinton EA, et al. Rationale and design of REDUCE-IT: Reduction of Cardiovascular Events with Icosapent Ethyl–Intervention Trial. *Clinical Cardiology*. 2017;40:138-148.

[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] Borow KM, Nelson JR, Mason RP. Biologic plausibility, cellular effects, and molecular mechanisms of eicosapentaenoic acid (EPA) in atherosclerosis. *Atherosclerosis*. 2015;242(1):357-366.

[7] Nelson JR, Wani O, May HT, et al. Potential benefits of eicosapentaenoic acid on atherosclerotic plaques. *Vascul Pharmacol*. 2017;91:1–9.

[8] Mason RP, Dawoud H, Jacob RF, et al. Eicosapentaenoic acid improves endothelial function and nitric oxide bioavailability in a manner that is enhanced in combination with a statin. *Biomed Pharmacother*. 2018;103:1231-1237.

[9] Takamura M, Kurokawa K, Ootsuji H, et al. Long-term administration of eicosapentaenoic acid improves post-myocardial infarction cardiac remodeling in mice by regulating macrophage polarization. *J Am Heart Assoc*. 2017;6(2). pii: e004560.

[10] American Heart Association. 2018. Disease and Stroke Statistics-2018 Update.

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

[12] Budoff M. Triglycerides and triglyceride-rich lipoproteins in the causal pathway of cardiovascular disease. *Am J Cardiol*. 2016;118:138-145.

[13] 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.

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

[15] Nordestgaard BG, Varbo A. Triglycerides and cardiovascular disease. *Lancet.* 2014;384:626–635.

Amarin Contact Information

Investor Relations:
Elisabeth Schwartz
Investor Relations and Corporate Communications
Amarin Corporation plc
In U.S.: +1 (908) 719-1315
investor.relations@amarincorp.com

Lee M. Stern
Trout Group
In U.S.: +1 (646) 378-2992
lstern@troutgroup.com

Media Inquiries:
Christy Maginn
Burson-Marsteller
In U.S.: +1 (646) 280-5210
Christy.Maginn@bm.com

Source: Amarin Corporation plc