Amarin Highlights New Evidence of Therapeutic Value of EPA in Reducing Cardiovascular Events in At-Risk Patients Presented at ACC.23/WCC

March 6, 2023

--In Vitro Data Presentations Support Antithrombotic and Antioxidant Effects of EPA Compared with DHA, No Impact of Mineral Oil on Rates of LDL Oxidation –-

DUBLIN, Ireland and BRIDGEWATER, N.J., March 06, 2023 (GLOBE NEWSWIRE) -- Amarin Corporation plc (NASDAQ:AMRN) today highlighted new in vitro data supporting the potential mechanistic effects of eicosapentaenoic acid (EPA) in reducing cardiovascular events in at-risk patients presented at the joint ACC.23 together with the World Congress of Cardiology (ACC.23/WCC) in New Orleans, LA, March 4-6, 2023.

“The findings shared at ACC.23/WCC provide additional insight into the unique role of EPA in reducing cardiovascular events in at-risk patients around the world. The potential novel antithrombotic mechanisms of EPA that may contribute to reduced ischemic events is particularly noteworthy given a new analysis from the REDUCE-IT trial showed that icosapent ethyl, a pharmaceutical formulation of EPA, significantly reduced the risk of first and total ischemic events in patients with recent acute coronary syndrome without significantly increasing bleeding,” said R. Preston Mason, PhD, MBA, Professor of Medicine at Harvard Medical School and Researcher

“Additionally, from these in vitro analyses we see that EPA is highly effective in reducing lipoprotein oxidation, a central driver of atherosclerosis, and would therefore be considered protective against heart disease. These mechanisms may help explain the significant risk reduction benefit demonstrated in the REDUCE-IT trial for icosapent ethyl. Our research also underscores confidence in the results of REDUCE-IT with mineral oil because that placebo comparator did not have any biologically active effects on LDL oxidation in our experiment.”

The ACC.23/WCC 2023 presentations were as follows:

- Eicosapentaenoic Acid (EPA) Modulated Expression of Proteins Linked to Platelet Activation and Thrombosis in Vascular Endothelial Cells during Inflammation

Highlights: This in vitro study suggests potential antithrombotic mechanisms for EPA that may contribute to reduced ischemic events. EPA modulated expression of proteins involved in platelet activation and thrombosis under inflammatory conditions, including increased levels of tissue factor pathway inhibitor in vascular endothelial cells. Importantly, these findings follow data from REDUCE-IT ACS, also presented at ACC.23/WCC, showing bleeding rates were not more frequent with icosapent ethyl than placebo despite extensive use of background antithrombotic therapy.

- Pharmaceutical Grade Mineral Oil and Corn Oil do not Influence Phospholipid Membrane Oxidation Rates Compared to Omega-3 Fatty Acids In Vitro

Highlights: This in vitro study compared the effects of pharmaceutical grade mineral oil, corn oil, EPA, or DHA on rates of membrane lipid oxidation and found that EPA had potent antioxidant effect in membranes that were sustained over time compared with DHA and that placebo oils had no effects on oxidation even at very high levels. The data showed EPA inhibited membrane oxidation by 89% compared to vehicle after 72 hours ($p<0.001$), while DHA mildly inhibited oxidation (21%) at this time point versus vehicle ($p<0.05$). There was no change in the oxidation rate in membranes incubated with either placebo through 72 hours.

- Comparing the Effects of Pharmaceutical Grade Mineral Oil, Corn Oil, Eicosapentaenoic Acid (EPA) and Docosahexaenoic Acid (DHA) in a Model of Atherosclerosis In Vitro

Highlights: This in vitro study found EPA had potent antioxidant effects in apolipoprotein B (ApoB) particles compared to DHA-containing formulations and that pharmaceutical grade mineral oil and corn oil did not influence LDL oxidation even at supra-pharmacologic levels. To compare the effects of these compounds on oxidation of LDL, LDL was isolated from human plasma, separated into test samples and incubated with pharmaceutical grade mineral oil, corn oil, EPA or DHA. All samples were then subjected to induced oxidation. At four hours, oxidation increased 15-fold and 57-fold in vehicle-treated small dense LDL (sLDL) and very-low-density lipoprotein (VLDL), respectively, and was unaffected by mineral oil or corn oil. By contrast, EPA significantly inhibited sdLDL and VLDL oxidation by 75% and 94%, respectively, compared with vehicle ($p<0.001$). While DHA exhibited antioxidant activity at 2 hours at a level less than EPA, this effect was eliminated by 4 hours.

About Amarin

Amarin is an innovative pharmaceutical company leading a new paradigm in cardiovascular disease management. From our scientific research foundation 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, and Zug in Switzerland as well as commercial partners and suppliers around the world. We are committed to rethinking cardiovascular risk through the advancement of scientific understanding of the impact on society of significant residual risk that exists beyond traditional therapies, such as statins for cholesterol management.

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.[1] 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%.[2] 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.[3,4,5]

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.[6] The primary results of REDUCE-IT were published in The New England Journal of Medicine in November 2018.[7] The total events results of REDUCE-IT were published in the Journal of the American College of Cardiology in March 2019.[8] These 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 capsules are the first prescription treatment approved by the U.S. Food and Drug Administration (FDA) comprised solely of the active ingredient, icosapent ethyl, a unique form of eicosapentaenoic acid. VASCEPA was launched in the United States in January 2020 as the first and only drug approved by the U.S. FDA for treatment of the studied high-risk patients with persistent cardiovascular risk after 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 over 18 million times. VASCEPA is covered by most major medical insurance plans. In addition to the United States, icosapent ethyl is approved and sold in Canada, Lebanon, Germany 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. The Great Britain Marketing Authorization for VAZKEPA applies to England, Scotland and Wales.

United States

Indications and Limitation of Use
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.

Europe

For further information about the Summary of Product Characteristics (SmPC) for VAZKEPA® in Europe, please click here.

Globally, prescribing information varies; refer to the individual country product label for complete information.

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 Amarin's key achievements in 2022 and the potential impact and outlook for achievements in 2023 and beyond; Amarin's 2023 financial outlook and cash position; Amarin's overall efforts to expand access and reimbursement to VAZKEPA across global markets; and the overall potential and future success of VASCEPA/VAZKEPA and Amarin generally. 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 2021. 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
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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