



Clinical Data and Other Research Results Regarding VASCEPA® (Icosapent Ethyl) and Its Unique Active Ingredient to Be Presented at the American College of Cardiology's 70th Annual Scientific Session

May 4, 2021

Amarin-Supported Research and Analyses from Academic Collaborators to Be Featured in Seven Presentations, Including REDUCE-IT® Heart Failure and Additional Analyses from EVAPORATE

DUBLIN, Ireland and BRIDGEWATER, N.J., May 04, 2021 (GLOBE NEWSWIRE) -- Amarin Corporation plc (NASDAQ:AMRN) today announced that new clinical data and other research results regarding VASCEPA® (icosapent ethyl) and its unique active ingredient will be presented at ACC.21, the American College of Cardiology's 70th Annual Scientific Session, being held virtually from May 15 – 17, 2021. These new findings will be presented in two moderated ePoster presentations plus five ePoster presentations from a variety of academic collaborators based on research and analyses supported by Amarin.

"Cardiovascular disease continues to be the leading cause of death worldwide, demanding new research to increase our understanding of how to effectively change the trajectory of this disease," said Craig Granowitz, M.D., Ph.D., Amarin's senior vice president and chief medical officer. "The need for unique scientifically-based solutions addressing residual cardiovascular risk is more pronounced than ever. Several scheduled presentations at ACC.21 provide new data on VASCEPA and its potential to address the needs of at-risk patients."

Featured Amarin-supported abstracts to be presented at ACC.21 include:

Moderated ePoster Presentations:

- "[REDUCTION IN HEART FAILURE WITH ICOSAPENT ETHYL: INSIGHTS FROM REDUCE-IT HF](#)" – presented on behalf of all authors by Deepak L. Bhatt, M.D., M.P.H., Brigham and Women's Hospital Heart and Vascular Center, Harvard Medical School, Boston, MA – Available from May 15
- "[EFFECT OF ICOSAPENT ETHYL ON PERCENT ATHEROMA VOLUME IN PATIENTS WITH ELEVATED TRIGLYCERIDES ON STATIN THERAPY: INSIGHTS FROM THE EVAPORATE TRIAL](#)" – presented on behalf of all authors by Suvasini Lakshmanan, M.D., M.S., The Lundquist Institute at Harbor-UCLA Medical Center, Torrance, CA – Available from May 15

ePoster Presentations:

- "[ICOSAPENT ETHYL REDUCES ISCHEMIC EVENTS IN PATIENTS WITH HIGH TRIGLYCERIDES AND LOW HIGH-DENSITY LIPOPROTEIN CHOLESTEROL LEVELS: REDUCE-IT HIGH TG/LOW HDL-C ANALYSES](#)" – presented on behalf of all authors by Xiaowen Wang, M.D., Brigham and Women's Hospital Heart and Vascular Center, Harvard Medical School, Boston, MA – Available from May 15
- "[ASSOCIATION OF BASELINE CORONARY PLAQUE BURDEN AND FRACTIONAL FLOW RESERVE DERIVED FROM CORONARY COMPUTED TOMOGRAPHY ANGIOGRAPHY \(CCTA\) IN THE EVAPORATE TRIAL](#)" – presented on behalf of all authors by Suvasini Lakshmanan, M.D., M.S., The Lundquist Institute at Harbor-UCLA Medical Center, Torrance, CA – Available from May 15
- "[ICOSAPENTAENOIC ACID \(EPA\) INCREASES HEME OXYGENASE-1 EXPRESSION IN ENDOTHELIAL CELLS UNDER CONDITIONS OF INFLAMMATION UNLIKE DOCOSAHEXAENOIC ACID \(DHA\)](#)" – presented on behalf of all authors by R. Preston Mason, Ph.D., Brigham and Women's Hospital, Boston, MA – Available from May 15
- "[PLATELET ENDOTHELIAL CELL ADHESION MOLECULE-1 \(PECAM-1\) AND NITROXIDATIVE STRESS REDUCED BY ICOSAPENTAENOIC ACID \(EPA\) DURING CYTOKINE EXPOSURE IN ENDOTHELIAL CELLS](#)" – presented on behalf of all authors by R. Preston Mason, Ph.D., Brigham and Women's Hospital, Boston, MA – Available from May 15
- "[GLOBAL CARDIOVASCULAR RISK ASSESSMENT IMPROVES RISK STRATIFICATION FOR MAJOR ADVERSE CARDIAC EVENTS ACROSS A WIDE RANGE OF TRIGLYCERIDE LEVELS IN STATIN-TREATED INDIVIDUALS: INSIGHTS FROM THE KP REACH STUDY](#)" – presented on behalf of all authors by Andrew P. Ambrosy, M.D., Kaiser Permanente San Francisco Medical Center, San Francisco, CA – Available from May 15

Additional REDUCE-IT® and icosapent ethyl (EPA)-related topics will be presented at ACC.21 and can be found [here](#).

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® (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 VASKEPA.

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 $\geq 3\%$ and $\geq 1\%$ 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 $\geq 1\%$ 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](http://www.vascepa.com) CAN BE FOUND AT [WWW.VASCEPA.COM](http://www.vascepa.com).

Forward-Looking Statements

This press release contains forward-looking statements, including statements regarding the potential impact of VASCEPA in various clinical uses. 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 such as further clinical evaluations failing to confirm earlier findings. 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 Quarterly Report on Form 10-Q. 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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AMARIN, REDUCE-IT, VASCEPA and VAZKEPA are trademarks of Amarin Pharmaceuticals Ireland Limited. VAZKEPA is a registered trademark in Europe and other countries and regions and is pending registration in the United States.

¹ American Heart Association. Heart Disease and Stroke Statistics—2020 Update: A Report From the American Heart Association. *Circulation*. 2020;141:e139-e596.

² 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.

³ Budoff M. Triglycerides and triglyceride-rich lipoproteins in the causal pathway of cardiovascular disease. *Am J Cardiol*. 2016;118:138-145.

⁴ 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.

⁵ Nordestgaard BG. Triglyceride-rich lipoproteins and atherosclerotic cardiovascular disease - New insights from epidemiology, genetics, and biology. *Circ Res*. 2016;118:547-563.

⁶ 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.

⁷ 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.

⁸ 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.