Amarin Highlights VASCEPA® (Icosapent Ethyl)-Related Data Presented at American College of Cardiology's Annual Scientific Session Together With World Congress of Cardiology (ACC.20/WCC)

March 31, 2020

DUBLIN, Ireland and BRIDGEWATER, N.J., March 31, 2020 (GLOBE NEWSWIRE) -- Amarin Corporation plc (NASDAQ:AMRN), hosted a webcast yesterday to discuss important data with study authors who presented at the American College of Cardiology's 69th Annual Scientific Session Together With World Congress of Cardiology (ACC.20/WCC), March 28-30. The data presented related to VASCEPA® (icosapent ethyl) capsules, the landmark clinical outcomes study REDUCE-IT®, as well as persistent cardiovascular risk in patients with elevated triglycerides, a type of fat in the blood.

- *Eicosapentaenoic Acid (EPA) levels from VASCEPA® (Icosapent Ethyl) in REDUCE-IT® strongly correlated to cardiovascular outcomes, more so than other biomarkers*
- *Over 70,000 cardiovascular events/year in US adults with known CVD or diabetes mellitus may be preventable from VASCEPA (Icosapent Ethyl) therapy, impacting persistent CV risk despite statin-controlled LDL-C*
- *Analysis supports determination that VASCEPA is highly cost-effective in patients from the REDUCE-IT USA subgroup and, as is rarely found for any therapy, may result in net healthcare cost-savings to patients, payers and society*
- *Mechanism of icosapent ethyl is distinct from docosahexaenoic acid (DHA) and other omega-3 fatty acids in providing antioxidant effects*

"Administration of 4 g/day of VASCEPA, a highly cost-effective therapy, can potentially prevent over 70,000 cardiovascular events per year," said Craig Granowitz, M.D., Ph.D., Amarin's senior vice president and chief medical officer commenting on presentations made at ACC.20/WCC. "It is apparent that icosapent ethyl administration results in serum EPA levels necessary to reduce cardiovascular events. This positive effect has not been demonstrated for any other therapy on top of statin therapy. These new and important data will help inform ways to manage persistent cardiovascular risk and help curb the number one killer of Americans."

About Cardiovascular Risk

The number of deaths in the United States attributed to cardiovascular disease continues to rise.[1,2] There are 605,000 new and 200,000 recurrent heart attacks per year (approximately 1 every 40 seconds), in the United States. Stroke rates are similar, accounting for 1 of every 19 U.S. deaths (approximately 1 every 40 seconds).[3] In aggregate, from cardiovascular disease there is one death, stroke or heart attack every 14 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% – but that still leaves a 65-75% risk remaining.[4] People with elevated triglycerides have 35% more cardiovascular events compared to people with normal (in range) triglycerides taking statins.[5,6,7]

Key Data Presented at ACC.20/WCC and Reviewed During Amarin's Webcast

"Eicosapentaenoic Acid Levels in REDUCE-IT and Cardiovascular Outcomes" – presented on behalf of all authors by Deepak L. Bhatt, M.D., M.P.H., Brigham and Women's Hospital

Highlights: Following administration of VASCEPA, a pure, stable, prescription EPA therapy, serum EPA levels showed an approximately 400% increase across the study from baseline (26.1 µg/mL) versus placebo, including to year 1 (144 µg/mL; $p=1x10^{-30}$). Docosahexaenoic acid (DHA) levels were measured and showed a decrease of 2.9% (p=0.002).

On-treatment EPA levels in the VASCEPA group were associated strongly with reduced cardiovascular events, including benefits observed in the primary and key secondary endpoints, each component of these endpoints such as cardiovascular death, as well as benefits in heart failure and total mortality with high on-treatment EPA levels.

These analyses suggest that achieved EPA levels with 4 g/day of VASCEPA is a marker for the majority of the relative risk reduction observed in REDUCE-IT. The EPA levels achieved in REDUCE-IT were well above levels that can be achieved with diet or with dietary supplements. The clinical results achieved with VASCEPA have not been demonstrated for any other therapy, reflecting the uniqueness of this FDA-approved prescription therapy and its high EPA content, in stable form, without offset or dilution by other omega-3 molecules each of which act differently (e.g., enhanced dosing of DHA is associated with increases in

LDL-cholesterol levels). Further study is needed to assess whether people with relatively large body mass might be safely and effectively treated with higher than 4 g/day of icosapent ethyl.

Biomarker analyses suggest minimal contribution of changes in measured lipid, lipoprotein, and inflammatory biomarkers to the cardiovascular benefit observed in REDUCE-IT.

"REDUCE-IT Eligibility and Preventable First and Total Cardiovascular Events in the US Population: An Analysis of the National Health and Nutrition Examination Survey (NHANES)" – Nathan D. Wong, Wenjun Fan, Peter P. Toth, Craig Granowitz, Sephy Philip

Highlights: The NHANES database was used to identify approximately 3 million REDUCE-IT eligible adults aged >45 years, 63% with prior CVD and 37% with DM + >1 risk factor. While this is not the full extent of VASCEPA's label, this is the population reviewed in this presented analysis.

Based on such eligibility criteria and event rate applied to the US population, it is estimated that administration of VASCEPA (icosapent ethyl) could prevent 71,391 cardiovascular events/year, consisting of 29,798/year fewer first occurrence of a cardiovascular events, such as stroke, heart attack or death, and 41,593/year fewer recurring cardiovascular events.

"Cost-effectiveness of Icosapent Ethyl in US REDUCE-IT Patients" – William S. Weintraub, Deepak L. Bhatt, Zugui Zhang, Cheng Zhang, Sarahfaye Dolman, William E. Boden, P. Gabriel Steg, Michael Miller, Eliot A. Brinton, Jordan B. King, Adam P. Bress, Terry A. Jacobson, Jean-Claude Tardif, Christie M. Ballantyne, Paul Kolm

Highlights: Based on a variety of cost-effectiveness analyses conducted, icosapent ethyl is shown to provide excellent value. The results show a dominant (better outcome, lower cost) cost-effectiveness profile overall and in patients with established atherosclerosis. Analyses conducted consistently put icosapent ethyl within US willingness-to-pay thresholds of <$50,000/QALY (Quality Adjusted Life Years) gained. Administration of icosapent ethyl may result in net healthcare cost-savings to patients, payers and society.

"Eicosapentaenoic Acid Inhibits Oxidation of Very Large Density Lipoproteins (VLDL) in a Dose-Dependent Manner over Time as Compared to Docosahexaenoic Acid In Vitro" – R. Preston Mason, Samuel C. R. Sherratt

"Eicosapentaenoic Acid Inhibits High Density Lipoprotein (HDL) Oxidation in a Synergistic Manner in Combination with Atorvastatin In Vitro" – R. Preston Mason, Samuel C. R. Sherratt

Highlights: In vitro studies were conducted to ascertain EPA behavior under 2 scenarios; antioxidant benefits in VLDL vs. DHA and effect on HDL oxidation in the context of use with ATM (active, ortho-hydroxy metabolite of atorvastatin.)

It was found that EPA exhibited concentration-dependent antioxidant effects. These antioxidant effects require pharmacologic concentrations for sustained activity over time. Furthermore, it was found that the antioxidant benefits with EPA in VLDL were not reproduced with DHA and that the antioxidant benefits for EPA were enhanced with a statin. EPA pretreatment prevented HDL oxidation in a significant fashion with this benefit more than doubling when combined with ATM, suggesting that synergistic antioxidant effects of EPA in combination with a statin may preserve atheroprotective functions for HDL. Such findings appear to be consistent with the multifactorial clinical effects attributed to icosapent ethyl.

All analyses highlighted above were funded by Amarin.

A replay of the call is available for a period of two weeks. To hear a replay of the call, dial 877-481-4010, PIN: 33498. A replay of the call is also available through the company's website beginning shortly after the call.

About Amarin

Amarin Corporation plc is a rapidly growing, innovative pharmaceutical company focused on developing and commercializing therapeutics to cost-effectively improve cardiovascular health. Amarin's lead product, VASCEPA® (icosapent ethyl), is available by prescription in the United States, Canada, Lebanon and the United Arab Emirates. Amarin, together with its commercial partners in select geographies, is pursuing additional regulatory approvals for VASCEPA in China, the European Union and the Middle East. For more information about Amarin, visit www.amarincorp.com.

About VASCEPA® (icosapent ethyl) Capsules

VASCEPA (icosapent ethyl) capsules are the first-and-only prescription treatment approved by the FDA comprised solely of the active ingredient, icosapent ethyl (IPE), a unique form of eicosapentaenoic acid. 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 eight million times and is covered by most major medical insurance plans. The new, cardiovascular risk indication for VASCEPA was approved by the FDA in December 2019.

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.

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 VASCEPA PRESCRIBING INFORMATION CAN BE FOUND AT WWW.VASCEPA.COM.

Forward-Looking Statements

This press release contains forward-looking statements, including statements regarding connections between EPA blood levels and cardiovascular risk reduction in patient use, the use of VASCEPA to help patients and the cost effectiveness of VASCEPA. These forward-looking statements are not promises or guarantees and involve substantial risks and uncertainties. Among the factors that could cause actual results to differ materially from those described or projected herein include the following: uncertainties associated generally with research and development and clinical trials. 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 its most recent Annual Report on Form 10-K. Existing and prospective investors are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. Amarin undertakes no obligation to update or revise the information contained in this press release, 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.

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[1] American Heart Association. Heart Disease and Stroke Statistics – 2019 Update: A Report from the American Heart Association. Published January 31, 2019.

[2] American Heart Association / American Stroke Association. 2017. Cardiovascular disease: A costly burden for America projections through 2035.

[3] American Heart Association: Heart Disease and Stroke Statistics -- 2019 At-a-Glance.

[4] 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.

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

[6] 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.

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