The CANTOS study results[1] announcement on August 27th 2017 serves as a reminder that, despite currently available standard of care treatments, patients with a prior heart attack and inflammatory atherosclerosis as measured by high-sensitivity C-reactive protein (hsCRP) levels of >=2mg/L, a known marker of inflammation, continue to be at an increased risk for cardiovascular disease and death.

The CANTOS study results appear to have validated the hypothesis that a long-term drug treatment focused on an anti-inflammatory mechanism in patients with a prior heart attack and inflammatory atherosclerosis can reduce cardiovascular events.

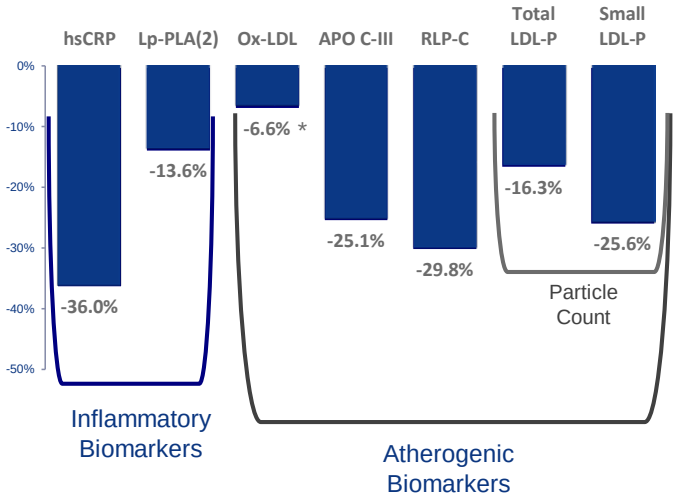
Amarin has demonstrated that Vascepa® (icosapent ethyl) capsules lowered triglyceride levels in two phase three clinical trials, MARINE and ANCHOR. These trial results also showed that Vascepa® affected inflammatory markers, including hsCRP and Lp-PLA2 and other lipid, lipoprotein, and inflammatory values. See the figure below.

MARINE and ANCHOR Studies on Vascepa® Key Published Findings (4g/day dose)

AMARIN

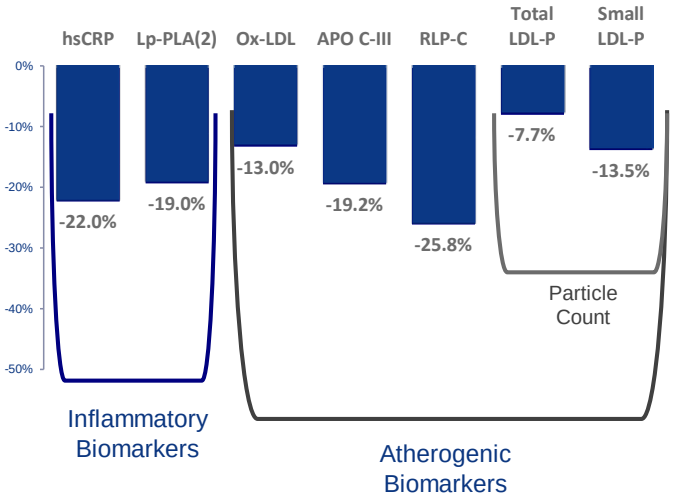
MARINE Trial:

Phase 3 median placebo-adjusted 12 week results for Vascepa 4g/day dose in patients with very high TGs (≥500 mg/dL)



ANCHOR Trial:

Phase 3 median placebo-adjusted 12 week results for Vascepa 4g/day dose in patients on statin therapy with persistent high TGs (200 to 499 mg/dL)



Sources:
Bays HE et al. Journal of Clinical Lipidology 2012; 6(6):565-572
Bays HE et al. American Journal of Cardiovascular Drugs 2013; 13(1):37-46
Ballantyne CM et al. Journal of Clinical Lipidology 2014; 8(3):313-314
Ballantyne CM et al. Journal of Clinical Lipidology 2015; 9(3):377-383
Ballantyne CM et al. Atherosclerosis 2016; 253:81-87

** All statistically significant results, except Ox-LDL reduction in MARINE Trial*

NOTE: The role of inflammatory biomarkers in cardiovascular disease has not been definitively determined.

Amarin believes that there are other factors beyond a drug's efficacy profile that impact whether a drug becomes broadly accepted by the medical community to combat the drug-appropriate disease states. These factors include a drug's cost-effectiveness, reimbursement availability, method of administration (e.g., injectable vs. oral), and side

effects. Vascepa has these characteristics as it is affordably priced, has broad managed care access, is dosed in capsule form, is administered orally and is well-tolerated. There are currently 150,000 patients on Vascepa therapy.

Vascepa is currently being studied for cardiovascular event reduction in the REDUCE-IT study. The REDUCE-IT study population includes both primary and secondary prevention patients. Study inclusion criteria includes:

- Men or women ≥45 years of age with established cardiovascular disease or ≥50 years of age with diabetes in combination with one additional risk factor for cardiovascular disease
- Fasting triglyceride levels ≥150 mg/dL and <500 mg/dL
- LDL-cholesterol levels >40 mg/dL and ≤100 mg/dL, stable statin therapy (± ezetimibe) for ≥4 weeks prior to the LDL-cholesterol and triglyceride qualifying measurements

Upon completion of the REDUCE-IT study we will look to assess the degree to which, if any, Vascepa reduced major adverse cardiovascular events in the at-risk patient population being studied. The extent to which such outcomes benefit is derived from the effect of Vascepa on levels of lipids, inflammation or other clinical effects will likely not be individually clarified by the REDUCE-IT study as it is the aggregate outcomes benefit which is being evaluated. Amarin believes that the aggregate benefit is most important.

For additional information on inflammation and associated biomarkers as seen in MARINE and ANCHOR as well as an *in vitro* study with EPA, please see the following journal articles:

- Mason RP, Sherratt SCR, Jacob RF. Eicosapentaenoic acid inhibits oxidation of ApoB-containing lipoprotein particles of different size in vitro when administered alone or in combination with atorvastatin active metabolite compared with other triglyceride-lowering agents. *J Cardiovasc Pharmacol.* 2016;68:33-40
- Bays HE, Ballantyne CM, Braeckman RA, Stirtan WG, Doyle RT Jr, Philip S, Soni PN, Juliano RA. Icosapent ethyl (eicosapentaenoic acid ethyl ester): effects upon high-sensitivity C-reactive protein and lipid parameters in patients with metabolic syndrome. *Metab Syndr Relat Disord*. 2015;13:239-247
- Bays HE, Ballantyne CM, Braeckman RA, Stirtan WG, Soni PN. Icosapent ethyl, a pure ethyl ester of eicosapentaenoic acid: effects on circulating markers of inflammation from the MARINE and ANCHOR studies. Am J Cardiovasc Drugs. 2013;13:37-46
- Brinton EA, Ballantyne CM, Bays HE, Kastelein JJ, Braeckman RA, Soni PN. Effects of icosapent ethyl on lipid and inflammatory parameters in patients with diabetes mellitus-2, residual elevated triglycerides (200-500 mg/dL), and on statin therapy at LDL-C goal: the ANCHOR study. Cardiovascular Diabetology. 2013; 12:100

and these press releases: ANCHOR Phase 3 Results, MARINE Phase 3 Results.

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 is known in scientific literature as AMR101.

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 (≥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.

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 (≥500 mg/dL) hypertriglyceridemia. VASCEPA is under various stages of development for potential use in other indications that have not been approved by the FDA. 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.

[1] Ridker, PM, et al. Anti-inflammatory Therapy with Canakinumab for Atherosclerotic Disease. The New England Journal of Medicine.2017; DOI: 10.156/NEJMmoa: 1707914.

Dated: August 29, 2017