Amarin Reports Overview of Latest Clinical Research Evaluating VASCEPA®/VAZKEPA (Icosapent Ethyl) and Eicosapentaenoic Acid (EPA) Presented at the American Heart Association Scientific Sessions 2021

November 16, 2021

VASCEPA/VAZKEPA found in prespecified and post hoc analyses to reduce total ischemic events by 32% in patients with prior PAD

DUBLIN, Ireland and BRIDGEWATER, N.J., Nov. 16, 2021 (GLOBE NEWSWIRE) -- Amarin Corporation plc (NASDAQ:AMRN) today reported an overview of new data relating to VASCEPA®/VAZKEPA (icosapent ethyl) presented at the American Heart Association (AHA) Scientific Sessions 2021, which took place virtually from November 13-15, 2021.

"We are committed to serving patients with cardiovascular (CV) disease and the data presented at this year's AHA annual meeting provide further evidence of the CV benefits of VASCEPA/ VAZKEPA in specified high-risk patients, potentially including those with peripheral artery disease," said Karim Mikhail, Amarin's president and chief executive officer. "We also continue to back investigator-led studies as they support the exploration of further potential mechanisms and clinical benefits of VASCEPA/VAZKEPA."

Key data presented at AHA 2021:

Rapid Fire Oral Session Presentation

- **"Benefits of Icosapent Ethyl in Patients with Prior Peripheral Artery Disease: REDUCE-IT PAD,"**– presented on behalf of all authors by Deepak L. Bhatt, M.D., M.P.H., Brigham and Women's Hospital

Highlights: The investigators concluded that, "Icosapent ethyl 4 g/day significantly reduced total (first and subsequent) primary endpoints by 32%, and trended toward a 22% reduction in first events, in patients with PAD. Icosapent ethyl provides substantial cardiovascular risk reduction in the high-risk REDUCE-IT population, with consistent benefits in patients with a history of PAD. Safety was generally consistent with the overall study. Overall tolerability and adverse events were generally similar between icosapent ethyl and placebo in patients with prior PAD. More atrial fibrillation/flutter occurred with icosapent ethyl versus placebo in patients with prior PAD (5.2% versus 2.6%, respectively; P=0.07). No differences in bleeding were observed between icosapent ethyl and placebo in patients with prior PAD, likely due to the sample size."

For more information on this presentation, see Amarin's previously issued press release, available here.

e-Poster Presentation

- **Eicosapentaenoic Acid (EPA) Restores Pulmonary Endothelial Nitric Oxide Bioavailability Following Exposure to Urban Air Pollution Small Particles"**– presented on behalf of all authors by R. Preston Mason, Ph.D., Brigham and Women's Hospital

Highlights: This study examined the effects of EPA on pulmonary endothelial cell (PEC) function and inflammatory state when challenged with air pollution particulate matter isolated from an urban environment. In this study, primary PECs were pre-treated with EPA (40 µM) for two hours in 2% FBS-containing medium and then challenged with urban particulate matter (50 µg/mL) for two hours. After two hours, media was washed out and HBSS buffer was added. Cells were then stimulated with a calcium ionophore and concurrent measurements of nitric oxide and ONOO- were performed using tandem electrochemical nanosensors. In parallel with the endothelial function analysis, soluble intracellular adhesion molecule-1 (sICAM-1) was detected [i].

The study authors concluded that, "EPA significantly improved pulmonary endothelial cell function under conditions of inflammation caused by air pollution particles, including reductions in nitroxidative stress and the soluble adhesion molecule ICAM-1. These effects of EPA in pulmonary tissue challenged with air particulate matter indicate a novel potential benefit for further exploration in people exposed to air pollution."

Late-Breaking Science Presentation

- **"Icosapent Ethyl Versus Placebo In Outpatients With COVID-19: The Main Results Of PREPARE-IT 2"** – presented on behalf of all authors and the PREPARE-IT 2 Trial Investigators by Rafael Diaz, M.D., Estudios Cardiologicos Latinoamerica (ECLA), Rosario, Argentina

Highlights: These data represent the first presentation of the topline results from the PREPARE-IT 2 study, which was an investigator-initiated trial (IIT) to evaluate the efficacy of icosapent ethyl (IPE) to reduce hospitalizations or death in approximately 2000 patients in Argentina with a positive diagnosis for the COVID-19 virus. In this study, subjects were randomized 1:1 to receive IPE or placebo and received a loading dose of 8g per day of IPE for the first three days followed by 4g per day of IPE thereafter from days 4-28. The primary endpoint is COVID-19 related hospitalizations or death assessed through day 28.

While the results of the PREPARE-IT 2 study in Argentina did not meet the primary and/or other endpoints studied, we believe it is valuable for Amarin to support pilot IITs of this nature to determine the safety and potential efficacy of VASCEPA/VAZKEPA in a diverse group of at-risk populations. Importantly, the study supports the safety and tolerability of VASCEPA/VAZKEPA at varying doses.

PREPARE-IT 1 and 2 are part of a series of IITs evaluating VASCEPA/VAZKEPA's potential benefit in preventing and/or treating COVID-19. Amarin

continues to support MITIGATE, another IIT study of IPE's potential efficacy in the prevention of COVID-19.

The results of this study have no relationship to or bearing on any approved indications for VASCEPA/VAZKEPA.

All analyses highlighted above were supported or funded by Amarin.

Additional REDUCE-IT and icosapent ethyl-related topics presented at AHA Scientific Sessions 2021 can be found here.

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.

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.[ii] 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%.[iii] 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. [iv,v,vi]

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.*[vii] The primary results of REDUCE-IT were published in *The New England Journal of Medicine* in November 2018.[viii] The total events results of REDUCE-IT were published in the *Journal of the American College of Cardiology* in March 2019.[ix] These and other publications can be found in the R&D section on the company's website at www.amarincorp.com.

About VASCEPA® (icosapent ethyl) Capsules
VASCEPA (icosapent ethyl) capsules are the first-and-only 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 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 ten million times. VASCEPA is covered by most major medical insurance plans. In addition to the United States, VASCEPA is approved and sold in Canada, 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.

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 (marketed as VAZKEPA in Europe); 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 September 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

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.

Amarin Contact Information

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

Solebury Trout
In U.S.: +1 (646) 378-2992
amarinir@troutgroup.com

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

[i] Mason RP et al. Biomed Pharmacother. 2018;103:1231- 1237

[ii] American Heart Association. Heart Disease and Stroke Statistics—2020 Update: A Report From the American Heart Association. *Circulation*. 2020;141:e139-e596.

[iii] 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.

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

[v] 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.

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

[vii] Bhatt DL, Steg PG, Brinton E, et al., on behalf of the REDUCE-IT Investigators. Rationale and Design of REDUCE-IT: Reduction of Cardiovascular Events with Icosapent Ethyl–Intervention Trial. *Clin Cardiol.* 2017;40:138-148.

[viii] Bhatt DL, Steg PG, Miller M, et al., on behalf of the REDUCE-IT Investigators. Cardiovascular Risk Reduction with Icosapent Ethyl for Hypertriglyceridemia. *N Engl J Med*. 2019;380:11-22.

[ix] Bhatt DL, Steg PG, Miller M, et al., on behalf of the REDUCE-IT Investigators. Reduction in first and total ischemic events with icosapent ethyl across baseline triglyceride tertiles. *J Am Coll Cardiol.* 2019;74:1159-1161.