New REDUCE-IT® Analyses Show VASCEPA® (icosapent ethyl) Associated with 29 Percent Relative Risk Reduction Compared with Placebo in Prespecified Subgroup of Patients with Metabolic Syndrome, but Without Diabetes at Baseline

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-- Analysis Also Found IPE Was Associated with a 41% Reduction in Total Events Compared with Placebo --

-- Subgroup Almost Exclusively Comprised of Patients with Established Cardiovascular Disease --

-- Findings Continue to Reinforce the Scientific Data and Clinical Use of VASCEPA®/VAZKEPA® to Reduce Cardiovascular Risk --

-- Results Presented Today at the American Heart Association (AHA) Scientific Sessions 2023 and Simultaneously Published in the European Heart Journal Open --

DUBLIN, Ireland and BRIDGEWATER, N.J., Nov. 12, 2023 (GLOBE NEWSWIRE) -- Amarin Corporation plc (NASDAQ:AMRN) today announced results from new REDUCE-IT analyses showing that among statin-treated patients in a prespecified subgroup with history of Metabolic Syndrome, but without diabetes at baseline, the addition of VASCEPA/VAZKEPA (icosapent ethyl) significantly reduced the risk of first and total cardiovascular events. This subgroup was almost exclusively comprised of patients with established cardiovascular disease. The results were presented today at the American Heart Association (AHA) Scientific Sessions 2023, taking place November 11 – 13, 2023 in Philadelphia, PA and simultaneously published in the *European Heart Journal Open*.

More than 1 out of every 3 adult Americans have Metabolic Syndrome, a cluster of 3 or more of 5 risk factors: 1) waist circumference ≥40 inches [102 cm] in men and ≥35 inches [88 cm] in women, 2) blood pressure ≥130/85 mmHg, 3) glucose ≥100 mg/dL, 4) triglycerides ≥150 mg/dL, and 5) HDL-C <40 mg/dL in men and <50 mg/dL in women.

Among patients with Metabolic Syndrome but without diabetes at baseline (n=2866), those who were allocated to icosapent ethyl (IPE) treatment with a median follow-up time of 4.9 years experienced a 29% relative risk reduction for the primary composite endpoint, defined as cardiovascular death, nonfatal myocardial infarction, nonfatal stroke, coronary revascularization, or unstable angina resulting in hospitalization (P <0.0001) (Absolute Risk Reduction [ARR]=5.9%; number needed to treat [NNT]=17) and a 41% reduction in total (first plus subsequent) events (P <0.0001) compared with placebo. The risk for the key secondary composite endpoint, defined as cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke was reduced by 20% (P=0.05) and there was a 27% reduction in fatal/nonfatal myocardial infarction (P=0.03), 47% reduction in urgent/emergent revascularization (P <0.0001) and 58% reduction in hospitalization for unstable angina (P <0.0001). Non-statistically significant reductions were observed in cardiac arrest (44%) and sudden cardiac death (34%).

The large relative and absolute risk reductions observed supports IPE as an important therapeutic option for patients with metabolic syndrome at high cardiovascular risk, despite lacking robust effects on any metabolic syndrome component.

“These subgroup findings provide us with valuable insight into the role icosapent ethyl may play in helping reduce the risk of cardiovascular events in patients with Metabolic Syndrome, but without concomitant diabetes, including those secondary prevention patients with established cardiovascular disease, a patient group particularly at high-risk of having another cardiovascular event,” said Michael Miller, M.D., cardiologist and Chief of Medicine, Corporal Michael J Crescenz Veterans Affairs Medical Center and Professor of Medicine, Hospital of the University of Pennsylvania in Philadelphia. “This is an area of growing concern for the medical community and for patients globally, given the steady rise in the number of patients with Metabolic Syndrome across the U.S. and around the world.”

Commenting on the findings, Amarin’s Chief Medical Officer Nabil Abadir said, “These data continue to reinforce the clinical value of IPE and expand the growing list of benefits attributable to the molecule, including secondary prevention patients such as those with prior myocardial infarction, percutaneous coronary intervention or coronary bypass grafting, chronic kidney disease, heart failure, and history of cigarette smoking.”

Limitations of these analyses, some of which are exploratory in nature, include the relatively small number of events in certain subgroups or for certain endpoints, such as cardiac arrest and sudden cardiac death. In addition, variation in subjective measures (e.g., waist circumference) may have affected classification of metabolic syndrome.

About Metabolic Syndrome

Metabolic Syndrome is a cluster of conditions that increase the risk of heart disease, stroke and Type 2 diabetes mellitus (T2DM).

Metabolic Syndrome is defined as the presence of any three of the following five risk factors: increased blood pressure, high blood sugar, excess body fat around the waist, low HDL cholesterol, or elevated/high triglyceride levels.[1] Metabolic Syndrome is increasingly common,[1] and more than 1 out of 3 people in the United States have it. Metabolic Syndrome is not only associated with a two-fold increased risk of adverse cardiovascular disease (CVD) outcomes (e.g., myocardial infarction, stroke and CV mortality), even in the absence of T2DM, but in recent years has also been linked to a variety of pathogenic phenotypes including heart failure and renal insufficiency.[2,3,4]

About Cardiovascular Risk

Cardiovascular disease is the number one cause of death in the world. In the United States alone, cardiovascular disease results in 859,000 deaths per year,[5] and the number of deaths in the United States attributed to cardiovascular disease continues to rise. In addition, in the United States there are 605,000 new and 200,000 recurrent heart attacks per year (approximately 1 every 40 seconds). Stroke rates are 795,000 per year (approximately 1 every 40 seconds), accounting for 1 of every 19 U.S. deaths. In aggregate, in the United States alone, there are more than 2.4 million major adverse cardiovascular events per year from cardiovascular disease or, on average, 1 every 13 seconds.

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 elevated triglycerides. Statin therapy has been shown to control LDL-C, thereby reducing the risk of cardiovascular events by 25-35%.[6] Significant cardiovascular risk remains after statin therapy. People with elevated triglycerides have 35% more cardiovascular events compared to people with normal (in range) triglycerides taking statins.[7,8,9]

About REDUCE-IT®

REDUCE-IT was a global cardiovascular outcomes study designed to 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).

REDUCE-IT, conducted over seven years and completed in 2018, 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.[10] The primary results of REDUCE-IT were published in The New England Journal of Medicine in November 2018[11]. The total events [12] and other publications can be found in the R&D section on the company's website at **www.amarincorp.com**.

About VASCEPA®/VAZKEPA® (icosapent ethyl) Capsules

VASCEPA (icosapent ethyl) capsules are the first prescription treatment approved by the U.S. Food and Drug Administration (FDA) comprised solely of the active ingredient, icosapent ethyl (IPE), a unique form of eicosapentaenoic acid. VASCEPA was launched in the United States in January 2020 as the first drug approved by the U.S. FDA for treatment of the studied high-risk patients with persistent cardiovascular risk despite being on statin therapy. VASCEPA was initially launched in the United States in 2013 based on the drug's initial FDA approved indication for use as an adjunct therapy to diet to reduce triglyceride levels in adult patients with severe (≥500 mg/dL) hypertriglyceridemia. Since launch, VASCEPA has been prescribed more than twenty million times. VASCEPA is covered by most major medical insurance plans. In addition to the United States, VASCEPA is approved and sold in Canada, China, Lebanon and the United Arab Emirates. In Europe, in March 2021 marketing authorization was granted to icosapent ethyl in the European Union for the reduction of risk of cardiovascular events in patients at high cardiovascular risk, under the brand name VAZKEPA. In April 2021 marketing authorization for VAZKEPA (icosapent ethyl) was granted in Great Britain (applying to England, Scotland and Wales). VAZKEPA (icosapent ethyl) is currently approved and sold in Europe in Sweden, Denmark, Finland, Austria, the UK, Spain and the Netherlands.

Indications and Limitation of Use (in the United States)

VASCEPA is indicated:

- As an adjunct to maximally tolerated statin therapy to reduce the risk of myocardial infarction, stroke, coronary revascularization and unstable angina requiring hospitalization in adult patients with elevated triglyceride (TG) levels (≥ 150 mg/dL) and
    - established cardiovascular disease or
    - diabetes mellitus and two or more additional risk factors for cardiovascular disease.
- As an adjunct to diet to reduce TG levels in adult patients with severe (≥ 500 mg/dL) hypertriglyceridemia.

The effect of VASCEPA on the risk for pancreatitis in patients with severe hypertriglyceridemia has not been determined.

Important Safety Information

- VASCEPA is contraindicated in patients with known hypersensitivity (e.g., anaphylactic reaction) to VASCEPA or any of its components.
- VASCEPA was associated with an increased risk (3% vs 2%) of atrial fibrillation or atrial flutter requiring hospitalization in a double-blind, placebo-controlled trial. The incidence of atrial fibrillation was greater in patients with a previous history of atrial fibrillation or atrial flutter.
- It is not known whether patients with allergies to fish and/or shellfish are at an increased risk of an allergic reaction to VASCEPA. Patients with such allergies should discontinue VASCEPA if any reactions occur.
- VASCEPA was associated with an increased risk (12% vs 10%) of bleeding in a double-blind, placebo-controlled trial. The incidence of bleeding was greater in patients receiving concomitant antithrombotic medications, such as aspirin, clopidogrel or warfarin.
- Common adverse reactions in the cardiovascular outcomes trial (incidence ≥3% and ≥1% more frequent than placebo): musculoskeletal pain (4% vs 3%), peripheral edema (7% vs 5%), constipation (5% vs 4%), gout (4% vs 3%), and atrial fibrillation (5% vs 4%).
- Common adverse reactions in the hypertriglyceridemia trials (incidence ≥1% more frequent than placebo): arthralgia (2% vs 1%) and oropharyngeal pain (1% vs 0.3%).
- Adverse events may be reported by calling 1-855-VASCEPA or the FDA at 1-800-FDA-1088.
- Patients receiving VASCEPA and concomitant anticoagulants and/or anti-platelet agents should be monitored for bleeding.

FULL U.S. FDA-APPROVED VASCEPA PRESCRIBING INFORMATION CAN BE FOUND AT WWW.VASCEPA.COM.

About Amarin

Amarin is an innovative pharmaceutical company leading a new paradigm in cardiovascular disease management. From our foundation in scientific research to our focus on clinical trials, and now our commercial expansion, we are evolving and growing rapidly. Amarin has offices in Bridgewater, New Jersey in the United States, Dublin in Ireland, Zug in Switzerland, and other countries in Europe as well as commercial partners and suppliers around the world. We are committed to increasing the scientific understanding of the cardiovascular risk that persists beyond traditional therapies and advancing the treatment of that risk.

Forward-Looking Statements

This press release contains forward-looking statements which are made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995, including beliefs about the potential for VASCEPA (marketed as VAZKEPA in Europe); beliefs about icosapent ethyl (IPE)'s potential role in helping reduce the risk of cardiovascular events in patients with Metabolic Syndrome, but without concomitant diabetes, as well as general beliefs about the safety and effectiveness of VASCEPA/VAZKEPA. These forward-looking statements are not promises or guarantees and involve substantial risks and uncertainties. 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 Amarin's annual report on Form 10-K for the full year ended 2022. Existing and prospective investors are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date they are made. Amarin undertakes no obligation to update or revise the information contained in its forward-looking statements, whether as a result of new information, future events or circumstances or otherwise. Amarin's forward-looking statements do not reflect the potential impact of significant transactions the company may enter into, such as mergers, acquisitions, dispositions, joint ventures or any material agreements that Amarin may enter into, amend or terminate. Availability of Other Information About Amarin communicates with its investors and the public using the company website (www.amarincorp.com) and the investor relations website (investor.amarincorp.com), including but not limited to investor presentations and 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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