

# Amarin Corporation

## VASCEPA® (Icosapent Ethyl) Found to Significantly Reduce Ischemic Events in Patients with Prior Coronary Artery Bypass Grafting (CABG) Procedures in Post Hoc Subgroup Analyses of Landmark REDUCE-IT® Study Presented at American Heart Association's Virtual

November 13, 2020

*VASCEPA®*, compared with placebo, significantly reduced primary composite first and total major adverse cardiovascular events (MACE) in post hoc exploratory analyses of patients with a history of CABG by 24% and 36%, respectively, and key secondary composite first hard MACE, comprised of heart attacks, stroke and cardiovascular death, by 31%

*Administration of VASCEPA resulted in robust absolute risk reductions of 6.2% and 6.0% and numbers needed to treat (NNT) of 16 and 17, respectively, for both primary and key secondary (hard MACE) composite endpoints in these subgroup analyses*

*Amarin to Webcast Discussion of Presented Data on November 18, 2020 at 4:30 p.m., Eastern Standard Time*

DUBLIN, Ireland and BRIDGEWATER, N.J., Nov. 13, 2020 (GLOBE NEWSWIRE) -- Amarin Corporation plc (NASDAQ:AMRN) today announced the presentation of REDUCE-IT® CABG at American Heart Association's (AHA) Virtual Scientific Sessions 2020, being held virtually from November 13 – November 17, 2020, adding to the growing body of knowledge on the clinical impact of VASCEPA® (icosapent ethyl). These new analyses supported by Amarin were presented by Subodh Verma, M.D., Ph.D., FRCSC, Professor and Cardiac Surgeon at University of Toronto.

"The REDUCE-IT CABG analysis results are another piece of the puzzle when looking at the potential use of icosapent ethyl in the procedural setting," commented Dr. Deepak L. Bhatt, M.D., M.P.H., Executive Director of Interventional Cardiovascular Programs at Brigham and Women's Hospital and Professor of Medicine at Harvard Medical School, principal investigator of REDUCE-IT. "The findings of benefit in at-risk patients with prior CABG are consistent with previously presented data on overall reductions in first and total coronary revascularization events, as well as in patients with prior percutaneous coronary interventions, and further strengthen the case for consideration of icosapent ethyl as an additional intervention for use by physicians to care for this patient population."

The REDUCE-IT CABG analysis examined 1,837 (22.5%) of the patients enrolled in REDUCE-IT, representing all patients who had undergone a prior coronary artery bypass grafting (CABG) procedure, a common form of surgical intervention to help treat coronary heart disease. Baseline characteristics were similar among patients randomized to VASCEPA versus placebo. *Post hoc* exploratory analyses of this subgroup showed that, for the composite endpoint of 5-point MACE, which was the prespecified primary endpoint for the full REDUCE-IT study cohort, time to first event was significantly reduced with VASCEPA versus placebo by 24% (p=0.004) and total (first and subsequent) events were also reduced by 36% (p=0.0002). For the REDUCE-IT study's key secondary composite endpoint of 3-point MACE, time to first event was reduced by 31% (p=0.001) in the subgroup of patients with a prior CABG.

Coronary revascularization procedures, such as CABG, are invasive, carry multiple risks, and can have significant direct and indirect costs. Patients with elevated triglycerides despite statin therapy have increased risk for ischemic events, including coronary revascularizations. These procedures, whether pre-scheduled or performed in an emergency, inevitably result in additional time spent in a healthcare setting. The latest statistical update from the American Heart Association (AHA) shows that, in 2014, an estimated 371,000 inpatient CABG procedures were performed in the United States with a mean inpatient hospital charge for CABG of \$168,541.<sup>1</sup>

"Revascularization procedures overall significantly impact the healthcare system, with CABG procedures adding to the burden and driving substantial costs," said Steven Ketchum, Ph.D., senior vice president and president, research & development and chief scientific officer, Amarin. "The subgroup data presented at AHA Virtual Scientific Sessions 2020 suggests another way in which VASCEPA can possibly alleviate the significant burden that at-risk patients and the healthcare system face with CABG procedures and how VASCEPA therapy can potentially reduce the risk of dangerous subsequent events."

REDUCE-IT was not specifically powered to examine individual cardiovascular endpoints or patient subgroups, therefore p-values presented for these revascularization analyses are nominal and exploratory with no adjustment for multiple comparisons. In addition, coronary revascularization as an endpoint can sometimes be considered subjective; however, these endpoints were adjudicated by an independent, blinded clinical endpoint committee. Results from the total coronary revascularization events analyses are consistent across the various recurrent event statistical models and are also consistent with the first coronary revascularization events results. Together, the REDUCE-IT first and total coronary revascularization events results support the robustness and consistency of the clinical benefit of VASCEPA therapy in reducing coronary revascularization.

These REDUCE-IT CABG results follow multiple scientific presentations of analysis results from other important patient subgroups in the REDUCE-IT study, including REDUCE-IT REVASC<sup>2</sup> and REDUCE-IT PCI. References to these other subgroup analyses are available on Amarin's website at [www.amarincorp.com](http://www.amarincorp.com).

Additional information on AHA Virtual Scientific Sessions 2020 can be found [here](#).

### Audio Webcast Information

Amarin will host an audio webcast on November 18, 2020, at 4:30 p.m. EST to discuss this and other VASCEPA-related information presented during the AHA Virtual Scientific Sessions 2020. To listen please register [here](#), listen live on the investor relations section of the company's website at [www.amarincorp.com](http://www.amarincorp.com), or via telephone by dialing 877-407-8033 within the United States, 201-689-8033 from outside the United States.

### 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<sup>®</sup> (icosapent ethyl), is available by prescription in the United States, Canada, Lebanon and the United Arab Emirates. VASCEPA is not yet approved and available in any other countries. Amarin, on its own or together with its commercial partners in select geographies, is pursuing additional regulatory approvals for VASCEPA in China, Europe and the Middle East. For more information about Amarin, visit [www.amarincorp.com](http://www.amarincorp.com).

#### **About Cardiovascular Risk**

The number of deaths in the United States attributed to cardiovascular disease continues to rise. 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 795,000 per year (approximately 1 every 40 seconds), accounting for 1 of every 19 U.S. deaths. Cardiovascular disease results in 859,000 deaths per year in the United States.<sup>1</sup> In aggregate, there are more than 2.4 million major adverse cardiovascular events per year from cardiovascular disease or, on average, one every 13 seconds in the United States alone.

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%.<sup>3</sup> 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.<sup>4,5,6</sup>

#### **About REDUCE-IT<sup>®</sup>**

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*.<sup>7</sup> The primary results of REDUCE-IT were published in *The New England Journal of Medicine* in November 2018.<sup>8</sup> The total events results of REDUCE-IT were published in the *Journal of the American College of Cardiology* in March 2019.<sup>9</sup> These and other publications can be found in the R&D section on the company's website at [www.amarincorp.com](http://www.amarincorp.com).

#### **About VASCEPA<sup>®</sup> (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 ( $\geq 500$  mg/dL) hypertriglyceridemia. Since launch, VASCEPA has been prescribed over eight million times. VASCEPA 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 ( $\geq 150$  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 ( $\geq 500$  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)
<b>Primary composite endpoint</b>					
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)
<b>Key secondary composite endpoint</b>					
Cardiovascular death, myocardial infarction, stroke (3-point MACE)	459 (11.2)	2.7	606 (14.8)	3.7	0.74 (0.65, 0.83)
<b>Other secondary endpoints</b>					
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 <sup>[1]</sup>	174 (4.3)	1.0	213 (5.2)	1.2	0.80 (0.66, 0.98)
Hospitalization for unstable angina <sup>[2]</sup>	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](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](http://www.amarincorp.com)), the investor relations website ([investor.amarincorp.com](http://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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  - <sup>3</sup> 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.
  - <sup>4</sup> Budoff M. Triglycerides and triglyceride-rich lipoproteins in the causal pathway of cardiovascular disease. *Am J Cardiol*. 2016;118:138-145.
  - <sup>5</sup> 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.
  - <sup>6</sup> Nordestgaard BG. Triglyceride-rich lipoproteins and atherosclerotic cardiovascular disease - New insights from epidemiology, genetics, and biology. *Circ Res*. 2016;118:547-563.
  - <sup>7</sup> 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.
  - <sup>8</sup> 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.
  - <sup>9</sup> 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.