Amarin Highlights Key Data Providing Mechanistic Insights into Eicosapentaenoic Acid (EPA) at ESC 2025

August 31, 2025

-- Data Further Advance Understanding of VASCEPA®/VAZKEPA® Potential Mechanisms of Action --

DUBLIN, Ireland and BRIDGEWATER, N.J., Aug. 31, 2025 (GLOBE NEWSWIRE) -- Amarin Corporation plc (NASDAQ:AMRN) today highlighted *in vitro* data assessing the effects of EPA on lipoprotein(a) [Lp(a)] oxidation and on cellular stress and inflammatory protein expression in endothelial cells and preliminary data showcasing the potential anti-inflammatory mechanism of icosapent ethyl (IPE) via modulation of nod-like receptor protein-3 (NLRP3) inflammasome by monocyte-derived macrophages (MDMs). The data was presented at the European Society of Cardiology (ESC) Congress 2025 in Madrid, Spain.

“These *in vitro* analyses provide additional insight into the mechanisms of action for VASCEPA/VAZKEPA, including the potential effect of reducing inflammation in atherosclerotic cardiovascular disease (ASCVD) as well as its reported impact on reducing cardiovascular (CV) events in at-risk patients with elevated Lp(a),” said Steven Ketchum, Ph.D., EVP, President of R&D, and Chief Scientific Officer at Amarin. "This data continues to advance understanding around potential underlying mechanisms of action for this molecule.”

The *in vitro* analyses and their key findings are outlined below:

Eicosapentaenoic acid (EPA) modulates inflammasome activation in monocyte-derived macrophages isolated from individuals with and without established atherosclerotic cardiovascular disease (ASCVD)

This analysis evaluated anti-inflammatory mechanisms of action of IPE, a purified form of EPA, that may be associated with cardiovascular risk reduction beyond triglyceride lowering.

Researchers focused on monocyte-derived macrophages (MDMs), which are thought to contribute to ASCVD progression in part via P2X7 receptor–mediated activation of the NLRP3 inflammasome and impairment of autophagy.

Key findings suggest that EPA may reduce extracellular ATP release and caspase 1 activation in stimulated MDMs from individuals with and without ASCVD. The analysis presents novel preliminary evidence that EPA may protect against inflammation in ASCVD by modulating the ATP–P2X7 axis and downstream NLRP3 activation in MDMs.

“These findings offer compelling preliminary evidence that eicosapentaenoic acid (EPA) may play a protective role against inflammation in atherosclerotic cardiovascular disease. By modulating the ATP–P2X7 axis and downstream NLRP3 inflammasome activation in monocyte-derived macrophages, EPA demonstrates potential mechanisms of cardiovascular risk reduction that extend beyond triglyceride lowering,” said Professors Kelvin Lee & Claire Elizabeth Hills, Consultant Interventional Cardiologist and Director of the Cardiovascular Research Program at Lincolnshire Heart Centre (Prof. Lee), United Lincolnshire Hospitals NHS Trust, and Professor of Renal Physiology, School of Life Sciences, Joseph Banks Laboratories, University of Lincoln (Prof. Hills). “This promising data suggest that the benefits of EPA may extend beyond triglyceride lowering, potentially influencing autophagy and inflammasome activity in ways that could meaningfully reduce cardiovascular risk.”

Eicosapentaenoic Acid (EPA) Inhibited Lipoprotein(a) [Lp(a)] Oxidation and its Effects on Expression of Oxidative Stress and Pro-Inflammatory Proteins in Endothelial Cells

Elevated Lp(a) is associated with an increased risk for ASCVD and aortic valve stenosis. Lp(a) is a major carrier of oxidized phospholipids (oxPLs). Atherogenic mechanisms for Lp(a) include increased endothelial dysfunction linked to its oxPL content.

This analysis assessed the effects of EPA on attenuation of Lp(a) oxidation and the effects of Lp(a) ± EPA on protein expression in endothelial cells during conditions of oxidative stress. Results showed that EPA attenuated Lp(a) oxidation and its effects on oxidative stress and pro-inflammatory protein expression.

IPE/EPA was reported to reduce CV events in high-risk patients with elevated Lp(a). Mechanistic insights suggest that EPA inhibits lipoprotein oxidation by a potent lipid-centric scavenging mechanism. By inhibiting Lp(a) oxidation, EPA may reduce its effects on endothelial dysfunction and inflammation.

About Amarin

Amarin is an innovative pharmaceutical company leading a new paradigm in cardiovascular disease management. We are committed to increasing the scientific understanding of the cardiovascular risk that persists beyond traditional therapies and advancing the treatment of that risk for patients worldwide. 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.

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-five 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, Australia, Lebanon, the United Arab Emirates, Saudi Arabia, Qatar, Bahrain, and Kuwait. 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, Finland, England/Wales, Spain, Netherlands, Scotland, Greece, Portugal, Italy, Denmark and Austria.

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 visit: https://www.ema.europa.eu/en/documents/product-information/vazkepa-epar-product-information_en.pdf

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 2024 and the potential impact and outlook for achievements in 2025 and beyond; Amarin's 2025 financial outlook and cash position; Amarin's overall efforts to expand access and reimbursement to VAZKEPA across global markets; expectations regarding potential strategic collaboration

and licensing agreements with third parties, including our ability to attract additional collaborators, as well as our plans and strategies for entering into potential strategic collaboration and licensing agreements and the overall potential and future success of VASCEPA/VAZKEPA and Amarin that are based on the beliefs and assumptions and information currently available to Amarin. All statements other than statements of historical fact contained in this press release are forward-looking statements. 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 quarterly report on Form 10-Q for the period ending June 30, 2025 and annual report on Form 10-K for the fiscal year ended 2024. 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. 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 (www.amarincorp.com/investor-relations) including but not limited to investor presentations and investor FAQs, U.S. Securities and Exchange Commission filings, press releases, public conference calls and webcasts

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 (investors.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.

Amarin Contact Information

Media Inquiries:

Tegan Berry

Amarin Corporation plc

PR@amarincorp.com

Investor Inquiries:

Bob Burrows

Western Avenue Advisers LLC

Investor.relations@amarincorp.com