

# Amarin Corporation

## Real-World Data Supports Association Between Elevated Triglyceride Levels and Increased Peripheral Arterial Revascularization in High Risk Statin-Treated Patients

August 25, 2018

**Management to Host Conference Call at 8:00 a.m. ET August 27, 2018 to Discuss Data Presented at European Society of Cardiology Congress**

BEDMINSTER, N.J. and DUBLIN, Ireland, Aug. 25, 2018 (GLOBE NEWSWIRE) -- Amarin Corporation plc (NASDAQ:AMRN), a biopharmaceutical company focused on the commercialization and development of therapeutics to improve cardiovascular health, supported the recent presentation of a scientific poster at the European Society of Cardiology (ESC) Congress in Munich, Germany. This analysis indicated that patients with elevated triglycerides (TG) were at a 37% higher rate of requiring a procedure for peripheral arterial revascularization per unit time than patients with normal TG levels. A conference call will be held Monday, August 27, 2018 to discuss this data and other data presented at ESC 2018 and related insights with respect to Amarin's potentially landmark cardiovascular outcomes study of Vascepa®, REDUCE-IT™. Top-line results from REDUCE-IT are anticipated before the end of September 2018.

The scientific poster #P739 is titled, "Triglycerides 150 mg/dL and above are associated with an increased risk of peripheral arterial revascularization in high-risk statin-treated patients: A real-world analysis." These data were based on a retrospective analysis of de-identified medical records from patient experiences within a leading national information and technology-enabled health services business. De-identified patient data is health information from a medical record that has been stripped of all "direct identifiers", that is, all information that can be used to identify the patient from whose medical record the health information was derived. The purpose of this retrospective analysis of a large medical claims database was to evaluate the real-world impact of elevated triglycerides on occurrence of peripheral arterial revascularization in high-risk statin-treated patients.

Patient data from the database were segmented into groups of people with elevated TG levels ( $\geq 150$  mg/dL, n=22,795) and a control cohort with normal TG levels ( $< 150$  mg/dL, n=22,884). In a multivariate analysis, patients with elevated TG levels were at a 37% higher rate of requiring a procedure for peripheral arterial revascularization per unit time than the control cohort. This analysis provides evidence to further support that elevated triglycerides are associated with higher rates of peripheral arterial revascularization.

This poster was authored by Peter P. Toth, MD, PhD, CGH Medical Center, Sterling, IL; Sephy Philip, RPh, PharmD, Amarin Pharma, Inc., Bedminster, NJ; Michael Hull, MS, Optum, Eden Prairie, MN; Djibril Liassou, BA, Optum, Eden Prairie, MN; Amy Anderson, MS, Optum, Eden Prairie, MN; and Craig Granowitz, MD, PhD, Amarin Pharma, Inc., Bedminster, NJ.

"We are pleased to present this new information that adds to our body of knowledge regarding the correlation of elevated TG levels to increased risk of revascularization procedure in patients with peripheral arterial disease (PAD). Development of PAD often has a significant effect on patient quality of life and drives healthcare utilization. Unfortunately, PAD is growing as a common disease condition along with changes in population demographics," said Peter Toth, MD, PhD.

PAD is associated with cardiovascular morbidity, reduced quality of life, and increased health care burden.<sup>1,2,3</sup> More than 200 million people are affected with PAD worldwide, including almost 40 million people in Europe.<sup>4</sup> In the United States, the prevalence of PAD is at least 6.8 million individuals, with more than 13,000 deaths in 2015 and more than 100,000 hospital discharges in 2014.<sup>1</sup> Interventions for peripheral vascular disease are one of a number of prespecified data points that are being collected in the Amarin REDUCE-IT cardiovascular outcomes study.

Previously, Amarin presented a real-world data analysis at the 2018 American College of Cardiology (ACC) 67th Annual Scientific Session and Expo in Orlando, Florida. This analysis reinforced that statin-treated patients at high cardiovascular (CV) risk with controlled low density lipoprotein cholesterol (LDL-C) and elevated triglyceride (TG) levels, TG  $\geq 150$  mg/dL, had worse CV outcomes and higher overall healthcare costs than statin-treated patients with controlled LDL-C and normal TG levels, TG  $< 150$  mg/dL, and normal high density lipoprotein cholesterol (HDL-C)  $> 40$  mg/dL.

Patients with diabetes mellitus and/or established atherosclerotic cardiovascular disease were followed longitudinally for up to five years. Those patients with elevated TG levels, defined as TG  $\geq 150$  mg/dL, as compared with the normal TG group defined as TG  $< 150$  mg/dL and HDL-C  $> 40$  mg/dL, were at increased risk of adverse CV outcomes after multivariable adjustment as follows:

- 26% increased risk for the composite initial major adverse CV event (MACE) (95% confidence interval [CI] 1.19-1.34)
- The increase in composite MACE in the elevated TG group was driven by a 32% (95% CI 1.20-1.45) increased risk of non-fatal myocardial infarction and a 46% (95% CI 1.33-1.61) increased risk of coronary revascularization
- 12% higher average total healthcare cost (95% CI 1.08-1.16)
- 13% higher rate of occurrence of initial inpatient hospital stay (95% CI 1.10-1.17)

### Conference Call and Webcast Information

Amarin will host a conference call at 8:00 a.m. ET, August 27, 2018 to discuss this presentation and other data presented at ESC 2018. The call will be accessible through the investor relations section of the company's website at [www.amarincorp.com](http://www.amarincorp.com). The call can also be heard via telephone by dialing 877-407-8033. A replay of the call will be made available for a period of two weeks following the conference call. To hear a replay of the call, dial 877-481-4010 (inside the United States) or 919-882-2331 (outside the United States). A replay of the call will also be available through the

company's website shortly after the call. For both dial-in numbers please use conference ID 37102.

## **About Amarin**

Amarin Corporation plc is a biopharmaceutical company focused on the commercialization and development of therapeutics to improve cardiovascular health. Amarin's product development program leverages its extensive experience in lipid science and the potential therapeutic benefits of polyunsaturated fatty acids. Vascepa® (icosapent ethyl), Amarin's first FDA-approved product, is a highly-pure, omega-3 fatty acid product available by prescription. For more information about Vascepa visit [www.vascepa.com](http://www.vascepa.com). For more information about Amarin visit [www.amarincorp.com](http://www.amarincorp.com).

## **About REDUCE-IT**

Amarin's clinical development program for Vascepa includes a trial known as the REDUCE-IT cardiovascular outcomes study, an 8,175-patient study commenced in 2011. REDUCE-IT is the first multinational cardiovascular outcomes study evaluating the effect of prescription pure EPA therapy, or any triglyceride lowering therapy, as an add-on to statins in patients with high cardiovascular risk who, despite stable statin therapy, have elevated triglyceride levels (150-499 mg/dL). A large portion of the male and female patients enrolled in this outcomes study are anticipated to also be diagnosed with type 2 diabetes. As reported previously, Amarin expects to announce top-line results of this important study by the end of September 2018. The REDUCE-IT trial is being conducted under a Special Protocol Assessment agreement with the U.S. Food and Drug Administration.

Additional information on clinical studies of Vascepa can be found at [www.clinicaltrials.gov](http://www.clinicaltrials.gov).

## **About VASCEPA® (icosapent ethyl) Capsules**

Vascepa® (icosapent ethyl) capsules are a single-molecule prescription product consisting of the omega-3 acid commonly known as EPA in ethyl-ester form. Vascepa is not fish oil, but is derived from fish through a stringent and complex FDA-regulated manufacturing process designed to effectively eliminate impurities and isolate and protect the single molecule active ingredient. Vascepa, known in scientific literature as AMR101, has been designated a new chemical entity by the FDA. Amarin has been issued multiple patents internationally based on the unique clinical profile of Vascepa, including the drug's ability to lower triglyceride levels in relevant patient populations without raising LDL-cholesterol levels.

### **FDA-Approved Indication and Usage**

- Vascepa (icosapent ethyl) is indicated as an adjunct to diet to reduce triglyceride (TG) levels in adult patients with severe ( $\geq 500$  mg/dL) hypertriglyceridemia.
- The effect of Vascepa on the risk for pancreatitis and cardiovascular mortality and morbidity in patients with severe hypertriglyceridemia has not been determined.

### **Important Safety Information for Vascepa**

- Vascepa is contraindicated in patients with known hypersensitivity (e.g., anaphylactic reaction) to Vascepa or any of its components.
- In patients with hepatic impairment, monitor ALT and AST levels periodically during therapy.
- Use with caution in patients with known hypersensitivity to fish and/or shellfish.
- The most common reported adverse reaction (incidence  $> 2\%$  and greater than placebo) was arthralgia (2.3% for Vascepa, 1.0% for placebo). There was no reported adverse reaction  $> 3\%$  and greater than placebo.
- Adverse events and product complaints may be reported by calling 1-855-VASCEPA or the FDA at 1-800-FDA-1088.
- Patients receiving treatment with Vascepa and other drugs affecting coagulation (e.g., anti-platelet agents) should be monitored periodically.
- Patients should be advised to swallow Vascepa capsules whole; not to break open, crush, dissolve, or chew Vascepa.

FULL VASCEPA PRESCRIBING INFORMATION CAN BE FOUND AT [WWW.VASCEPA.COM](http://WWW.VASCEPA.COM).

Vascepa has been approved for use by the United States Food and Drug Administration (FDA) as an adjunct to diet to reduce triglyceride levels in adult patients with severe ( $\geq 500$  mg/dL) hypertriglyceridemia. Nothing in this press release should be construed as promoting the use of Vascepa in any indication that has not been approved by the FDA.

## **About Cardiovascular Disease**

Worldwide, cardiovascular disease (CVD) remains the #1 killer of men and women. In the United States CVD leads to one in every three deaths – one death approximately every 38 seconds – with annual treatment cost in excess of \$500 billion.<sup>1, 5</sup>

Beyond the cardiovascular risk associated with LDL-C, genetic, epidemiologic, clinical and real-world data suggest that patients with elevated triglycerides (TG) (fats in the blood), and TG-rich lipoproteins, are at increased risk for cardiovascular disease.<sup>6, 7, 8, 9</sup>

Leading clinical investigations seeking to address cardiovascular risk reduction beyond lowering LDL-C focus on interrupting the atherosclerotic process (e.g., plaque formation and instability) by beneficially affecting other lipid, lipoprotein and inflammation biomarkers and cellular functions thought to be related to atherosclerosis and cardiovascular events.

## **Forward-Looking Statements**

This press release contains forward-looking statements, including statements about the patient risk profiles thought to be related to triglyceride levels as well as statements concerning the REDUCE-IT cardiovascular outcomes study such as the anticipated inclusion of certain patient populations, related timing and announcements with respect to final outcomes and the anticipated successful completion of the REDUCE-IT study. 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 uncertainties associated generally with retrospective subset analyses, research on biomarkers thought to be relevant in the treatment of cardiovascular disease, research and development and clinical trial risk generally, including the risk that study results in modest sample sizes may not be predictive of future results in larger studies, that studied parameters may not have clinically meaningful effect and the risk that patents may not adequately protect Vascepa against competition. 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.

#### Availability of Other Information About Amarin

Investors and others should note that Amarin communicates with its investors and the public using the company website (<http://www.amarincorp.com/>), the investor relations website (<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.

#### References

- <sup>1</sup> Benjamin EJ, et al. American Heart Association. 2018. Disease and Stroke Statistics-2018 Update. *Circulation*. 2018;137:e67-e492.
- <sup>2</sup> Creager MA. Protecting Life and Limb in Peripheral Artery Disease. *Circulation*. 2018;137:351-3.
- <sup>3</sup> Valdivielso P, et al. Peripheral arterial disease, type 2 diabetes and postprandial lipidaemia: Is there a link? *World J Diabetes*. 2014;5:577-85.
- <sup>4</sup> Fowkes FG, et al. Comparison of global estimates of prevalence and risk factors for peripheral artery disease in 2000 and 2010: a systematic review and analysis. *Lancet*. 2013;382:1329– 40.
- <sup>5</sup> American Heart Association. 2017. Cardiovascular disease: A costly burden for America projections through 2035. At: [http://www.heart.org/idc/groups/heart-public/@wcm/@adv/documents/downloadable/ucm\\_491543.pdf](http://www.heart.org/idc/groups/heart-public/@wcm/@adv/documents/downloadable/ucm_491543.pdf) Accessed August 23, 2018.
- <sup>6</sup> Budoff M. Triglycerides and triglyceride-rich lipoproteins in the causal pathway of cardiovascular disease. *Am J Cardiol*. 2016;118:138-145.
- <sup>7</sup> Toth PP, Granowitz C, Hull M, et al. High triglycerides increase cardiovascular events, medical costs, and resource utilization in a real-world analysis of statin-treated patients with high cardiovascular risk and well-controlled low-density lipoprotein cholesterol [abstract]. *Circulation*. 2017;136(suppl 1):A15187.
- <sup>8</sup> Nordestgaard BG. Triglyceride-rich lipoproteins and atherosclerotic cardiovascular disease - New insights from epidemiology, genetics, and biology. *Circ Res*. 2016;118:547-563.
- <sup>9</sup> Nordestgaard BG, Varbo A. Triglycerides and cardiovascular disease. *Lancet*. 2014; 384: 626–635.

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