

# Amarin Corporation

## Latest Clinical Research Evaluating VASCEPA® (Icosapent Ethyl) in Patients with Residual Cardiovascular Risk to be Presented at ESC Congress 2020, the Annual Meeting of the European Society of Cardiology

August 17, 2020

### Amarin-Supported Research and Analyses from Academic Collaborators to Be Featured in Five Presentations, Including Late-Breaking Science Presentation of Final EVAPORATE Study Results

DUBLIN, Ireland and BRIDGEWATER, N.J., Aug. 17, 2020 (GLOBE NEWSWIRE) -- Amarin Corporation plc (NASDAQ:AMRN) today announced that new data that add to the growing body of knowledge on VASCEPA® (icosapent ethyl) in patients at risk for major adverse cardiovascular events will be presented at ESC Congress 2020, the annual meeting of the European Society of Cardiology (ESC), being held virtually from August 29 - September 1, 2020. These new findings will be presented in one Late-Breaking Science presentation and four rapid fire abstract and e-poster presentations from a variety of academic collaborators based on research or analyses supported by Amarin.

"Cardiovascular disease is an ever-increasing global challenge commanding both attention and action," said Craig Granowitz, M.D., Ph.D., Amarin's senior vice president and chief medical officer. "Often devastating, cardiovascular disease demands new research to increase our understanding of how to address residual cardiovascular risk. Several scheduled presentations at ESC provide new data on VASCEPA and its potential to address heart health in at-risk patients."

Featured Amarin-supported abstracts to be presented at ESC Congress 2020 include:

#### **Late-Breaking Science Presentation**

- **Session: Late-Breaking Science in Lipids**

"[Effect of Icosapent Ethyl on Progression of Coronary Atherosclerosis in Patients with Elevated Triglycerides on Statin Therapy: Final results of the EVAPORATE Study](#)" – presented on behalf of all authors by Matthew Budoff, M.D., The Lundquist Institute – August 29, 8:50-9:20 a.m. CEST (Central European Summer Time)

#### **Rapid Fire Abstracts and e-Poster Presentations**

- **Session: Rapid Fire Abstracts**

"[REDUCE-IT: Accumulation of Data Across Prespecified Interim Analyses to Final Results](#)" – presented on behalf of all authors by Brian Olshansky, M.D., University of Iowa – Available from August 30

- **Session: Rapid Fire Abstracts**

"[REDUCE-IT: Total Ischemic Events Reduced Across the Full Range of Baseline LDL Cholesterol and Other Key Subgroups](#)" – presented on behalf of all authors by Deepak L. Bhatt, M.D., M.P.H., Brigham and Women's Hospital – Available from August 30

- **Session: Rapid Fire Abstracts**

"[Are the Results of Clinical Trials Relevant in The Real World? The Applicability of REDUCE-IT to the FAST-MI Registry](#)." – presented on behalf of all authors by Jean Ferrières, M.D., M.Sc., FESC, Toulouse Rangueil University Hospital – Available from August 30

- **Session: e-Poster**

"[REDUCE-IT: Outcomes by Baseline Statin Type](#)" – presented on behalf of all authors by Deepak L. Bhatt, M.D., M.P.H., Brigham and Women's Hospital – Available from August 28

Additional REDUCE-IT® and icosapent ethyl (EPA)-related topics will be presented at ESC Congress 2020 and can be found at <https://www.escardio.org/Congresses-&-Events/ESC-Congress>.

#### **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, 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>2</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>3,4,5</sup>

#### 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*.<sup>6</sup> The primary results of REDUCE-IT were published in *The New England Journal of Medicine* in November 2018.<sup>7</sup> The total events results of REDUCE-IT were published in the *Journal of the American College of Cardiology* in March 2019.<sup>8</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® (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
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	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 [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](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>1</sup> American Heart Association. Heart Disease and Stroke Statistics—2020 Update: A Report From the American Heart Association. *Circulation*.

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<sup>2</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>3</sup> Budoff M. Triglycerides and triglyceride-rich lipoproteins in the causal pathway of cardiovascular disease. *Am J Cardiol*. 2016;118:138-145.

<sup>4</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>5</sup> Nordestgaard BG. Triglyceride-rich lipoproteins and atherosclerotic cardiovascular disease - New insights from epidemiology, genetics, and biology. *Circ Res*. 2016;118:547-563.

<sup>6</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>7</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>8</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.