Amarin Announces New REDUCE-IT® Data at ACC.23/WCC Showing Benefit of VASCEPA®/VAZKEPA® (Icosapent Ethyl) in High-Risk Patients with a Recent Acute Coronary Syndrome Event

March 5, 2023

--Post-Hoc Analysis Shows IPE Significantly Reduced Risk of First, Total Ischemic Events by 37% and 36% Respectively in Patients with Recent ACS Without Increased Bleeding--

--Analysis Builds on Consistently Demonstrated Positive Outcomes for VASCEPA/VAZKEPA Across Sub-Populations in REDUCE-IT, Including in Patients with Prior Myocardial Infarction (MI), Prior Revascularization, Prior Peripheral Arterial Disease (PAD) and Diabetes--

DUBLIN, Ireland and BRIDGEWATER, N.J., March 05, 2023 (GLOBE NEWSWIRE) -- Amarin Corporation plc (NASDAQ:AMRN) today announced a new analysis from the VASCEPA/VAZKEPA (icosapent ethyl) cardiovascular outcomes REDUCE-IT study showing the effectiveness of VASCEPA®/VAZKEPA® in patients with recent acute coronary syndrome (<12 months before randomization). This post-hoc analysis showed that icosapent ethyl (IPE) substantially and significantly reduced the risk of first and total ischemic events by 37% and 36% respectively in patients with recent acute coronary syndrome (ACS) without increasing bleeding, supporting early initiation of IPE after ACS. The data were presented at the American College of Cardiology's 72nd Annual Scientific Session together with the World Heart Federation's World Congress of Cardiology in New Orleans, LA.

"Patients who have experienced acute coronary syndrome are at very high risk of a recurrent event, which can be life threatening, particularly in the weeks following the index event," [1] said Philippe Gabriel Steg, MD, Chief of Cardiology at Hôpital Bichat, Greater Paris University Hospitals – AP-HP, and professor at Université Paris -Cité, France. "These results demonstrate that the addition of icosapent ethyl to the treatment regimen of patients who have experienced ACS within the last 12 months can substantially reduce their risk of another cardiovascular event, (with an absolute risk reduction of 9.3%) and that the earlier a patient begins treatment with icosapent ethyl after ACS, the greater the absolute risk reduction for those patients."

In this post hoc ACS analysis of the landmark REDUCE-IT study, 840 (10.3% of the total trial cohort) patients who experienced recent ACS, defined as myocardial infarction (MI) or unstable angina <12 months before randomization were compared to 3,651 patients with ACS ≥12 months before randomization to assess the efficacy of VASCEPA/VAZKEPA on first and total primary events endpoints. The absolute risk reduction for first events with IPE treatment over 5 years for the primary composite endpoint was 9.3% with a number needed to treat (NNT) of 11. The absolute risk reduction for first events with IPE treatment in patients with ACS ≥12 months was 4.7% with an NNT of 21. Overall tolerability and adverse event patterns with IPE and placebo in patients with recent ACS were consistent with the full study. Bleeding event rates were no more frequent with IPE than placebo despite extensive use of dual antiplatelet therapy.

"As we know, the REDUCE-IT trial demonstrated the clear risk reduction benefits of icosapent ethyl in reducing ischemic events among patients at high risk for cardiovascular disease," said Nabil Abadir, MB. CH.B., Chief Medical Officer and Head of Global Medical Affairs, Amarin. "This data not only underscore the benefit for patients at risk for a cardiovascular event within 12 months following ACS, but it also builds on the consistency of data across sub-populations in REDUCE-IT with demonstrated positive outcomes for patients, including those with prior MI, prior revascularization, prior PAD and diabetes."

Limitations include that REDUCE-IT was not powered for multiple subgroup analyses, and this was a post hoc defined subset among post ACS patients.

All analyses highlighted above were funded by Amarin. Dr. Steg received research funding paid to Fondation Assistance Publique –Hôpitaux de Paris, France from Amarin for his role as an investigator on the REDUCE-IT study and personal funding as a speaker or consultant to Amarin.

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.[2] 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%.[3] 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.[4,5,6]

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.[7] The primary results of REDUCE-IT were published in The New England Journal of Medicine in November 2018.[8] The total events results of REDUCE-IT were published in the Journal of the American College of Cardiology in March 2019.[9] 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.

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.

Key clinical effects of VASCEPA on major adverse cardiovascular events are included in the Clinical Studies section of the prescribing information for VASCEPA as set forth below:

Effect of VASCEPA on Time to First Occurrence of Cardiovascular Events in Patients with Elevated Triglyceride levels and Other Risk Factors for Cardiovascular Disease in REDUCE-IT

	VASCEPA	Placebo	VASCEPA vs

					Placebo
	N = 4089 n (%)	Incidence Rate (per 100 patient years)	N = 4090 n (%)	Incidence Rate (per 100 patient years)	Hazard Ratio (95% CI)
Primary composite endpoint					
Cardiovascular death, myocardial infarction, stroke, coronary revascularization, hospitalization for unstable angina (5-point MACE)	705 (17.2)	4.3	901 (22.0)	5.7	0.75 (0.68, 0.83)
Key secondary composite endpoint					
Cardiovascular death, myocardial infarction, stroke (3-point MACE)	459 (11.2)	2.7	606 (14.8)	3.7	0.74 (0.65, 0.83)
Other secondary endpoints					
Fatal or non-fatal myocardial infarction	250 (6.1)	1.5	355 (8.7)	2.1	0.69 (0.58, 0.81)
Emergent or urgent coronary revascularization	216 (5.3)	1.3	321 (7.8)	1.9	0.65 (0.55, 0.78)
Cardiovascular death[1]	174 (4.3)	1.0	213 (5.2)	1.2	0.80 (0.66, 0.98)
Hospitalization for unstable angina[2]	108 (2.6)	0.6	157 (3.8)	0.9	0.68 (0.53, 0.87)
Fatal or non-fatal stroke	98 (2.4)	0.6	134 (3.3)	0.8	0.72 (0.55, 0.93)

[1] Includes adjudicated cardiovascular deaths and deaths of undetermined causality.
[2] Determined to be caused by myocardial ischemia by invasive/non-invasive testing and requiring emergent hospitalization.

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

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 world-wide market potential for VASCEPA; expectations regarding financial metrics and performance such as prescription growth, revenue growth, operating expenses, inventory purchases, and managed care coverage for VASCEPA, including the impact of the COVID-19 pandemic, the disappointing outcome of patent litigation and the launch of generic competition on these metrics; beliefs that Amarin is well positioned to deliver on its goals to grow VASCEPA in the U.S. and beyond; beliefs about patient needs for VASCEPA; effects of the COVID-19 pandemic on Amarin's operations and on the healthcare industry more broadly, which effects continue to be fluid; beliefs that Amarin's strategy for reducing the effects of cardiovascular disease is sound and that Amarin is efficiently reaching physicians, payors, pharmacists and patients; plans for Amarin's go-to-market model; the timing and outcome of regulatory reviews, recommendations and approvals and related reimbursement decisions and commercial launches in Europe, the China region and elsewhere; plans for Amarin's expected launch of VASCEPA directly in major markets in Europe, directly and indirectly; beliefs about the cardioprotective and other benefits of VASCEPA; beliefs about the strength of data in market access dossiers and other reports; expectations for the timing, effectiveness and outcome of promotional activities, including patient-oriented campaigns, conference and posted presentations and education of healthcare professionals; commercial and international expansion, prescription growth and revenue growth and future revenue levels, including the contributions of sales representatives and the new leadership team; beliefs that Amarin's current resources are sufficient to fund projected operations; ongoing patent litigation efforts; and the impact of the COVID-19 pandemic on all of the forgoing. These forward-looking statements are not promises or guarantees and involve substantial risks and uncertainties. Amarin's ability to effectively commercialize VASCEPA and maintain or grow market share will depend in part on Amarin’s ability to continue to effectively finance its business, VASCEPA approval in geographies outside the U.S., efforts of third parties, Amarin’s ability to create and increase market demand for VASCEPA through education, marketing and sales activities, to achieve broad 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 secure, maintain and defend its patent protection for VASCEPA. Among the factors that could cause actual results to differ materially from those described or projected herein include the following: the possibility that VASCEPA may not receive regulatory approval in the China region or other geographies on the expected timelines or at all, the risk that additional generic versions of VASCEPA will enter the market and that generic versions of VASCEPA will achieve greater market share and more commercial supply than anticipated, particularly in light of the recent and disappointing outcome of Amarin's litigation against two generic drug companies and subsequent requests for appeal; the risk that the scope and duration of the COVID-19 pandemic will continue to impact access to and sales of VASCEPA; the risk that Amarin has overestimated the market potential for VASCEPA in the U.S., Europe and other geographies; risks associated with Amarin's expanded enterprise; 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 be determined to not be infringed or not be valid 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 Amarin’s quarterly report on Form 10-Q for the quarter ended June 30, 2021, filed on or about the date hereof. 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

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.

Amarin Contact Information
Investor Inquiries:
Investor Relations
Amarin Corporation plc
In U.S.: +1 (908) 719-1315
IR@amarincorp.com (investor inquiries)

Solebury Trout
amarinir@troutgroup.com

Media Inquiries:
Communications
Amarin Corporation plc
In U.S.: +1 (908) 892-2028
PR@amarincorp.com (media inquiries)

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