

# Amarin Corporation

## Real-World Data Supports Association Between High Triglyceride Levels and Increased Cardiovascular Events and Healthcare Costs in People with Diabetes Mellitus

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### Data Underscores the Need for the REDUCE-IT™ Cardiovascular Outcomes Study

BEDMINSTER, N.J. and DUBLIN, Ireland, June 25, 2018 (GLOBE NEWSWIRE) -- Amarin Corporation plc (NASDAQ:AMRN), a biopharmaceutical company focused on the commercialization and development of therapeutics to improve cardiovascular (CV) health, announced the presentation of three scientific presentations this week at the American Diabetes Association (ADA) Scientific Sessions in Orlando, FL, June 22-26, 2018. These analyses highlight the need for further research in patients with diabetes mellitus and elevated or high triglyceride (TG) levels despite statin therapy due to the association with increased cardiovascular disease (CVD) risk.

The poster titled "Diabetes Mellitus and High Triglycerides Are Significant Predictors of Major Cardiovascular Events and Increased Health Care Costs and Resource Utilization: A Real-World Analysis of High-Risk Statin-Treated Patients" studied patients with diabetes mellitus and atherosclerotic cardiovascular disease (ASCVD). Groups were segmented into people with high TGs (200–499 mg/dL, n=13,411), as compared to a cohort with normal TGs (<150 mg/dL) and high-density lipoprotein cholesterol (HDL-C) >40 mg/dL (n=32,506). The analysis showed that patients with high TGs were at a 35% increased risk of having an initial major CV event per unit time. Diabetes mellitus was also found to be a significant predictor of CV events, costs, and risk of inpatient hospital stay. This poster was authored by Peter P. Toth, MD, PhD, CGH Medical Center, Sterling, IL; Craig Granowitz, MD, PhD, Amarin Pharma, Inc., Bedminster, NJ; Michael Hull, MS, Optum, Eden Prairie, MN; Sephy Philip, RPh, PharmD, Amarin Pharma, Inc., Bedminster, NJ.

The poster titled "Increased Cardiovascular Risk in Patients with Diabetes, Statin-Controlled LDL Cholesterol and Residual Hypertriglyceridemia" reported data from electronic health records of the Kaiser Permanente Northwest and Southern California regions. The patients selected had a diagnosis of type 2 diabetes and a prior diagnosis of myocardial infarction, ischemic stroke, peripheral artery disease or at least one other CV risk factor, and were on statin therapy with LDL-C between 40-100 mg/dL. Patients were grouped into high (200-499 mg/dL, n=5,542) or normal (<150 mg/dL, n=22,411) TG and followed for a mean of five years. After statistical adjustment for known CV risk factors, patients in the high TG group had a 34% increased risk of non-fatal myocardial infarction, a 25% increased risk of non-fatal stroke, a 60% increased risk of hospitalization due to unstable angina, and a 30% increased risk of coronary revascularization. This poster was authored by Gregory A. Nichols, PhD, Kaiser Permanente Northwest Center for Health Research, Portland, OR; Sephy Philip, RPh, PharmD, Craig B. Granowitz, MD, PhD, Amarin Pharma, Inc., Bedminster, NJ; Kristi Reynolds, PhD, MPH, Kaiser Permanente Southern California, Pasadena, CA; Sergio Fazio, MD, PhD, Oregon Health & Science University, Portland, OR.

The research in the oral presentation titled "Prevalence and Predictors of Residual Hypertriglyceridemia According to Statin Use in US Adults with Diabetes" reported that elevated and high TG levels remain common in more than one-third (approximately 10 million) of US adults with diabetes mellitus, even among statin users with well-controlled low-density lipoprotein cholesterol (LDL-C) levels. A limitation of this study was that information on statin dosage, duration, or adherence was not available. This presentation was authored by Wenjun Fan, MD, MS, Heart Disease Prevention Program, Division of Cardiology, University of California, Irvine School of Medicine, Division of Cardiology; Sephy Philip, RPh, PharmD, Craig Granowitz MD, PhD, Amarin Pharma, Inc., Bedminster, NJ; Peter P. Toth, MD, PhD, CGH Medical Center, Sterling, IL; Nathan D. Wong, PhD, Heart Disease Prevention Program, Division of Cardiology, University of California, Irvine School of Medicine.

"The medical community should take note of these important findings reporting the prevalence and increased costs associated with diabetes mellitus and high triglyceride levels despite statin therapy," said Nathan Wong, PhD, of the University of California, Irvine. "REDUCE-IT, a potentially landmark CV outcomes study of over 8,000 patients, is the first global study to assess a medical intervention in this patient group. I look forward to learning the results of this study."

#### 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 pure EPA (eicosapentaenoic acid) and 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™. The REDUCE-IT cardiovascular outcomes study, a multi-national, 8,175-patient study which commenced in 2011. REDUCE-IT is a first-of-its-kind cardiovascular outcomes study evaluating the effect of prescription pure EPA therapy as an add-on to statin therapy in patients with high cardiovascular risk who have elevated TG 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 before the end of Q3 2018. Notably, the REDUCE-IT trial is an event-driven CV outcomes study and is not designed to validate the effect of lowering triglycerides. REDUCE-IT 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 pure 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.
- 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.
- Patients receiving treatment with Vascepa and other drugs affecting coagulation (e.g., anti-platelet agents) should be monitored periodically.
- In patients with hepatic impairment, monitor ALT and AST levels periodically during therapy.
- Patients should be advised to swallow Vascepa capsules whole; not to break open, crush, dissolve, or chew Vascepa.
- Adverse events and product complaints may be reported by calling 1-855-VASCEPA or the FDA at 1-800-FDA-1088.

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, 2</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>3, 4, 5, 6</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 potential relevance of elevated triglyceride levels to cardiovascular risk and clinical outcomes and on the healthcare system 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 with research on biomarkers thought to be relevant in the treatment of cardiovascular disease, healthcare costs and clinical trial risk, 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>American Heart Association. 2018. Disease and Stroke Statistics-2018 Update.

<sup>2</sup>American Heart Association. 2017. Cardiovascular disease: A costly burden for America projections through 2035.

<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 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>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> Nordestgaard BG, Varbo A. Triglycerides and cardiovascular disease. *Lancet*. 2014; 384: 626–635.

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